Volume 58, Supplement 1, September 2021

ISSN 0924-8579

ELSEVIER

INTERNATIONAL JOURNAL OF Antimicrobial Agents

2021 ISAAR Virtual

Supplement:

Abstracts from the 13th International Symposium on Antimicrobial Agents and Resistance (ISAAR)

"Navigating Uncharted Waters: Antimicrobial Resistance in the Era of Pandemic"

Virtual Congress, September 9–10, 2021

Antibacterial Therapy

Antiviral Therapy

Antiparasitic Therapy

Antifungal Therapy

Immunotherapy

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liposomal amphotericin B

2017

You've worked hard and your patient is recovering. Then signs of an invasive fungal infection appear – and time starts running out. Consider AmBisome. Effective against major fungal pathogens[1-4], it helps survivors survive[2-6]

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The Innovative Liposomal Amphotericin B to Target Life-Threatening Fungal Infections [1,2]

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- Low Incidence of Nephrotoxicity, even in High Dose Therapy [4]
- Broad Spectrum Fungicidal Action Including in Neutropenic Patients [5]
- Impressive Response in Invasive Aspergillosis [6]

KRAMB0048_v1.0(2016.01.25)

AmBisome Injection (amphotericin B liposome for injection)

[Indications] Following systemic fungal infections sensitive to this drug: cryptococcosis, North American Blastomycosis, disseminated candidiasis, coccidioidomycosis, aspergillosis, mucormycosis and some cases of American mucocutaneous leishmaniasis Fever of unknown origin show in patients with neutropenia (Persistent fever of unknown origin which is not improved even after 96-hour treatment with antibiotics) Primary treatment of visceral leishmaniasis in immunocompetent adults and children Primary treatment of visceral leishmaniasis in immunocompromised patients (HIV-positive patients etc.) **[Dosage and Administration]** This drug should be administered via intravenous infusion for 30~60 mins. For doses greater than 5 mg/kg/day, intravenous infusion over 2 hour period is recommended. The recommended concentration in the intravenous infusion is 0.2~2.0 mg/mL of amphotericin B. The dosage of amphotericin B as AmBisome must be adjusted to the specific requirements of each patient. • Systemic fungal infections: Although 1.0 mg(titer)/kg/day is usually administered, the dosage can be gradually increased to 5.0 mg(titer)/kg/day, if required. • Fever of unknown origin show in patients with neutropenia: 1.0 mg(titer)/kg/day is administered as initial dose, which can be increased to 3.0 mg(titer)/kg/day according to symptoms. • Visceral leishmaniasis: 1.0~1.5 mg(titer)/kg/dayis administered for 21 days or 3.0 mg(titer)/kg/day for 10 days. Maintenance therapy or responsive therapy is performed if required due to the risk of recurrence. **[Warnings]** This drug is not used for common clinically inapparent fungal infections due to its strong activity. A positive skin serum test for fungus is not sufficient for administration. In addition, it is not used for bacterial infections or viral diseases due to no efficacy. In the treatment of fever of unknown origin, it is not used for fever caused by infections due to usual viruses, parasites or mycobacterium. **[Contraindications]** Patients with the hypersensitivity to this drug or any component of the drug **[General precautions]** It is recommended to check susceptibility for the prevention of the occurrence of resistant bacteria and to administer this drug for the minimum period required for the treatment. If a severe anaphylactic / anaphylactoid reaction occurs, the infusion should be immediately discontinued It was found that the incidence rates of increased serum creatinine, hypokalemia and hypomagnesemia were notably higher in the high dose groups. Patient management should include routine laboratory evaluation of hepatic, renal and hematopoietic function. Amphotericin B has nephrotoxicity. Patients with diabetes should bear in mind that each vial contains 900 mg of white sugar. This drug should not be given during the dialysis. **[Adverse Reactions]** The following adverse reactions may be caused by this drug. Their incidences were based on a clinical trial. (1) 10% : Fever, coldness/chills, hypokalemia, nausea, vomiting (2) 1~<10%: Elevations in creatinine and BUN, hypomagnesemia, hypocalcemia, hyperglycemia, hyponatremia, increased ALP, bilirubinemia, abnormal liver function test results, diarrhea, abdominal pain, dyspnea, flushing/vasodilation, hypotension, headache, low back pain, chest pain, rapid pulse rate (tachycardia) and rash (3) 0.1~<1%: Convulsion, bronchospasm, thrombocytopnea, anaphylactoid reaction, anemia and phlebitis (4) Frequency not known: anemia, anaphylactic reactions, hypersensitivity, cardiac arrest, arrhythmia, renal failure, renal insufficiency, angioneurotic edema, rhabdomyolysis(associated with hypokalemia) and musculoskeletal pain(described as arthralgia or bone pain) In post-marketing surveillance, anaphylactic reaction was uncommonly reported and angioedema was very rarely reported. Occasionally, there were cases of not severe hypersensitivity. Hematological changes, temporary hearing impairments, tinnitus, visual impairments, double vision, increase and decrease in blood pressure, arrhythmia, cardiac arrest, reversible increase of liver enzyme levels (transaminase), leukocytopenia, agranulocytosis, increase in leukocytes and eosinophil, and rarely reversible renal dysfunction may occur. Rhabdomyolysis accompanied by hypokalemia may be caused by amphotericin B. Therefore, if myalgia, feelings of burnout, increases in creatine kinase (CK, CPK) and increase of myoglobin in the blood and urine occur, administration should be discontinued and appropriate actions be taken. Interference with Phosphorous Chemistry Assays: False elevations of serum phosphate may occur when samples from patients receiving AmBisome are analyzed using the PHOSm assay. **[Use in pregnant women and nursing mothers & pediatric use]** The safety of this drug has not been established in pregnant women and nursing mothers. Safety and effectiveness in pediatric patients below the age of one month have not been established. **[Importer]** Gilead Sciences Korea (26 Euljiro 5-gil, Jung-gu, Seoul, 100-210, Korea, 02-6030-3330) **[Distributor]** yuhan Corp. (AMB-1605-01)

※ Please read full product information at www. gilead.co.kr or http://nedrug.mfds.go.kr before prescription.

References : 1. Boswell et al. J Clin Pharmacol 1998;38:583-592. 2. Wingard et al. Clin Inf Dis 2000;31:1155-1163. 3. Lipid formulations of amphotericin B. In: Sobel JD, Vazquez JA, editors. Contemporary Diagnosis and Management of Fungal Infections. Handbook in Healthcare, 2006:18-19. 4. Walsh et al. N Engl J Med 1999;340:764-771. 5. Lass-Flörl et al. Antimicrob Agents Chemother 2008;52:3637-3641. 6. Cornely et al, for the AmBiLoad Trial Study Group. Clin Infec Dis 2007;44:1289-1297.

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International Journal of

Antimicrobial Agents

Abstracts from the

13th International Symposium on Antimicrobial Agents and Resistance

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Publication of this supplement is supported by the Asia Pacific Foundation for Infectious Diseases (APFID).

International Journal of
Antimicrobial Agents

Volume 58/3 (2021)

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※ 수술 또는 의학적 시술을 진행 하게 될 환자에서 타이가실 100mg 을 iv로 단회 투여시 bile, gall bladder, colon 및 lung에서의 tissue/fluid농도가 simultaneous serum 농도보다 높았습니다.[2]

References **1.** Stein GE. Craig WA. Tigecycline: a critical analysis. *Clin Infect Dis.* 2006 Aug 15;43(4):518-24. **2.** Rodvold KA, *et al.* Serum, tissue and body fluid concentrations of tigecycline after a single 100 mg dose. *J Antimicrob Chemother.* 2006 Dec;58(6):1221-9. **3.** Rose WE, Rybak MJ. Tigecycline: first of a new class of antimicrobial agents. *Pharmacotherapy.* 2006 Aug;26(8):1099-110. **4.** 타이가실® 제품설명서(개정년월일: 2020.05.21) **5.** Babinchak *et al.* The Efficacy and Safety of Tigecycline for the Treatment of Complicated Intra-Abdominal Infections: Analysis of Pooled Clinical Trial Data. Clin Infect Dis. Sep 1;41 Suppl 5:S354-67. **6.** Oliva ME, *et al.* A multicenter trial of the efficacy and safety of tigecycline versus imipenem/cilastatin in patients with complicated intra-abdominal infections [Study ID Numbers: 3074A1-301-WW; ClinicalTrials.gov Identifier: NCT00081744]. *BMC Infect Dis.* 2005 Oct 19;5:88.

주요 안전성 정보 아나필락시스/아나필락시양 반응이 발생하였다는 보고가 있었으며, 그 증상은 생명을 위협할 수 있다. 이 약은 테트라사이클린계 항생제와 구조적으로 유사하므로 테트라사이클린계 항생제에 과민증의 병력이 있는 환자에게는 이 약을 신중하게 투여해야 한다. • 타이가실®의 안전성과 유효성은 18세 미만의 환자에 대해서는 확립되지 않았다. • Clostridium difficile에 의한 설사 "Clostridium difficile"-associated diarrhea(CDAD)는 타이가실®을 포함하여 거의 모든 항생제에서 나타나는 것으로 보고되고 있으며, 증상의 중등도는 경증의 설사에서 생명을 위협하는 치명적인 대장염까지 다양하다. • 경증-중등도의 간장애 환자(Child Pugh A와 Child Pugh B)에서 이 약의 용량조절은 필요하지 않다. 신장애환자나 혈액투석을 받고 있는 환자에서 이 약의 용량조절은 필요하지 않다.[4]

타이가실® 제품 요약 정보 [효능 · 효과] 적응증 성인(18세 이상)에서의 · 복잡성 피부 및 피부조직 감염 · 복잡성 복강내 감염 · 지역사회 획득 세균성 폐렴 [용법 · 용량] 초기용량으로 100mg을 투여한 후, 매 12시간마다 50mg씩 투여하는 것이 권장됩니다. 이 약은 30-60분 동안 점적 정맥 주사합니다. 권장 투여기간은 복잡성 피부 및 피부조직 감염, 복잡성 복강내 감염의 경우 5~14일이며, 지역사회 획득 세균성 폐렴의 경우 7~14일 입니다. 투여기간은 감염의 정도와 부위, 환자의 임상적 및 세균학적 경과에 따라 정해져야 합니다. [신중 투여] 1) 테트라사이클린계 항생제에 과민증의 병력이 있는 환자 글리실사이클린계 항생제와 구조적으로 유사하므로 테트라사이클린계 항생제에 과민증의 병력이 있는 환자에게는 이 약을 신중하게 투여해야 합니다. 2) 중증 간장애 환자 경증-중등도의 간장애 환자(Child Pugh A와 Child Pugh B)에서 이 약의 용량조절은 필요하지 않습니다. 악동학적 프로파일에 근거하여 중증 간장애 환자(Child Pugh C)에서는 이 약의 유지용량이 50% 감소되어야 하며 성인용량은 초기용량 100mg 투여 후 매 12시간마다 25mg씩 투여하고 치료반응을 모니터링해야 합니다. [이상 반응] 가장 흔한 치료관련 이상반응은 투여 후 처음 1-2일에 나타나는 구역 및 구토였습니다. 이 약과 대조약과 관련된 구역 및 구토 경우는 대부분 경증 또는 중등도였습니다. ※제품에 대한 자세한 정보는 최신의 제품설명서를 참고하시기 바라며, 홈페이지(www.pfizer.co.kr)를 통해 확인하실 수 있습니다. 설명서 개정년월일 : 2020.05.21

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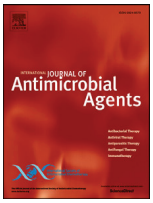

Contents

Note:
For DOIs and abstract article numbers please consult the Full text version of the abstracts which will be made available in the online publication of the supplement on ScienceDirect.

PROGRAM-AT-A-GLANCE

"Navigating Uncharted Waters: Antimicrobial Resistance in the Era of Pandemic"

	September 9 (Thu.)			September 10 (Fri.)			
	Room 1	Room 2	Room 3	Room 1	Room 2	Room 3	
9:00	Opening Ceremony (9:00~9:10)						9:00
9:10	Symposium 1 "Public health response to COVID-19" (9:10~11:10)	Symposium 2 "Gram-negative bacteria" (9:10~11:10)	Symposium 3 "How I treat difficult-to-treat infections (interactive)" (9:10~11:10)	Symposium 7 "Pros and cons (interactive)" (9:00~11:00)	Symposium 8 "Gram-positive bacteria" (9:00~11:00)	Symposium 9 "Infection prevention and control" (9:00~11:00)	
11:00				Break (11:00~11:10)			11:00
11:10	Plenary Lecture 1 Michael T. Osterholm (11:10~11:50)			Plenary Lecture 4 Robin Patel (11:10~11:50)			11:10
11:50	Plenary Lecture 2 Jerome H. Kim (11:50~12:30)			Plenary Lecture 5 Dennis M. Dixon (11:50~12:30)			11:50
12:30	Break (12:30~13:30)			Break (12:30~13:30)			12:30
13:30	Satellite Symposium 1 (13:30~15:00) GILEAD	Satellite Symposium 2 (13:30~15:00) Pfizer 한국화이자제약		Satellite Symposium 3 (13:30~15:00) GILEAD	Satellite Symposium 4 (13:30~15:00) Pfizer 한국화이자제약		13:30
15:00	Break (15:00~15:10)			Break (15:00~15:10)			15:00
15:10	Plenary Lecture 3 David Livermore (15:10~15:50)			Plenary Lecture 6 David Paterson (15:10~15:50)			15:10
15:50	Symposium 4 "Clinical management of COVID-19" (15:50~17:20)	Symposium 5 "Diagnostics/ clinical microbiology" (15:50~17:20)	Symposium 6 "Antimicrobial stewardship" (15:50~17:20)	Symposium 10 "Fungus" (15:50~17:20)	Symposium 11 "Vaccine" (15:50~17:20)	Symposium 12 "HIV" (15:50~17:20)	15:50
17:20							17:20

Program of Symposium Presentations and Plenary Lectures

September 9, 2021 – Day 1

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†In the safety analysis including 46 clinical trials, nausea and vomiting was reported in 1.4% to be related to treatment with meropenem.[5]

References.

1. 식약처 의약품 제조품목 허가증. 2020.4.24 2. J Antimicrob Chemother 1995; 36(Suppl A): 1-17 3. Drugs 2008:68(6):803-838 4. J Antimicrob Chemother 1998; 41(Suppl D):25-41 5. Scand J Infect Dis1999;31(1):3-10 6. J Antimicrob Chemother 1995; 36(Suppl A): 179-189 7. Diagn Micorbiol infect Dis 1998; 31: 405-410 8. Antimicrob Agents and Chemother 1995; 39(5): 1140-1146

제품요약정보 — 전문의약품

유한메로펜® 주사 0.5그램 [원료약품 및 분량] 1 바이알 중 유효성분: 메로페넴·건조탄산나트륨(별규) 604mg(메로페넴으로서 500mg(역가)) **[성상]** 백색~담황색의 결정성 분말을 충진한 바이알 **[효능·효과] 1. 유효균종:** 제품 허가사항 참조 **2. 적응증:** 패혈증, 표재성 화농성질환, 림프절염, 항문주위농양. 외과 정형외과 영역 감염증(골수염, 관절염, 창상감염), 호흡기 감염증(폐렴, 편도주위농양, 만성호흡기질환의 2차 감염, 폐화농양, 농흉), 요로감염증(신우신염, 복잡성방광염), 간 담도감염증(담낭염, 담관염, 간농양), 복막염, 산부인과영역 감염증(자궁부속기염, 자궁내감염, 자궁방결합직염), 이비과영역 감염증(중이염, 부비동염), 세균성 수막염(3개월 이상의 소아), 호중구감소증 환자에서의 의심되는 감염, 낭포성 섬유증 **[용법·용량]** • 성인: 메로페넴수화물으로서 1일 0.5 ~ 1g(역가)을 2 ~ 3회 분할하여 30분 이상에 걸쳐 점적정맥주사한다. 병원성 폐렴, 복막염, 호중구감소증 환자에서의 의심되는 감염, 패혈증에는 8시간마다 1g(역가)을 점적정맥주사한다. 낭포성섬유증, 수막염에는 8시간마다 2g(역가)을 점적정맥주사한다. • 소아: 3개월 이상의 소아에 대한 세균성 수막염의 경우 병원균의 감수성과 환자의 상태, 감염의 종류에 따라 8시간마다 체중 kg 당 40mg을 30분 이상에 걸쳐 점적정맥주사한다. 또한 증상에 따라 적절히 증감하지만 중증, 난치성 감염증에는 1일 2g(역가)까지 증량할 수 있다. ※ 신장애 환자 등 기타 자세한 용법·용량은 제품 허가사항 참조 **[사용상의 주의사항] • 다음 환자에는 투여하지 말 것.** 1) 이 약에 대해 쇼크의 병력이 있는 환자 2) 발프로산나트륨을 투여 받고 있는 환자(이 약과의 병용투여에 의해 발프로산의 혈중농도가 저하되어 간질발작이 재발할 수 있다.) 3) 이 약 또는 이 약의 구성성분에 대해 과민반응 또는 그 병력이 있는 환자 4) 다른 카바페넴계 항생물질에 대해 과민반응(에, 심각한 피부 반응)의 병력이 있는 환자 5) 다른 베타락탐계 항생물질(에, 페니실린 또는 세팔로스포린)에 중증의 과민반응(에, 아나필락시스반응, 중증의 피부반응) 환자 **[저장방법]** 밀봉용기, 실온보관 **[개정연월일]** 2019. 5. 14 **[제조 판매자]** ㈜유한양행 본사: 서울 동작구 노량진로 74, 공장: 충청북도 청주시 청원구 오창읍 연구단지로 219 홈페이지: www.yuhan.co.kr 소비자상담실: 080-024-1188 (수신자 요금부담) **※자세한 허가사항은 식약처 의약품통합정보시스템 홈페이지 (http://nedrug.mfds.go.kr/)를 참조하여 주시기 바랍니다. 요약 허가사항에 반영되지 않은 허가 변경이 상기일자 이후에 있을 수도 있습니다.**

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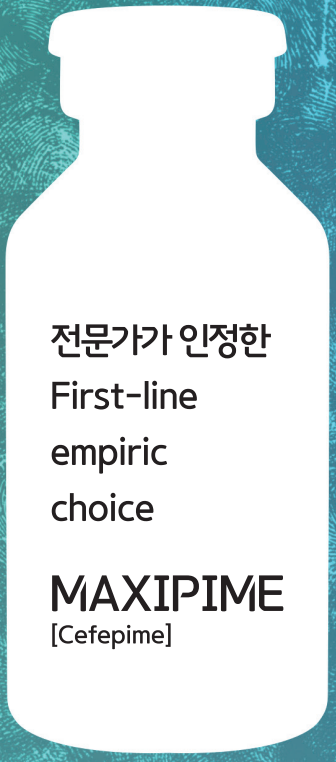
CAP
community-acquired pneumonia

AVELOX® 400mg FILM-COATED TABLETS, AVELOX® 400mg/250ml SOLUTION FOR INFUSION (MOXIFLOXACIN): Refer to local prescribing information for full details before prescribing. **Tablets** each contain 400mg moxifloxacin as hydrochloride. **Solution for Infusion** contains moxifloxacin 1.6mg/ml (400mg/250ml), as moxifloxacin hydrochloride. **Indications:** Bacterial infections caused by moxifloxacin susceptible bacteria as follows: **Tablets: adequately** diagnosed acute exacerbation of chronic bronchitis and acute bacterial sinusitis only when it is considered inappropriate to use antibacterial agents that are commonly recommended for the initial treatment of these infections or when these have failed to resolve the infection; community acquired pneumonia, except severe cases only when it is considered inappropriate to use antibacterial agents that are commonly recommended for the initial treatment of this infection; mild to moderate pelvic inflammatory disease without an associated tubo-ovarian or pelvic abscess in combination with another appropriate agent unless moxifloxacin resistant Neisseria gonorrhoeae can be excluded. **Solution for Infusion:** community acquired pneumonia and complicated skin and skin structure infections in patients requiring initial parenteral therapy only when it is considered inappropriate to use antibacterial agents that are commonly recommended for the initial treatment of these infections. Consideration should be given to official guidance on the appropriate use of antibacterial agents. Refer to SmPC and/or local laboratory guidelines for microbiological activity. Dosage/Use: Adults: Tablets 400mg once daily for 5-10 days in acute exacerbation of chronic bronchitis, 7 days in acute sinusitis, 10 days in community acquired pneumonia and 14 days in mild to moderate pelvic inflammatory disease. **Solution for Infusion intravenous dose** of 400mg once daily (can be administered via a T-tube, with compatible infusion solutions), the duration of infusion should not be less than the recommended 60 minutes and the intravenous dose of 400 mg once a day should not be exceeded (QT prolongation may increase with increasing plasma concentrations due to rapid i.v. infusion). Initial i.v. use may be followed by oral administration. For sequential administration total treatment duration depends on indication, type and severity of disease and clinical response: community acquired pneumonia, 7-14 days; complicated skin and skin structure infections, 7-21 days. No dose adjustment in elderly or patients with low body weight, in impaired renal function or in patients on chronic dialysis. Insufficient data in patients with severely impaired liver function. Efficacy and safety not established in children and adolescents.

보령제약

Mass Pick, Smart Pick



For
Hospital-acquired pneumonia (HAP)
Ventilator-associated pneumonia (VAP)
Febrile neutropenia

1. Excellent in vitro activity against both G(+) and G(−)
2. 대부분의 β-lactamase 에 대해 매우 안정합니다.
3. FDA 로부터 Febrile neutropenia 에 Empiric Monotherapy 로 최초로 그 적응증을 인정받은 항생제 입니다.
4. IDSA, NCCN 가이드 라인에서 HAP&VAP 및 Febrile neutropenia 1차 경험요법제로 추천되었습니다.
5. Pneumonia, Urinary tract infections, Pediatric infections 에 우수한 효과를 나타냅니다.

First-Line Empiric Therapy
맥스핌
[Cefepime HCl 0.5g / 1g IV/IM]

#[대한감염학회 2010] 경증 또는 중등증 지역사회획득 복잡성 복강 내 감염을 가진 성인 환자의 경험적 치료 (BII)[4,5] [질병관리본부 2018] 요로 패혈 관련 신우신염의 경험적 치료(A2)[7,8] [IDSA 2010] 경증 또는 중등증 지역사회획득 복잡성 복강내 감염을 가진 성인 환자의 경험적 치료 (AI)[5,1] [SIS 2017] 경증 지역사회획득 복잡성 복강내 감염을 가진 성인 또는 소아 환자의 경험적 치료 (1A)[6,1]

* [Strength of Recommendation] **A** Good evidence to support a recommendation for (or against use): **B** Moderate evidence to support a recommendation for (or against use); **C** Poor evidence to support a recommendation [Quality of Evidence] **I** ≥ 1 properly randomized controlled trial **II** ≥ 1 well-designed clinical trial without randomization or cohort or case-controlled analytic studies (preferably >1 center) or multiple time-series or dramatic results from uncontrolled experiments **III** opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees[4] / [Strength of Recommendation] **A** Good evidence to support a recommendation for use; **B** Moderate evidence to support a recommendation for use; **C** Poor evidence to support a recommendation [Quality of evidence] **Level 1** Evidence from at least 1 properly designed randomized, controlled trial; **Level 2** Evidence from at least 1 well-designed clinical trial, without randomization: from cohort or case-controlled analytic studies (preferably from >1 center): from multiple time series: or from dramatic results of uncontrolled experiments; **Level 3** Evidence from opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees[5] / [Class of Evidence] **A** High quality evidence from RCTs, meta-analyses of such trials, or methodologically sound epidemiologic studies; **B** Moderate quality evidence from lower quality prospective studies, retrospective case control studies, and large observational, cohort, or prevalence studies, based on clearly reliable data; **C** Weak quality evidence from smaller observational studies, studies relying on retrospective or less reliable data, authoritative opinions expressed in reviews, or expert opinions of task force members: None Insufficient evidence [Rating Scale for recommendations] **1** Strong recommendation generally based on moderate to high quality evidence. "We recommend..."; **2** Weak recommendation generally based on weak to moderate quality evidence. "We suggest..."; **None** No recommendation[6] / [Strength of Recommendation] **A** Good evidence to support a recommendation for (or against use); **B** Moderate evidence to support a recommendation for (or against use); **C** Poor evidence to support a recommendation [Quality of Evidence] **I** ≥ 1 properly randomized controlled trial; **II** ≥ 1 well-designed clinical trial without randomization or cohort or case-controlled analytic studies (preferably >1 center) or multiple time-series or dramatic results from uncontrolled experiments; **III** opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees[7]

FDA : US Food and Drug Administration, IDSA : Infectious Diseases Society of America, SIS : Surgical Infection Society

※ 이 약은 생후 3개월 미만의 영아에 대한 자료는 없으므로 생후 3개월 미만의 영아에게는 권장되지 않습니다.[1]

References 1. 인반즈주 허가사항. 식품의약품안전처. 2. 식약처 의약품통합정보시스템. 특허목록 검색-에르타페넴. Available at <https://nedrug.mfds.go.kr/searchPatent?page=1&searchYn=true&itemName=&mainIngr=에르타페넴> Accessed Dec. 01, 2020. 3. 식약처 의약품통합정보시스템. 의약품등 정보검색>에르타페넴. Available at <https://nedrug.mfds.go.kr/searchDrug?sort=&sortOrder=false&searchYn=true&page=1&searchDivision=detail&itemName=&entpName=&ingrName1=에르타페넴> Accessed Dec. 01, 2020. 4. 대한감염학회·대한화학요법학회·대한임상미생물학회. 소화기계 감염 진료지침 권고안. *Infect Chemother.* 2010;42(6):323-361. 5. Solomkin JS, *et al.* Diagnosis and management of complicated intra-abdominal infection in adults and children: guidelines by the Surgical Infection Society and the Infectious Diseases Society of America. *Clin Infect Dis.* 2010;50(2):133-164. 6. Mazuski JE, *et al.* The Surgical Infection Society Revised Guidelines on the Management of Intra-Abdominal Infection. *Surg Infect (Larchmt).* 2017;18(1):1-76. 7. 질병관리본부, 대한감염학회, 대한비뇨기과학회, 대한신장학회, 대한요로생식기감염학회. 요로 감염 항생제 사용지침. 2018. 8. Food and drug administration. Drug@FDA : FDA-Approved Drugs. INVANZ. Available at <https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=BasicSearch.process> Accessed Dec. 01, 2020.

Selected Safety Information 인반즈(에르타페넴-나트륨) [효능·효과] 1. 유효균종: *Escherichia coli* (균혈증을 동반한 경우를 포함), *Clostridium clostridioforme, Eubacterium lentum, Peptostreptococcus* 종, *Bacteroides fragilis, Bacteroides distasonis, Bacteroides ovatus, Bacteroides thetaiotaomicron, Bacteroides uniformis, Staphylococcus aureus* (methicillin 감수성 균종), *Streptococcus pyogenes, Streptococcus pneumoniae* (페니실린 감수성 균주, 균혈증을 동반한 경우를 포함), *Haemophilus influenzae* (beta-lactamase 음성 균주), *Moraxella catarrhalis, Klebsiella pneumoniae, Streptococcus agalactiae, Porphyromonas asaccharolytica, Proteus mirabilis* 혹은 *Prevotella bivia*. 2. 적응증 1) 치료 - 복잡성 복부내 감염, 복잡성 피부 및 피부조직 감염 (성인에서 골수염을 동반하지 않은 당뇨성 족부감염 포함), 지역사회 획득성 폐렴, 복잡성 요로감염, 급성 골반 감염 (분만후 자궁실질염·난관염, 패혈성 유산, 수술후 부인과 감염 등) 2) 예방 (성인) - 계획된 직장결장수술로 인한 수술부위 감염 예방: 직장관 경제로 원인균을 분리 확인하고, 이 약에 대한 감수성 여부를 확인한다. 시험결과를 확인하기 전에 경험적으로 이 약의 투여를 시작할 수도 있으며, 시험결과가 확인된 후에는 그에 따라 적절하게 항균제를 투여하여야 한다. **[용법·용량]** 1. 13 세 이상의 환자에게는 에르타페넴으로서 1.0g 을 1 일 1 회 투여합니다. 생후 3 개월 이상 12 세 이하의 환자에게는 1 일 1g 을 초과하지 않는 범위에서 15mg/kg 을 1 일 2 회 투여합니다. 2. 정맥주사하는 경우 14 일까지 투여할 수 있으며, 근육주사의 경우에는 7 일까지 투여한다. 정맥주사시에는 30 분 동안 주입해야 한다. **[사용상의 주의사항] [경고]** 1) 베타락탐계 약물을 투여 받은 환자 중에서 때때로 중대한 치명적 과민반응(아나필락시 반응)이 보고되었다. 이러한 반응은 다양한 항원에 대한 과민반응의 병력을 가진 환자의 경우 발생될 가능성이 더욱 높았다. 또한 페니실린에 과민반응의 병력을 가진 환자에게 다른 베타 락탐계 약물을 투여하였을 때, 중증의 과민반응이 나타났다는 보고가 있었다. 따라서 이 약을 투여하기 전에 환자가 페니실린, 세팔로스포린, 다른 베타 락탐계 약물 및 기타 항원에 대하여 이전에 과민반응을 나타낸 적이 있었는지 주의 깊게 조사하여야 한다. 만약 이 약에 대해 알려지 반응이 나타날 경우 이 약의 투여를 즉시 중단한다. 중대한 아나필락시 반응이 나타날 경우 즉각적인 응급조치(에피네프린, 산소, 스테로이드 정맥주사, 기도삽관 등 기도 처치)등을 취해야 한다. 이외에도 다른 치료약물을 투여할 수도 있다. 2) 이 약의 투여시 발작, 기타 중추신경계 이상반응이 보고된 적이 있다. 3) 이 약을 포함하여 거의 모든 항균제에 의해 위막성 대장염이 발생하였다는 보고가 있으며, 증상은 경증에서부터 생명을 위협하는 정도까지 다양하였다. 따라서 항균제 투여 후 설사를 하는 환자의 경우 위막성 대장염을 고려할 필요가 있다. 4) 항균제의 투여는 정상 장내세균총을 변화시킬 수 있으며, Clostridium 속 균종의 과도한 성장을 유도할 수 있다. 연구결과, Clostridium difficile에 의해 발생하는 독소가 "항균제-관련 대장염"의 주요한 원인인 것으로 알려졌다. 5) 위막성 대장염으로 진단된 후에는 적절한 치료를 해야 한다. 경증인 경우에는 통상 이 약의 투여를 중단하면 회복될 수 있다. 중등도 내지 중증의 경우에는 수액 및 전해질, 단백질을 보충하거나, Clostridium difficile에 의한 대장염에 유효한 항균제의 투여를 고려해야 한다. 6) 문헌에 따르면, 이 약을 포함한 카바페넴계 항균제를 발프로산(valproic acid) 또는 디발프로엑스나트륨(divalproex sodium)을 투여받는 환자에게 병용투여했을 때, 발프로산 농도의 감소가 보고되었다. 이러한 약물상호작용으로 인해 발프로산 농도가 치료 농도 이하로 감소될 수 있으며, 이로 인해 발작의 위험이 높아질 수 있다. 발프로산 또는 디발프로엑스나트륨의 용량을 높이는 것이 약물 상호작용을 극복하는 데에 충분하지 않을 수 있다. 이 약과 발프로산 또는 디발프로엑스나트륨의 병용투여는 권장되지 않는다. 발프로산 또는 디발프로엑스나트륨으로 발작이 잘 조절되는 환자의 감염증 치료에는 카바페넴계 외의 항균제 사용을 고려하여야 한다. 만약 이 약의 투여가 필요할 때에는, 혈중 발프로산의 농도를 모니터링하며, 추가적인 항경련 요법을 고려하여야 한다. 7) 이 약의 근육주사시 희석제로 염산리도카인 용액이 사용되므로, 염산리도카인에 대한 첨부문서를 참고한다. **[금기]** 1) 이 약의 성분 혹은 동일한 계열의 다른 약물에 과민증이 있는 환자. 2) 베타 락탐계 약물에 아나필락시성 반응의 병력이 있는 환자. 3) 이 약의 근육주사 시 희석제로 염산리도카인 용액이 사용되므로, 아미드계열의 국소마취제에 과민증이 있는 환자에게는 이 약을 근육주사하여서는 안된다. **[신중투여]** 1) 설인 환자를 대상으로 한 임상시험에서 이 약과의 관련성과 상관없이 시험기간 및 14일간 추적조사동안 환자의 0.5%에서 발작이 보고되었다(4. 이상반응 항 참조). 이 시험반응은 중추신경계질환(예, 뇌 손상 혹은 발작의 병력) 및/또는 신기능 저하 환자에서 더욱 빈번하게 발생하였다. 따라서 발작증상을 일으킬 인자가 알려진 환자에서는 권장용량을 초심히 지킬 것이 요구되며, 발작질환이 있는 환자는 항경련제 투여를 지속하여야 한다. 국소성 진전, 간대성 근경련, 혹은 발작이 발생한 경우에는 신경학적으로 검사하여 임원하지 않은 경우라면 항경련제 요법을 받아야 하고, 이 약을 감량할 것인지 이 약의 투여를 중단할 것인지 결정하기 위하여 이 약의 용량을 검토하여야 한다. 2) 신부전환자: 이 약의 투여시 용량을 조절하여야 한다. **[이상반응]** 1)성인: 임상시험에서 1,954명의 환자가 이 약을 투여받았다. 몇 임상시험에서는 이 약의 투여 후 적절한 경구 항균제로 교체되었다. 임상시험에서 보고된 이상반응의 대부분은 경증 내지 중등도이었으며, 이상반응으로 인하여 이 약의 투여를 중단한 환자는 전체 중 4.7% 이었다. 다음 표 1은 임상시험에서 1.0% 이상의 환자에서 발생한 이상반응을 나타낸 것이다. 경구 항균제로 교체한 환자를 포함하여 이 약을 투여받은 모든 환자에서 약물과 관련된 것으로 가장 빈번하게 보고된 이상반응은 설사(5.5%), 주사부위 혈관 합병증(3.7%), 구역(3.1%), 두통(2.2%),질염(2.1%), 정맥염/혈전성정맥염(1.3%), 구토(1.1% 이었다. 복부내 감염 합병증 환자를 대상으로 한 임상시험에서 이 약을 투여받은 환자에서 4.7%(15/316), 대조약을 투여받은 환자에서 2.6%(8/307)가 사망하였으나, 사망한 환자들은 중대한 합병증과 중증 감염증으로 인하여 사망한 것이며, 시험자의 판단으로 이 약과의 연관성은 없다고 여겨졌다. 임상시험에서 시험기간 및 14일간 추적조사동안 이 약을 투여받은 환자의 0.5%, Piperacillin/Tazobactam을 투여받은 환자의 0.3%, ceftriaxone을 투여받은 환자의 0% 에서 발작이 보고되었다. **[일반적주의]** 1) 다른 항균제와 마찬가지로 이 약을 장기간 투여하였을 때는 이 약에 감수성이 없는 미생물의 과도한 증식을 유발시킬 수 있다. 이 약을 투여하는 동안 환자의 상태를 지속적으로 관찰하여야 하며, 만약 균교대감염이 관찰되면 적절한 조치를 취하여야 한다. 2) 감수성균에 의한 감염이거나 그러한 균으로 상당히 의심되는 감염이 아닌 경우 또는 예방의 목적으로 이 약을 처방하는 것은 환자에게 유익하지 않을 수 있으며 약물내성균의 발생 위험을 증가시킨다. 약물내성균의 발생률을 감소시키고 이 약과 다른 항균제의 유효성을 지속시키기 위해 이 약에 감수성이 있는 균으로 인한 감염이거나 그러한 균으로 상당히 의심되는 감염에 한하여 치료나 예방의 목적으로 이 약을 사용하여야 한다. 배양결과와 감수성 정보가 확인된 후에는 그에 따라 항균제를 선택하거나 변경하는 것을 고려해야 한다. 이러한 정보가 없는 경우 그 지역의 역학이나 감수성 양상에 대한 정보가 이 약을 경험적으로 선택하는데 도움이 될 수 있다. 3) 이 약을 근육주사할 때는 혈관내로 주사하지 않도록 주의하여야 한다(용법 • 용량 참조). 이 약의 근육주사시 희석제로 염산리도카인 용액이 사용되므로, 염산리도카인에 대한 첨부문서를 참고한다. 4) 이 약은 베타락탐계 항균제와 유사한 특성을 가지므로, 장기간 투여시에는 신장, 간, 조혈계 등 장기의 기능을 주기적으로 검사하는 것이 바람직하다. 5) 이 약은 투여량 1.0 g당 약 8.0 mEq(약 137 mg)의 나트륨을 포함하므로, 나트륨 조절 식이 환자는 이를 고려해야 한다. **[상호작용]** 1) 이 약과 Probenecid(500 mg, 6시간마다 경구투여)를 병용하였을 때, probenecid의 이 약의 최소관 농동분비와 경쟁하여 이 약의 AUC를 25% 증가시켰으며, plasma 및 renal clearance를 각각 20%, 35% 감소시켰다. 반감기는 4.0시간에서 4.8시간으로 증가시켰다. 그러나 이 약의 반감기에 미치는 영향은 작기 때문에, 이 약의 반감기를 연장시키기 위하여 Probenecid를 병용하는 것은 바람직하지 않다. 2) In vitro 시험에서 이 약은 P-glycoprotein을 매개로 하는 digoxin 혹은 vinblastine의 수송을 억제하지 않았으며, P-glycoprotein을 매개로 하는 수송의 기질이 아니었다. 또한 사람의 간 마이크로좀을 이용한 In vitro 시험에서 이 약은 주요한 6종의 cytochrome P450(CYP) 효소(1A2, 2C9, 2C19, 2D6, 2E1, 3A4)에 의해 매개되는 대사를 억제하지 않았다. 따라서 이 약은 P-glycoprotein을 매개로 하는 약물의 배설 혹은 CYP에 의한 약물의 대사 등을 억제하는 기전의 약물상호작용은 없을 것으로 여겨진다. 3) Probenecid 외 특정한 약물과의 상호작용은 연구되지 않았다. 4) 문헌에 따르면, 이 약 등의 카바페넴계 항균제를 발프로산 또는 디발프로엑스나트륨을 투여받는 환자에게 병용투여했을 때, 발프로산 농도의 감소가 보고되었다. 이러한 약물 상호작용으로 인해 발프로산 농도가 치료 농도 이하로 감소될 수 있으며, 이로 인해 발작의 위험이 높아질 수 있다. 약물상호작용의 작용기전은 명확히 밝혀지지 않았으나, in vitro 및 동물시험 자료를 통해 발프로산의 글루쿠로니이드 대사체(VPA-g)가 가수분해되어 발프로산으로 전환되는 것을 카바페넴계가 저해함으로써, 발프로산의 혈중 농도를 감소시키는 것으로 생각된다. **[임부에 대한 투여]** 마우스 및 랫드에게 정맥으로 700mg/kg/day 용량(마우스의 경우, 체표면적에 근거하여 사람의 권장용량인 1g의 3배 용량, 랫드의 경우 혈중 AUC에 근거하여 사람의 권장용량인 1g의 1.2배 용량)까지 투여하고 태자의 외표기형, 내장기형, 골격기형 등을 측정하였을 때, 발생독성의 증거는 없었다. 그러나 마우스에서 700mg/kg/day 용량 투여 시, 태자의 체중감소와 전미골 최추의 골형성 감소가 관찰되었다. 이 약은 랫드에서 태반을 통과하였다. 그러나 임부를 대상으로 한 적절한 비교임상시험은 없다. 동물생식시험이 항상 사람에서의 반응을 예측할 수는 없으므로, 임신시에는 이 약물이 반드시 필요하다고 판단되는 경우에만 신중히 투여한다. **[수유부에 대한 투여]** 이 약은 사람의 모유중으로 배설되므로 이 약을 수유부에 투여할 때는 주의하여야 한다. 수유부에게는 이 약물의 유익성이 위험성을 상회한다고 판단되는 경우에만 투여한다. **[소아에 대한 투여]** 생후 3개월에서 17세의 환자에 대한 이 약의 안전성과 유효성은 다음 임상시험의 자료에 근거하여 아래 감염증에 대해서 확인되었다. 성인에서의 적절한 대조임상시험, 소아환자에서의 약동학시험, 생후 3개월에서 17세 환자에서의 활성약 대조임상시험 1)복잡성 복부내 감염 2)복잡성 피부 및 피부조직 감염 3)지역사회 획득성 폐렴 4)복잡성 요로감염 5)급성 골반 감염. 이 약은 생후 3개월 미만의 영아에 대한 자료는 없으므로 생후 3개월 미만의 영아에게는 권장되지 않는다 이 약은 뇌척수액으로 충분히 통과하지 못하므로 소아의 수막염 치료에는 권장되지 않는다. **[고령자에 대한 투여]** 제Ib/IIIa 상 임상시험에서 이 약을 투여받은 1,835명의 환자 중 대략 26%가 65세 이상이었으며, 75세 이상은 약 12%였다. 이 약의 유효성 및 안전성은 고령자(65세 이상)와 젊은 연령층간에 차이가 없었다. 그 외 임상경험에서도 고령자와 젊은 연령층간에 차이는 보고된 바 없으나, 일부 고령자에서 감수성이 증가할 가능성은 배제할 수 없다. 이 약은 신장으로 대부분 배설되므로, 신장애환자의 경우 이 약의 의한 독성반응의 위험성이 커질 수 있다. 고령환자는 신기능이 저하될 가능성이 있으므로, 용량설정시 주의하여야 하며 신장기능을 계속 관찰할 필요가 있다. **[간장애 환자에 대한 투여]** 간장애 환자에서 이 약의 약동학은 확립된 바 없다. 총 임상시험에서 이 약 1g을 투여받은 환자 37명과 대조약을 투여받은 환자 36명이 Child-Pugh Class A,B, 혹은 C 간장애로 진단받았으며, 간장애환자에서 이상반응의 발생률은 이 약의 투여군과 대조약 투여군에서 유사하게 나타났다. 개정일 : 2020년 4월 1일

※ 처방하시기 전에 각 항목에 대한 자세한 내용은 제품설명서 전문을 참조하시기 바랍니다.

KR-CAR-00076 12/2022

보건의료전문가용

도바토정
돌루테그라비르나트륨/라미부딘

gsk

이제는 2제로[1,2]

새로운 2제 DTG/3TC 복합제
도바토로 HIV 치료를 시작하세요

* 실제 환자가 아닌, 이해를 돕기 위한 이미지 예시입니다.

PM-KR-DLL-JRNA-200001 | Mar 2021

Dovato(dolutegravir/lamivudine) Important Safety Information 전문의약품 수입의약품

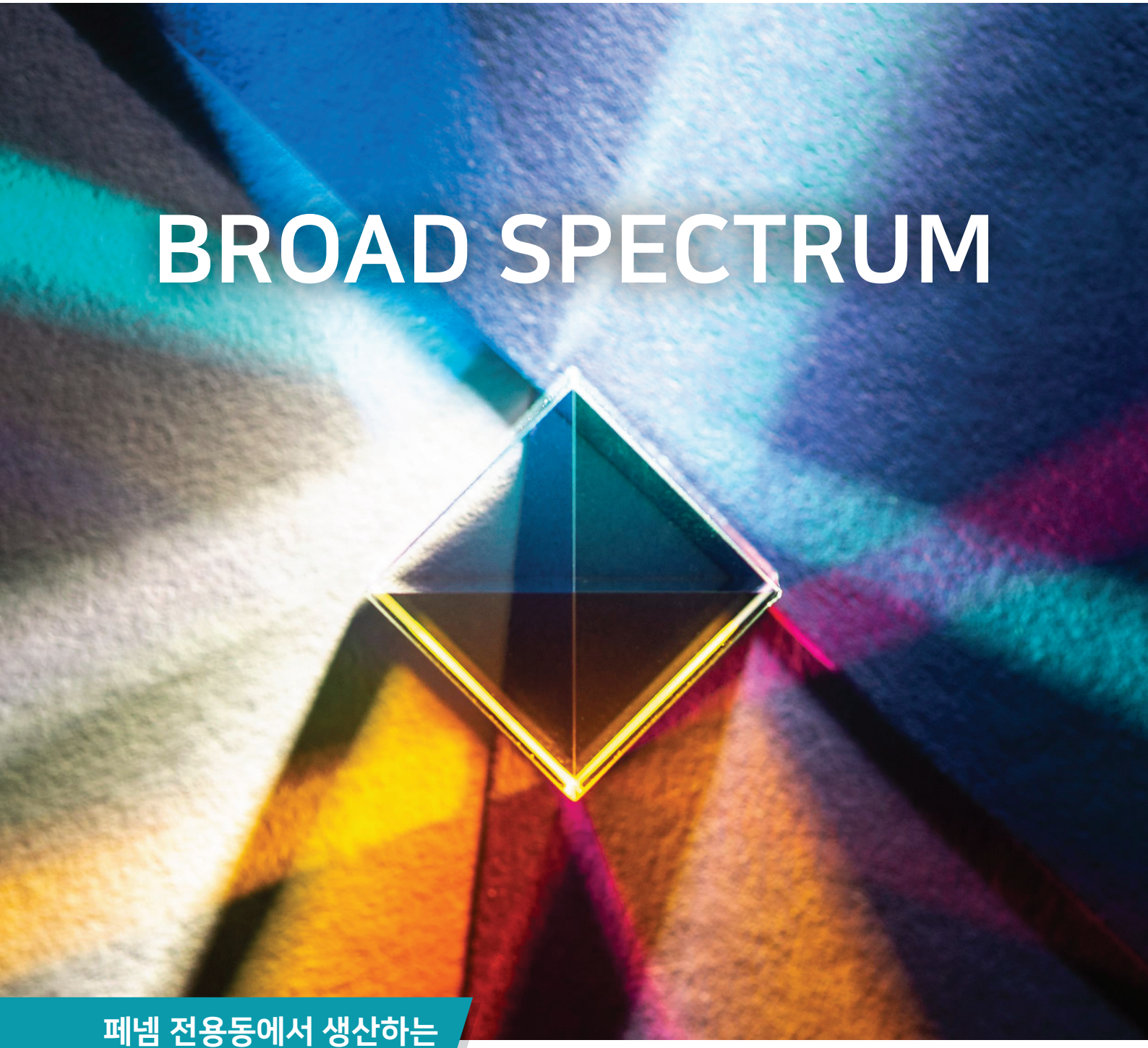
1) 과민반응: 발진과 전신 소견, 때때로 중증의 간 반응을 포함한 장기 기능 이상을 특징으로 하였다. 2) B형 간염 바이러스 동시 감염 시 중단에 의한 B형 간염 바이러스 출현이 보고되었다. 3) 이미 간기능 장애가 있는 환자들은 항레트로바이러스 병용요법을 받는 동안 간기능 이상의 빈도가 증가하며 표준 진료에 따라 반드시 모니터링해야한다. 4) 유산산증: 라미부딘을 포함한 뉴클레오시드 유사체의 단독 또는 병용 사용에 의하여 알반적으로 간비대 및 간지방증과 연관이 있는 유산산증이 보고되었다. 알파인터페론과 리바비린을 병용투여받고 있는 C형 간염에도 감염된 환자의 경우 특별한 위험이 발생할 수 있다. 5) 태아 독성: 태아에 대한 신경관 결손 발생 위험이 있으므로, 이 약을 투여하는 동안 임신 계획이 있거나 임신 첫 3개월 이내인 것으로 확인된 경우, 다른 항레트로바이러스 요법으로 전환하는 것 대비 이 약의 투여 지속에 대한 위험성과 유익성을 평가해야 하며 임부에 기대되는 유익성이 태아에 대한 잠재적 위험성을 상회하는 경우에만 투여해야 한다. 임신 가능한 여성은 이 약의 투여를 시작하기 전에 임신 검사를 해야 하며 치료하는 동안 효과적인 피임법을 사용하도록 지속적으로 권고해야 한다. Reference: 도바토 제품설명서

Dovato(dolutegravir/lamivudine) Abbreviated PI version 01

[원료약품 및 분량] 도바토: 1정 (918.0밀리그램) 중 주성분: 돌루테그라비르-나트륨(비분화)(벌규) 52.6 밀리그램 (돌루테그라비르로서 50mg) 과 라미부딘 300 밀리그램 **[효능효과]** 이 약의 개별 항레트로바이러스 성분에 대하여 알려진 또는 의심되는 내성 관련 치환이 없는 성인 및 12세 이 상(체중 40 kg 이상) 청소년의 인체면역결핍바이러스(HIV-1) 감염 치료 **[용법용량]** 이 약은 HIV-1 감염 치료에 경험이 있는 의사에 의해 처방되어야 하며, 경구로 투여한다. 음식물의 섭취와 상관없이 투여할 수 있다. 1. 성인 및 12 세 이상 청소년(체중 40kg 이상) 권장 용량은 1일 1회, 1정. 감량이 불가능한 고정용량 정제임. 이 약은 구성성분 중 어느 것에라도 내성이 있는 경우 권장하지 않는다. 2. 복용을 잊은 경우- 환자가 이 약의 복용을 잊은 경우 다음 번 투여시점까지 4시간 이상 남아있으면 가능한 빨리 이 약을 복용한다. 만약 다음 번 투여시점이 4시간 이내이면 잊은 정제를 복용하지 않고 평소 투여 일정대로 복용을 다시 시작한다. 3. 환자가 이 약의 복용을 잊은 경우 다음 번 투여시점까지 4시간 이상 남아있으면 가능한 빨리 이 약을 복용한다. 만약 다음 번 투여시점이 4시간 이내이면 잊은 정제를 복용하지 않고 평소 투여 일정대로 복용을 다시 시작한다. 4. 2정씩 1회 복용 – 경증 또는 중증의 간장애 환자(Child-Pugh score A 또는 B)에서 용량 조절은 필요하지 않다. 중증 간장애 환자(Child-Pugh score C)에 대한 자료는 없으므로, 중증 간장애 환자에게는 이 약을 주의하여 투여한다. **[사용상의 주의사항]** 1. 경고 1) 과민반응 – 돌루테그라비르 투여 시 과민반응이 보고되었는데, 발진과 전신 소견, 때때로 중증의 간반응을 포함한 장기 기능 이상을 특징으로 하였다. 과민반응의 징후 또는 증상이 발생하면(중증의 발진이나 간 효소의 상승을 수반한 발진 발열, 전신 권태감, 피로, 근육통, 관절통, 수포, 구강병변, 결막염, 안면부종, 호산구 증가증, 혈관부종을 포함하나 이에 국한되지는 않음), 이 약과 다른 의심되는 약물의 투여를 즉시 중단해야 한다. 2) B형 간염 바이러스 동시 감염: 돌루테그라비르는 이러한 활성이 없다. 라미부딘 단일요법은 B형 간염 내성 발생 위험이 높기 때문에 알반적으로 B형 간염에 대한 적절한 치료법으로 간주되지 않는다. (치료 가이드라인 참고). 3) 간독성 – 만성 활성 간염을 포함하여 이미 간기능 장애가 있는 환자들은 항레트로바이러스 병용요법을 받는 동안 간기능 이상의 빈도가 증가하며 표준 진료에 따라 반드시 모니터링해야 한다. 4) 유산 산증 – 라미부딘을 포함한 뉴클레오시드 유사체의 단독 또는 병용 사용에 의하여 알반적으로 간비대 및 간지방증과 연관이 있는 유산산증이 보고되었다. 이들 사례의 대부분은 여성에게서 보고되었다. 5) 태아 독성: 태아에 대한 신경관 결손 발생 위험이 있으므로, 이 약을 투여하는 동안 임신 계획이 있거나 임신 첫 3개월 이내인 것으로 확인된 경우, 다른 항레트로바이러스 요법으로 전환하는 것 대비 이 약의 투여 지속에 대한 위험성과 유익성을 평가해야 하며 다른 요법으로 전환하는 것을 고려해야 한다. 2. 다음 환자에는 투여하지 말 것 1) 돌루테그라비르, 라미부딘 또는 이 약의 성분에 과민증이 있는 환자. 2) 도파테랄라이드, 필시키이니드, 또는 팜프리딘(담팜프리딘으로도 알려짐)을 포함하여 유기양이온수송체 2 (OCT2)의 기질이고 좁은 치료역을 갖는 의약품과 병용투여해서는 안 된다. 3. 이상반응 1) 안전성 프로파일 요약 이 약을 사용한 임상적 안전성 자료는 제한적이다. 3상 임상 시험에서 돌루테그라비르와 라미부딘을 병용 투여한 HIV-1 감염 환자 716명에서 돌루테그라비르와 라미부딘 병용투여와 관련되었을 가능성이 있다고 판단된 가장 빈번하게 보고된 이상반응은 두통(3%), 설사(2%), 구역(2%) 및 불면증(2%)이었다. 돌루테그라비르 투여와 관련되었을 가능성이 있는 가장 중증의 이상 사례(제2b상 및 제3상 임상시험 통합)는 한 환자에서 관찰된 과민반응이었으며, 이는 발진 및 중증 간 영향을 포함하였다. 2) 이상반응–임상시험 및 시판 후 경험에서 적어도 이 약의 성분인 돌루테그라비르 및 라미부딘 투여와 관련성이 있을 것으로 판단된 이상반응을 발현계/발현기간 및 빈도에 따라 제시하였다. 빈도에 대한 정의는 다음과 같다: 매우 흔하게(≥1/10: 두통, 구역, 설사, 두통, 구역, 설사, 흔하게 (≥1/100 및 <1/10: 우울증, 불안, 불면증, 비정상적 꿈, 어지러움, 기면, 구토, 고장, 복통, 복부, 불쾌감, 우울증, 불안, 불면증, 비정상적 꿈, 어지러움, 기면, 구토, 고장, 복통, 복부 불쾌감, 발진, 가려움증, 탈모, 관절통, 근육 이상(근육통 포함), 피로, CPK 상승, ALT 및/또는 AST 상승), 흔하지 않게(≥1/1,000 및 <1/100: 호중구감소증, 빈혈, 혈소판감소증, 과민반응, 면역재구성증후군, 자살관념, 자살시도, 간염), 드물게(≥1/10,000 및 <1/1,000: 췌장염, 급성간부전, 혈관부종, 횡문근 융해, 아밀라아제 상승), 매우 드물게(<1/10,000: 진성적혈구무형성증, 유산산증, 말초신경병증, 이상감각). 4. 알반적 주의 5. 상호작용 – 1) 다른 약물이 돌루테그라비르와 라미부딘의 약동학에 미치는 영향. ㄱ> 돌루테그라비르는 UGT1A3, UGT1A9, CYP3A4, P-당단백질(Pgp), 유방암저항단백질(BCRP)의 기질이기도 하다. ㄴ> 유기음이온수송운반체(OATP)1B1, OATP1B3, 또는 유기음이온수송체1(OCT1)의 기질이 아니므로, 단독으로 이러한 수송체를 조절하는 약물들이 돌루테그라비르 혈청농도에 영향을 미칠 것으로 예상되지 않는다. ㄷ> 금속 양이온을 함유하는 특정 제산제 및 보충제는 돌루테그라비르의 흡수를 감소시킨다. ㄹ> 라미부딘은 신장으로 제거된다. 돌루테그라비르는 OCT 및 MATE1의 저해제이다. ㅁ> 라미부딘은 CYP효소에 의해 주요하게 대사되지 않는다. ㅂ> 칼슘 보충제, 철분 보충제, 또는 증합비타민제는 이 약의 복용과 충분한 시간 간격을 두고 복용하여야 한다(최소한 2시간 전이나 6시간 후). ㅅ> 항당조절을 유지하기 위하여, 메트포르민을 투여받는 환자에게 이 약 투여를 시작 또는 중단할 때 메트포르민의 용량 조절이 고려되어야 한다. 중등증 신장애 환자에서 메트포르민 농도 증가로 인한 유산 산증 위험이 증가할 수 있으므로, 이 약을 병용 투여할 때 메트포르민의 용량 조절을 고려해야 한다. 9. 과량투여시의 처치 – 돌루테그라비르 또는 라미부딘의 급성 과량투여 후, 이상 반응으로 보고된 것 이외의 특정 증상이나 징후는 확인된 바 없다.

■ **최종허가변경일** 2020.03.16 이 개정 이후 변경된 내용 및 제품 정보 전문은 kr.gsk.com에서 확인하실 수 있습니다. GSK 제품 사용 중 발생한 이상사례(부작용)는 080-901-4100 또는 kr-medical.drug-safety@gsk.com으로 보고해 주시기 바랍니다.

[References] 1. Cahn et al. Durable efficacy of dolutegravir (DTG) plus lamivudine (3TC) in antiretroviral treatment-naïve adults with HIV-1 infection: 3-year results from the GEMINI studies. Journal of the International AIDS Society 2020, 23(S7):e25616. Abstract P018, 2. Van Wyk et al. Switching to DTG/3TC fixed-dose combination (FDC) is non-inferior to continuing a TAF-based regimen (TBR) in maintaining virologic suppression through 96 weeks (TANGO study). Journal of the International AIDS Society 2020, 23(S7):e25616, Abstract O441.



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Reference. 1. 포스페넴®주 식약처 허가사항. 2. Drugs 2000 Mar; 59 (3): 653-680

JW 중외제약

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International Journal of Antimicrobial Agents 58S1 (2021) 106419

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Introduction

On behalf of the organizing committee of the ISAAR 2021 (13th International symposium on Antimicrobial Agents and Resistance), we are very pleased to have the esteemed opportunity to publish the supplement of the International Journal of Antimicrobial Agents (IJAA), which includes abstracts of all presentations at ISAAR 2021 Virtual Congress, from September 9 to 10, 2021. ISAAR is the most representative international meeting on antimicrobial resistance and infectious diseases in the Asia-Pacific region, which has been hosted by the Asia Pacific Foundation for Infectious Diseases (APFID), since 1997. The scientific program of ISAAR 2021 is packed with state-of-the-art knowledge and information on epidemiology and mechanisms of antimicrobial resistance, treatment of antimicrobial-resistant bacterial and fungal infections, diagnostic microbiology, vaccines, HIV infection, infection prevention and control, and antimicrobial stewardship as well as a global pandemic of COVID-19. The supplement includes abstracts of six keynote plenary lectures, forty scientific presentations by invited speakers, and two hundred e-poster presentations, which were presented during the congress, and until one month after the event through the ISAAR 2021 Virtual Platform (www.isaar.org).

It is our wish that physicians and scientists from around the world can share the vital information on antimicrobial resistance and emerging infectious disease threats from ISAAR 2021. All members of the organizing committee of ISAAR 2021 are very grateful to all invited speakers and poster presenters, as well as IJAA and Elsevier, who helped us prepare the supplement. Thank you very much.

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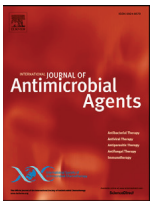
International Journal of Antimicrobial Agents 58S1 (2021) 106420

Contents lists available at ScienceDirect

International Journal of Antimicrobial Agents

journal homepage: www.elsevier.com/locate/ijantimicag



Abstracts from the 13th International Symposium on Antimicrobial Agents and Resistance (ISAAR 2021) – Symposium Presentations and Plenary Lectures

Public health response to COVID-19: National perspective from Taiwan

Hsien-Ho Lin

National Taiwan University, Taipei, Taiwan

During the first few months of the Covid-19 pandemic, Taiwan was considered a high-risk country for large outbreaks because of its close geographic and economic relationships with China, the original epicenter of the disease. In 2020, however, Taiwan was able to maintain low incidence and mortality rates among all countries in the absence of strict lockdown or school closure. By February 28, 2021, a cumulative 955 confirmed cases of COVID-19 (4.1 per 100,000 population) were reported in Taiwan, and only 77 (8.1%) of the cases were locally acquired.

At the beginning of the outbreak, the epidemic command center implemented a "containment-as-mitigation," or elimination, strategy. This approach included border control, case-based interventions for COVID-19 patients, and population-based measures for the general public. Border control was initially applied to incoming travelers (citizens and non-citizens) from a list of high risk countries, but was quickly expanded to all incoming travelers. All had to be quarantined in a quarantine hotel or at home (with isolated bedroom and bathroom) for 14 days. Case-based interventions included case finding and isolation, and contact tracing and quarantine. In the year of 2020 the case finding efforts were mainly based on symptomatic cases presenting to healthcare facilities and receiving Covid-19 diagnosis. Contact tracing was quickly initiated when a newly confirmed case of Covid-19 was reported. Close contacts identified by contact tracing were all required to be quarantined for 14 days (regardless of symptoms). Population-based measures included all the nonpharmacological interventions (npis) that were applied to the general population. This included social distancing, facial masking, and handwashing.

In the first few months of the epidemic, locally acquired cases occurred due to the transmission from imported cases that were not fenced off by border control. Nonetheless, these local cases did not result in large scale community outbreaks. Using the detailed information from epidemiological investigation and contact tracing, we evaluated the impact of case-based interventions and population-based interventions on the control of local transmission of Covid-19. We found that case finding and contact tracing substantially contributed to the containment effort and reduced the reproduction number by 39%, but this was not sufficient to bring down the epidemic if the basic reproduction number was 2.5. We further found that population-based measures including facial masking and social distancing contributed to 48% decline of the reproduction number. The combination of the both population-based and case-based interventions contributed to successful suppression of transmission and resulted in a reproduction number of less than 1.

Despite the success in 2020, Taiwan faced a serious outbreak from the alpha variant starting late April 2021. The causes of this outbreak are multifold. First, the increased transmissibility of the alpha variant (with a reproduction number of up to 3.5 to 4.0) made the containment efforts more challenging. Second, there was a lack of awareness in the community and healthcare setting in the beginning of the outbreak because of the previous success and the absence of reported local cases for a long time. Third, by the time the outbreak was detected, the number of cases were increasing rapidly and overwhelmed the public health system and healthcare facilities. This made the efforts of extensive case finding and contact tracing much more challenging. Fourth, the low vaccination rate in Taiwan made the population particularly vulnerable to community outbreaks.

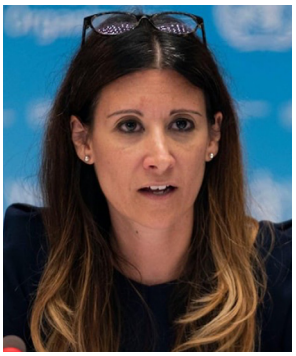
Given the worsening situation the Central Epidemic Command Center issued a level 3 alert nationally on May 19, 2021, and people were encouraged to stay at home except for work. Six weeks after the level 3 alert, the situation gradually improved. By June 30th2021 the daily number of notified cases decreased by 90% compared to the number in the peak of the epidemic, and the public health system and medical system were gradually recovering. While the country is rushing to scale up the vaccination efforts, continuous surveillance assisted by active testing and screening, extensive contact tracing, and a high level of adherence to npis will be all essential before a high vaccination rate is achieved.

Public health response to COVID-19: Regional perspective

Sharon Salmon

World Health Organization, Philippines

The COVID-19 pandemic caught the world unprepared despite decades of warnings of the threat of a global pandemic and years of planning. While the pandemic is not over, we must take opportunity to review this experience so that the Regions are better positioned to cope with potential future surges of the current pandemic and be prepared for future pandemic threats. The World Health Organization (WHO) Western Pacific Regional Office (WPRO) was the first to respond and continues to encourage countries to improve detection of COVID-19 transmission, to respond to detection with quick and targeted measures, and to focus efforts on preventing transmission among the vulnerable.



Public health response to COVID-19: Global perspective

Maria Van Kerkhove

World Health Organization, Switzerland

Since the beginning of the pandemic, the COVID-19 epidemiological scenarios across countries have been heterogenous, as well as the national strategies adopted to control transmission. The ability of the virus to spread rapidly in certain settings has meant that COVID-19 has sometimes overwhelmed even the most resilient health systems. In addition, increasing indirect mortality has been documented worldwide as disruptions to health services associated with the pandemic and response measures have impacted care for other health conditions.

In the second year of the COVID-19 pandemic, our efforts to end the pandemic have been strengthened by deployment of safe and effective COVID-19 vaccines. However, we are now faced with two new challenges in 2021: the emergence of virus variants that have demonstrated increased transmissibility and possible escape from immune responses, as well as pandemic fatigue, leading to poorer adherence to public health and social measures. The global situation remains highly unstable, health systems and global supply chains remain under significant pressure, and inequities are prolonging the impact and duration of pandemic.

The work of the World Health Organization for COVID-19 is guided by the COVID-19 Strategic Preparedness and Response Plan. This is intended to help guide the public health response to COVID-19 at national and subnational levels, and to provide global strategic priorities in support of this effort. The strategic objectives for COVID-19 are to suppress transmission, reduce exposure, counter misinformation, protect the vulnerable, reduce mortality and morbidity and accelerate equitable access to COVID-19 vaccines, diagnostics and therapeutics.

This talk will cover the global epidemiological situation, the World Health Organization's comprehensive strategy for coordinated public health action, and the factors driving the current global epidemiological situation, including an update on the evolution and impact of SARS-CoV-2 variants of concern.

Strategies to flatten the curve: Current evidence and practical pitfalls

Paul Ananth Tambyah

National University of Singapore, Singapore

This current pandemic has been truly unique among pandemics of the last two centuries in terms of the draconian responses from societies all over the world. While the global cholera pandemics and the 1918 influenza pandemic caused much higher mortality and morbidity especially among younger people, the extent to which global travel ground to a halt is truly unprecedented. Despite WHO not recommending any travel restrictions, most countries have imposed significant limitations on travel which are only recently being lifted mainly for vaccinated travelers. In addition, cultural life in many cities and local commuting have been markedly constrained. Some of these movement restrictions have had unintended consequences such as amplifying transmissions in large households and also leading to rises in non-COVID morbidity. There also seems to be a reluctance among most public health leaders to accept the fact that this virus, like all other pandemic pathogens throughout history has become endemic. A dwindling number of countries at the time of writing are still pursuing a "zero covid" strategy which is probably based on the experience of the SARS epidemic which affects only a handful of countries significantly. For the rest of the world, a focus on protecting the vulnerable and minimizing the impact on the healthcare system are the most important steps aided by vaccine rollout and a sensible approach to non-pharmacological interventions. It is critically important that we review what we have done with this pandemic as the next pandemic is surely just around the corner and we cannot afford to repeat the mistakes made again.

Epidemiology and impact of carbapenem-resistant Acinetobacter and Pseudomonas species

Po-Ren Hsueh

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Carbapenems constitute the mainstay of therapy against infections caused by Gram-negative bacilli. However, the increased resistance to carbapenems, particularly in non-fermenting gram-negative bacilli,[3] greatly limits therapeutic options. Carbapenem resistance is closely associated with increased mortality from *Pseudomonas aeruginosa* and *Acinetobacter baumannii* infections. The mortality rate could be as high as 30% and 80% in individuals infected with carbapenem-resistant *P. aeruginosa* (CRPA) and *A. baumannii* (CRAB), respectively. The spread of CNSPA and CNSAB poses a major challenge to global health. Prior inappropriate antimicrobial therapy is associated with a higher risk of mortality in individuals infected with both *P. aeruginosa* and *A. baumannii*. Moreover, carbapenem resistance could serve as a primary cause for incorrect treatment and result in substantially worse outcomes. Novel antibacterial agents, such as cefiderocol, new β-lactamase inhibitor (BLI) combinations (cefepime/enmetazobactam, cefepime/zidebactam, cefoperazone/sulbactam, ceftazidime/avibactam, and ceftolozane/tazobactam), and new tetracycline analogs (eravacycline and omadacycline) have been used clinically over the past few years. However, most of these novel agents are not globally available, and their geographic availability varies greatly. Significant resistance be developed even before a novel agent becomes commercially available. In conclusion, CRPA and CRAB can cause a range of serious infections in hospitalized patients, requiring the prompt initiation of appropriate antibiotic treatment.

Epidemiology and impact of carbapenem-resistant Enterobacteriaceae

Anucha Apisarnthanarak

Thammasat University Hospital, Thailand

Carbapenem-resistant Enterobacteriaceae (CRE) are a serious public health threat. Infections due to these organisms are associated with significant morbidity and mortality. Mechanisms of drug resistance in gram-negative bacteria (GNB) are numerous; β-lactamase genes carried on mobile genetic elements are a key mechanism for the rapid spread of antibiotic-resistant GNB worldwide. Transmissible carbapenem-resistance in Enterobacteriaceae has been recognized for the last 2 decades, but global dissemination of carbapenemase-producing Enterobacteriaceae (CPE) is a more recent problem that, once initiated, has been occurring at an alarming pace. In this presentation, I will address the clinical and relevant molecular epidemiology, the clinical impact of CRE as well as hospital infection control strategy.

Emergence of intrinsically resistant Gram-negative bacteria with an environmental primary habitat

José Luis Martínez*, Fernando Sanz-García, Pablo Laborda, Teresa Gil-Gil, Luz Edith Ochoa-Sánchez, Sara Hernando-Amado

Centro Nacional de Biotecnología, CSIC, Madrid, Spain

Bacterial pathogens can be broadly classified into two categories: those that infect healthy people and those that infect persons with basal diseases, immunocompromised or debilitated. The first are problematic both at hospitals and in the community, while the organism forming the second category, which have been dubbed as opportunistic pathogens are important mainly at hospitals; their relevance for causing infections in the community is minor in comparison. Classical opportunistic pathogens are those forming part of the human microbiome. These bacteria are commensals when present at the right location of the human body, but they can cause problematic infections when present in other locations that are naturally axenic (i. e. blood, urine bladder or peritoneum). Commensal bacteria, as well as classical bacterial pathogens, were susceptible to antibiotics before these compounds began to be used in therapy; hence, infections by this type of commensal-opportunistic pathogens were easily treated, although the acquisition of antibiotic resistance determinants is currently compromising such treatment. However, several environmental bacteria present low susceptibility to antibiotics regularly used in therapy and, when they produce infections, antibiotic treatment can be more difficult and even fail. This is the situation concerning different Gram-negative non-fermenters as *Pseudomonas aeruginosa*, *Acinetobacter baumannii, Burkholderia cepacia* or *Stenotrophomonas maltophilia*, among others. These organisms have a primary environmental habitat, display low susceptibility to antibiotics and, though they rarely infect healthy people, they constitute a relevant problem at hospitals and in people with underlying diseases, like cystic fibrosis. The increasing prevalence of these pathogens is likely linked to their low natural antibiotic susceptibility rather than their evolution towards an increased virulence. Actually, previous antibiotic therapy is a risk factor for being infected by some of these pathogens. Further, in most cases, there is no clear distinction between infective and environmental isolates of these opportunistic pathogens. Although some clones are more prevalent in hospitals than others, they can also be found in natural ecosystems. Altogether, this means that these opportunistic environmental pathogens acquired their virulence determinants and their intrinsic resistome before they became to be a relevant problem for human health.

In this presentation, examples on the population structure of these pathogens, together with the potential reasons for the selection of their virulence and antibiotic resistance phenotypes in nature will be provided. As aforementioned, clinical isolates of environmental opportunistic pathogens are not a specific phylogenetic branch that has evolved to increase virulence/infectivity. However, this does not mean that all clones are fully equivalent or do not evolve along infection. Indeed, epidemic clones have been reported for most of these pathogens, supporting that these clones are better adapted to the human host than others. Nevertheless, these epidemic clones are also found in natural ecosystems, frequently in high prevalence, indicating that the characteristics that make them epidemic were selected in those environments before they began to infect the human host.

Regarding their evolution, the best studied situation concerns chronic infections, particularly in cystic fibrosis patients. Common patterns of evolution have been found, but isolates that infect a patient for the first time usually present a wild-type phenotype, not an evolved one, indicating that this kind of evolution would unlikely end in a speciation process. It fits more in what has been dubbed as short-sighted evolution. Despite these organisms present low susceptibility to different antibiotics, their evolution of also include the acquisition of further antibiotic resistance genes/mutations. However, this acquisition is due to the recent (in evolution terms) selective pressure due to the use of antibiotics in clinical practice and will not be discussed in detail in this communication. Rather, the physiological functions -beyond antibiotic resistance- that the intrinsic resistance genes that these organisms harbour may have in the natural habitats they colonise, will be discussed.

Antimicrobial therapy for carbapenem-resistant gram-negative bacteria

Yohei Doi

University of Pittsburgh School of Medicine, USA

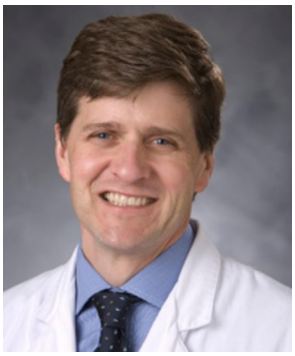
Carbapenem-resistant gram-negative bacteria are highly concerning as few safe and effective treatment options remain for infections caused by these pathogens. The three major ones are Enterobacterales, Pseudomonas aeruginosa and Acinetobacter baumannii, and each has unique characteristics that have implications in therapy.

By number, P. aeruginosa is the most common carbapenem-resistant gram-negative pathogen, and it appears to be less prone to epidemics than other carbapenem-resistant pathogens. While some strains remain susceptible to non-carbapenem beta-lactams or fluoroquinolones, the rest are resistant to all beta-lactams and fluoroquinolones thus can be defined as difficult-to-treat strains. Ceftolozane-tazobactam has sometimes been used successfully in the treatment of such cases. Imipenem-relebactam is the latest addition to the armamentarium, which is active against a higher proportion of carbapenem-resistant P. aeruginosa than ceftolozane-tazobactam, though clinical experience with this combination is yet to be accumulated.

Carbapenem-resistant A. baumannii has decreased in incidence over the last ten years, but it is still the most carbapenem-resistant bacteria after excluding intrinsically resistant species, with over 30% of the isolates being resistant in the U.S., down from nearly 60% a decade ago. Treatment options are still scarce since the majority of these isolates meet the definition of difficult to treat and the newer beta-lactam-beta-lactamase inhibitor combinations are generally inactive against carbapenem-resistant A. baumannii. This leaves polymyxins (colistin or polymyxin B) as the first line option, but the complex pharmacokinetics and frequent toxicity make them challenging to use in clinical practice. Cefiderocol, a recently approved cephalosporin, is generally active against carbapenem-resistant A. baumannii. While there is some concern over the mortality observed among patients infected with this pathogen and treated with cefiderocol in one of the pivotal clinical trials, further clinical experience and data are awaited to define its potential role in the treatment of carbapenem-resistant A. baumannii infection.

Carbapenem-resistant Enterobacterales (CRE), previously carbapenem-resistant Enterobacteriaceae, triggered a global concern when carbapenemase-producing CRE surged in many countries and caused nosocomial outbreaks. This epidemic was initially caused by Klebsiella pneumoniae strains producing KPC-group carbapenemases that spread across the U.S. early this century and subsequently in Europe, Latin America, China and other regions. This was followed by the spread of K. pneumoniae and E. coli strains producing NDM-group metallo-beta-lactamases in many countries. Fortunately, ceftazidime combined with avibactam, a new beta-lactamase inhibitor that was initially developed to block both extended-spectrum beta-lactamases and AmpC beta-lactamases, turned out to be an excellent inhibitor of KPC-group carbapenemases, was highly active against KPC-producing CRE and became the standard of care in the treatment of these infections where the combination was available for use. While randomized trials are lacking, multiple well adjusted observational studies suggest its superiority over conventional therapy such as polymyxins in the treatment of infections causes by KPC-producing CRE. Meropenem-vaborbactam, another new combination, also appears to be a reasonable treatment option. However, these new beta-lactam-beta-lactamase inhibitor combinations are not active against CRE producing NDM-group carbapenemases or other metallo-beta-lactamases. Cefiderocol is active against the majority of CRE strains including metallo-beta-lactamase-producing ones, but it is not as potent against the latter as it is against other carbapenem-resistant gram-negative bacteria. Treatment of infections caused by these metallo-beta-lactamase-producing CRE therefore remains a major clinical challenge.

Overall, thanks to the advent of newer agents the providers are better equipped to manage carbapenem-resistant gram-negative bacterial infections than they were ten years ago. However, gaps remain for certain species-carbapenemase combinations, and also in terms of availability of these treatment options in less resourced countries or regions that bear the brunt of the burden from these pathogens.



How I treat persistent S. aureus bacteremia

Vance Fowler

Duke Department of Medicine, USA

Persistent *Staphylococcus aureus* bacteremia is poorly understood. Prognosis is poor, no standard therapy exists, and even its definition has changed over time. In this lecture, I will review the “Who?”, “What?”, “When?”, “Where?”, “Why?”, and “How?” of persistent *S. aureus* bacteremia.

How I treat vascular graft infections

M. Rizwan Sohail

Baylor College of Medicine, USA

Infection is a major complication of use of prosthetic vascular grafts. Microbial seeding of the graft at the time of implantation or in the immediate postoperative period is most common mechanism of vascular graft infections (VGI). However, spread from a contiguous focus or hematogenous seeding of the graft are other potential mechanisms of VGI. Emergency surgery, groin incision, bacteremia during index hospitalization, and repeated surgical interventions further increase risk of VGI.

Infection rates and clinical presentation of VGI varies based on location of the prosthetic vascular graft and the causative pathogens. Infection with more virulent organisms (such as *S aureus* or Pseudomonas) tend to present early and frequently with systemic manifestations. VGI with less virulent organisms such as coagulase negative staphylococci, Cutibacterium, or Corynebacterium tend be more indolent and may present months to years after graft implantation.

Computed tomography (CT) scan is the preferred imaging modality for diagnosis of VGI. Perigraft fluid or fat stranding are typical finding of VGI on CT scan. Mycotic aneurysm or poor incorporation of graft in the surrounding tissues may also be noted. In cases where CT findings are inconclusive, magnetic resonance imaging (MRI) or nuclear medicine imaging (Indium-labeled WBC scan or 18 FDG-PET) may be considered. Ultrasound can be helpful for diagnosis of extra-cavitary graft infections and associated complications such as abscess or pseudoaneurysm formation. Endoscopy is indicated when an aortoenteric fistula is suspected due to underlying VGI.

For extra-cavitary (peripheral) VGI, graft preservation and 2 to 4 weeks of antibiotic therapy may be an option if infection is limited to skin and soft tissue and does not involve anastomotic site. For more extensive infections, resection of infected graft and extra-anatomic bypass is usually preferred. These patients should be treated with 4 to 6 weeks of intravenous antimicrobial therapy followed by 3 to 6 months of suppressive therapy. Chronic antimicrobial suppressive therapy may be indicated when infection is caused by methicillin-resistant *S aureus* (MRSA), Pseudomonas, or MDR bacteria and in patients who are not candidates for re-operation.

For intra-cavitary (abdominal or thoracic) VGI, most cases are managed by resection of infected graft and in-situ reconstruction using arterial allograft or homograft. These cases should be managed with 6 week of parenteral induction therapy followed by 6 months of suppressive oral therapy. In cases where in-situ reconstruction is done using prosthetic graft or infection is caused by MRSA, Pseudomonas, or MDR bacteria, lifelong suppressive therapy is indicated.

How I treat CMV infection in high-risk pediatric patients?

Yae-Jean Kim

Department of Pediatrics, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

Cytomegalovirus (CMV) infection is ubiquitous and mainly asymptomatic in individuals with a competent immune system. However, it is a clinically significant complication in cancer patients with impaired cellular immunity, particularly hematopoietic stem cell transplantation recipients, solid organ transplantation recipients. In addition, certain primary immunodeficiencies and congenital CMV infection are of importance in the field of pediatrics.

When treating high-risk patients, the possibility for resistant and refractory CMV infection should be considered with the background immunocompromised condition and organ dysfunction caused by primary disease treatment. In addition, adverse reactions of the antiviral agents such as bone marrow suppression and tissue distribution, including central nervous system penetration, should also be considered.

This presentation will discuss options to consider when treating high-risk patients with CMV infection in selected example cases.

COVID-19: Lessons from the Unfolding Pandemic

Michael T. Osterholm

University of Minnesota, USA

No abstract received.

Vaccines against SARS-COV-2

Jerome H. Kim

International Vaccine Institute

The SARS-CoV-2 pandemic has made several important points about vaccine research, testing, manufacturing, and implementation under urgent circumstances, and several of these developments could, under non-pandemic circumstances, create enormous value for global health: (1) It is possible to develop a vaccine in less than 5–10 years (lab to licensure); (2) the Coalition for Epidemic Preparedness Innovations (CEPI) did what it was intended to do; (3) Vaccine manufacturers contracted/licensed vaccines to other qualified companies to make billions of doses; (4) COVAX is a mechanism for near concurrent access to vaccines in all countries; (5) Can we move from childhood to lifetime vaccination; (6) mRNA and adenovirus vaccines can prevent disease; (7) Innovation, agility and partnership – biotechs, DCVMs are the heroes of the story – not necessarily the big vaccine companies.

In the second year of the pandemic, the year of vaccination we find that we don't have enough vaccine, we have incomplete knowledge of impact (for the various vaccines), and we have a growing threat of variant viruses undermining the progress made to date. In this global pandemic, we must engage fully, systematically, and impactfully for the threat of COVID-19 to be finally controlled.

Overview of the current status of antimicrobial resistance

David M. Livermore

Norwich Medical School, University of East Anglia, Norwich, United Kingdom

Despite widespread concern about resistance, the situation has improved markedly against gram-positive pathogens in the past 20 years. In 2000, three internationally-marketed antibiotics from two chemical classes were widely active against MRSA. This total has now grown to 16 antibiotics in nine classes. For the first time in two generations, new anti-tuberculosis antibiotics have begun to be launched. The situation is less rosy against gram-negative pathogens, which head the WHO and CDC lists of pathogens where resistance is a concern; nonetheless new anti-gram-negative antibiotics are now becoming available, after a long fallow period. They include ceftolozane/tazobactam, ceftazidime/avibactam, meropenem/ vaborbactam, imipenem/relebactam, cefiderocol, eravacycline and plazomicin, all of which have some utility against multi-resistant gram-negative bacteria. Several are active against the producers of one or more carbapenemase types. These are welcome developments.

Disturbingly, though, resistance has already been seen emerging to the newest anti-gram-negative agents.

In the case of ceftolozane/tazobactam – a combination mostly of interest due to its activity against *Pseudomonas aeruginosa* – structural mutations in pseudomonal AmpC chromosomal β-lactamase confer resistance and have been reported as being selected during therapy. Interestingly, these changes typically also confer resistance to ceftazidime/avibactam, but lower resistance to imipenem, which co-depends on AmpC activity as well as loss of porin OprD.

For ceftazidime/avibactam – a combination active against Enterobacterales with KPC and OXA-48 carbapenemases – mutations to the bla_{KPC} gene can confer resistance. The most frequent and important leads to an Asp179Tyr substitution in the enzyme, making it a more powerful ceftazidimase, and therefore harder to inhibit. Meropenem/vaborbactam – a combination principally of interest against Enterobacterales with KPC carbapenemases – can be compromised through porin mutations, reducing uptake by these organisms. Again, such mutations have been seen emerging during therapy, leading to clinical failure.

There is less experience to date with the catechol cephalosporin cefiderocol, which has the widest spectrum of all the new anti-gram-negative agents. Its MICs are quite widely scattered *within* resistance types, suggesting a major influence of factors beyond those normally considered, potentially including lesions in the iron uptake system. Notably, resistance evolved in several *Acinetobacter* strains during a Phase III resistant pathogens, although the precise mechanism(s) remain to be established.

Before leaving the novel β-lactams, it should be added that several, as well as the developmental agent aztreonam/avibactam, can be compromised by 4-amino-acid insertions, typically Tyr-Gly-Ile-Asn/Lys, in PBP3 of *E. coli*, making this target less vulnerable to inhibition. *E. coli* with this modification, which has not been seen in other Enterobacterales, are scattered across Asia, Europe and the Middle East, and seem particularly prevalent in India.

For eravacycline, like tigecycline, increased expression of chromosomal RND efflux pumps can confer resistance. This has been described as emerging during therapy for tigecycline, and (so far) only in vitro for eravacycline.

Another risk is that new agents suppress pathogens with mechanisms that are covered, whilst facilitating expansion of strains with uncovered mechanisms. For example, deployment of ceftazidime/avibactam in Patras (Greece) was followed by a rise of *Klebsiella* with metallo carbapenemases, which evade inhibition by avibactam. Plazomicin overcomes most resistance due to aminoglycoside-modifying enzymes but carries the hazard of instead selecting strains with ArmA and Rmt ribosomal methyltransferases. These confer aminoglycoside pan-resistance and often are genetically linked with NDM carbapenemases; they are prevalent in Asia, less so in Europe and are very uncommon in North America.

Ultimately, one point is clear: that the new agents are no more immune to resistance than their predecessors. It is vital therefore that we use them prudently. This should increasingly be facilitated using rapid diagnostics, better matching the choice of antibiotic to the pathogen's specific resistances. A final, and major, concern should also be highlighted too: that many of the new agents are not proving commercially successful. Developers of three of the seven recently-licensed anti-gram-negative agents (Melinta, Achaogen and Tetraphase) have failed or required substantial refinancing. Unless this market failure is addressed, antibiotics will continue to be seen as an unattractive area for pharmaceutical investment.

Do you have anything for this Cough? State of Treatments and Research for Outpatient COVID

Davey Smith

University of California San Diego, USA

In this talk Dr. Smith will summarize the natural history and how this relates to COVID-19 treatments. This talk will also review SARS-CoV-2 lifecycle and what treatments can be used at particular points in the viral lifecycle. The talk will then describe the state of treatments available for early COVID-19, and those that are in clinical trials. The talk will also cover the development and the use of monoclonal antibody therapy. Variants will also be discussed and how they may impact the use of the various treatments.

Therapeutics for COVID-19

Yaseen M. Arabi

King Abdulaziz Medical City, Ministry of National Guard Health Affairs, Riyadh, Kingdom of Saudi Arabia

In less than 2 years, coronavirus disease-19 (COVID-19) has spread globally, to cause infection among more than 200 million people and to cause more than 4 million deaths. In parallel, there have been accelerated advancements in understanding the management of COVID-19. Based on in vitro and observational studies, several antiviral agents including hydroxychloroquine, remdesivir, lopinavir/ritonavir, and interferon-beta were suggested as COVID-19 therapeutics. Hydroxychloroquine was widely used around the globe until several large randomized controlled trials (RCTs) showed that lack of benefit, and probable harm. An RCT showed that early inhaled interferon-beta in patients with mild COVID-19 may be effective, although a large RCT in hospitalized patients demonstrated no reduction in mortality. Several RCTs have demonstrated that corticosteroid therapy reduces mortality in patients with severe COVID-19, although important questions remain regarding the dose, time, duration, and drug. RCTs have demonstrated that IL-6 receptor antagonists (IL-6ra) among critically ill patients and deteriorating hospitalized patients with signs of inflammation reduce mortality and reduce time on organ support. A multiplatform RCT demonstrated that in non-critically ill patients with COVID-19, therapeutic anticoagulation was reduced time on organ support and mortality compared to thromboprophylaxis. For critically ill patients, therapeutic anticoagulation was not better compared to thromboprophylaxis, and that intermediate-dose thromboprophylaxis was not better compared to standard-dose thromboprophylaxis. Data on the role of monoclonal antibodies are emerging, and this therapy may have a role in seronegative patients.

Long-term sequelae of COVID-19

Bin Cao

National Clinical Research Center for Respiratory Diseases, PR China

No abstract received.

The future is here: Rapid diagnosis of antimicrobial resistance

Robin Patel

Mayo Clinic, USA

Diagnostic testing for infectious diseases is undergoing a rapid revolution. In this presentation, specific technologies and applications that enable rapid diagnosis of antibacterial resistance thereby informing potential appropriate use of antibacterial agents will be highlighted. Rapid nucleic acid amplification technologies, panel-based molecular diagnostics, proteomics, metagenomics and advances in phenotypic susceptibility testing will be overviewed.

Next-generation sequencing for diagnosing infectious diseases

John W. A. Rossen

Department of Medical Microbiology and Infection Prevention, University of Groningen, The Netherlands

Infectious diseases require rapid, sensitive, and accurate diagnostics, including information on antimicrobial susceptibility, to ensure timely and effective treatment and prevent the spread of pathogens. Laboratories are rapidly adopting clinical metagenomics for comprehensive and unbiased pathogen detection and profiling. Although shotgun metagenomics is the broadest approach, it comes with several challenges and disadvantages, including variable sensitivity and variable AMR marker detection, as well as the presence of a high host DNA background. Precision metagenomics is a method in which pathogens and antimicrobial resistance markers, including markers encoding resistance against antivirals, are enriched. Whereas amplicon-based sequencing has a low mismatch tolerance and limited scope, precision metagenomics allows detection of hundreds of pathogens, accurate AMR marker detection, and is sensitive and specific. In addition, it has shorter turn-around times and a high mismatch tolerance. This presentation will discuss different next-generation sequencing approaches to identify pathogens and predict antibiotic and antiviral resistance. Moreover, it will show that the use of an internal calibrator and an automated data analysis workflow provides accurate quantification without the need for a standard curve using the quantification of SARS-cov-2 in clinical samples as an example. Combining pathogen detection, classification, AMR identification, and pathogen quantification with one unified and automatable workflow allows laboratories to further consolidate metagenomics-based testing while providing comprehensive results to clinicians in a timely way.

How to combine novel techniques with stewardship: A real-world experience

Tristan Timbrook

Biomérieux, The University of Utah, USA

Antimicrobial stewardship programs (ASP) have developed to improve patient care and combat the public health problem of antimicrobial resistance (AMR). Asps strive to avoid the use of inappropriate antibiotic therapy along with improving efficacy and safety in antimicrobial therapy which improves clinical outcomes, decreases adverse effects and severe complications such as Clostridioides difficile infection, and reduces healthcare costs. To this end, antimicrobial stewardship goals can be summarized as aiming for right diagnosis, right drug, right dose, and right duration. ASP teams are well positioned towards these quality improvement goals through their expertise and multidisciplinary collaborations. Their team is ideally comprised of an infectious diseases physician, clinical pharmacy specialist, microbiologist, nurse, infection control professional, information system specialist, and hospital epidemiologist. Together this team impacts patient care and antimicrobial use both at the individual patient level and an institutional level. The former is achieved through collaborations on specific patient cases while the latter is completed through the development of clinical pathways, processes, electronic medical record tool implementation, etc. Novel diagnostic techniques have arisen in recent years as an essential tool for achieving these quality improvement goals by providing clinicians earlier and more comprehensive information leading to ability to streamline management of patient care. This development has established a synergistic relationship between asps and novel diagnostics.

Real-world experience with ASP implementation of novel diagnostics is heterogeneous in technologies employed, implementation strategies, and outcomes observed. Given the diverse landscape of healthcare facilities and delivery, considerations should be given to local facility characteristics, the information being derived from the diagnostics, and how best it can be leveraged for improving care within the setting. This lecture will review the importance of combining novel techniques with stewardship in terms of demonstrated effectiveness and safety. The incremental value of rapid diagnostic technology for AMR detection will be explored through assessments in its benchmarking against AMR risk prediction scores based on patient-specific factors. Firsthand experience of real-world implementation of novel diagnostics with ASP interventions at the initial diagnostic result will be examined. Additionally, experience with an antimicrobial stewardship bundle for uncomplicated gram-negative bacteremia as an approach to streamline the patient encounter will be discussed. Finally, considerations around design and implementation of novel diagnostics within an ASP pathway will be reviewed. Given the predominance of evidence for these technologies in bloodstream infections, this syndrome and related literature will be focused on throughout the lecture though many of the concepts and topics discussed will be generalizable to other infectious syndromes and novel technologies utilized by asps.

Shorter the better: Current evidence for the shorter duration of antibiotic therapy

David Paterson

University of Queensland, Australia

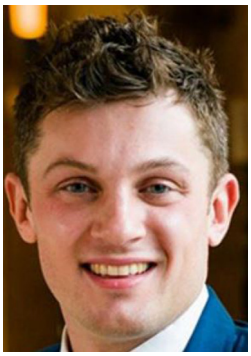
For many years, prescribers have been more concerned with the type of antibiotic to prescribe rather than its mode of delivery (IV vs oral) or the duration of the antibiotic course. There is now evidence from RCTs that short duration is the preferred option for community and ventilator associated pneumonia, complicated urinary tract infection, intra-abdominal infection, cellulitis, Gram negative bloodstream infection, bone and native joint infections and acute exacerbations of chronic bronchitis. Exceptions to this rule include prosthetic joint infection, otitis media in young children and streptococcal throat infections treated with penicillin.

Capacity for antimicrobial stewardship in the Asia Pacific

David Lye

National Centre for Infectious Diseases, Tan Tock Seng Hospital, Yong Loo Lin School of Medicine, Lee Kong Chian School of Medicine, Singapore

Antimicrobial resistance remains a pressing global public health issue. Within healthcare settings, infection control and antimicrobial stewardship are two effective solutions to contain and reduce antimicrobial resistance. Antimicrobial stewardship comprises a package of necessary components in order to optimise antibiotic use, reduce toxicity and resistance. Firstly, microbiology services are important, from collection of right samples for the right infection, correct microbiology testing, to the timely reporting of antibiotic susceptibility to guide doctors in empiric and culture guided antibiotics. The development of empiric antibiotic guideline requires accurate annual hospital antibiogram. Pharmacy services are another essential component. From rational formulary management, drug use evaluation, development and implementation of antibiotic guidelines, monitoring antibiotic usage to intervening in inappropriate antibiotic use, trained and skilled pharmacists in antimicrobial stewardship are essential. Finally, a medical advocate is needed to drive antimicrobial stewardship who is regarded as an expert in antibiotic use. I will review the capacity across Asia Pacific in these areas and compare with other regions of the world.



Antimicrobial stewardship during the COVID-19 pandemic

Timothy M. Rawson

Health Protection Research Unit for Healthcare Associated Infections and Antimicrobial Resistance, Imperial College London, London, UK

The SARS-CoV-2 pandemic may have a complex long-term impact on antimicrobial resistance (AMR). We will review the reported impact of COVID-19 on antimicrobial prescribing and AMR in the community and hospital settings. We will explore the links between bacterial infection and COVID-19 and discuss potential solutions to mitigate the negative impact of the pandemic on antimicrobial stewardship and AMR. Finally, we will explore the ongoing development of co-ordinated strategies at the individual, health-care and policy levels to inform necessary actions to reduce the potential longer-term impact on AMR and on access to effective antimicrobials.

Pro) Early oral transition for endocarditis

José M. Miró

Hospital Clínic of Barcelona, Spain

It has been a dogma for more than 60 years that antibiotic treatment for infective endocarditis (IE) should be given intravenously with one or more antibiotics for 4-6 weeks. In the **Partial Oral Endocarditis Treatment (POET)** clinical trial (1), this paradigm has changed. Using criteria very similar to those of the **Outpatient Parenteral Antibiotic Treatment (OPAT)** for IE (2), hemodynamically stable patients with infective endocarditis with or without previous cardiac surgery could complete antibiotic treatment at home by oral route. Briefly, in this noninferiority, multicenter clinical trial, 400 adults in stable condition (see table 1) who had endocarditis on the left side of the heart caused by streptococcus, *Enterococcus faecalis*, *Staphylococcus aureus*, or coagulase-negative staphylococci and who were being treated with intravenous antibiotics were randomized to continue intravenous treatment (199 patients) or to switch to oral antibiotic treatment (201 patients, see oral regimens in table 2). In all patients, antibiotic treatment was administered intravenously for at least 10 days. If feasible, patients in the orally treated group were discharged to outpatient treatment. The primary outcome was a composite of all-cause mortality, unplanned cardiac surgery, embolic events, or relapse of bacteremia with the primary pathogen, from the time of randomization until 6 months after antibiotic treatment was completed. After randomization, antibiotic treatment was completed after a median of 19 days (interquartile range, 14 to 25) in the intravenously treated group and 17 days (interquartile range, 14 to 25) in the orally treated group (P = 0.48). The primary composite outcome occurred in 24 patients (12.1%) in the intravenously treated group and in 18 (9.0%) in the orally treated group (between-group difference, 3.1 percentage points; 95% confidence interval, −3.4 to 9.6; P = 0.40), which met noninferiority criteria. The authors concluded that in patients with IE on the left side of the heart who were in stable condition, changing to oral antibiotic treatment was noninferior to continued intravenous antibiotic treatment. This POET strategy has been confirmed at long term (3). In any case, the results of this trial must be confirmed in new randomized clinical trials that are ongoing in France and in Spain. However, my opinion is antibiotic treatment of IE has changed and oral therapy has come to stay in clinical practice. From now on and as summarized in Figure 1, patients with IE should be treated initially (10-14 days) with combinations of bactericidal antibiotics that quickly clear up bacteremia and reduce the density of bacteria in cardiac vegetations and that together with cardiac surgery in order to eliminate abscesses and intracardiac foreign bodies (valve prostheses, cables), allowing in a second phase (from 2 to 6 weeks) the oral antimicrobial treatment of IE in order to eliminate the resting bacteria responsible for relapses. Whether the oral treatment or the intravenous antibiotics are better at the patients' homes, only the clinical trials that are being carried out (in Spain the OROPAT-IE-GAMES) will give us the answer.

Table 1: Criteria for Partial Oral Endocarditis Treatment (based on the POET study by Iversen et al. (1))

Description of criteria	Specifications
Adults with left sided endocarditis due to streptococci, *S. aureus*, *E. faecalis* or coagulase-negative staphylococci	≥ 18 years
Appropriate parenteral initial antibiotic treatment	≥ 10 days IV antibiotic treatment (appropriate) ≥7 days IV antibiotic treatment after cardiac valve surgery
Satisfactory response to treatment	Temp<38.0 C for minimum 2 days CRP <25% of peak level or <20 mg/l Leukocytes<15×10^9/l
Transthoracic and transesophageal echocardiography	Performed within 48 hours of switch to oral antibiotics No signs of abscess or valve abnormities requiring surgery
Absence of factors that make oral treatment ineffective	BMI <40 No abdominal disorder causing reduced absorption No suspicion of reduced compliance
Absence of other infection requiring IV antibiotics	No other indications for prolonged IV antibiotics
Bacterial susceptibility testing	Bacteria susceptible to two different classes of orally administered antibiotics*

*Suggested oral antibiotic regimens are shown in table 2

Table 2: Oral antibiotic combinations used for Partial Oral Endocarditis Treatment in the POET study (based on Iversen et al. (1))

Penicillin and methicillin susceptible *S. aureus* & CONS	**Methicillin susceptible *S. aureus* & CONS**	**Methicillin resistant CONS**	***Enterococcus faecalis***	**Streptococci with penicillin MIC < 1mg/L**	**Streptococci with penicillin MIC > 1mg/L**
Amoxicillin 1 g × 4* **Rifampicin 600 mg × 2**	**Dicloxacillin 1 g × 4** **Rifampicin 600 mg × 2**	**Linezolid 600 mg × 2** **Fusidic acid 750 mg × 2**	**Amoxicillin 1 g × 4** **Moxifloxacin 400 mg × 1**	**Amoxicillin 1 g × 4** **Rifampicin 600 mg × 2**	**Linezolid 600 mg × 2** **Rifampicin 600 mg × 2**
Amoxicillin 1 g × 4	Dicloxacillin 1 g × 4	**Linezolid 600 mg × 2**	**Amoxicillin 1 g × 4**	**Amoxicillin 1 g × 4**	Moxifloxacin 400 mg × 1
Fusidic acid 750 mg × 2	Fusidic acid 750 mg × 2	**Rifampicin 600 mg × 2**	**Linezolid 600 mg × 2**	**Moxifloxacin 400 mg × 1**	Rifampicin 600 mg × 2
Moxifloxacin 400 mg × 1	Moxifloxacin 400 mg × 1		Amoxicillin 1 g × 4	Amoxicillin 1 g × 4	Linezolid 600 mg × 2
Rifampicin 600 mg × 2	Rifampicin 600 mg × 2		Rifampicin 600 mg × 2	Linezolid 600 mg × 2	Moxifloxacin 400 mg × 1
Linezolid 600 mg × 2	Linezolid 600 mg × 2		Linezolid 600 mg × 2	Linezolid 600 mg × 2	
Rifampicin 600 mg × 2	Rifampicin 600 mg × 2		Moxifloxacin 400 mg × 1	Rifampicin 600 mg × 2	
Linezolid 600 mg × 2	Linezolid 600 mg × 2		Linezolid 600 mg × 2	Linezolid 600 mg × 2	
Fusidic acid 750 mg × 2	Fusidic acid 750 mg × 2		Rifampicin 600 mg × 2	Moxifloxacin 400 mg × 1	

Abbreviations: POET, partial oral endocarditis treatment; CONS, coagulase-negative staphylococci; MIC, minimal inhibitory concentration.
***Most frequently used regimens in the POET study are mentioned first and marked in bold.**

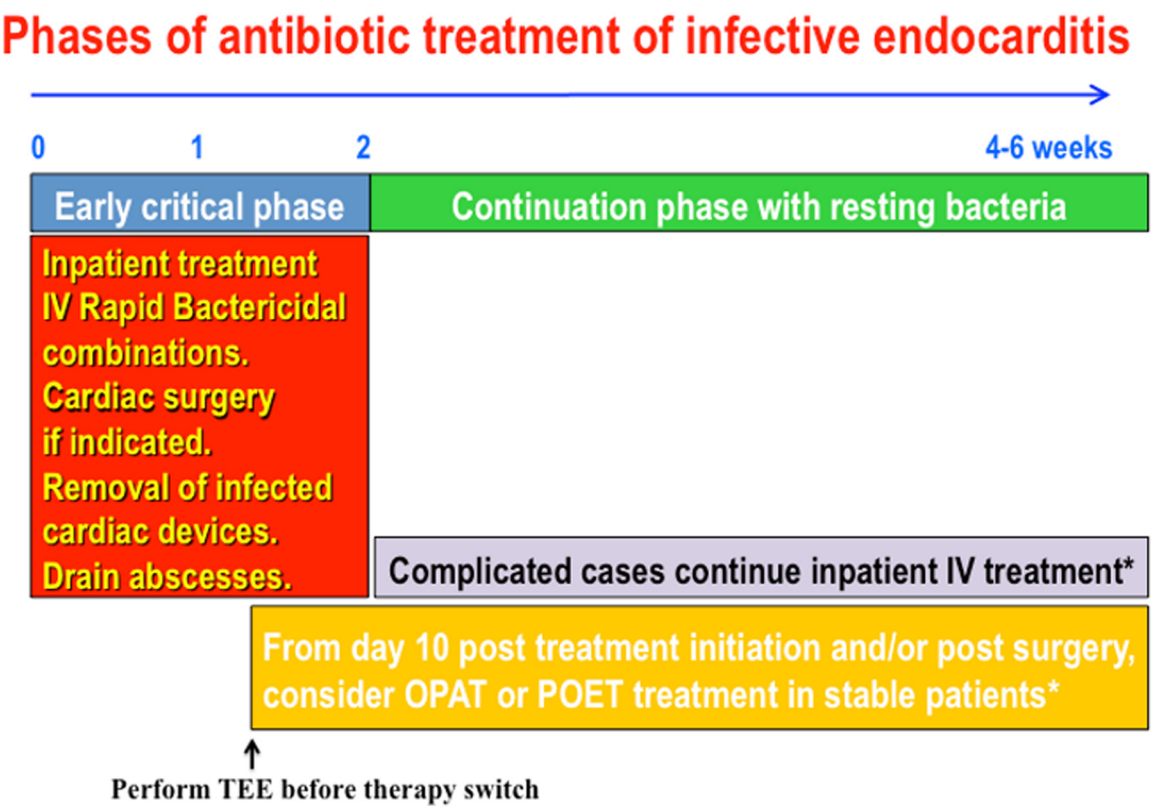


Figure 1 Phases of intravenous and oral antibiotic treatment for infective endocarditis
Abbreviations: OPAT, outpatient parenteral antibiotic treatment; POET, partial oral endocarditis treatment; TEE, transesophageal echocardiography.
*Criteria for switching to outpatient oral or parenteral antibiotic treatment must follow POET (1) and OPAT (2) guidelines.

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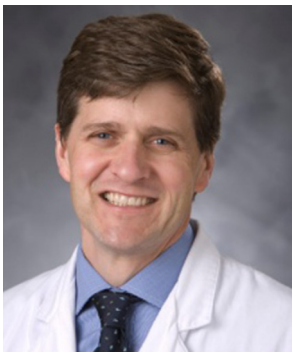


Con) Early oral transition for endocarditis

Vance Fowler

Duke Department of Medicine, USA

Untreated, infective endocarditis is invariably fatal. For this reason, it has been almost universally treated with parenteral antibiotics for more that a generation. In my response to Dr. Miro's presentation, I will argue why early oral transition for endocarditis should not be undertaken in most clinical settings.

Pro) Piperacillin-tazobactam for ESBL-producing Enterobacterales

Jesús Rodríguez-Baño

Hospital Universitario Virgen Macarena/Universidad de Sevilla, Spain

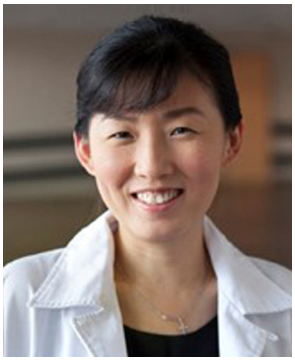
In a context of rampant increase in carbapenem resistance among gram negative bacteria, finding alternatives to carbapenems for the treatment of infections so that the selection pressure caused by these drugs can be reduced, is important. A considerable number of ESBL-producing Enterobacterales show in vitro susceptibility to piperacillin-tazobactam. Some observational studies and meta-analyses suggested that it might be as effective as carbapenems for the treatment of bloodstream infections caused by these isolates. However, piperacillin-tazobactam did not reach the non-inferiority pre-established criteria for the primary endpoint (30-day all-cause mortality) compared to meropenem in the MERINO trial. The authors of this trial must be commended for performing this investigator-initiated, multinational randomized trial. However, its results must be interpreted with caution since piperacillin-tazobactam dosing used may not have been the most appropriate, mortality was unrelated to infection in most cases, and more importantly, because ESBL-producing isolates from an important proportion of recruited patients were later showed to be actually resistant to piperacillin-tazobactam, although considered susceptible in initial susceptibility testing (and therefore should have not been recruited as the trial was performed to test the drug as definitive therapy). The reason for this false susceptibility is related to co-production of the OXA-1 beta-lactamase, which may jeopardise the susceptibility testing results for this drug when using strip gradient or automatic microdilution tests. Another trial (PETERPEN) is recruiting at the time of writing, in order to check for the reproducibility of the MERINO results. In the meantime, and based on data from well-designed and analysed observational studies performed in areas where co-production of OXA-1 is less frequent, we think that piperacillin-tazobactam should not be abandoned as a potential option for ESBL-producer; in fact, we consider it is a reasonable alternative in patients with isolates susceptible to amoxicillin-clavulanic acid (which reasonably discard OXA-1) presenting without sepsis or shock, and with a urinary or biliary tract source. This is relevant because an important proportion of patients with invasive infection due to ESBL-producers would be included in this group. Of course, we recommend the use of a carbapenem for patients either presenting with sepsis or septic shock, or with other sources of infection, and when resistance to piperacillin-tazobactam cannot be discarded.

Con) Piperacillin-tazobactam for ESBL-producing Enterobacterales

Patrick N A Harris

The University of Queensland, Australia

ESBL-producing Enterobacterales are increasingly common worldwide and compromise empirical antibiotics such as third-generation cephalosporins. Many ESBL-producing *E. coli* or *Klebsiella* will test susceptible in vitro to piperacillin-tazobactam, but the clinical efficacy of this drug in bloodstream infections caused by these organisms has been uncertain. In the MERINO trial, piperacillin-tazobactam failed to demonstrate non-inferiority in comparison to meropenem for this indication. Post hoc microbiological analysis has suggested that some of this effect reflected inaccuracies in routine susceptibility testing systems for these challenging organisms, especially in the presence of other beta-lactamases such as OXA-1. In this debate, reasons for caution in using piperacillin-tazobactam for EBSL-producers will be explored with reference to the available clinical and laboratory evidence.



Pro) Combination regimen for carbapenem-resistant Acinetobacter infections

Andrea Kwa

Singapore General Hospital, Singapore

Infections caused by carbapenem-resistant (CR) Acinetobacter baumannii (AB) constitute a major therapeutic challenge. Whether combination antibiotic therapy is superior to monotherapy remains unknown. In recent years, the combination of antibiotics has become the preferred treatment strategy for CR-GNB infection, including CR AB. However, robust evidence to support this approach is lacking. This talk serves to go through the current evidence to-date.

Con) Combination regimen for carbapenem-resistant Acinetobacter infections

Visanu Thamlikitkul

Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand

No abstract received.

Update on antimicrobial resistance of Staphylococcus

Michael Otto

National Institute of Allergy and Infectious Diseases, U.S. National Institutes of Health, Bethesda, Maryland, USA

Staphylococcus aureus is an important human pathogen that causes a wide variety of many in part serious and fatal infections worldwide, ranging from moderately complicated skin and soft tissue infections to severe lung, bone, and blood infections. It is particularly infamous as a leading nosocomial pathogen, but also often causes community-associated infections. The continued high morbidity and mortality that is associated with S. Aureus infections stems to a great extent from widespread resistance to antibiotics, among which that to methicillin is considered most impactful owing to the efficacy that this antibiotic otherwise exerts toward S. Aureus isolates. Many countries report frequency of resistance in hospital-associated methicillin-resistant S. Aureus (HA-MRSA) isolates of up to 50% or even higher. Health-care personnel and hospitalized patients are often colonized asymptomatically with MRSA and there is now also considerable distribution of colonizing MRSA in the community, although there is great variation of colonization frequencies in different settings and locations. MRSA carriage is of great concern, as carriage of S. Aureus predisposes to infection. Specific clonal complexes of MRSA dominate in different geographic locations, and they are also generally different between HA- and community-associated (CA) isolates. As compared to HA-MRSA, CA-MRSA clones characteristically have higher virulence, although this is accompanied by reduced resistance levels to methicillin.

More recently, clonal differences between HA- and CA-MRSA have started to become less distinct, as for example the USA300 pulsed-field type, which started as a typical CA-MRSA clone, has also become the most predominant clone causing hospital infections in the U.S. Recent years have seen a decline in MRSA infection in hospitals of industrialized nations and a shift of the focus of antibiotic drug development on Gram-negative bacteria due to the pan-resistance observed in some Gram-negative pathogens. Nevertheless, S. Aureus remains a leading cause of nosocomial infections and is still the most common cause of mortality due to an antibiotic-resistant pathogen for example in the U. S. Furthermore, there is development of resistance to methicillin alternatives (sulfamethoxazole/trimethoprim, clindamycin, vancomycin, daptomycin, linezolid, minocycline, etc.) Which also generally have limitations as for efficacy and applicability as compared to methicillin. While resistance to vancomycin, the most frequently used antibiotic for MRSA infections, remains sporadic, intermediate resistance to vancomycin is on the rise. Lastly, despite the success of public health efforts to reduce the frequency of nosocomial MRSA infections, there is ongoing concern about community-associated MRSA as well as the increasing realization that highly virulent MSSA strains and antibiotic-resistant coagulase-negative staphylococci also represent an immense danger and cause for fatalities. There are several approaches to develop alternatives to antibiotics to treat and prevent S. Aureus infections, such as vaccines, decolonization efforts, bacteriophages, probiotics, and anti-virulence drugs, but these have either failed for a long time – in the case of vaccines – or are in their infancy and need more and better research. As for anti-virulence drugs, the respective efforts are complicated by a variety of factors, one of which is the considerable geographic variation in S. Aureus and MRSA clonal complexes and their virulence factor repertoires, which significantly complicates across-the-board strategies.

Genomic insights into vancomycin-resistant Enterococcus faecium

Glen Carter

Doherty Institute, Department of Microbiology and Immunology, The University of Melbourne, Victoria, Australia

Enterococci are considered a normal part of the gastrointestinal microflora. Despite this, several species are considered important human pathogens, with *Enterococcus faecium* in particular being a significant nosocomial pathogen. *E. faecium* has a high propensity for horizontal gene transfer, which has resulted in the emergence of multi-drug resistant strains. The most serious of these, vancomycin resistant enterococci (VRE), is classified as a "serious threat" to human health by the US Centers for Disease Control and Prevention.

E. faecium is easily transmitted within the hospital environment where it causes potentially life-threatening infections that are typically difficult to treat. Although vancomycin can be an effective first line therapy, the increasing prevalence of vancomycin-resistant *E. faecium* (VREfm) means that treatment options are becoming limited. VREfm infections are increasingly associated with high levels of morbidity and mortality and often require the use of last-line antimicrobials such as linezolid and daptomycin. As a consequence, most hospitals have implemented infection prevention and control (IPC) measures designed to limit the spread of VREfm. An important component of IPC involves typing *E. faecium* clinical and screening isolates, since this assists infection control teams to identify potential VRE outbreaks within or between hospitals.

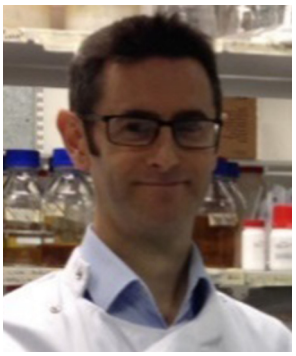
Here we describe the use of whole genome sequencing (WGS) to characterise a large number of VREfm isolates collected from patients within the Australian Healthcare system. This genomic data has provided invaluable information on the dominant VREfm types that cause infections within Australia, and the transmission networks associated with these strains. Furthermore, WGS has delivered unparalleled insights in the genes and mutations that are associated with antimicrobial resistance, including to last line antimicrobials, in contemporary VREfm isolates that are currently circulating within Australian Hospitals.

How to dose vancomycin: Time to go Bayesian?

Jennifer Le

University of California San Diego, Skaggs School of Pharmacy and Pharmaceutical Sciences, USA

The 2020 guidelines on vancomycin dosing and therapeutic monitoring underscored the importance of evaluating pharmacokinetic (PK) model-informed, Bayesian-guided area-under-the-curve over 24 hours to minimum inhibitory concentration (AUC_{24}/MIC) dosing and monitoring to optimize efficacy and minimize nephrotoxicity in the treatment of serious methicillin-resistant *S. aureus* (MRSA) infections in adults and children. This session will present on an old concept but new application of the Bayesian estimation to improve dosing and monitoring of vancomycin. A brief review of AUC will also be provided.



Novel therapeutic approaches to bacterial infection

Andrew M. Edwards

MRC Centre for Molecular Bacteriology and Infection, Imperial College London, UK

Staphylococcus aureus causes several different infections, including those of the bloodstream, heart, bones, joints, soft tissues and indwelling medical devices. Staphylococcal infections are often hard to treat, frequently leading to chronic or recurrent infections despite apparently appropriate antibiotic therapy and a potent host immune response. One of the key aims for research in my group is to understand how S. Aureus is able to persist in the hostile host tissues, with the long-term aim of exploiting this information for the development of new therapeutics. Recent work from the group has shown that DNA repair is essential for staphylococcal survival in host tissues, at least in part because it enables the pathogen to survive DNA damage caused by the oxidative burst of neutrophils. Key DNA repair components included the addab family helicase/nuclease complex rexab, which processes DNA double strand breaks and triggers the SOS response. In addition to promoting staphylococcal survival in host tissues, induction of the SOS response due to DNA damage caused by oxidative stress results in an increase in the mutation rate due to the expression of an error-prone DNA polymerase. This results in an increased frequency of antibiotic resistant isolates and also the emergence of small colony variants (scvs), which are associated with chronic infection. Scvs are resistant to various antibiotics and also highly resistant to killing by neutrophils, providing an explanation for their ability to survive in host tissues.

In addition to host defences, we have also found that several classes of clinically relevant antibiotics cause DNA damage and induction of the SOS response. As for DNA damage caused by the oxidative burst, rexab made a significant contribution to repair of damage caused by antibiotics and was required for induction of the SOS response. Therefore, there are similarities in the damage caused to S. Aureus by host defences and several classes of antibiotics and these stresses not only select for resistance, they also promote its emergence by increasing the mutation rate. This information provides an opportunity to develop a new therapeutic approach for S. Aureus and possibly other pathogens. By targeting bacterial DNA repair, we can sensitise S. Aureus to both host defences and several different antibiotics, and reduce the mutation rate associated with the acquisition of drug resistance. For example, rexab-deficient mutants were killed more efficiently by neutrophils and the antibiotics oxacillin, daptomycin and co-trimoxazole compared to wild-type bacteria. Furthermore, the rexab-deficient mutants did not increase their mutation rates in response to oxidative or antibiotic-mediated DNA damage, reducing the emergence of scvs and drug-resistant strains. To identify small molecule inhibitors of DNA repair, we undertook a cell-based screen using a *reca-gfp* reporter strain in which DNA damage was triggered by a sub-lethal dose of ciprofloxacin. This talk will give an overview of the project and update on progress of the development of small molecule inhibitors of bacterial DNA repair as a novel therapeutic approach.

Indoor transmission of SARS-CoV-2

Hua Qian

South East University, China, PR China

It is essential to understand where and how SARS-CoV-2 is transmitted. We identified all outbreaks involving three or more cases and reviewed the major characteristics of the enclosed spaces in which the outbreaks were reported and associated indoor environmental issues at the early stage of COVID spreading in China. It was found that almost all infections were occurred in indoor environment. Home outbreaks were the dominant category followed by transport. Results confirms that sharing indoor spaces is a major SARS-CoV-2 infection risk. Typical cases were detailed analysed to identify the role of ventilation and airflow pattern.

Infection control for COVID-19: Theory and practice

Kalisvar Marimuthu

National Centre for Infectious Diseases, Singapore

COVID-19 pandemic continues to challenge infection prevention and control (IPC) in many different ways. Existing dogma and work practices are challenged by accumulating evidence, limited resources, and expectations from both decision-makers and users on the ground. This talk will address some of these issues and give a broad overview of how the National Centre for Infectious Diseases (NCID), Singapore, implemented IPC during the COVID-19 pandemic.

Environmental cleaning & disinfection: Current controversies

Stephan Harbarth

Geneva University Hospitals, Switzerland

The impact of environmental contamination on nosocomial infections and the cost-effectiveness of surface disinfection as opposed to detergent-based cleaning remains a scientifically unresolved issue, despite a growing body of literature. However, with respect to hospital cleaning and terminal cleaning in particular, a broad consensus exists that high standards are essential. The essential role of the environment as potential reservoir of multidrug-resistant organisms (mdros) has recently gained new momentum. Several well-conducted clinical studies have highlighted the importance of thorough cleaning practices to avoid transmission of mdros that are capable of surviving in the environment for extended periods. For instance, the recently published Researching Effective Approaches to Cleaning in Hospitals (REACH) trial showed the important role of thorough environmental cleaning in the prevention of hais. The study demonstrated that the implementation of a multi-modal cleaning bundle consisting of component training, technique, product, audit and communication not only improved the performance, knowledge and attitude of the environmental services staff, but may also reduce the occurrence of clinically important hospital pathogens.

In my presentation, I will discuss various issues, including topics covered in a recent expert review (O Assadian et al, J Hosp Infect 2021): Key elements of environmental cleaning and disinfection, choice of appropriate disinfectants and cleaning equipment, definitions for standardized cleaning processes and the relevance of structured training, with additional focus on practical topics and implementation.

Outbreak control in healthcare settings

Doo Ryeon Chung

Division of Infectious Diseases, Department of Internal Medicine, Seoul, Korea

Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea;

Center for Infection Prevention and Control, Samsung Medical Center, Seoul, Korea

"Epidemics" or "outbreaks" in communities have been a big concern for mankind in the past, and large-scale outbreaks such as the plague, cholera, smallpox, and measles have resulted in many deaths or morbidity. Although the importance of hand hygiene or the cause of infection was not known, the concept of 'quarantine' has been applied to block the spread for a very long time. In modern times, such large community epidemic has decreased due to the advances in medicine, improved personal hygiene, development of vaccines and so on. Instead, increasing attention has been paid to the control of outbreaks in healthcare facilities.

Outbreaks in healthcare settings are caused by complex factors including an increase in immunocompromised hosts, an increase in invasive procedures or surgeries, an excessive number of patients compared to medical staff and facility infrastructure, contamination of the hospital environment, a long hospital stay, and long-term use of broad-spectrum antibiotics. In addition, weakness of the hospital's infection control system and low adherence to hand hygiene or inadequate aseptic techniques of medical staff can promote outbreaks.

Outbreak control in healthcare settings usually starts with the identification of a potential outbreak and leads to developing hypotheses and testing, interpretation, and control measures. The specific process differs depending on the type and cause of the outbreak. Hypotheses about the cause of outbreak are established based on the epidemiological information collected, previously published literatures, and expert opinions. The epidemic curve of the outbreak cases can be of great help in understanding the nature of outbreak. Epidemiological studies such as case-control studies or cohort studies are sometimes performed to prove the hypothesis. The role of the microbiology laboratory is very important, so it carries out storage of the specimens or positive cultures, identification of microorganisms and antibiotic susceptibility testing, and furthermore, molecular typing. In recent years, as whole genome sequencing (WGS) has been established as the complete and universal method for microbial typing, it has become an essential investigative tool in the outbreak investigation. As the outbreak through environmental contamination increases, environmental investigation is also very important. It is often necessary to include the investigation of not only the surface of medical devices or equipment but also air or water in the hospital. When the cause is identified, control measures are implemented to end the outbreak. Depending on the circumstances, these actions may have to be preemptively carried out at the same time as the outbreak investigation begins.

If the WGS has brought breakthrough developments and change in the recent trend investigation and control of outbreak in the healthcare settings, one of the things expected in the future with the development of science and technology is an artificial intelligence-based automatic early detection system for outbreaks. If such studies are successful, infection preventionists will be able to focus on more important tasks.

In the context of the current COVID-19 pandemic, all healthcare institutions are making their utmost efforts to prevent the spread of COVID-19 among patients, visitors, and the healthcare workers. These new and painful experiences will greatly contribute to preparing for the future epidemics of emerging infectious diseases with high contagiousness.

The Trifecta of Diagnostic Stewardship, Antimicrobial Stewardship, and Value Assessment of New Diagnostic Tests

Robin Patel

Mayo Clinic, USA

The past two years have made us all acutely aware of the ravages infectious diseases can wreak. At the same time, we've seen what science can deliver to combat devastating situations. The rapid development of SARS-cov-2 diagnostic tests, and their deployment in innovative ways, has been unprecedented, possibly accelerating the microbial diagnostics field by half a decade, if not more. But SARS-cov-2 is just one of many microbes impacting human health. Underneath the COVID-19 pandemic lurks another pandemic, that of antimicrobial resistance. In many ways the antimicrobial resistance crisis is more challenging than COVID-19, involving so many types of bacteria (and fungi), alongside an assortment of antimicrobial resistance mechanisms.

Fortunately, as with SARS-cov-2, we have witnessed gradually increasing availability of tests to address the antimicrobial resistance crisis. This is great news. However, given the complexity of antimicrobial resistance, it is not always clear how novel diagnostics for antimicrobial resistance should be applied to demonstrate the greatest value. In this presentation, the new frontier of the 'science' needed to define appropriate utilization of microbiology diagnostics will be highlighted, emphasizing the trifecta of diagnostic stewardship, antimicrobial stewardship, and value assessment of new diagnostic tests.

Promoting the development of novel therapeutic agents

Dennis M. Dixon

NIH, NIAID. United States

The National Institute of Allergy and Infectious Diseases (NIAID) at the U.S. National Institutes of Health (NIH) is unique in having a dual role of advancing the science and public health countermeasures for a contemporary set of pathogens and diseases, as well as rapidly responding to newly emerging pathogens. Key examples include the emergence of novel seasonal and pandemic influenza strains and SARS coronavirus, as well as the profound, current example of the emergence of SARS-Cov-2. New bacterial and fungal pathogens include several *Rickettsia* spp, *Neoehrlichia* spp. And *Candida auris*. Perhaps more challenging for bacteria is the endless evolution of novel resistance genes and mechanisms in well established pathogens.

Strategies to confront this relentless tide include the development of novel therapeutic agents such as next generation candidates from existing classes, development of new classes, and development of new or non-traditional approaches. Few examples of truly new classes have appeared and been successful in recent years. Current enthusiasm is increasing for novel approaches such as bacteriophage therapy in the contemporary regulatory environment, as well as virulence inhibitors and alternative approaches such as antimicrobial peptides that may have an indirect mechanism of action rather than direct inhibitory action. Each of these concepts poses individual pathway development uncertainties, and NIAID is exerting substantial efforts to advance the field. In the U.S., the recognition of artificially emerging agents after 9/11was a crucial to the increased focus on countermeasure development. NIAID's efforts, including a spectrum of special, targeted funding announcements for traditional grant and contract mechanisms, have been instrumental in paving the path forward in product development.

Designing and conducting clinical trials that change the practice

David Paterson

University of Queensland, Australia

Most clinical trials are for the purpose of registering new antibiotics by regulatory authorities (for example, the FDA). While these are essential for the availability of new antibiotics for unmet clinical needs, they do not always change clinical practice. Investigator-initiated clinical trials (sometimes called clinician-directed trials) have the potential to change clinical practice since they may evaluate generic antibiotics or strategies of management of infection (for example, evaluating duration of therapy or IV to PO stepdown therapy). Investigator-initiated clinical trials typically involve networks of clinicians (for example, via ARLG or ECRAID) and may use innovative designs such as use of “platforms” and “response adaptive randomisation”.

Epidemiology and impact of anti-fungal resistance in Asia

Ban Hock Tan

Singapore General Hospital, Singapore

No abstract received.

The confluence between viral and fungal infections

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Invasive fungal disease (IFD) and viral infections frequently occur in immune compromised hosts, with viral infection preceding IFD. The first awareness of this interaction came from the observation that solid and stem cell transplant recipients who developed end organ cytomegalovirus (CMV) invasive disease were at a significantly increased risk of developing IFD, particularly Aspergillosis and Pneumocystis pneumonia. Further studies showed that CMV DNAemia, antigenemia and recipient CMV serostatus also increased the risk of both early and late onset IFD. The inter-relationship between fungal infection and CMV will be discussed including treatment related risk factors, viral and fungal immunity and genetic predisposition.

More recently the association of community acquired respiratory viruses (CARV) and IFD in both immunocompromised and previously immunocompetent hosts has been recognised. The complex relationship between CARV and IFD will be discussed with reference to Influenza associated pulmonary Aspergillosis (IAPA), and SARS COV-2 and Aspergillosis, Mucormycosis and other fungal pathogens. Indeed, the COVID-19 pandemic has seen the identification of 2 new syndromes: COVID-19-associated pulmonary aspergillosis (CAPA) and COVID-19-associated mucormycosis (CAM). All involve airway damage and hyperinflammation due to virus infection. The different presentation of and risk factors for these IFDs will be discussed.

Viral infection may increase the risk of IFD due to a number of common and pathogen-specific, host, treatment and environmental risk factors. Further research is warranted to determine the biological interaction between viruses and IFD in order to better identify future patients at high risk of developing IFDs and interventions to decrease the risk.

Novel therapeutic options for invasive fungal infections

David W. Denning

The University of Manchester and Global Action Fund for Fungal Infections, UK; www.aspergillus.org.uk; www.LIFE-Worldwide.org; www.GAFFI.org

New antifungal agents are required for multiple reasons including: both intrinsic and acquired resistance, especially to the triazole class, drug interactions which prevent optimal therapy in many patients, drug intolerance and toxicity and in many instances, in adequate efficacy. The last 3 agents approved by the FDA were both posaconazole and andulafungin in 2006 and isavuconazole in 2015. In 2021, a new class of compound, a Triterpenoid, was approved for use and called ibrexafungerp. It is oral and inhibits glucan synthase, but in a different molecular location to the echinocandins.

New systemic antifungals in clinical development include:

- Manogepix (or Foxmanogepix). An inhibitor of fungal glycosylphosphatidylinositol biosynthesis (Amplyx; APX001A)
- Olorofim. An orotomide inhibiting dihydro orotate dehydrogenase (DHODH) (F2G; F901318)
- Oteseconazole and other novel CYP inhibitors (Mycovia; VT1598/1161)
- Resafungin. A long acting echinocandins (Cidara; CD101)
- An arylamide, active against mitochondrial membranes (Toyama; T-2307)
- New formulations of amphotericin B (Matinas; AMB nanoparticles, cochleate AMB)

In addition, some inhaled antifungals are also in development:

- Itraconazole (Pulmatrix)
- Triazole antifungal (Pulmocide; PC945)
- Voriconazole (Zambon and TFF Pharmaceuticals)

The next decade promises to be a very interesting period in antifungal chemotherapy.

Future role of vaccines on antibacterial resistance

Paul Ananth Tambyah

National University of Singapore, Singapore

Vaccines have made a significant impact on global public health from the eradication of smallpox to the near elimination of measles and polio. Other diseases which have declined significantly due to vaccines include hepatitis B and liver cancer as well as HPV and cervical cancer. However, vaccines for bacterial diseases are rare with a few notable exceptions such as the pneumococcal vaccines as well as the pertussis vaccines. There have been a number of disappointments with vaccines against *S. aureus* and *C. difficile* which have not progressed. However, there are benefits from viral vaccines that can reduce infections by reducing the incidence of respiratory tract infections. Antimicrobial resistance is a major problem in respiratory tract infections and thus reducing these infections through deployment of effective vaccines would have a significant impact on secondary bacterial infections and possibly by extension resistance. Perhaps the most significant contribution of vaccines to the control of antimicrobial resistance is the development of novel technologies which may be effective in protecting those at risk of infections caused by antimicrobial resistant pathogens.

Novel technologies for vaccine development

Kaitlyn M. Morabito

DMID, NIAID, NIH, USA

Traditional vaccine development involves starting with the virus or pathogen and developing vaccines based on empirical evaluation. Most licensed vaccines currently fall within this category including whole-inactivated vaccines, live-attenuated vaccines that have been attenuated through passage methods, or proteins that have been purified from virus preparations, or produced in vitro using wild-type sequences. In contrast, rational vaccine design starts with knowledge of protective or presumably protective immune responses against a virus and designing vaccines to elicit that specific immune response. The recent shift towards rational vaccine designs has been enabled by the development of new technology. These transforming technologies include structure-based vaccine design, advances in sorting, sequencing and bioinformatics which enable a more in-depth analysis of immune responses, and rapid DNA synthesis which allows more rapid high-throughput evaluation of monoclonal antibodies and screening of antigens. Additionally, advances in gene editing have enhanced transgenic or humanized mouse models for vaccine evaluation and technologies for gene-based delivery of vaccine antigens have also improved. The development of these technologies has improved both the precision of vaccines by shifting the balance towards protective immune responses and away from non-protective responses, and the speed at which the immune response can be analyzed, and vaccines can be evaluated and manufactured. Rational vaccine design provides new solutions to old problems such as RSV and influenza, enables rapid response to emerging pathogens such as SARS-CoV2, and has the potential to improve vaccine safety for pathogens such as dengue virus.

What we learned from COVID-19 vaccination

Eui-Cheol Shin

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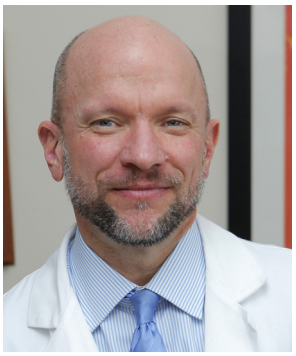
The current pandemic disease, coronavirus disease 2019 (COVID-19) is caused by infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Since its emergence in late December 2019, SARS-CoV-2 has been spreading rapidly worldwide. In response to the rapid spread of COVID-19, vaccines have been developed at an unprecedented pace. In particular, novel platform technologies such as mRNA and viral vectors were adopted for rapid development of COVID-19 vaccines. However, variant viruses have been emerging, and neutralizing antibodies elicited by vaccination have reduced activity against variants. In the present lecture, I will talk about 'what we learned from COVID-19 vaccination' in various aspects, including antibody and T cell immunogenicity, adverse reactions, and immune responses elicited by viral vectors. In addition, I will discuss the generation of memory cells by COVID-19 vaccination compared to that by natural infection.



Current strategies for antiretroviral therapy

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Currently, there are 33 antiretroviral drugs approved for the treatment of HIV infection in 8 broad mechanistic classes: nucleoside analogue reverse transcriptase inhibitors (nrtis), non-nucleoside reverse transcriptase inhibitors (nnrtis), protease inhibitors (pis), integrase inhibitors (iis) and 4 types of HIV entry inhibitors (CD4 attachment inhibitors, CD4 post-attachment inhibitors, CCR5 antagonists, and fusion inhibitors). ART guidelines worldwide recommend starting an initial 2- or 3-combination drug treatment regimen in all patients with HIV infection. Current ART regimens are potent, safe, tolerable, and convenient and current virologic suppression rates can exceed 90%. However, some patients experience virologic failure with the associated emergence of drug resistance. While less common today, some patients cycle through multiple regimens and can develop complex drug-resistance patterns.

The diagnostic approach to the heavily treatment-experienced patient with a complex drug-resistance pattern initially is to take a detailed history of antiretroviral use, focusing on adherence, tolerability and drug toxicities, and drug-interactions with prior regimens; all available prior resistance test results should be obtained and reviewed. In such a patient, conducting both genotypic and phenotypic resistance testing while the patient continues their current antiretroviral regimen is recommended, including assessment of resistance to nrtis, nnrtis, pis, and integrase inhibitors and identifying susceptible drugs and drug classes. Viral tropism testing also should be obtained to assess susceptibility to the CCR5 antagonist, maraviroc.

The goal of therapy is to address prior reasons for regimen failure and design a new regimen with 2 fully active drugs (with at least one having a high barrier to resistance such as the integrase inhibitors bictegravir or dolutegravir, or the boosted protease inhibitor, darunavir) that will achieve maximal virologic suppression (HIV RNA below the limit of detection). If no fully active drug with a high barrier to resistance is identified, then 3 fully active drugs should be used in the next regimen. Adding one active antiretroviral agent to a failing regimen is not recommended as this likely will lead to selection of resistance. For some heavily treatment-experienced patients with extensive drug resistance, full virologic suppression may not be achievable – in this case antiretrovirals should be continued with the goal of partial virologic suppression that still may help preserve CD4 cell counts and delay clinical progression.

In heavily treatment-experienced patients, newer and investigational antiretroviral agents may offer benefits. Newer nnrtis (e.g. Doravirine, etravirine), pis (e.g. Boosted darunavir), and integrase inhibitors (bictegravir, dolutegravir) may demonstrate activity against drug-resistant viruses. Approved drugs with newer mechanisms of action, fostemsavir (CD4 attachment inhibitor), ibalizumab (CD4 post-attachment inhibitor), maraviroc (CCR5 antagonist) and enfuvirtide (fusion inhibitor) demonstrate activity against viruses resistant to the standard antiretroviral drug classes. New investigational agents with novel mechanisms of action (e.g. The capsid inhibitor, lenacapavir) also demonstrate activity in heavily treatment-experienced patients.

We currently can control HIV infection long-term with potent, safe, and convenient antiretroviral treatment in most patients, leading to prolonged healthy survival. Treatment-experienced patients with complex drug-resistance pose challenges and further innovations and strategies for this group of patients are needed.

PrEP and disparities in access in the Asia Pacific

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Pre-exposure prophylaxis (prep) is a biomedical form of intervention that has been proven effective for the prevention of virus transmission in HIV uninfected people at high risk of infection. In 2012, US FDA approved the daily use of co-formulated tenofovir disoproxil fumarate 300 mg and emtricitabine 200 mg (TDF/FTC) for prep. Subsequently co-formulated emtricitabine 200 mg and tenofovir alafenamide 25 mg (F/TAF) was approved in 2019. While new prep modalities continued to be experimented, TDF/FTC has remained the most commonly used regimen worldwide. In many countries, men who have sex with men (MSM) constitute a prioritised community whose access of prep is crucial for controlling HIV spread. Globally, the coverage of prep is heterogeneous and the pattern of uptake has varied from place to place. As of the end of March 2021, just over 1 million prep initiations have been recorded worldwide (https://data.prepwatch.org/).

Despite rising awareness of prep among MSM and other people at risk of infection, there exists “prep gaps” in the Asia pacific as a result of barriers at different levels. For individuals, the main obstacles are cost, varied perception of risk, concern about efficacy and safety. Community-level obstacles include social stigma and low acceptance in some MSM networks. On programme level, funding, feasibility and technical capacity are grossly insufficient to enable prep services to be implemented. At the government level, the lack of policy direction is common. In many jurisdictions, there is also the “purview paradox”, which refers to contradictory beliefs about the right setting for delivering prep. Despite the cumulation of scientific evidence on the effectiveness of prep, neither HIV physicians, primary care clinics nor public health services consider it within one’s practice domain. As a strategy that centers on the delivery of a prescription medicine, an agreed clinical home for prep is often lacking.

Among prep services in operation in the Asia Pacific, 4 delivery models can be distinguished which differ by the setting (community or public service) and fee (fee or free), each of which appeals to people with different needs and preferences. To date, only Thailand and Vietnam have reported relatively large-scale implementations of prep, whereas others are organised as pilots for small number of people. Research in prep delivery is common, which offers an opportunity for pilot and time-limited services to be established. In Hong Kong, for example, three pilot studies have been launched since 2017, providing prep access to over 400 persons. Through these studies, data analyses were conducted to help understand the acceptability of different regimen, affordability of partially self-financed prep, incorporation of point-of-care testing for monitoring, and feasibility of novel service models.

While a central public-funded prep service is not yet in sight in many Asia Pacific jurisdictions, the coverage of prep in people at risk has clearly increased. Since early 2020, however, the COVID-19 outbreak has inadvertently slowed the progress of prep programme expansion. The UNAIDS target of a global coverage of 3 million prep users by 2020 was missed. Policy commitment, funding support as well as innovation in programme development are crucial in ensuring that the world is on track in promoting prep for achieving the HIV prevention targets by 2030.

International Journal of Antimicrobial Agents 58S1 (2021) 106421

Contents lists available at ScienceDirect

International Journal of Antimicrobial Agents

journal homepage: www.elsevier.com/locate/ijantimicag

Abstracts from the 13th International Symposium on Antimicrobial Agents and Resistance (ISAAR) – e-Poster Presentations

PAG-001

The genome of *Micrococcus luteus* MST-118984C isolated from Australian soil harbours a bacteriocin biosynthetic gene cluster and biocide/multidrug efflux genes

Soo Sum Lean[1*], Alex Zhuo Shang[1], Thomas Booth[1], Ernest Lacey[2], Yit-Heng Chooi[1]. [1]*School of Molecular Sciences, University of Western Australia, Western Australia;* [2]*Microbial Screening Technologies, Smithfield 2164, Australia*

Background: *Micrococcus luteus* is a Gram positive, high GC content (>70%) free-living coccoid Actinobacteria. *M. luteus* survives in both biotic and abiotic environments such as soil, air, on plants, animals and the human body. *M. luteus* is also a nosocomial pathogen which targets immunocompromised patients, causing diseases such as bacteraemia and endocarditis. While other Actinobacteria (such as *Streptomyces* spp.) are in the limelight for secondary metabolites (SMs) production, information on potential SM production in *M. luteus* are scarce.
Objective: In this study, we describe the genome of *M. luteus* MST-118984C and unearth its novel SM production.
Methods: *M. luteus* MST-118984C was isolated from Australian soil and sequenced on the Illumina platform. Genome assembly was carried out using Unicycler pipeline before downstream analysis. SMs prediction, precursor peptide determination, core and accessory genome analysis were performed using antiSMASH, NeuRiPP and Roary bioinformatic tools, respectively
Results: The assembled draft genome was 2 625 402 bp with G + C content of 72.58%. No antibiotic resistance genes were found in the genome of MST-118984C but it harboured the *qac*C resistance determinant (encoding quaternary ammonium compound resistance protein C) and the *mac*B-encoded multidrug efflux pump. MST-118984C together with 81 *M. luteus* genomes obtained from the NCBI database were analysed to uncover the different types and distribution of biosynthetic gene clusters potentially encoding for SMs. This led to the discovery of a bacteriocin gene cluster in MST-118984C which was found on the same contig with genes encoding the synthesis of carotenoid, a signature yellow pigmentation in *M. luteus*.
Conclusion: Closest match of the bacteriocin cluster showed >80% similarity to uberolysin family from *Pseudarthrobacter chlorophenolicus*, suggesting the cluster may be a result from horizontal gene transfer.
Keywords: *M. luteus*, bacteriocin, uberolysin.

PAG-002

Antibacterial effects of tetraspanin CD9 against *Pseudomonas aeruginosa*

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Background: Tetraspanins are a family of transmembrane proteins that form multi complexes at the cell surfaces, through their tetraspanin-enriched microdomains (TEMs). Their role as a gateway of infectious disease has gained our attention, which evidently shown in previous studies by bacteria hijacking the tetraspanin adhesion platforms on the cell membrane, to adhere and proceed with the pathogenesis.
Objective: *Pseudomonas aeruginosa* infections are very challenging to eradicate due to antimicrobial resistance against most conventional antibiotics. Therefore, it is crucial to find a targeted alternative therapeutic approach to combat the infections that may simultaneously reduce the occurrence of resistance.
Methods: In this study, the antibacterial effects of synthetic tetraspanin peptide CD9 against *Pseudomonas aeruginosa* standard strain ATCC 27853 and a clinical multidrug-resistant (MDR) *Pseudomonas aeruginosa* isolate were investigated by the direct disc diffusion method. The minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) were performed by microdilution method following the guidelines by the Clinical Laboratory Standards Institute (CLSI) using cefotaxime, imipenem, and polymyxin B as the control.
Results: This study revealed an excellent inhibitory effect of the CD9 peptide on *Pseudomonas aeruginosa* ATCC 27853 with an approximately 12 mm inhibitory zone. However, CD9 peptide had no effect against MDR *Pseudomonas aeruginosa*. The MIC value of the CD9 peptide was 28.5 μM against both isolates. The MBC of CD9 peptide against both isolates could not be detected due to the presence of bacterial colonies (CFU) even with the highest concentrations of CD9 peptide.
Conclusion: This study has shown that CD9 peptide has inhibitory effects against *Pseudomonas aeruginosa* ATCC strain only. This could indicate that the peptide may have no direct antagonist effects on bacterial isolates and show the significant role of tetraspanin CD9 as a facilitator for bacterial-cell adhesion.
Keywords: *Pseudomonas aeruginosa, p. aeruginosa,* peptide CD9, antibacterial, disc diffusion, MIC, MBC.

PAG-003

Assessment of vancomycin pharmacokinetics in an obese patient receiving extracorporeal membrane oxygenation

R. Morales, Junior *, V. Juodinis, I. Santos, P. Okumura, F. Leite, B. Ribeiro, B. Lima, L. Barbosa, G. Ferriani, R. Moura. *Sírio-Libanês Hospital, São Paulo, Brazil*

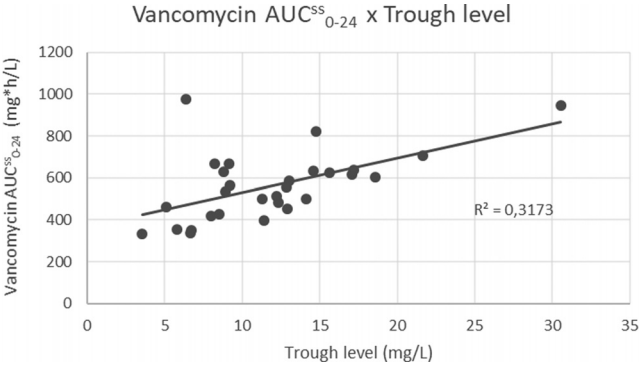
Background: Vancomycin is frequently prescribed to prevent or to treat gram-positive bacterial infections in patients receiving extracorporeal membrane oxygenation (ECMO). The use of ECMO combined with critical illnesses may affect pharmacokinetics of hydrophilic drugs such as vancomycin.
Case Presentation Summary: A 46-year-old, 130 kg, 185 cm man without any important medical history, hospitalized for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), receiving extracorporeal membrane oxygenation (ECMO), started vancomycin with loading dose of 2 g followed by 1 g every 8 h. Blood culture reported *Staphylococcus epidermidis* with vancomycin MIC 1 mg/L. Two steady-state blood samples were collected within the same dose interval and the one-compartment model with first-order kinetics was used to estimate the pharmacokinetic parameters. The found vancomycin clearance, volume of distribution and half-life values were, respectively, 6.0 L/h, 61.9 L and 7.2 hours. The vancomycin area under the curve (AUC), estimated by logarithmic trapezoidal rule, was 502.2 mg/L.h. A week later, serum levels were rechecked and the patient presented a slight increase in the vancomycin volume of distribution (71.1 L) but the AUC remained at the therapeutic target and the dose was maintained. The blood culture became sterile and the patient remained hospitalized for treatment of the underlying disease.
Conclusion: Obese patients undergoing ECMO may require higher vancomycin daily doses than those recommended by the empirical dose regimen. The vancomycin AUC-guided monitoring permits specific dose adjustments based onindividuals' pharmacokinetic parameters and it can be implemented in clinical practice to maximize antimicrobial target attainment in critically ill patients requiring life support devices.

PAG-004

Vancomycin area under the curve–guided monitoring in critically ill patients

R. Morales, Junior*[1,2], F. Leite[1], V. Juodinis[1], I. Santos[1], P. Okumura[1], B. Ribeiro[1], B. Lima[1], L. Barbosa[1], R. Moura[1], S. Santos[2]. *[1]Sírio-Libanês Hospital; [2]São Paulo University, São Paulo, Brazil*

Background: Vancomycin is largely prescribed to critically ill patients with confirmed or suspected gram-positive bacterial infections. We aim to analyze the vancomycin target attainment and nephrotoxicity using a pharmacokinetics-pharmacodynamics approach.
Methods: Critically ill adult patients with normal renal function were included. Therapy started with 750–1500 mg q12 h, one-hour infusion. The one-compartment model with first-order kinetics was used to estimate the pharmacokinetic parameters from two steady state drawn levels. Therapeutic target was defined as area under the curve/minimum inhibitory concentration (AUC^{ss}_{0-24}/MIC) ≥400 and <600. Nephrotoxicity was defined as an increase in serum creatinine of 0.5 mg/dL or 50% from baseline.
Results: This study included 19 patients, median age of 63 years. The found vancomycin clearance, volume of distribution and half-life values were, respectively, 4.5 (IQR 3.2–5.7) L/h, 41.1 (IQR 29.9–57.5) L and 6.2 (IQR 4.9–8.5) hours. The therapeutic target was initially achieved in 5 (26%) patients. We rechecked the vancomycin AUC after adjusting the dose based on individual parameters in 8 of 14 patients who did not reach the target with initial regimen, and then 7 of them reached the target. Trough levels and AUC showed low correlation value ($R^2 = 0.32$). Vancomycin related nephrotoxicity occurred in 2 (11%) patients and both presented an initial AUC^{ss}_{0-24}/MIC >600.



Conclusions: With a two-sample AUC-guided monitoring strategy, it was possible to individualize the therapy in real time to improve target attainment. Since most of patients did not reach the target with the initial dose regimen, it is prudent to monitor the exposure to vancomycin directly by AUC^{ss}_{0-24}/MIC ratio to maximize antimicrobial efficacy and decrease the occurrence of nephrotoxicity.

PAG-005

In vitro activity of WCK 5222 (cefepime/zidebactam) against bioterror pathogen *Burkholderia pseudomallei*

Balaji Veeraraghavan[1*], Yuvasri Manokaran[1], Shalini Anandan[1], Abirami Shankar[1], Yamuna Devi Bakthavatchalam[1], Binesh Lal[1], Karthik Gunasekaran[2], Ramya Iyyadurai[2]. *[1]Department of Clinical Microbiology, Christian Medical College, Vellore, India; [2]Department of Medicine, Unit V, Christian Medical College, Vellore, India*

Background: *Burkholderia pseudomallei* causes melioidosis, a potentially fatal infection in human. The organism is endemic in certain tropical geographies and is designated as Category B bioterror pathogen by CDC. Due to the fulminating infection and the need of highly bactericidal drug to manage initial aggressive therapy to deal with acute phase of infection, the clinical performance of existing antibiotics such as ceftazidime is sub-optimal against this pathogen. Resistance to ceftazidime has also been reported. Moreover, there is no FDA-approved therapy for *B. pseudomallei* infections suggesting lack of antibiotics with a novel mechanism of action. Evaluating newer antibiotics with favourable pharmacokinetic/pharmacodynamic features for the activity against *B. pseudomallei* including those resistant to ceftazidime is warranted. WCK 5222 (cefepime/zidebactam, FEP/ZID) is a novel β-lactam enhancer mechanism-of-action based antibiotic in advanced clinical development. The combination is active against multi-drug/extensive-drug resistant nosocomial Gram-negative pathogens. In the present study, comparative activity of FEP/ZID against clinical isolates of *B. pseudomallei* was evaluated by MIC determination and time kill studies. Impact of high ceftazidime MICs of lab-selected ceftazidime-resistant *B. pseudomallei* on the activity of FEP/ZID was also studied by MIC determination.
Methods: *B. pseudomallei* clinical isolates (n = 50) used in this study were collected at Christian Medical College Vellore, Tamil Nadu, India during (2017–2020) The organism was isolated from routine blood culture and identified by MALDI-TOF mass spectrometry. The MICs of FEP/ZID (1:1 ratio) and comparator antibiotics were

Table 1: (abstract PAG-005): Activity of cefepime/zidebactam and comparators against 50 isolates of *B. pseudomallei*

Antibacterial agents	No. of isolates inhibited (cumulative %) at respective MIC (mg/L)								MIC_{50}	MIC_{90}	%S*
	≤0.5	1	2	4	8	16	32	64			
FEP					4 (8.0)	29 (66.0)	17 (100.0)		16	32	NA
ZID						4 (8.0)	30 (68.0)	16 (100.0)	32	64	NA
FEP/ZID (1:1)			7 (14.0)	29 (72.0)	7 (86.0)	7 (100.0)			4	16	100^
CAZ			1 (2.0)	24 (50.0)	23 (96.0)	1 (98.0)	1 (100.0)		4	8	96
MEM	11 (22.0)	27 (76.0)	9 (94.0)	3 (100.0)					1	2	NA

%S: % susceptibility; NA: Not applicable.
*CLSI criteria.
^PK/PD breakpoint was applied.

determined by reference broth dilution method as per CLSI (M07-A12, 2018). The antibiotic susceptibilities were determined based on CLSI breakpoints (M100-S31, 2021) except FEP/ZID for which reported PK/PD breakpoint of ≤64 mg/L was applied. Bactericidal activity of FEP/ZID was determined using time kill studies. Briefly, three isolates of *B. pseudomallei* grown on blood agar plates, the colonies from each plate were emulsified and adjusted to 0.5 McFarland turbidity. About 6.1–6.3 $\log_{10}$ CFU/mL final inoculum was prepared and exposed to fold-MIC concentrations of test antibiotics in 2 mL CaMHB and time-dependent changes in bacterial counts were monitored by plating the serial dilutions of the bacterial cultures (at 2, 4, 6, 8, 24 h) on blood agar (5%) plates. To develop the ceftazidime-resistance, 5 *B. pseudomallei* isolates were subjected to daily sequential transfer of inoculum from 0.5× MIC tube on ceftazidime for 8 days. Terminal mutants were preserved and the MIC determination of cefepime/zidebactam was undertaken against these mutants.

Results: The MICs of cefepime, zidebactam, FEP/ZID, ceftazidime and meropenem against *B. pseudomallei* isolates are shown Table 1. FEP/ZID was active against all *B. pseudomallei* isolates with MICs 2–16 mg/L, which are well-below its proposed breakpoint of ≤64 mg/L. The MICs of cefepime/zidebactam was better than either of the individual agents (8 to 32 mg/L for cefepime and 32 to 64 mg/L for zidebactam). In time kill studies, standalone cefepime and zidebactam failed to elicit bactericidal activity in all the three *B. pseudomallei* isolates, while FEP/ZID displayed a potent bactericidal activity with 2–3-$\log_{10}$ CFU reduction in the bacterial load by 8 h at 1× MIC (8–16 mg/L). Serial transfer of 5 *B. pseudomallei* isolates in ceftazidime containing media for 8 days resulted in substantial increase in ceftazidime MICs and even after 15 drug-free passages, the resistance was stable. Despite high level resistance to ceftazidime, FEP/ZID remained active with a MIC range of 8–16 mg/L, which was well within the proposed PK/PD susceptibility breakpoint of ≤64 mg/L.

Conclusions: In the present study, FEP/ZID exhibited therapeutically relevant in vitro activity against *B. pseudomallei* isolates including those resistant to ceftazidime. Moreover, FEP/ZID was highly bactericidal for *B. pseudomallei* suggestive of its potentially utility during initial intensive antibiotic therapy phase. Results of present study support evaluation of FEP/ZID in translational animal models of *B. pseudomalle*i.

PAG-006

In vitro activity of β-lactam-β-lactam enhancer combination, cefepime/zidebactam (WCK 5222, FEP/ZID) against multi-clonal, colistin-resistant *Klebsiella pneumoniae*

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Background: Relentless increase in the carbapenem resistance among clinically important Gram-negative organisms has led to surge in colistin use, resulting in world-wide emergence and dissemination of 'almost untreatable' colistin-resistant pathogens. Lack of Gram-negative active antibiotics with ability to comprehensively tackle the multiplicity of resistance mechanisms has led to extensive morbidity and mortality in hospital settings. FEP/ZID is an investigational β-lactam and β-lactam enhancer combination being developed for the treatment of multi-/extensively-drug resistant Gram-negative organisms including carbapenem-resistant isolates. Herein, we comparatively evaluated the activity of FEP/ZID against Indian clinical isolates of *K. pneumoniae* exhibiting both colistin and carbapenem resistance. These isolates were also screened for the presence of colistin resistance conferring genes *mcr1* and *mcr3*, changes in *mgrB* and also presence of genes encoding carbapenemases. Further, all the isolates were profiled for multi-locus sequence type (MLST).

Methods: Non-duplicate *K. pneumoniae* isolates (N = 127) resistant to carbapenems (imipenem and meropenem) and colistin based on CLSI susceptibility breakpoints were included in this study. The MIC determination of FEP/ZID (1:1 ratio), colistin, carbapenems, ceftazidime-avibactam, imipenem-relebactam and amikacin was undertaken by broth micro-dilution method as per CLSI (M07-A12, 2018). Susceptibility rates of comparator antimicrobial agents were arrived on the basis of CLSI criteria (M100-S31, 2021). Carbapenemase genes (NDM and OXA-48-like) were detected using multiplex PCR based gene amplification. MLST analyses were undertaken as described previously. The presence/absence of colistin resistance conferring genes was identified using whole genome sequencing. For FEP/ZID, the susceptibility rates were based on cefepime's current SDD CLSI breakpoints.

Results: Table 1 provides the activity of FEP/ZID and comparator agents against colistin- and carbapenem-resistant *K. pneumoniae*. Overall, 122/124 isolates showed presence of carbapenemase genes, 71.8% (89/124) carried $bla_{\text{OXA-48-like}}$ gene and 25% isolates (31/124) carried dual carbapenemase genes; $bla_{\text{OXA-48-like}}$ and bla_{NDM}; of the remainder, two isolates carried bla_{NDM} and two isolates lacked carbapenemases gene despite being carbapenem-resistant. None of the isolates showed presence of *mcr1* and *mcr3*. Out of 109 isolates analysed for *mgrB*, 36 showed mutational changes. The MLST profile revealed at least 14 unique sequence types with ST231 being the dominant clone. All the isolates showed colistin MICs >2 mg/L and were non-susceptible to carbapenems. FEP/ZID demonstrated potent activity with MIC_{50} and MIC_{90} of 1 and 2 mg/L, respectively. MIC_{90}s of amikacin, ceftazidime-avibactam and imipenem-relebactam were >32 mg/L.

Conclusions: FEP/ZID combination was highly active against multi-clonal, colistin-resistant *K. pneumoniae* isolates expressing OXA-48-like (Ambler class D) or/and NDM (Ambler class B) carbapenemases. Though, zidebactam is not an inhibitor of class B and D β-lactamases, activity of FEP/ZID combination is attributable to β-lactam enhancer mechanism.

Table 1: (abstract PAG-006): Activity of cefepime/zidebactam and comparators against colistin-resistant *K. pneumoniae*

Antibiotic	Number of isolates inhibited at MIC (mg) (percentage cumulative inhibition)										MIC_{50} (mg/L)	MIC_{90} (mg/L)	%S[a]
	0.12	0.25	0.5	1	2	4	8	16	32	>32			
Cefepime					1 (0.8)	1 (1.6)	3 (4.0)	0 (4.0)	0 (4.0)	119 (100)	>32	>32	4
Zidebactam	1 (0.8)	1 (1.6)	10 (9.7)	22 (27.4)	27 (49.2)	14 (60.5)	2 (62.1)	5 (66.1)	1 (66.9)	41 (100)	4	>32	NA[b]
Cefepime/zidebactam	1 (0.8)	3 (3.2)	26 (24.2)	59 (71.8)	26 (92.7)	5 (96.8)	4 (100)				1	2	100[c]
Colistin						4 (3.2)	5 (7.3)	33 (33.9)	58 (80.6)	24 (100)	32	>32	0
Imipenem					40 (32.3)	39 (63.7)	5 (67.7)	6 (72.6)	5 (76.6)	29 (100)	4	>32	0
Meropenem							16 (12.9)	58 (59.7)	11 (68.5)	39 (100)	16	>32	0
Amikacin		1 (0.8)	3 (3.2)	7 (8.9)	4 (12.1)	2 (13.7)	1 (14.5)	1 (15.3)	0 (15.3)	105 (100)	>32	>32	15.3
Ceftazidime/avibactam		6 (4.8)	25 (25.0)	44 (60.5)	12 (70.2)	2 (71.8)	1 (72.6)	0 (72.6)	0 (72.6)	34 (100)	1	>32	72.6
Imipenem-relebactam				16 (12.9)	50 (53.2)	16 (66.1)	3 (68.5)	8 (75.0)	2 (76.6)	29 (100)	2	>32	12.9

Cefepime/zidebactam MIC was determined at 1:1 ratio.
Inhibitors were tested at 4 mg/L.
[a]Percentage susceptibility determined based on CLSI interpretive criteria (M100-S31, 2021).
[b]Not applicable.
[c]Final breakpoints are not awarded; susceptibility is determined based on cefepime high-dose breakpoint of 8 mg/L.

PAG-007

Activity of WCK 5222 (cefepime/zidebactam, FEP/ZID) against *Stenotrophomonas maltophilia* collected from a large Indian tertiary-care hospital during 2018–2020

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Background: Multi-drug resistant Gram-negative bacterial pathogens have evoked heightened attention among the scientific community owing to their ability to cause life-threatening infections. Within Gram-negatives, infections caused by non-fermenters in hospital settings pose higher degree of challenges as treatment options are extremely limited. *Stenotrophomonas maltophilia* is an emerging non-fermenter pathogen implicated in nosocomial pneumonia and also in cystic fibrosis. Currently, minocycline, ceftazidime, trimethoprim-sulfamethoxazole and levofloxacin are the therapeutic options but their effectiveness is suboptimal due to PK/PD drawbacks and increasing resistance rates. Moreover, newly approved β-lactam and β-lactamase inhibitor combinations do not cover *S. maltophilia* as this organism intrinsically carries MBL. WCK 5222 is a β-lactam enhancer mechanism based combination of FEP and ZID slated to enter Phase 3 clinical development for the indications of complicated urinary tract infections (cUTI) and ventilated-nosocomial pneumonia. Previously, therapeutic potential of WCK 5222 for the infections caused by carbapenem-resistant *Acinetobacter baumannii* and *Pseudomonas aeruginosa* has been demonstrated through in vitro and in vivo studies. In the present study, in vitro activity of WCK 5222 and comparator antibiotics was evaluated against a recent collection of carbapenem-resistant *S. maltophilia*.

Methods: A total of 200 non-duplicate clinical isolates of *S. maltophilia* were collected from various clinical specimens such a blood and sputum at Christian Medical College, Vellore, India during 2018–2020. Identification *of S. maltophilia* was confirmed using MALDI-TOF mass spectroscopy. The MICs of FEP/ZID (1:1) and various comparators - cefepime, zidebactam, ceftazidime, trimethoprim/sulfamethoxazole, minocycline and levofloxacin were determined as per CLSI (M07-A12). For percent susceptibility determinations, CLSI breakpoints were employed except for cefepime (M100-S31, 2021). Reported PK/PD breakpoint of ≤64 mg/L was applied for FEP/ZID.

Results: Table 1 shows the activity of FEP/ZID and comparator agents against *S. maltophilia*. The $MIC_{50/90}$ of FEP/ZID was 4/16 mg/L and the combination inhibited 96.5% of isolates at its PK/PD breakpoint. Trimethoprim-sulfamethoxazole was the second most active agent with an $MIC_{50/90}$ of 1/4 mg/L; 86.1% of isolates were inhibited at susceptibility breakpoint. Other comparator antibiotic such as minocycline, ceftazidime and levofloxacin showed a limited activity with susceptibility rates of 76.6, 38.8 and 76.6%, respectively.

Conclusions: Among all the studied antibiotics, cefepime/zidebactam was found to be the most active antibiotic combination. Despite the presence of an inherent MBL enzyme, owing to ZID mediated enhancer mechanism of action, FEP/ZID was active against *S. maltophilia*. The therapeutic potential of FEP/ZID against this pathogen needs to be further evaluated through in vivo PK/PD studies.

PAG-008

Vancomycin dose adjustment against Gram-positive MIC 2 mg/L strains in critically ill adult burn patients by pharmacokinetic-pharmacodynamic approach

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Background: The vancomycin empiric dose regimen may not reach the target in critically ill adult patients against the most common pathogens and it can impact the desired outcome. The rational of this study was to compare the vancomycin empirical dose with adjusted doses based on pharmacokinetic-pharmacodynamic (PK/PD) approach in septic burn patients.

Table 1: (abstract PAG-007): MIC distribution of cefepime/zidebactam and other comparators against *S. maltophilia*

Antibiotics	No. of isolates inhibited (% cumulative inhibition) at MIC (mg/L)													MIC_{50}	MIC_{90}	% S
	0.12	0.25	0.5	1	2	4	8	16	32	64	128	256	512	>512			
Cefepime						11 (5.47)	22 (16.4)	52 (42.3)	55 (69.7)	42 (90.5)	13 (97)	2 (98)	4 (100)		**32**	64	NA
Zidebactam									2 (1)	4 (2.9)	21 (13.4)	63 (44.8)	54 (71.6)	57 (100)	512	>512	NA
Cefepime/ zidebactam		1 (0.5)	2 (1.5)	8 (5.5)	47 (28.9)	58 (57.7)	46 (80.6)	25 (93)	6 (96.5)	1 (99)	5 (99)	0 (99)	2 (100)		4	16	99.0
Ceftazidime				4 (1.9)	13 (8.5)	30 (23.4)	31 (38.8)	31 (54.2)	31 (69.7)	15 (77.1)	20 (87.1)	9 (91.5)	5 (94)	12 (100)	16	256	38.8
Trimethoprim/ sulfamethoxazole	8 (3.9)	29 (18.4)	61 (48.8)	50 (73.6)	25 (86.1)	13 (92.5)	6 (95.5)	2 (96.5)	4 (98.5)	2 (99.5)	1 (100)				1	4	86.1
Minocycline	10 (4.9)	12 (10.9)	24 (22.9)	24 (34.8)	39 (54.2)	45 (76.6)	27 (90)	15 (97.5)	4 (99.5)	1 (100)					2	8	76.6
Levofloxacin	1 (0.5)	6 (3.48)	33 (19.9)	57 (48.3)	36 (66.2)	32 (82.1)	18 (91)	12 (97)	4 (99)	2 (100)					2	8	66.2

%S: percentage susceptibilities based in CLSI 2021 breakpoints except cefepime/zidebactam for which PK/PD breakpoint of ≤64 mg/L was applied.
NA: not applicable.

Methods: Patients receiving vancomycin were investigated after the initial dose and, if required, after dose adjustment. Therapy started with 1 g q12 h, one hour pump infusion and the dose was adjusted based on PK/PD target: area under the curve/minimum inhibitory concentration (AUC^{ss}_{0-24}/MIC) >400. Blood at the steady state was sampling at the 3rd and 11th of the starting of infusion. Serum levels were analyzed by liquid chromatography. The one compartment open model was applied to investigate the pharmacokinetics.
Results: We included 14 septic adult burn patients (2F/12M) receiving vasopressors, 27 yrs, 74.5 kg, 30% total burn surface area, SAPS3 63, medians. Pharmacokinetics was altered at the earlier period of septic shock. The target was attained up to MIC 1 mg/L for all patients and after dose adjustment (0.75–1 g q8 h) it was extended for 57% of burn patients against Staphylococcus spp. with MIC 2 mg/L. Clinical cure occurred for all patients.
Conclusion: Vancomycin serum levels were reduced at the earlier period of septic shock, as consequence of increases in total body clearance and reduction of biological half life in burn septic patients with vasopressors requirements, impacting target attainment. The vancomycin dose must be adjusted soon to eradicate gram-positive susceptible strains, including strains with MIC 2 mg/mL.

PAG-009

Meropenem extended infusion against nosocomial MIC 4 mg/L strains to guarantee drug effectiveness in burn patients at the earlier period of septic shock

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Background: Meropenem with intermittent infusion usually cannot achieve the target in critically ill septic patients against the most common nosocomial MIC > 2 mg/L strains, with impact on the desired outcome.The subject of this study was to investigate meropenem 3 g/daily administered by extended infusion based on pharmacokinetic-pharmacodynamic (PK/PD) approach in burn patients.
Methods: Burn patients undergoing meropenem treatment at the earlier period of septic shock receiving 1 g q8 h with 3 hrs-infusion were investigated. Two blood samples were collected (2 mL/each) at the steady state for drug serum measurement by liquid chromatography. The PK parameters obtained were compared with data previously described in healthy volunteers. PK/PD approach was performed to estimate the probability of target attainment based on the predictive index of drug effectiveness: 100%$f\Delta T$ > MIC.
Results: We included 13 septic adult burn patients (2F/11M) receiving vasopressors, 27.5 yrs, 70 kg, 34% total burn surface area, SAPS3 62, medians. Effective free serum trough levels above 4 mg/L occurred for all patients after 3 hrs-extended infusion. Total isolates at the earlier period of septic shock were stratified in *Enterobacteriaceae* and *Pseudomonas aeruginosa*. Clinical cure occurred for all patients.
Conclusion: Meropenem 3 hrs-extended infusions provided drug effectiveness up to MIC 4 mg/L for 100% of dosing interval. Serum levels measurement can be applied to achieve clinical success and to avoid microbial resistance.

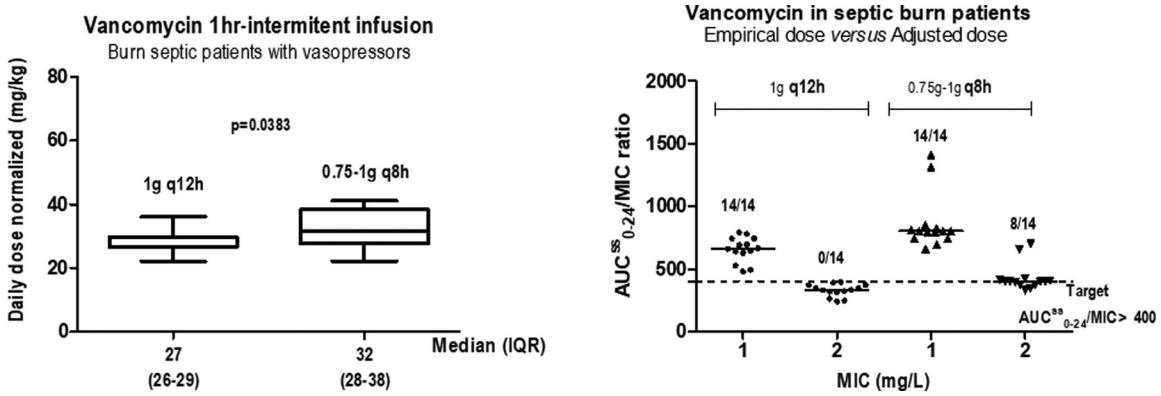

Figure: (abstract PAG-008)

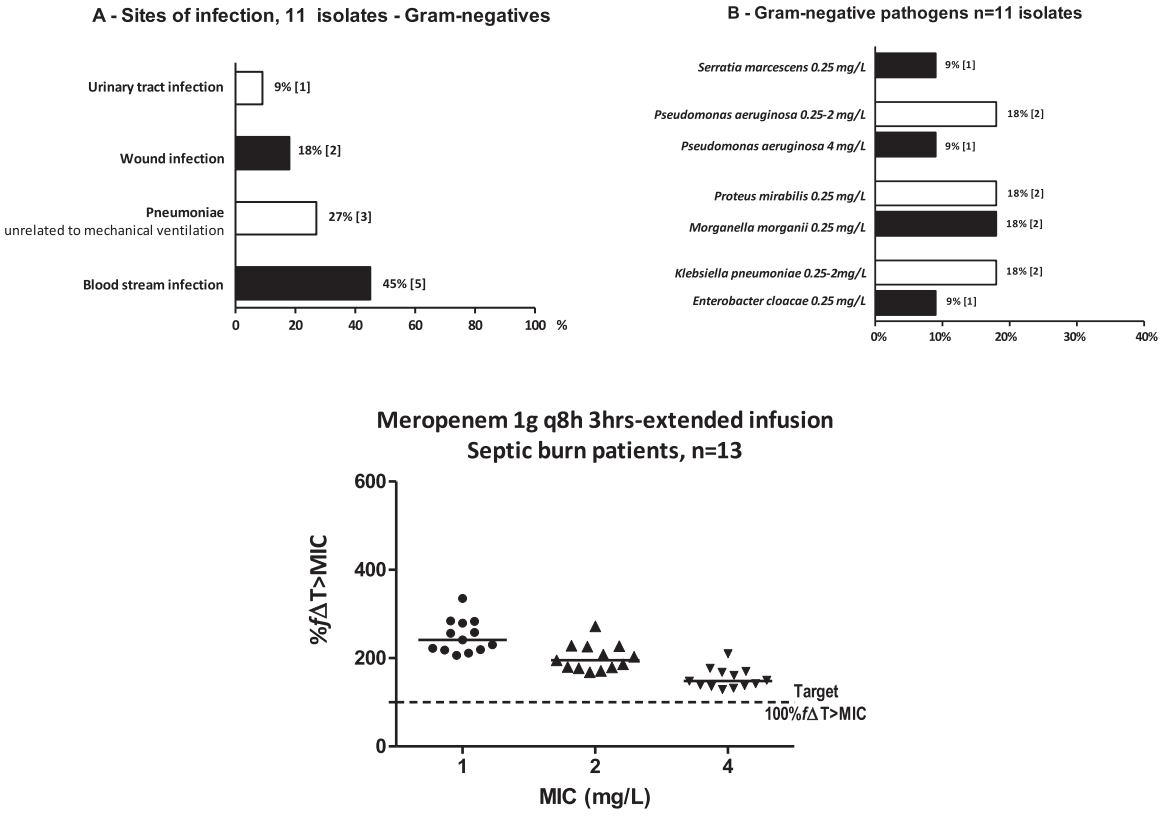

Figure: (abstract PAG-009)

PAG-010

Meropenem extended infusion versus intermittent infusion against nosocomial MIC 4 mg/L strains to guarantee drug effectiveness by PK/PD approach in burn patients at the earlier period of septic shock

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Background: Extended infusion of β-lactams can improve target attainment in critically ill patients. Rational of this study was to investigate whether a 3-hour extended infusion of meropenem achieves the therapeutic target against the most common nosocomial MIC > 2 mg/L strains in septic burn patients.

Methods: Burn patients at the earlier period of septic shock receiving meropenem 1 g q8 h were included and they were stratified in two groups: G1 - intermittent infusion (0.5 hr) and G2 - extended infusion (3 hr). Two blood samples were collected (2 mL/each) at the 3rd hr and at the 5th hr of the starting the infusion for drug serum measurement by liquid chromatography. The pharmacokinetic-pharmacodynamic (PK/PD) approach was performed to estimate the probability of target attainment based on the predictive index of drug effectiveness: 100%*f*T > MIC.

Results: We included 25 septic burn patients (7F/18M) receiving vasopressors, inhalation injury (20/25), 32 yrs, 70 kg, 45% total burn surface area, SAPS3 62, medians. Drug effectiveness was impacted due to different changes on pharmacokinetics as a consequence of duration of infusion. Colistin was required for 11 patients after A.baumannii isolated from blood cultures. With

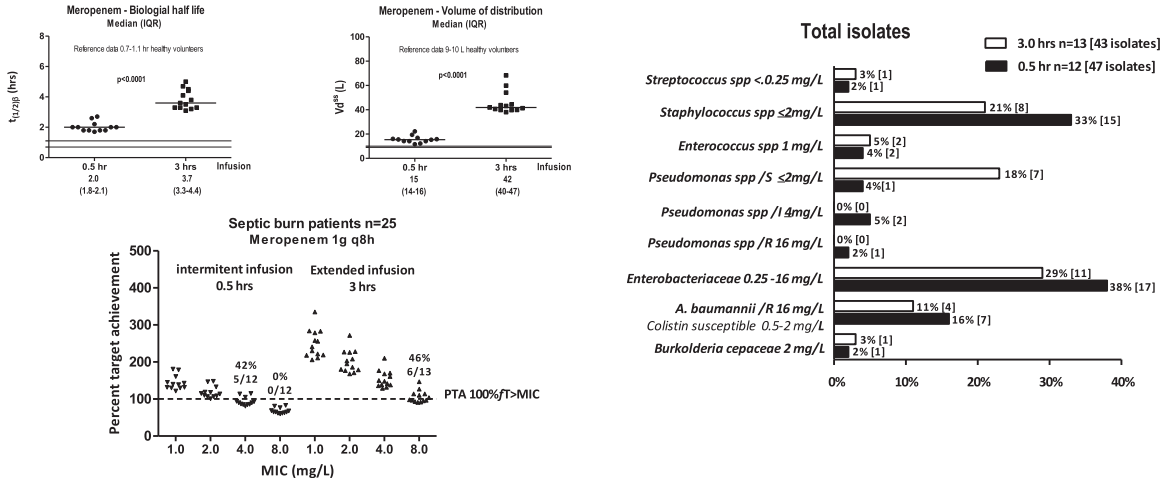

Figure: (abstract PAG-010)

3 h-infusion, the target was attained for all patients against of gram-negative nosocomial pathogens MIC 2–4 mg/L and up to MIC 8 mg/L in 46% of patients.

Conclusion: Superiority of meropenem therapy by 3 hr-extended infusion over 0.5 hr-intermittent infusion occurred as consequence of changes on pharmacokinetics. Extended infusion must be applied to optimize target attainment and to avoid the development of microbial resistance.

PAG-011

Vancomycin target attainment in critically ill septic pediatric burn *versus* non-burn patients against *Staphylococcus spp.*

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Background: Vancomycin initial dose regimen is recommended for critically ill pediatric patients with infections caused by gram-positive strains. We evaluate if dose adjustment at the earlier

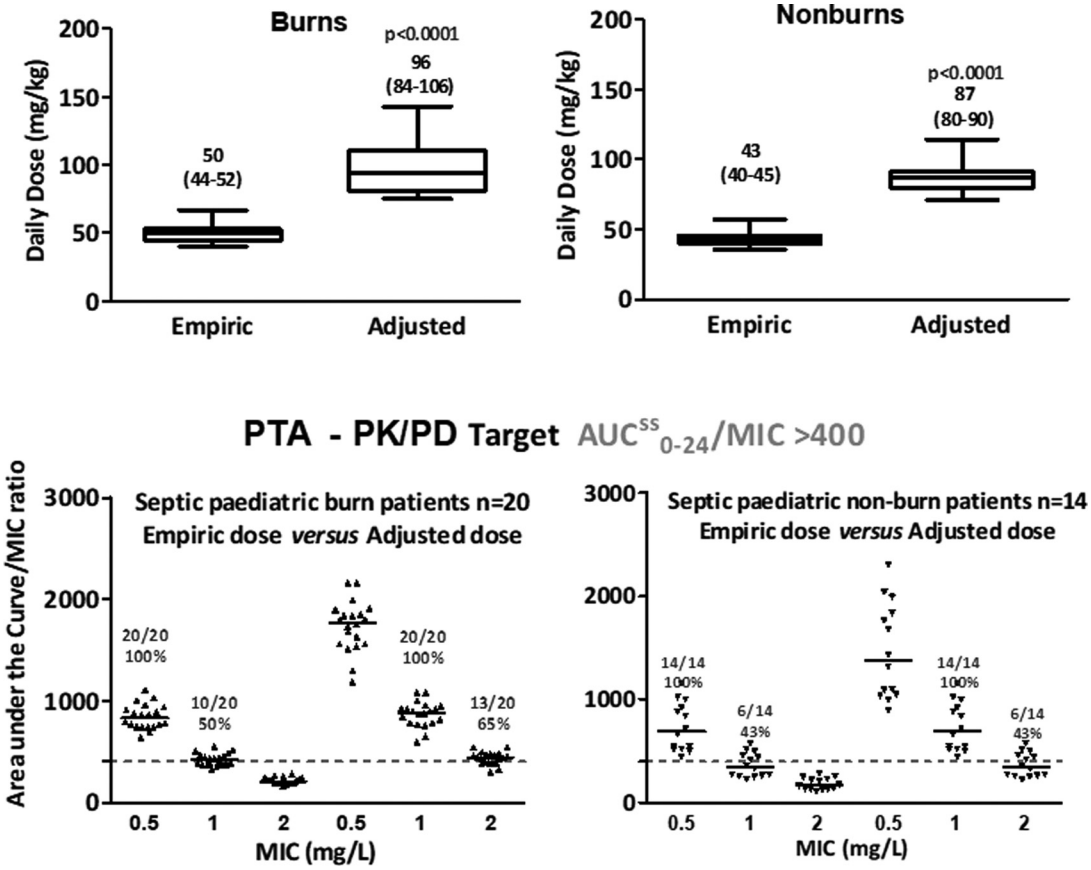

Figure: (abstract PAG-011)

period of septic shock must be done based on pharmacokinetics-pharmacodynamics (PK/PD) approach by comparison of burns with non-burns pediatric patients.
Methods: Patients receiving vancomycin were investigated after the empiric daily dose and after individualization of therapy. Therapy started with 40–60 mg/kg daily, one hour pump infusion, and the dose was adjusted if required based on PK/PD target: area under the curve/minimum inhibitory concentration (AUC^{ss}_{0-24}/MIC) >400. Blood was sampling at the 3rd hr and 5th hr of the starting of infusion, 2 mL/each. The one compartment open model was used to investigate pharmacokinetic parameters.
Results: We included 34 Septic pediatric patients (12F/20M) with preserved renal function; 20 burns and 14 non-burns; 5–10 yrs, 16–22 kg body weight (quartiles). Significant differences were found between the initial and individualized dose in both groups. Changes on pharmacokinetics occurred by increases on total body clearance and shortening half life in both groups when compared with healthy volunteer's data. After dose adjustment, the target was attained up to MIC 1 mg/L for all patients and it was extended against *Staphylococcus spp.* with MIC 2 mg/L in 65% of burn patients and in 43% of non-burns. Clinical cure occurred for all patients.
Conclusion: Since pharmacokinetics was altered at the earlier period of septic shock in ICU pediatric patients, the vancomycin dose must be adjusted soon to eradicate gram-positive susceptible strains.

PAG-012

Meropenem 3hrs-extended infusion improves effectiveness in critically ill burn patients at the earlier period of septic shock against *P. aeruginosa* intermediate susceptibility MIC 4–8 mg/L

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Background: Meropenem recommended dose with bolus infusion cannot achieve the target against nosocomial gram-negative strains with MIC > 2 mg/L. We aim to investigate meropenem effectiveness after 3hrs-extended infusion by application of pharmacokinetics-pharmacodynamics (PK/PD) approach in septic burn patients to avoid carbapenem resistance in *P. aeruginosa* strains.
Methods: Burn patients undergoing therapy of septic shock with meropenem 1 g q8h3h-infusion were considered. Blood was sampling (2 mL/each) at the 3rd and at the 5th of the starting of infusion. Drug serum measurements were done by liquid

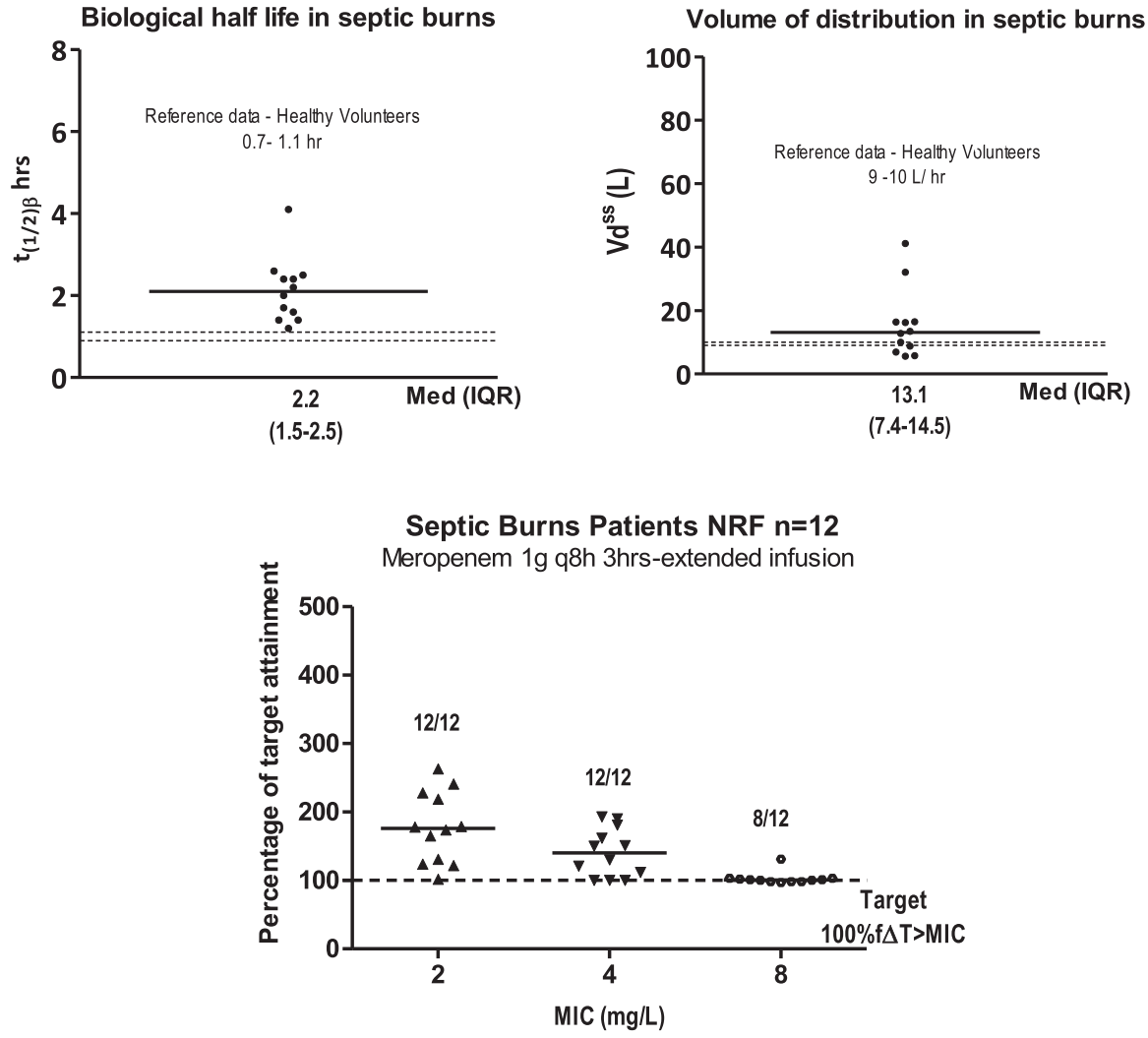

Figure: (abstract PAG-012)

chromatography mass spectrometry (LC-MS/MS). PK/PD target was considered based on the predictive index of effectiveness: 100% *f*T>MIC.

Results: Twelve critically ill burn patients (6M/6F) were included. The patients had: 31 (24–35) yrs, 72 (61–75) kg body weight, 32 (19–43) total burn surface area, SAPS3 57 (32–62), medians (IQR). Vasopressors were required for all of them. Pharmacokinetics of meropenem were altered in patients compared to healthy volunteers by increases on volume of distribution and on half-life. Clinical and microbiological cure occurred for all patients by eradication of pathogens up to MIC 4 mg/L. The target was also attained against *P. aeruginosa* isolates with MIC 8 mg/L in 75% of patients.

Conclusion: Burn patients with septic shock presented pharmacokinetic changes that impact meropenem target attainment. The 3 hrs-extended infusion must be applied to eradicate the pathogens, including intermediate susceptibility, to reach earlier the desired outcome.

PAG-013

Piperacillin/tazobactam effectiveness in septic burn patients requiring vasopressors by applying pharmacokinetics-pharmacodynamics approach

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Background: Piperacillin/tazobactam initial dose cannot achieve the target against nosocomial after intermittent infusion. Subject of study was to investigate piperacillin/tazobactam effectiveness with 3hrs-extended infusion based on pharmacokinetics-pharmacodynamics (PK/PD) approach in septic burn patients against intermediate susceptibility strains.

Methods: Burn patients undergoing therapy of septic shock with piperacillin/tazobactam 4.5 g every 8 hrs (5 patients) or every 6 hrs (11 patients) were included. Two blood samples were collected (2 mL/each) at the 3rd hr and at the 5th hr of starting the infusion. Drug serum measurements were done by liquid chromatography mass spectrometry (LC-MS/MS). PK/PD target was considered based on the predictive index of effectiveness: 100%*f*T>MIC.

Results: Characteristics of patients at admission were: 32 (24–41) yrs, 70 (62–75) kg body weight, 22 (14–37) % total burn surface area, SAPS3 62 (35–67), medians (IQR). Vasopressors were required in all of them. Pharmacokinetic changes occurred in the beta-lactam agent after the extended infusion over the intermittent infusion previously reported. Target was attained up to MIC 16 mg/L in those patients receiving 4.5 g q6 h at the initial therapy. Dose adjustment was required in 5/16 patients receiving 4.5 g q8 h and then clinical and microbiological cure occurred for all patients.

Conclusion: We have demonstrated the superiority of piperacillin/tazobactam 4.5 g q6 h over 4.5 g q8 h for burn patients in septic shock. Piperacillin serum monitoring should be done routinely to ensure eradication of *K. pneumonia* and *P. aeruginosa* up to MIC 16 mg/L.

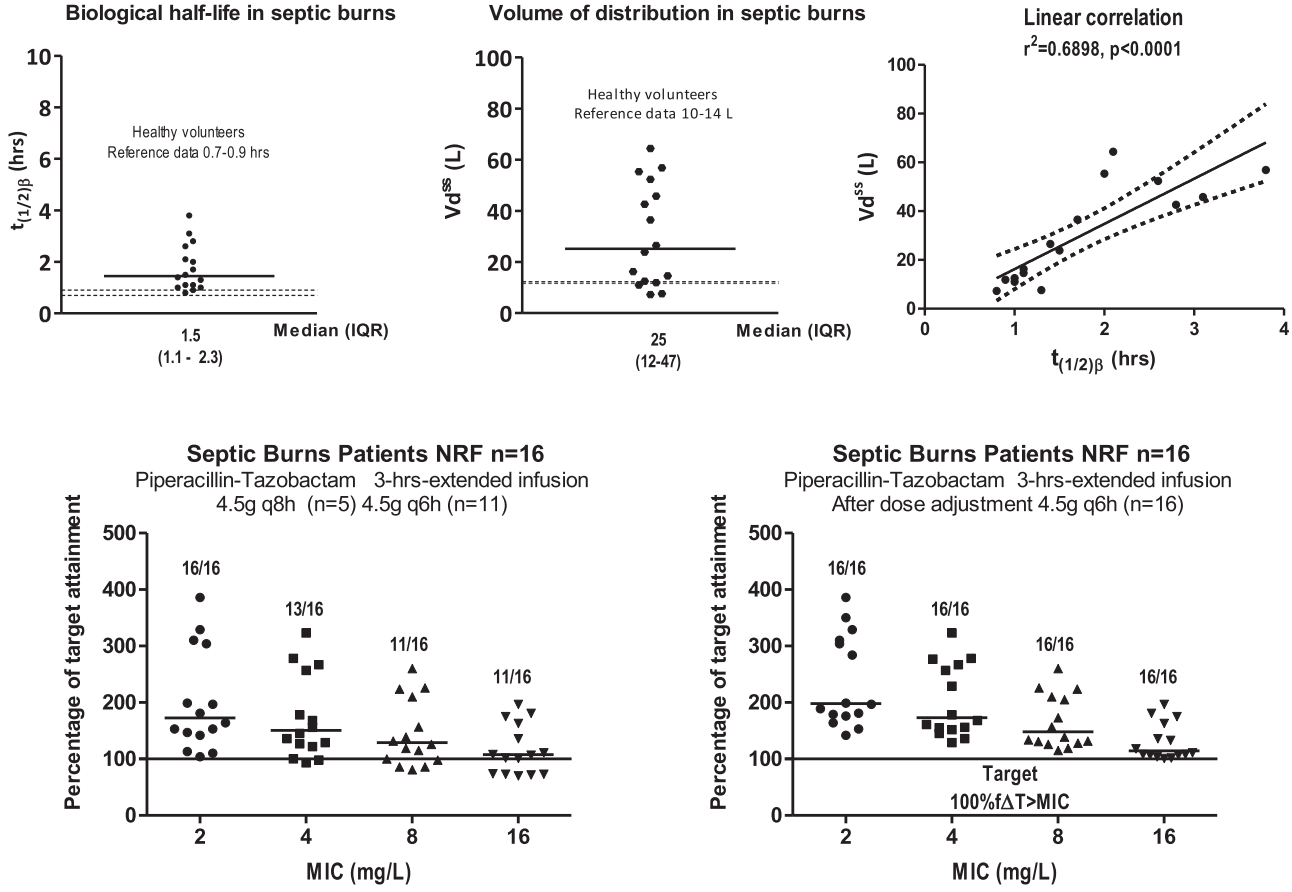

Figure: (abstract PAG-013)

PAG-014

Extended infusion improves meropenem and piperacillin/tazobactam effectiveness in septic burn patients with normal renal by applying pharmacokinetics-pharmacodynamics approach

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Background: Piperacillin/tazobactam and meropenem are largely prescribed to critically ill patients with nosocomial infections. We aim to investigate drug effectiveness after the 3hrs-extended infusion of both agents by pharmacokinetics-pharmacodynamics (PK/PD) approach in septic burn patients.
Methods: Patients undergoing therapy of septic shock were stratified in two groups: G1 – receiving meropenem 1 g q8 h and G2 – receiving piperacillin/tazobactam 4.5 g q6 h. Two blood samples were collected (2 mL/each) at the 3rd and at the 5th hours of starting the infusion. Drug serum measurements were done by liquid chromatography mass spectrometry (LC-MS/MS). PK/PD target was considered based on the predictive index of effectiveness: 100%*f*T>MIC.
Results: Twenty eight burn patients (18M/10F) at the earlier period of septic shock were included. The patients had (G1 vs G2): 31 vs 32 yrs, 72 vs 70 kg body weight, 32 vs 22% total burn surface area, medians. Vasopressors were required in all of them. Pharmacokinetic changes occurred for both beta-lactam agents after 3 h-infusion with increases on trough levels and consequent drug accumulation. Clinical and microbiological cure occurred by eradication of susceptible strains MIC 4 mg/L and *K. pneumoniae and P. aeruginosa* with intermediate susceptibility in meropenem therapy. Desired outcome was also reached in piperacillin therapy for all patients up to MIC 16 mg/L strains.
Conclusion: β-lactam3 hrs-extended infusion must be prescribed to critically ill septic patients to achieve clinical success and microbiological eradicationbased on PK/PD approach.

PAG-015

Phenotypic determination of phage susceptibility among multidrug-resistant bacteria isolated from clinical samples of patients of tertiary care center, Nepal

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Background: Emergence of multidrug-resistant (MDR) bacterial strains have become a global threat that has led to increased interest in therapeutic alternatives. Bacteriophages (BPs) have been studied as a therapeutic agent to treat the bacterial infections for around 100 years. The lytic BPs can lyse bacteria without attacking on mammalian cells. Thus, it is thought that BPs are significantly safer and better tolerated, and utilize the novel mechanisms of action to achieve antibacterial activity.
Methods: BPs were isolated from different environmental sources: river sites, ponds and sewages. Presence of phage was determined by the Double layer agar assay. Concentrations of phage were determined in Plaque forming unit per milliliter (PFU/mL) by Plaque assay and susceptibility test was done by observing their lytic effect on pre-identified MDR bacteria.
Results: A total of 73 BPs were obtained from 11 different sources, out of which 52 (71.2%) showed clear lysis. BPs recovered against specific MDR isolates were ΦEC-21.3%, ΦPS-17.3%, ΦKP-19.2%, ΦCF-19.2%, ΦPR-11.5% and ΦSA 11.5%. Majority of the isolated phages had lytic effect on their respective specific MDR bacteria with varying degree, mostly high efficacy (+++) showing high specificity. However, ΦCF showed minimum lytic effect even on *Citrobacter freundii*, indicating narrow spectrum. Phages specific for *Proteus* spp. i.e., ΦPR42 and ΦPR44 had wider spectrum of lytic effect on

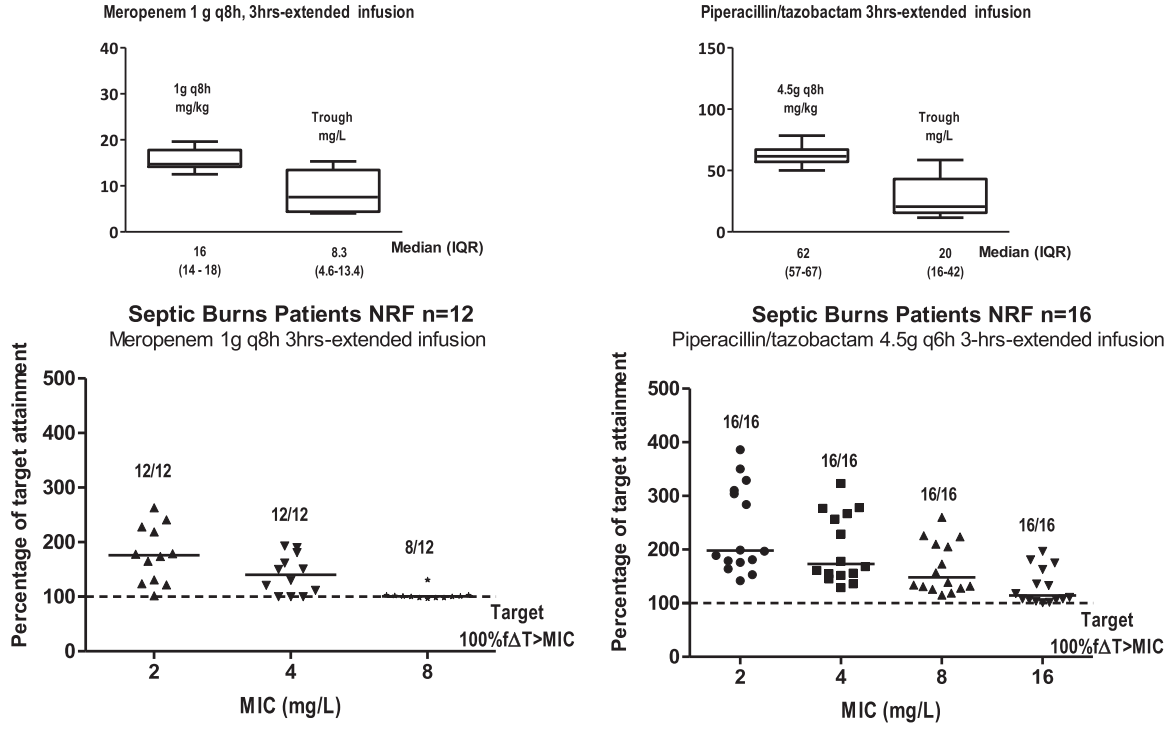

Figure: (abstract PAG-014)

majority of the MDR isolates. Overall, phages specific for Gram Negative Bacilli (GNB) and Gram-positive cocci (GPC) showed lytic effect predominantly on GNB and GPC respectively.
Conclusion: Phage therapy can be a promising alternative to antibacterial therapy for treatment of patients with severe MDR bacterial infections.

PAR-001

Co-occurrence of *cfr*-mediated linezolid resistance in sequence type (ST) 398 livestock-associated methicillin-resistant *Staphylococcus aureus* and coagulase-negative staphylococci (CoNS) isolated from a pig farm

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Background: Linezolid resistance mediated by the *cfr* gene, which confers multiresistant phenotypes to phenicols, lincosamides, oxazolidinones, pleuromultilins, and streptogramin A ($PhLOPS_A$), has emerged in *S. aureus*. However, despite the interspecies transferability of *cfr* gene, little or no attention has been paid to the occurrence of linezolid resistance in CoNS.
Methods: A total of 26 staphylococci were isolated from a pig farm, where a linezolid-resistant MRSA strain was previously identified. Antimicrobial susceptibility assays were performed and the presence of *cfr* and *fexA* genes was determined. Moreover, whole-genome sequencing (WGS) analyses were performed on *cfr*-positive linezolid-resistant *S. aureus* and CoNS strains.
Results: Linezolid resistance along with the $PhLOPS_A$ phenotypes was identified in 3 ST398 MRSA and 11 CoNS isolates. All the linezolid-resistant staphylococci carried both *cfr* and *fexA* genes for resistance to phenicols. Comparative whole genome analyses of the linezolid-resistant MRSA and CoNS strains revealed that the *cfr*-containing regions on a plasmid and/or transposons were conserved among MRSA, *S. epidermidis*, *S. pasteuri*, and *S. cohnii* by showing ≥99% nucleotide sequence identity.
Conclusion: These results suggest that ST398 LA-MRSA and CoNS may develop $PhLOPS_A$ resistance phenotype through intra- and inter-species acquisition of *cfr*-containing plasmids, which frequently co-carry additional resistance genes such as *fexA* and *erm* (C) genes.

PAR-002

Antimicrobial resistance profiles and molecular characteristics of extended-spectrum β-lactamase-producing *Escherichia coli* isolates from pigs in South Korea

Hyun-Ju Song[*], Dong Chan Moon, Soon-Seek Yoon, Suk-Kyung Lim. *Bacterial Disease Division, Animal and Plant Quarantine Agency*

Background: The widespread use of third-generation cephalosporins has led to the emergence and dissemination of extended-spectrum β-lactamase (ESBL)-producing *Enterobacteriaceae*. This study aimed to determine the susceptibility profiles of *E. coli* isolated from pigs and to investigate the molecular characteristics of identified ESBL-producing *E. coli*.
Methods: *E. coli* isolates from weaner (n = 99) and finisher (n = 74) pigs in South Korea (2017) were investigated by broth microdilution and molecular methods.
Results: *E. coli* isolates exhibited high (>60%) ampicillin, chloramphenicol, streptomycin, and sulfisoxazole resistance rate. About 76% of pig isolates were resistant to multiple antimicrobials, including those considered critically important for humans. The *qnrs* gene was detected in 12.7% of the isolates, predominantly from finishers. ESBL production was noted in eight isolates and the ESBL genes belonged to $bla_{CTX\text{-}M\text{-}14}$, $bla_{CTX\text{-}M\text{-}55}$, and $bla_{CTX\text{-}M\text{-}65}$. Notably, the $bla_{CTX\text{-}M\text{-}65}$ and *qnrS1* genes were found to be carried together in two isolates from finisher pigs. Phylogenetic analysis demonstrated that $bla_{CTX\text{-}M}$-carrying isolates belonged mainly to diverse subgroups including subgroups B2 and D. Conjugation confirmed the transferability of $bla_{CTX\text{-}M}$ genes, as well as non-β-lactam resistance traits from seven of $bla_{CTX\text{-}M}$-positive strains to a recipient *E. coli* J53. The $bla_{CTX\text{-}M}$ genes belonged to the IncI1α, IncFII, and IncHI2 plasmids. The ISECP, IS903, and orf477 elements were detected in the upstream or downstream regions. In addition, the majority of ESBL-producing isolates exhibited heterogeneous PFGE profiles.
Conclusion: This study showed that healthy pigs act as reservoirs of ESBL-producing *E. coli* that can potentially be transmitted to humans.

PAR-003

Resistance profiling and molecular characterization of methicillin-resistant *Staphylococcus pseudintermedius* isolated from dogs and cats

Su-Jeong Kim[*], Dong Chan Moon, Soon-Seek Yoon, Suk-Kyung Lim. *Bacterial Disease Division, Animal and Plant Quarantine Agency*

Background: Methicillin-resistant *Staphylococcus pseudintermedius* (MRSP) pose a threat to companion animals and human worldwide. This study examined the antimicrobial resistance profiles and molecular characteristics of MRSP isolated from dogs and cats in Korea.
Methods: Staphylococcal isolates were collected from skin/ear scrapping specimens of dogs and cats. Identification of *S. pseudintermedius* was performed using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry or Polymerase chain reaction (PCR). The broth microdilution and molecular methods were used to determine the susceptibility profiles and molecular characteristics of MRSP isolates.
Results: MRSP accounted for 37.5% (251/670) of the *S. pseudintermedius* isolates. The majority of MRSP isolates (96%) were multidrug resistant (MDR) and co-resistance to clindamycin, erythromycin, and marbofloxacin was noted in 41.8% of these isolates. PCR analysis detected *erm*(*B*), *mecA*, a*ph*(*3′*)-*IIIa*, and *aac(6′)-Ie-aph(2″)* genes in the majority (>94%) of the MDR-MRSP isolates that exhibited co-resistance to clindamycin, erythromycin, and marbofloxacin. We found amino acid substitutions in *gyrA* (Ser84Leu, Glu88Lys, and Glu88Gly) and *grlA* (Ser80Ile and Asp84Asn) genes. As well, we identified the co-existence of Ser84Leu (*gyrA*) and Ser80Ile (*grlA*) amino acid substitutions in most (91.4%) of the MDR-MRSP isolates. MLST analysis revealed 50 different sequence types, and 24 were novel. Furthermore, a pRE25-like element carrying the *erm*(*B*), *msrC*, *aphA(3′)-III*, *sat4*, and *aac(6′)-Ie-aph(2″)* genes, two copies of IS256, and an IS1182 element was noted in one of the MDR-MRSP strains.
Conclusion: These findings demonstrated that companion animals could be potential sources of genetically diverse and novel MDR-MRSP clones.

PAR-004

Molecular characteristics of extended-spectrum β-lactamase/AmpC-producing *Salmonella enterica* serovar Enteritidis isolated from chickens in South Korea

Jong Hoon Lee*, Dong Chan Moon, Soon-Seek Yoon, Suk-Kyung Lim. *Bacterial Disease Division, Animal and Plant Quarantine Agency*

Background: Global dissemination of non-typhoidal *Salmonella* producing extended-spectrum β-lactamase (ESBL) is a public health concern. This study examined molecular characteristics of *S.* Enteritidis isolates resistant to extended-spectrum cephalosporins (ESCs).
Methods: *S.* Enteritidis isolates were collected from fecal and carcass specimens of cattle, pigs, and chickens. Identification was performed using MALDI-TOF mass spectrometry or Polymerase chain reaction (PCR). The broth microdilution and molecular methods were used to determine the susceptibility profiles and molecular characteristics of ESBL-producing isolates.
Results: We obtained 237 *S.* Enteritidis isolates from fecal and carcasses samples of cattle, pigs, and chickens during 2010–2017, and observed high ESC-resistance (43%, 102/237); all of the resistant isolates were obtained from chickens. ESCs -resistant *S.* Enteritidis isolates (n = 102) showed significantly higher resistance rates to other antimicrobials. All ESC-resistant *S.* Enteritidis produced CTX-M-15-type ESBL (n = 102) and co-existence of $bla_{\text{CTX-M-15}}$ and $bla_{\text{CMY-2}}$-genes was noted in 21 isolates. ESC-resistant S. *Enteritidis* represented 11 pulsotypes, predominantly composed of type VI (31.4%) and III (29.4%). Conjugation confirmed the transferability of $bla_{\text{CTX-M-15}}$ genes, as well as other resistance markers in 20.6% (21/102) $bla_{\text{CTX-M-15}}$-positive strains to a recipient *E. coli* J53 strain. The conjugative plasmids carrying $bla_{\text{CTX-M-15}}$ and $bla_{\text{CMY-2}}$ genes predominantly belonged to ST2-IncHI2/FIIs. In addition, the ISECP and orf477 elements were detected in the upstream or downstream regions of most of the $bla_{\text{CTX-M-15}}$ and $bla_{\text{CMY-2}}$ carrying isolates.
Conclusion: Our results show a high prevalence of ESBL-producing S. *Enteritidis* in chickens.

PAR-005

Molecular characterization of extended-spectrum/plasmid-mediated AmpC β-lactamase-producing *Escherichia coli* isolated from companion animals in South Korea

Ji Hyun Choi*, Dong Chan Moon, Soon-Seek Yoon, Suk-Kyung Lim. *Bacterial Disease Division, Animal and Plant Quarantine Agency*

Introduction: The dissemination of extended-spectrum β-lactamase (ESBL)/plasmid-mediated AmpC β-lactamase (pAmPC)-producing isolates poses a serious risk to both animal and human health. Recently, the prevalence of *E. coli* resistant to third-generation cephalosporins has been increasing in companion animals in Korea. This study aimed to explore the molecular characteristics of ESBL/pAmpC-producing *E. coli* isolated from dogs and cats.
Methods: *E. coli* isolates from dogs (n = 699) and cats (n = 128) in Korea (2018 and 2019) were investigated by broth microdilution and molecular methods.
Results: Co-resistance to marbofloxacin, enrofloxacin and ceftiofur were noted in 11.1% (78/699) and 8.6% (11/128) of the isolates from dogs and cats, respectively. CTX-M-15-type ESBLs were detected in 62.9% (56/89) of these isolates, while the remaining (37.1%) isolates belonged to TEM-type ESBLs. The most common CTX-M types were CTX-M-14 (24.7%, 22/89) and CTX-M-15 (21.3%, 19/89). In addition, 43.8% (39/89) of the isolates belonged to TEM-type ESBLs, predominantly $bla_{\text{CMY-2}}$. A few isolates carried $bla_{\text{CTX-M-3}}$, $bla_{\text{CTX-M-55}}$, $bla_{\text{CTX-M-65}}$, and bla_{DHA} genes. Notably, 11 of the ESBL/pAmpC -producing isolates were found to co-harbor at least one plasmid-mediated quinolone resistance gene. All the ESBL/pAmpC-producing isolates harbored one or more-point mutations in the quinolone resistance determining region of *gyrA* and *parC*. Multilocus sequence typing demonstrated that the most prevalence sequence type (ST) was ST131 (18.0%, 16/89), followed by ST405 (12.4%, 11/89) and ST457 (9.9%, 9/89).
Conclusion: This study showed that companion animals act as reservoirs of ESBL/pAmpC-producing *E. coli* that can potentially be transmitted to humans.

PAR-006

Characterization of *NDM-5*-producing *Escherichia coli* isolates from dogs in Korea

Abraham Fikru Mechesso*, Suk-Kyung Lim, Soon-Seek Yoon, Dong Chan Moon. *Bacterial Disease Division, Animal and Plant Quarantine Agency, Republic of Korea*

Background: Carbapenems are critically useful antimicrobial agents that are reserved for the treatment of infections caused by multidrug-resistant Gram-negative bacteria. With the increasing use of carbapenems in clinical practice, the emergence of carbapenem-resistant pathogens poses a public health threat. This study aimed to determine the occurrence and molecular characteristics of carbapenem-resistant *E. coli* isolated from dogs and cats in Korea.
Methods: We collected 1835 *E. coli* isolates from healthy and diseased dogs and cats in seven provinces of South Korea in 2019 and 2020. Antimicrobial susceptibility was determined using the broth microdilution method. Genes conferring resistance to carbapenem were examined by PCR and sequencing. In addition, $bla_{\text{NDM-5}}$-carrying isolates were characterized using molecular techniques. Further, the genomic DNA was sequenced by the combined analysis of 20-kb PacBio SMRTbell and PacBio RS II.
Results: We identified five imipenem-resistant isolates carrying the $bla_{\text{NDM-5}}$ gene from diseased dogs. The isolates exhibited additional resistance to multiple antimicrobials, including aminoglycosides, fluoroquinolones, and third-generation cephalosporins. The $bla_{\text{NDM-5}}$ carrying isolates belonged to ST410 (n = 5) and ST70 (n = 1). The $bla_{\text{NDM-5}}$ gene was identified in the IncX3, IncFIIs, and IncN plasmids. It was also transferred to *E. coli* J53 recipient strain. The ST70 strain presented a unique pulsed-field gel electrophoresis pattern. The $bla_{\text{NDM-5}}$-carrying plasmid (CP049051) in this study was closely related to those previously reported in *E. coli* from humans in China and India. To the best of our knowledge, this is the first report of $bla_{\text{NDM-5}}$-carrying ST70 *E. coli* in South Korea.
Conclusion: Our findings support One Health approach is necessary to prevent the dissemination of this high-risk gene.

PAR-008

Methotrexate hinders the expression of *Drosomycin* induced via Toll/NF-KB pathway in both acute and chronic inflammation

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Background: Methotrexate (MTX) is an anti-folate metabolite that competitively targets and inhibits the DHFR enzyme thereby ameliorating the disease of rapid cell proliferation. Our prior publication showed the mitigating effects of MTX on the hyperactive JAK/STAT pathway. We observed that MTX also exhibited an effect on the antimicrobial peptide (AMP) expression in mutants of JAK/STAT pathway carrying blood tumors. With this

clue we extended to test MTXs efficacy on the production of AMP under the regulation of Toll/Dorsal pathway.
Methods: We studied the effects of MTX on *Toll/NF-kB*, and its downstream AMP targets (*Drosomycin* and *Metchinkowin*) in the hemolymph of wild type (controls), wasp infested (acute inflammation) and mutants of *Ubc9*$^{-/-}$ (chronic inflammation). Immunofluorescence assay and RT-qPCR were performed to determine the nuclear localization of dorsal in different immune tissues and to examine gene expression of different AMPs respectively.
Results: Toll pathway triggered due to wasp infestation was clearly inhibited by MTX displaying low penetrance and expressivity of the encapsulated bodies in host larva. Nuclear localization of NF-κB in the larvae was retained in the cytoplasm after MTX treatment. *Drosomycin* (*Drs*) showed reduction in its gene expression, while *Iκ-B* showed up-regulation after MTX treatment.
Conclusion: We deduce from our results that MTX treatment suppresses *Drs* expression, hematopoietic proliferation, and blood tumor formation. Our studies suggest that AMPs that are specific targets of Toll pathway such as *Drosomycin* and *Metchinkowin* can be the targets for various therapeutics. We can utilize the *Drosophila* model for understanding the impact of AMPs on hematopoiesis, blood tumor formation and immune regulation.

PAR-009
SETDB1 mutants are immune compromised with decreased AMP expression and hematopoietic defects
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Background: To ensure proper genome maintenance cells have to also ensure balanced epigenetic regulation. SETDB1 methylates Histone-3 at lysine-9 silencing target genes. SETDB1 in mice regulates non-hematopoietic genes in hematopoietic cells. Deregulation of various genes important for maintaining hematopoietic "stemness" and progenitor state leads to development of acute leukaemia. *SETDB1*$^{-/-}$ mutants exhibit hematopoietic defects in *Drosophila* larva. In these genetic backgrounds i.e. LOF of SETDB1 we observe not only abnormal haematopoiesis but also development of hematopoietic tumors.
Method: We performed microarray studies to determine differential gene expression changes in mutants of SETDB1 comparing them to their heterozygote siblings. We validated the microarray results using qRT-PCR experiments. We performed immunofluorescence to determine protein levels of genes affected.
Results: Upon studying the differential gene expression through microarray studies we found the downregulation of several antimicrobial peptide genes (AMP). We observed statistically significant differences in the expression of *Drosocin*, *Metchinkowin*, *Diptericin*, and *Attacin* in *SETDB1*$^{-/-}$ mutants compared to their heterozygote siblings. These results were corroborated with qRT-PCR studies and consistent results were observed.
Conclusion: AMPs are crucial in defending host against microbial infections. AMPs are gaining immense attention for their regulation in cancer progression and development and also for their anticancer behaviour. Since *Drosophila* is a compatible model to study human diseases it widely used as a disease therapeutic model. Hence, Drosophila provides an ideal platform to expose the unknown effects of AMPs and epigenetic mechanisms in hematopoiesis and hematopoietic tumors.

PBI-001
The epidemiology and clinical spectrum of melioidosis in a tertiary hospital in a north-eastern state of Malaysia: A three-year review
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Backgroud: Melioidosis seen commonly in tropical countries caused by the *Burkholderia pseudomallei which is a* facultative intracellular gram-negative bacterium. It is commonly seen in soil and fresh water source which spreads via direct contact both to humans and animals. Transmission occurs via percutaneous inoculation mainly and lung infection after percutaneous infection been documented, which is attributed to hematogenous spread. The incubation period is from 1 to 21 days and acute disease defined as symptoms less than two months while chronic disease if symptoms persisting for longer than two months.
Method: This is retrospective study of 98 adult patients who admitted to tertiary care hospital [Hospital Raja Perempuan Zainab II (HRPZ II), Kelantan State Hospital, Malaysia] in whom *Burkholderia pseudomallei* isolated for period of 3 years (1st January 2018 to 31st December 2020).
Results: Higher incidence noted among those more than 50 years old which is 55 cases (56%), Main isolates were from blood which is 75 cases (76.5%) and followed by pus 14 cases (14.3%). Patient with diabetes mellitus was predisposed for infection where 73 cases (74.5%) was recorded. Overall mortality was 31 cases (31.6%) and higher incidence associated with diabetes mellitus patients which is 22 cases (30.1%). Multiple complications been recorded including 36 cases of pneumonia (36.7%), 40 cases of bacteremia (40.8%) and 39 cases of septicemic shock (39.8%).
Conclusion: Mortality was high among elderly male population especially with underlying diabetes mellitus and those progressed to septicemic shock (66.7%), High clinical suspicion advocated especially among those high risk population with appropriate sample collection which can lead us to prompt early initiation of treatment and to avoid undesirable patient outcome.

PBI-002
Clinical characteristics and prediction of poor outcome in *Clostridium innocuum* infection: A Case-Control study
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Background: Recent evidence suggested that *Clostridium innocuum* could cause gastrointestinal disease indistinguishable from *Clostridioides difficile* (CD) infection (CDI). More importantly, *C. innocuum* is intrinsically resistant to vancomycin.
Methods: A retrospective case-control study involving 152 *C. innocuum*-infected patients treated at a medical center from 2014 to 2019 was conducted. All bacterial isolates were identified using MALDI-TOF MS Biotyper. Age-matched cases with CDI were selected as the controls.
Results: The study enrolled 456 patients (152:304 matched pairs). Baseline characteristics such as age, gender, and Charlson's comorbidity score were similar between the two groups. *C. innocuum* (CI) group tended to present with more extra-intestinal

clostridial infection (EICI) (36.8% *vs* 8.2%, $P < 0.001$) and gastrointestinal tract-related complications, including ileus, bowel perforation, sepsis and shock (26.3% *vs* 11.2%, $P < 0.001$), than the CD group. The 30-day mortality and the overall mortality rate in the CI group was 14.5% and 23.0%, respectively. Chronic kidney disease (odds ratio [OR] 8.55; 95% CI, 2.57 to 28.42, $P < 0.001$), solid tumor (OR 3.46; 95% CI, 1.00 to 12.00, $P = 0.051$), ICU admission (OR 7.27; 95% CI, 2.41 to 21.94, $P < 0.001$) and shock status (odds ratio 7.99; 95% CI, 2.35–27.21, $P < 0.001$) were four independent risk factors for both in patients with *C. innocuum* infection.
Conclusions: *C. innocuum* is an important pathogen causing EICI and gastrointestinal infection with the risk of severe complications. In patients with symptoms typical of CDI but negative antigen and toxin tests and not responding to vancomycin treatment, *C. innocuum* should be considered.

PBI-003

Don't bring home that bacon: a report of two simultaneous cases of *Streptococcus suis* meningitis

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Background: *Streptococcus suis (S. suis)* is an emerging zoonotic pathogen known to cause severe infection in people who have close contact with infected pigs and pork-derived products. To date, despite a worldwide estimate of >1600 cases of *S. suis* infection, predominantly in Southeast Asia, there remains no available local data of the total distribution of reported clinical *S. suis* human infections in the Philippines.
We report two simultaneously documented *S. suis* meningitis with associated sequelae of bilateral hearing loss, through a unique case series of a husband and wife, presenting with fever and neurologic symptoms after consumption of an infected pork-derived product.
Methods: We obtained the medical records of two Filipino patients whose cerebrospinal fluid (CSF) and blood cultures tested positive for *S. suis*.
Results: Both were healthy individuals who had high grade fever associated with headache, neck rigidity and hearing loss a week after consuming grilled pork at a local restaurant. Cranial MRI of both patients showed leptomeningeal enhancement suggestive of meningitis. Blood cultures and CSF samples of both patients isolated *S. suis* through PCR. They were given high dose Penicillin G and dexamethasone which resolved the symptoms. On follow-up, residual hearing loss remained and both were advised ENT work-up.
Conclusion: *S. suis*, an emerging pathogen, can cause significant morbidity through bacteremia, meningitis, and persistent hearing loss warranting prompt intervention to avoid worsening complications. Because human infections are mostly seen in pork-consuming countries such as the Philippines, the distribution of *S. suis* needs to be fully elucidated through better diagnostics and identification methods. Health authorities, clinicians and at-risk groups must be aware of the disease risk posed to better save lives.

PBI-004

Novel broad-spectrum peptide therapy reverses respiratory infections with multidrug-resistant gram-negative bacteria

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Background: Respiratory infections caused by biofilm producing multidrug-resistant (MDR) *Pseudomonas aeruginosa* and *Acinetobacter baumannii* affect hundreds of millions of people globally.
Objective and Methods: Activity of 15 novel polycationic peptide candidates were evaluated against 450 MDR clinical isolates of *P. aeruginosa*, and *A. baumannii* via a novel high-throughput assay. Further investigated its synergistic activity with antibiotics covering all major classes. The ability of candidate peptides to eliminate acute and chronic biofilm lung infections were finally assessed using *in vivo* mouse model.
Results: Two peptides were bactericidal against MDR *P. aeruginosa,* and *A. baumannii* at low concentrations (4–16 μg/ml). CDP101was the most potent peptide, effectively restorated bacterial sensitivity to colistin (0.5 μg/ml) amikacin (2 μg/ml), tobramycin (2 μg/ml), imipenem (2 μg/ml) and ciprofloxacin (1 μg/ml). CDP101 was well tolerated to trypsin/pepsin/papain (20 mg kg^{-1}) at 37°C for 12 h. Single inhale dose of CDP101 induced >90% bio-volume/bacterial reduction in mouse airway and >97% reduction in combination with antibiotics.
Conclusion: Our findings provide novel therapeutic option using broad-spectrum peptide adjuvants in combination existing antibiotics on MDR *P. aeruginosa,* and *A. baumanni*i.

PBI-005

Novel subtypes and multiple transfer units of *tmexCD-toprJ* gene clusters were identified in clinical carbapenem-resistant *E. cloacae* and *K. oxytoca*

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Background: Tigecycline is the last-resort antibiotics used to treat lethal infections with carbapenem-resistant *Enterobacteriaceae*, and plasmid-borne tigecycline resistance *tmexCD-toprJ* gene clusters rendered tigecycline ineffective in clinical treatment.
Methods: Herein, five non-duplicate isolates of different species were isolated from patients across China during November 2018 to June 2019, which carrying the *tmexCD-toprJ* gene clusters or its novel subtypes. The whole genome sequences were performed on the Illumina and Nanopore platform. The phylogenetic tree was constructed using a data set of 77 sequences carrying *tmexCD-toprJ* gene cluster, 72 of which were downloaded from NCBI with blastn identity cutoff of 95%.
Results: In total, six different transfer units and two novel subtypes (*tmexC1D1.2-toprJ1* and *tmexC2D2.2-toprJ2*) of the *tmexCD-toprJ* gene clusters were detected in this study. Among the six transfer units, three are mediated by *IS*26, and the rest are presumed to be mediated by *Tn*5393, hypothetical integrases (*xerD-hp clusters-umuC*-integrases-*tnfxB2-tmexC2D2-toprJ2-umuC*) and hypothetical units composed of *hp-hp-hp-tnfxB2-tmexC2D2.2-toprJ2-*Δ*Tn*5393-*Tn*6292. Moreover, two *tmexCD-toprJ* gene clusters were located on

the same plasmids with bla_{NDM} in five isolates. Phylogenetic analysis revealed that the *tmexCD-toprJ* gene clusters may originated in the *Pseudomonas* spp., and mainly in *Pseudomonas* spp. and *Klebsiella* spp. (64/77). Most of the *tmexCD-toprJ* gene clusters in *Enterobacteriaceae* are located on plasmids, indicating that the gene clusters has a higher interspecies transfer risk after transferred to *Enterobacteriacea*e.

Conclusion: In short, this is the first time that the *tmexCD-toprJ* gene clusters has been isolated from *Enterobacter cloacae* and *Klebsiella oxytoca* and the multiple transfer units of *tmexCD-toprJ* gene clusters deserves our vigilant.

Keywords: plasmids, mobile genetic elements, tigecycline resistance, *tmexCD-toprJ* gene clusters.

PBI-006

Invasive Elizabethkingia meningoseptica infections – a descriptive study from South India

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Background: Elizabethkingia meningoseptica is a multi-drug-resistant organism associated with high mortality and morbidity in newborns and immunocompromised patients. Despite ubiquitous presence in soil, water and hospital settings, it is probably underreported or misinterpreted as pseudomonas species in many of the laboratories by conventional methods. Though it is of low virulence, can be life threatening in certain hosts. Prolonged hospital stay and empirical antibiotics and central line catheter are some of the established independent risk factors.

Method: This was a retrospective 2.5-year descriptive study conducted between January 2019 and March 2021 at a tertiary care teaching medical hospital in South India. Individuals of all ages and sex with a positive culture for E. meningoseptica from any sterile site were included. Cases were identified from the hospital laboratory database. Patients' medical records were reviewed and the following information was extracted: age, gender, length of hospital stay prior to sterile site infection, clinical diagnosis, immunological status, presence of central venous access and removal (if applicable), antibiotic susceptibility, choice and duration of antibiotic treatment, clinical outcome, microbiological cure (defined as two successive negative blood cultures) and the ward or unit the patient was staying in at the time of laboratory confirmation. The institutional ethics committee approval was obtained prior to analysis and publication.

Blood and other sterile body fluid cultures were performed by BACTEC FX40 automated blood culture system. We used the Vitek2 compact (bioMérieux,) system to identify E. meningoseptica. Antimicrobial susceptibility test interpretation was performed using Clinical and Laboratory Standards Institute (CLSI) criteria for 'Pseudomonas species.".

Results: During the study period, there were 8 patients with E. meningoseptica (blood-6, pleural fluid and blood-1, CAPD fluid-1). Table 1 shows the clinical characteristics of these patients. Their ages ranged from 45 days to 84 years, with a median age of 66 years

Table 1: (abstract PBI-006): Clinical characteristics of the patients

	1	2	3	4	5	6	7	8
Age	79	40	64	75	1	68	22	84
Gender	M	M	M	F	M	M	M	M
Culture positive	November 2018	December 2018	January 2019	July 2019	September 2019	December 2019	January 2021	February 2021
Diagnosis	Metabolic encephalopathy	Acute cerebrovascular accident with left hemiparesis	Right foot 1st metatarsal osteomyelitis/ triple vessel disease/ bilateral pleural effusion	Acute pulmonary thromboembolism/ Pneumonitis	Extreme preterm baby	Diabetic foot ulcer with cellulitis-	CAPD peritonitis	Large bowel obstruction with sigmoid volvulus, chronic kidney disease/septic shock
Recent hospitalization and procedures	Yes, below knee amputation done 2 weeks back	Right frontotemporoparietal decompressive craniectomy and tracheostomy done a week back	Wound debridement and removal of remnant bone done a week back	Laparoscopy assisted vaginal hysterectomy with Bilateral salpingooopherectomy done a week back		Left below knee amputation		Emergency laparotomy with sigmoid colon resection and descending colostomy done 2 weeks back and Blood culture-Kleb. Pneumoniae (CRE)
ICU stay	Speciality ICU	Neurology ICU	Speciality stepdown ICU	No, Medical ward	Neonatal ICU	Respiiratory ICU	No, Surgery ward	Surgical ICU
Duration of hospitalisation	10 days	40 days	25 days	2 days	102 days	26 days	14 days	41 days
Diabetes	Yes	Yes	Yes	No	No	Yes	Yes	No
Mechanical ventilation	No	Yes	No	No	Yes	Yes	Yes	Yes
Central Line	No	Yes	No	No	Yes	Yes	No	Yes
No of ICU days prior to bacteremia	6	9	10 days	No	48 days	22 days	No	21
Renal failure	No	No	Yes	No	No	Yes	Yes	Yes
Treatment	Ciprofloxacin	Meropenem, Piptaz	Piptaz, Ciprofloxacin	Meropenem, Levofloxacin	Piptaz, Meropenem	Ciprofloxacin, Cotrimoxazole	Intraperitoneal ciprofloxacin for	Piptaz, Meropenem
Duration of therapy	9 days	9 days	8 days	5 days	10 days	7 days	14 days	8 days
Microbiological clearance	Yes	Yes	No	Yes	Yes	No	Yes	No
Outcome	Survived	Survived	AMA	Survived	Survived	AMA	Survived	Died

AMA-Against medical advice.

with male preponderance (7 out of 8 patients). All but one was bacteraemic. Five patients had recent hospitalization with surgeries performed. Newborn was extreme preterm twin baby with prior blood cultures at various periods growing Escherichia coli (Carbapenem resistant and sensitive only to colistin), Sphingomonas paucimobilis, Multidrug resistant Acinetobacter baumanii sensitive only to colistin. Cocktails of antibiotics with colistin could have predisposed to Elizabethkingia meningoseptica infection. Five patients had diabetes mellitus and four had renal failure. Five were mechanically ventilated and three were on central line.

The average length of stay in ICU prior to developing E. meningoseptica bacteraemia was (range 6 to 48 days; median 9.5 days). Six patients acquired E. meningoseptica bacteraemia in the intensive care unit (ICU), while two patients each from general ward and dialysis unit. All cases occurred sporadically, with no outbreaks or clusters of infection. All isolates demonstrated 100% susceptibility to minocycline, and variable susceptibility topiperacillin tazobactam (2/8) trimethoprim/sulfamethoxazole (3/8) and fluoroquinolones (ciprofloxacin 4/8, levofloxacin 4/8). All patients were treated with combination antibiotics. Ciprofloxacin with piperacillin tazobactam was the most common antibiotic combination followed by piperacillin/tazobactam with a fluroquinolone. Six patients including a newborn in this study survived. Outcome of two patients was not known as they were discharged against medical advice due to financial constraints. Six patients who survived achieved microbiological clearance.

We identified some limitations in our study. It was a retrospective descriptive study, with a small number of patients included. Vitek 2 Automated Identification System (bioMérieux) contain only a portion of Elizabethkingia species in their reference databases. The concordances of species identification between these machines and 16S rRNA gene sequencing were only 24.5%–26.5%[1]. Similar to the report of Lau et al, E. meningoseptica could be accurately identified by Vitek 2, but almost all E. anophelis species were misidentified as E. meningoseptica by Vitek 2.[2] In the current study, there is a possibility that species identification could have been wrong and confirmation with 16SrRNA sequencing was not performed.

Conclusion: *E. meningoseptica,* is an important emerging pathogen associated with healthcare associated infection. Future studies with randomized controlled trials of various combination therapies could be considered to evaluate efficacy.

PBI-007

Binary toxin-producing *Clostridioides difficile* shows diverse multilocus sequence typing (MLST) clade and types in Korea

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Background: Binary toxin has been supposed to contribute to a severity in *Clostridioides difficile* infection (CDI) since the outbreak of ribotype 027 (ST1 in clade 2) in North America and ribotype 078 (ST11 in clade 5) in Europe. The aim of this study is to investigate distribution and change of multilocus sequence typing (MLST) types of *C. difficile* strains producing binary toxins over 10 years in Korea.

Materials and methods: Through 2009 to 2018, all isolates of *C. difficile* were collected from a tertiary hospital in Korea. Multiplex PCR for toxin genes was performed and binary toxin producing strains were selected. MLST typing was performed for the strains.

Results: A total of 58 *C. difficile* isolate possessed binary toxin genes. Annual number of binary toxin-producing isolates ranged from 1 to 12. MLST typing was performed with clade classification. Among 58 binary positive strains, 13 belonged to clade 2 (22.4%), 31 to clade 3 (53.4%), 12 to clade 5 (20.7%) and 2 to unknown clade (3.4%). Thirteen STs were identified among 58 isolates, and ST5 (14, 24.1%), ST11 (11, 19%), ST221 (10, 17.2%), ST201 (7, 12.1%) and ST1 (5, 8.6%) were popular strains. ST11 strains looked to increase since 2011, and 3 of 5 binary producing strains in 2018 were ST11. On the contrary, ST5 was most commonly found ST in 2009, but decreased since 2013. ST1 showed similar annual incidence since first identification in 2011.

Binary positive strains of clade 2 contains the most diverse STs: ST1 (ribotype 027), 5 isolates; ST192, 3 isolates; ST67, 97, 130, 232, 371, each 1 isolate. Clade 3 was composed with 3 STs: ST5, 14 isolates; ST201, 7 isolates; ST221, 10 isolates. Among the isolates of clade 5, ST11 (ribotype 078) was the most popular (11 isolates) and one ST415 strain was found. Two ST122 strains which was not known for clade were identified in 2014.

Conclusions: MLST of binary toxin-producing *C. difficile* showed a diverse distribution of ST and clades in Korea.

PBI-008

Efficacy of teicoplanin for bloodstream infection caused by *Enterococcus faecium*: a post-hoc analysis of a nationwide surveillance

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Background/Aims: Vancomycin and teicoplanin are both glycopeptides with activity against *Enterococcus faecium*. However, information regarding the clinical efficacy of teicoplanin is limited. This study compared the therapeutic efficacy of teicoplanin and vancomycin in *E. faecium* bacteremia.

Methods: Patients with bloodstream infections have been identified prospectively from Jul 2015 through Dec 2016 in 14 hospitals as a part of a multicenter nationwide surveillance. Patients with *E. faecium* monomicrobial bacteremia were selected, and the medical records of the patients were reviewed for demographic, clinical, microbiologic characteristics and patient outcome. Teicoplanin and vancomycin groups were defined as the patients who were treated with either agent for ≥48 hours. Primary outcome was 30-day all-cause in-hospital mortality. Cox proportional hazard model with inverse probability weighting was used to account for the imbalance in baseline characteristics between two groups.

Result: Among 97 patients identified with *E. faecium* bacteremia, 33 (34%) was treated with teicoplanin and 64 (66%) with vancomycin. There were no significant differences in 30-day in-hospital mortality (18.2% vs. 26.6%, P = 0.358), 7-day mortality (6.1% vs. 15.6%, P = 0.212), and infection attributable mortality (9.1% vs. 15.6%, P = 0.533). Multivariable analysis also showed that the use of teicoplanin was not significantly associated with mortality (aOR, 0.62; 95% confidence interval [95% CI], 0.13–2.95; P = 0.555).

Conclusion: No significant difference in clinical outcome was observed between the treatment with teicoplanin and vancomycin for *E. faecium* bacteremia. Teicoplanin could be a useful alternative to vancomycin.

PBI-009

Septic pelvic thrombophlebitis: A "pain in the back"

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Background: Postpartum fever is a common obstetric complication. Septic pelvic thrombophlebitis (SPT) is an uncommon puerperal complication typically presenting with fever and abdominal pain, within one week of caesarean section. Here we describe a patient with SPT who presented with fever and flank pain.

Case Description: 23-year-old G1P1 healthy female who was nine days post-partum, presented with a four-day history of fevers, rigors, myalgias, lower back and left flank pain. She was febrile, tachycardic and with lower abdominal and left costovertebral angle tenderness. Urinalysis revealed leukocyturia and hematuria. She was started on ceftriaxone and clindamycin and later switched to piperacillin-tazobactam and vancomycin. Still, she persisted with daily fevers and pain for seven days. A Computerized Tomography demonstrated left salpingitis, thrombosis of the left renal and left gonadal veins and left renal wedge-shaped cortical infarction. Final cultures grew Dialister micraerophilus. Piperacillin-tazobactam was switched to ampicillin-sulbactam with anticoagulation. After two days, her abdominal pain resolved.

Discussion: Postpartum fever is concerning for surgical site infection, mastitis, or endometritis; However, this patient's lower abdominal and costovertebral angle tenderness suggested pyelonephritis. Her urine had no growth, and fever and pain did not improve on antibiotics. This prompted further imaging which confirmed SPT and renal infarction, explaining her pain. Blood cultures grew Dialister micraerophilus, an anaerobe found in gynecological tract samples. Dialister species have shown decreased susceptibility to piperacillin and better response to ampicillin sulbactam.

Conclusion: Ultimately, this case was a unique presentation of postpartum fever and abdominal pain, utilizing a multidisciplinary team.

PBI-010

Clinical spectrum of extended spectrum β-lactamase producing Enterobacteriaceae in a tertiary care hospital

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Background: Enterobacteriaceae family includes *Escherichia coli* (*E. coli)* and *Klebsiella pneumoniae. With growing usage of antibiotics these organisms develop adapting resistance mechanism by production of* Extended Spectrum Beta-Lactamase (ESBL) enzyme that breaks down the commonly used antibiotics. This complicates therapy and limit treatment options. Here we describe clinical spectrum of ESBL producing Enterobacteriaceae in a tertiary hospital.

Method: This was retrospective study of 108 adult patients admitted to general medical wards and Intensive Care Unit (ICU) Hospital Raja Perempuan Zainab II with ESBL producing Enterobacteriaceae isolated for a period of 6 months from 1st January 2020 to 30th June 2020.

Results: Majority was more than 50 years old which 78 cases (72%). Main isolates were from blood which 38 cases (35.1%) and tracheal aspirate 30 cases (27.8%); more than half were Klebsiella Pneumonia 59 cases (54.6%) Overall mortality rate was 21.3%. Higher mortality was seen in infections caused by Klebsiella Pneumonia 30.5% as compared to E Coli 10.2%. Mortality rate was also higher in older age group more than 70 years old (26.3%). Chronic kidney disease (40%) and diabetes mellitus (36.1%) were main contributors associated with highest number of deaths. 53 cases (49%) were treated with carbapenem including Meropenem and ertapenem. 32 cases (29.6%) was on carbapenem sparing antibiotic like piperacillin/tazobactam and cefepime. Mortality was highest among those treated with ertapenem 12 (52%).

Conclusion: Mortality was high in elderly age group and those with comorbidites of diabetes mellitus and chronic kidney disease Carbapenems remain the drugs of choice for infections caused by ESBL-producing organism however fourth generation cephalosporins (cefepime) and beta lactam/b lactamase inhibitor (piperacillin/tazobactam) can be therapeutic alternatives for mild-to-moderate infections.

PBI-011

Hospital acquired pneumonia: Microbial pathogens and antibiotic resistance trend

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Background: The microbial agents causing hospital acquired pneumonia are not only bacterial and fungal but also non-culture pathogens such as atypical bacteria and viruses. Therefore, the real-time PCR solution must be used in order to detect all of the pathogenic microorganism presented in the sputum specimens taken from the patients.

Aims of the study: Analysis of the real-time PCR results from the examination of the sputum samples taken from patients with pneumonia hospitalized at the ICU of the hospitals that were sent to the laboratory to detect the microbial pathogens existed in the specimens.

Objects and methods: The objects were the sputum samples taken from patients with pneumonia hospitalized at the ICU of the hospitals and sent to the laboratory for real-time PCR testing to detect 72 possible microbial pathogens including 7 community bacteria, 7 atypical bacteria, 21 hospital bacteria, 19 viral and 17 fungal pathogens. This test is done in the laboratory during the last 6 months of 2019. The study method is retrospective. In addition, in order to understand the situation and the trend of the antibiotic resistance of the major bacterial pathogens, the study also included a review of the hospital acquired pneumonia cases who were hospitalized at the ICU of Nguyen Tri Phuong Hospital during 4 years from 2016 to 2019.

Results: There were 158 cases of adult and 240 cases of children with hospital acquired pneumonia (HAP) were collected for analyzing of the real-time PCR results. The results showed that in adult with HAP, there were 4 major bacterial pathogens detected, that were: A. baumannii (28.5%), K. pneumoniae (27.9%), S. aureus (12.7%) and P. aeruginosa (12%). In addition, there was a significant ratio of the virus detected at 46.84%, of which CMV was predominant (29.75%). In children with HAP, A. baumannii was also the leading bacterial pathogen (20.0%), K. pneumoniae (8.75%) and S. aureus (6.25%) followed; P. aeruginosa is detected with very low ratio, only 1.25%. The study also noted a high rate of detecting viral agents (72.92%) with CMV (37.5%) and EBV (10.83%) in children with HAP. Not only that, community bacteria can still be detected at up to 27.08% in cases of HAP children. The analysis of the situation and the trend of the antibiotic resistance also shows with a worrying signal, that is, a very high rate of Gram [-] rod pathogens were highly resistant to Imipenem: A. baumannii (97.7%), P. aeruginosa (52.6%) and K. pneumoniae (43.9%); At the same time, the trend of increasing MRSA rate was also detected.

Conclusions: In order to fully know the spectrum of microorganisms causing hospital acquired pneumonia, the use of real-time PCR solution in microbiological examination of the sputum samples is necessary. Real-time PCR results can be delivered to physicians very early in treatment so that physicians can adjust the appropriate antibiotic therapy by understanding the situation and tendency to resist key antibiotics. This work also provides information on antibiotic resistance and hopefully this is the useful information.

Keywords: Hospital acquired pneumonia; Multiplex real-time PCR; Antibiotic resistance.

PBI-012

Prevalence of Extended Spectrum Beta Lactamase (ESBL) producers among *Escherichia coli* from various clinical isolates

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Abstract: Broad spectrum antimicrobials are widely used for empirically treating infections. In a clinical setting i one of the frequently diagnosed infectious agent is *Escherichia coli*. Multidrug resistant *Escherichia coli* with extended-spectrum β-lactamase (ESBL) are adversely affecting the therapeutic management. (ESBLs) producing pathogens exhibit resistance not only to newer β-lactams, including third generation cephalosporins and monobactams, but also to other classes of antibiotics. The study aimed to characterize extended-spectrum β-lactamase (ESBL) and AmpC β-lactamase (AmpC) producing *Enterobacteriaceae* isolated from clinical specimens. More effective surveillance will help in deriving better treatment plans and more effective outcomes.

Materials and methods: The present research work was a hospital based cross-sectional study which was conducted in the Microbiology Department at Karuna Medical College, Chittur from April, 2019 to January, 2020. *Escherichia coli* strains isolated from clinical samples such as urine, blood, sputum, and swabs from out patients and hospitalised patients were collected for the study. We screened about two hundred and eighty six (286), E.coli from positive cultures for susceptibility against third generation cephalosporins. The multidrug resistant E. coli isolates were screened for ESBL by double disc synergy test and confirmed with combined disc diffusion test. Phenotypic AmpC activity was detected using two different tests. First, *AmpC beta-lactamase* strains were screened using disk diffusion method in which cefoxitin 30 μg disc was used. Isolates showing an inhibitory zone diameter ≤18 mm were suspected to be AmpC β-lactamase producers. Secondly, AmpC beta-lactamase production, was judged by the Ceftazidime-Imipenem antagonism test (CIAT). The *p-value* <0.05 was considered as statistically significant.

Results: Phenotypic screening found that 104/286 (36.3%) organisms had resistance to third generation cephalosporins; 69/286 (24.12%) of isolates exhibited ESBL activity, 4.89% (14/286) had *AmpC* activity, and 0.69% (2/286) had both ESBL and *AmpC* activity. There was no significant difference ($p > 0.05$) between the antimicrobial resistance phenotypes of the organisms associated with community and hospital-acquired infections.

Conclusions: ESBL production was found in the *E. coli isolated* from in patients and outpatients which points towards the spread of ESBL producing isolates in community. To prevent the spread of these strains, the implementation of appropriate infection control measures and an antibiotic policy must be in place, as it should not be neglected.

PBI-013

Post-mortem microbiology: *Klebsiella* isolates in sudden unexpected death of infants and children

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Background: Sudden unexpected deaths due to bacterial infections contribute largely to the death of infants and children (SUDI/SUDC) worldwide. *Klebsiella* species, particularly *K. pneumoniae* infections have been linked to hospitalizations and bloodstream infections with case fatalities. However, little data on *Klebsiella* infections are established in SUDI/SUDC cases. This study aims to identify and characterize sudden unexpected death of <5-year-olds with *Klebsiella* isolates from post-mortem microbiology sampling and establish their incidence as contributor to the cause of death.

Methods: Post-mortem databases of two tertiary centres in Klang Valley, Malaysia were searched to identify all SUDI/SUDC cases with *Klebsiella* isolates performed from 2018 to 2020.

Results: A total of 74 autopsies were conducted with 61/74 (82%) post-mortem microbiology samplings performed with aseptic technique and <48 hours. *Klebsiella* isolates were found in 16/61 (26.2%) (12 cases of *K. pneumoniae* and 4 cases of *Klebsiella spp*). Majority of the cases (12/16, 75%) occurred in infants ≤3 months. They have mostly been isolated from lungs (12/16) and blood (6/16) samples. Six cases showed consistency of isolates from more than one sampling sites. Evidence of tissue haemorrhages (7/16) and pneumonic (9/16) changes were identified from histopathological examinations. They were identified and concluded as main and secondary contributors to the cause of death in 10/16 and 2/16 cases respectively, either pneumonia, sepsis or both.

Discussion and Conclusion: Infants less than one-year-old are generally predisposed to bacterial infections due to immaturity of the immune system. Possibility of an infection by a hypervirulent strain associated with post-mortem isolates compared to hospitalized children should not be overlooked as it can be acquired in the community. Hence, post-mortem microbiological findings remain to have critical value in SUDI/SUDC investigations. Inclusion of both epidemiological and clinicopathological data are important in understanding *Klebsiella* infections in these cases. This is part of a study funded by the Fundamental Research Grant Scheme, Ministry of Education, Malaysia (USIM/FRGS/FPSK/055002/51319).

PBI-014

Molecular epidemiological study of *Haemophilus influenzae* by multilocus sequence typing

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Background: *Haemophilus influenzae* (HI) is a pleomorphic gram-negative coccobacillus, which can be either capsulated or non-capsulated and is strictly a human pathogen. Encapsulated isolates of *Haemophilus influenzae* serotype B (Hib) is a significant causative agent of meningitis, pneumonia, epiglottis and other severe infections. Since the introduction of Hib conjugated vaccine in 2002 in Malaysia, the incidence of both disease and carriage of Hib has been intensely reduced. This study was conducted to study the genotypic characteristics of HI in children attending child care centres in Wilayah Kuala Lumpur post vaccination era.

Methods & materials: The study was conducted from year 2018–2019. 436 healthy children ranging from age 2–4 years old,

attending child care centres in Kuala Lumpur were included in this study. Throat swabs were cultured for HI. The isolates were identified by API NH and reconfirmed by 16srRNA. Twenty-four isolates confirmed as HI were preceded with multi locus sequence typing (MLST) using seven housekeeping genes (*adk, atpG, frdB, fucK, mdh, pgi* and *recA*).

Results: Out of 436 children, only 24 (5.5%) throat swabs cultures were positive for HI. The most predominant sequence types (STs) in among the 24 isolates were ST 411 (three isolates), ST103 (two isolates), and ST727 (two isolates). The two strains ST103 were from the same daycare centre and both strains were also serotype B. Six new STs were found which are ST2113, ST2114, ST2115, ST2116, ST2117, and ST2172. Three of this newly found STs were serotype B, which is ST 2113, ST 2115, and ST2116. In total there were five serotype B isolates.

Conclusion: Through this study it is noted that HI is diverse among the carriers and MLST serves an important role in studying the genetic characteristic of the HI strains among the carriers.

Keywords: Haemophilus Influenza, MLST, childcare centre.

PBI-015

Pulsed-field gel electrophoresis of *Haemophilus influenzae* isolated from children attending childcare centres in Kuala Lumpur

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Background: *Haemophilus influenzae* is a Gram-negative coccobacillus found in human respiratory tract. The infection is mainly caused by its capsulated type and can be classified into six serotypes, a to f with the most invasive was serotype b. The incidence of type b disease in Malaysia was approximately 52.2%, occurring mostly in children under 5years old. This study was conducted to characterize the Hib strains isolated from healthy children attending childcare centres in Kuala Lumpur by pulsed-field gel electrophoresis.

Methods: Throat swab samples were taken from 436 children aged 2–4 years old in 33 childcare centres. Isolates were identified using API NH and 16 s rRNA sequencing. Fourteen *Haemophilus influenzae* isolates were subjected to pulse-field gel electrophoresis (PFGE) with run time parameters of 2.3 s to 63.8 s for 19 hours, using Sma1 restriction enzyme.

Results: The PFGE analysis showed 12 pulsotypes (A to L) from the 14 isolates. Two isolates showed identical pulsotype H. The identical HI strains were isolated from children from the same childcare. Hib strains demonstrated 3 different pulsotypes (A, G, L). Strains with Pulsotype L was subtype to L1 and L2 and was also isolated from children attending the same childcare centre (Dice coefficient 97.6%). The other 12 pulsotypes were not related (Dice coefficient 49% to 75%).

Conclusion: In summary, most of the isolates are genetically diverse including those the same serotype B. Eventhough all these children were vaccinated, Hib can be isolated from them. There may be transmission of strains between the children based on the similar or identical pulsotypes discovered from those attending the same childcare centre.

Keywords: *Haemophilus influenzae*, pulse-field gel electrophoresis (PFGE), childcare centres.

PBI-016

Clinical characteristics of hypermucoviscous *Klebsiella pneumoniae* bacteremia with non-hepatobiliary infection

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Background: Hypermucoviscous strain of *Klebsiella pneumoniae* (Kp) is associated with invasive liver abscess syndrome. However, little has been known in the characteristics of this phenotype in non-hepatobiliary infection. In this study, we investigated the clinical characteristics of patients with hypermucoviscous Kp (hmvKp) bacteremia from non-hepatobiliary tree infection.

Methods: This retrospective cohort study was implemented in Samsung Changwon Hospital. From March 2018 through December 2019, adult patients (≥18-year-old) with non-hepatobiliary Kp bacteremia were enrolled. Hypermucoviscousity was defined by the string test. Clinical characteristics between patients with hmvKp and non-hmvKp bacteremia were compared. 30-day all-cause mortality of each phenotype was calculated and independent risk factors associated with mortality were evaluated using the Cox-regression model.

Results: Among 179 cases of non-hepatobiliary KP bacteremia, 67 (37.4%) and 112 (62.6%) isolates were classified as hmvKp and non-hmvKp, respectively. In hmvKp group, metastatic infection (7.5% vs. 0.9%, P = 0.028) and purulent or necrotizing infection (31.3% vs. 9.8%, P < 0.001) were more common. On the other hand, non-hmvKp had more resistance to cefotaxime (11.9% vs. 38.4%, P < 0.001). 30-day All-cause mortality was similar in hmvKp (41.8%) and non-hmv-Kp (39.3%) groups (P = 0.643). In multivariable analysis, septic shock (adjusted hazard ratio [aHR] 2.99, 95% confidence interval [CI] 1.19–7.48) and Pitt bacteremia score (aHR 1.23 per 1-point, 95% CI 1.14–1.333) were associated with increased mortality in patients with Kp bacteremia; however, urinary tract infection (aHR 0,33, 95% CI 0.16–0.70) were associated with decreased mortality.

Conclusion: hmvKp was associated with lesser drug resistance and metastatic-purulent presentation in non-hepatobiliary infection, as in hepatobiliary infection. However, hmvKp was not associated with clinical outcomes.

PBI-017

Differences of virulence factors, and antimicrobial susceptibility according to phylogenetic group in uropathogenic *Escherichia coli* strains isolated from Korean patients

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Background: *Escherichia coli* is among the most common uropathogens. Alternative therapeutic options including vaccines against uropathogenic *E. coli* (UPEC) have been developed. In this study, we compared the genotypic characteristics and antimicrobial susceptibility of UPEC according to phylogenetic groups.

Methods: We retrospectively reviewed the medical records of pyelonephritis patients with UPEC between February 2015 and June 2018. We compared the clinical and genotypic characteristics of UPEC according to phylogenetic groups. The phylogenetic groups and 29 virulence factors were identified using multiplex polymerase chain reaction.

Results: Phylogenetic group analysis revealed that most uropathogenic *E. coli* belonged to groups B2 and D: B2 (276, 77.7%), D (62, 17.5%), B1 (12, 3.4%), and A (5, 1.4%). Among the virulence factors, *fyuA, fimH, traT, iutA, papG allele II,* and *papC* were the most frequently observed. Phylogenetic group B2 was more closely related to virulence factors, including *fimH, sfa/focED, focG, hlyA,*

cnf1, fyuA, and *PAI*, than group D. Groups B2 and D showed similar clinical presentations and complications. Group B2 had mostly healthcare-associated infections and antimicrobial resistance. Group D mostly had community-acquired infections. The K1 serotype was prevalent in group B2, and K5 was the most prevalent in group D.

Conclusions: Phylogenetic group B2 had more proportions and types of virulence factors than group D. An increased presentation of antimicrobial resistance and healthcare-associated infections was also noted. Considering the genetic characteristics of UPEC, alternative therapeutic options targeting frequent virulence factors might be considered in addition to antibiotics.

PBI-018

Infections caused by the *Enterococcus* species and its antimicrobial resistance pattern – A hospital based study

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Background: Enterococci are inhabitants with a remarkable adaptive capacity to evolve and transmit antimicrobial resistance determinants. Enterococci infections are common in individuals with comorbidities such as diabetes mellitus, patients on long-term dialysis, in intensive care units, and an immunocompromised state. The emergence of high-level aminoglycoside-resistant (HLAR) enterococci and vancomycin-resistant enterococci (VRE) pose great problems in clinical anti-infective therapy. Antimicrobial resistance profile of clinically significant species varies in different geographical areas. Understanding the ecology, epidemiology, virulence, development of antibiotic resistance in *Enterococcus* spp are important for managing the infections and avoiding the further development of antibiotic resistance.

Methods: It was a prospective study conducted in a teaching medical college hospital, Mangalore India. Clinically significant *Enterococcus* spp. isolated from the clinical samples were identified from tertiary care hospitals. All clinically significant isolates of *Enterococcus* spp, where in gram staining shows gram-positive cocci in pairs along with pus cells. *Enterococcus* spp isolated from sterile body fluids, deep tissue, pus, and urine. In the case of urine, bacteria grown in counts 10 0000 cfu/ml was considered significant. Enterococci isolated from stool, vaginal swab, throat swab, and sputum were excluded from the study. Species identification is carried out by standard biochemical tests. Antibiotic susceptibility testing carried out for the isolates by Kirby-Bauer disk diffusion method on Mueller Hinton agar as per the CSLI. Statistical Analysis was done by descriptive statistics and association was carried out by the chi-square test. A statistical package SPSS version 25.0 used for the analysis. Haemolysin production was screened by cultivation on blood agar, and observing for the production of complete (alpha) hemolysis, partial (beta) hemolysis or no hemolysis on blood agar (gamma) hemolysis.

Results: 110 clinical specimens were collected and identified. In 74/110 samples *E faecalis* (67.2%) was identified, *E. faecium* in 31/110 of samples (28/2), *E raffinosus* was isolated in (4/110) samples and in one sample *E. casselifavus* was isolated. The majority of samples were urine (42/110), blood (34/110), and pus swabs (25/110). *Enterococcus* spp. infection was maximum in age group 61–70 years 26 (23.63%). The common type of infections noted in our study were urinary tract infections (42/110), sepsis (34/110) and wound infection (19/110). In terms of antimicrobial resistance profile 87/110 (79%) of enterococci were resistant to Erythromycin followed by penicillin in 76/110 (69%). High Level Aminoglycoside resistance noted in 57/110 of samples. 23% of samples were resistant to Linezolid, Vancomycin in 9/110 (8%).Only 28 samples showed alpha hemolytic property.

Conclusions: Urinary tract infections followed by sepsis were commonly seen in our cohort. The commonest species was *E fecalis.* Resistance to Teicoplanin and Vancomycin was noted in 11% and 8% of samples respectively by disk diffusion method.

Abstract withdrawn

PBI-020

Optimising culture results of orthopaedic infections using blood culture bottles

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Introduction: Bone & joint infections, particularly Orthopaedic Implant Associated Infections (OIAI) constitute a complex diagnostic challenge. For any surgeon, reliability and yield of culture method is important. An accurate diagnosis is crucial for treatment success. To ensure that the appropriate antibiotic regimen is inititated, the identification and sensitivity testing of the causal pathogen is crucial. We tried to evaluate the performance of blood culture bottle in comparison to routine culture bottles.

Materials & methods: Cultures were sent for 59 patients between 2017 and 2019. Routine cultures methods (Swab, Culture bottle) were used to send samples in 41 patients. Blood culture bottles (BD BACTEC™) were used to send samples in 11 patients. Both routine and blood cultures were sent in 5 patients.

Results: Routine cultures gave a positive yield for 21 patients out of 46 samples (45.6%). Blood culture bottle gave a positive yield for 09 patients out of 17 samples (53%). Blood culture gave a positive yield in 3 out of 5 patients (60%) where results were negative for culture sent in routine bottles.
Conclusion: Blood culture bottle can be used to send fluids/tissue collected during orthopaedic surgeries to improve yield of culture results. Further large scale studies are necessary to confirm results of this abstract.

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PBI-023
Predictive and prognostic factors associated with undrainable liver abscesses
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Introduction: Percutaneous drainage is crucial for treatment of liver abscess. However, inadequate liquefaction, which makes drainage impossible at the time of diagnosis is not infrequent. If left undrained, this might lead to treatment failure.
Method: We reviewed medical records of patients who were diagnosed with liver abscess between July 2017 and Jun 2020. Study population was divided according to whether drainage was performed or not. To identify potential factors associated with feasibility of abscess drainage, demographic variables, underlying diseases, laboratory and radiologic findings were compared. Cox proportional hazard model was used to find variables related to 90-day recurrence-free survival.
Result: A total of 169 patients were included. 94 underwent drainage immediately after diagnosis, 22 later during hospitalization. Patients with larger abscesses (mean 64.7 mm vs. 44.6 mm, odds ratio [OR] 1.05, confidence interval [CI] 1.02–1.08, $p < 0.001$), current hepatopancreaticobiliary (HPB) malignancy (OR 21.02, 95% CI 2.44–181.17, $p = 0.006$) and *K. pneumoniae* infection (OR 4.20, 95% CI 1.65–11.03, $p = 0.003$) were more likely to undergo drainage. Immediate drainage was related to shorter time to defervescence (median 2 days vs. 3 days, $p = 0.036$). Current HBP malignancy (OR 8.60, 95% CI 2.82–26.22, $p < 0.001$) and higher Charlson comorbidity indices (OR 1.21, 95% CI 1.04–1.42, $p = 0.017$) were predictive of 90-day recurrence-free survival, but abscess drainage was not.
Conclusion: Abscess drainage did not have significant impact on adverse outcome except time to defervescence. Comorbidities,

especially current HPB malignancy, were associated with 90-day recurrence-free survival.

Abstract withdrawn

PBI-025

Risk factors of repeat bacterial sexually transmitted infections (STI) in Hong Kong

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Background: Repeat sexually transmitted infections (STI) are often related to continued practice of risky sexual behaviours. This study aims to identify risk factors of repeat STI.
Method: In Hong Kong, Social Hygiene Clinics provide free STI examination and treatment in the public service. From 2009–16, attendance records were retrieved from 7 clinics with dates of visit, diagnoses, socio-demographics, and sex partnerships. Male patients with first notification of bacterial STI (i.e. syphilis, gonorrhoea, chlamydia, non-gonococcal urethritis) and trichomoniasis in 2009–14 were included, allowing ≥2 years of follow-up. With the earliest record as baseline, repeated diagnosis >6-month window or different diagnosis >3-month window were classified as repeat infection. Bivariable and multivariable logistic regression were performed.
Results: Among 40657 male patients, 21389 (53%) were analysed, with 1272 (6%) self-reporting as men who have sex with men (MSM) and none were commercial sex worker. Percentages of patients ever diagnosed with syphilis, gonorrhoea, chlamydia, non-gonococcal urethritis and trichomoniasis were 16%, 26%, 11%, 70% and 1% respectively. A total of 2235 (10%) patients had repeat infection. In the final model, risk of repeat infection reduced with older age at first notification (aOR = 0.99, 95% CI = 0.98–0.99). Married (single as reference, aOR = 0.58, 95% CI = 0.52–0.64) patients had lower risk. MSM (non-MSM as reference, aOR = 1.34, 95%CI = 1.14–1.57) were at higher risk. Ethnicity was an insignificant predictor.
Conclusion: Repeat STI were common among MSM attending the clinics. Their prevention needs would require focused attention to reduce the population burden of STI.

PBI-027

Eczematous skin colonization pattern with potential bacterial pathogens in paediatric population at a tertiary care setting, in Sri Lanka

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Background: Atopic dermatitis (AD) is a chronic skin disease primarily in childhood. AD skin is at greater risk of bacterial adhesion. We evaluated antibiotic sensitivity of colonizing bacteria associated with eczematous skin.
Methods: Study carried out at dermatology clinic of a children's hospital. Surface swabs of lesions from 50 patients cultured. Isolates identified by biochemical and molecular methods. Susceptibility determined using CLSI disc diffusions.

Results: Total 98% (n = 49) showed bacterial colonization and 34% (n = 17) carried *Staphylococcus aureus.* Of 101 different isolates from 49 subjects, 65.3% (n = 66) were coagulase negative staphylococci (CoNS), 18.8% (n = 19) *S.aureus*, 11.9% (n = 12) *Micrococci*, 3% Gram negative bacteria ((n = 2) *Acinetobacter* sp., (n = 1) *Bordetella bronchiseptica* and 1% (n = 1) *Streptococcus agalactiae*. *S. aureus* showed resistance to erythromycin (36.8%) clindamycin (21%) and 31.6% were MRSA. CoNS showed resistance to cefoxitin (68.2%), erythromycin (65.2%), clindamycin (33.3%) and tetracycline (1.5%). All *Acinetobacter sp*. were sensitive to gentamycin, ceftazidime and meropenem.
Conclusions: *Staphylococcus aureus* colonization is much lower compared to the previous data available locally. Majority of the CoNS showed resistance while *Acinetobacter* sp. and *Streptococcus agalactiae* sensitive to all antibiotics tested. However, MRSA colonization has to be evaluated periodically to avoid further spread.

PBI-028

Antibiotic resistance – the problem of modernity

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Background: Antibiotic resistance is a natural biological evolution of microorganisms, which today is one of the most serious threats to human health. The purpose: to study changes in antibiotic resistance in children with acute leukemia in 2020 compared to 2015.
Methods: The retrospective descriptive study included 123 medical records of patients, who were admitted to the oncology and hematology departments of the SCP&PS in the period from May to July 2015 and in the same period in 2020. Of these, 65 cases were related to 2015, 58-to 2020. All patients underwent bacteriological examination from various loci.
Results: The study showed a tendency to increase antibiotic resistance. At the same time, resistance to 2 or more groups of antibacterial drugs increased from 69.7% in 2015 to 90.4% in 2020 ($p < 0.01$). There is an increase in the number of groups of antibiotics from five in 2015 to nine in 2020, to which the sown flora is resistant. Bacterial pathogens resistant to 7–9 groups of antibiotics include: *Str. anginosus* and *dysgalactiae*, group B *streptococci, Staph. hominis* and gram-negative ones: *P. vulgaris.* The analysis of monitoring of antibioticograms revealed the appearance of resistant strains of *Staph.aureus* to oxacillin in 2020, which indicates the identification of *MRSA*, which is also resistant not only to beta-lactams, but also to vancomycin. In addition to the increase in resistance to vancomycin from 3.2% to 26.4%, vancomycin-resistant enterococcus was detected.
Conclusions: There is a significant increase in multi-resistance to antibiotics, which requires an urgent revision of the algorithms and standards of antibacterial therapy. The results of the study show the need for regular monitoring of antibioticograms to optimize antimicrobial therapy in children with hemoblastosis. The obtained data can be useful in the approach to the rational appointment of antibacterial therapy.

PBI-029

Causative microorganisms, antibiotic resistance and empiric therapeutic choices in Cobra-bite wound infections

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Background: Snakebite is a medical problem in Taiwan where the climate ranges from humid subtropical to tropical monsoon. Snakebite develops clinical illness and even leads to death from complications. Naja atra (Cobra) bite causes more severe bacterial infection than other kinds of snakebites. Here we review 24 cases suffered from Cobra bites and their presentation.
Methods: Patients with wound infection after Cobra bite between January 2009 to December 2016 were included in the retrospective study at a tertiary medical center in Taiwan. Case patients were defined as local symptoms or signs such as pain, erythema, localized warmth, swelling, lymphangitis, delayed healing, malodor, crepitus in soft tissues, discolored or friable granulation tissue, or wound breakdown or dehiscence as well as purulence/abscess and organisms isolated from the fluid/tissue/blood after Cobra bite. The guilty snake was identified definitively by inspection, patient identification via a photograph, or laboratory testing of the venom by the treating specialist in the facility. We acquired the results of deep tissue or biopsy culture conducted during surgical debridement, or blood culture performed during febrile episodes.
Results: 24 cases with cobra envenomation were identified during the period, 16 (66.67%) of them developed wound infection. 9 (56.25%) cases sustained polymicrobial infection. In this report, aerobic bacteria isolated in pathogenic organism of Cobra bite wound, Morganella morganii and Enterococcus faecalis were the most common bacteria.
Conclusion: Snakebites carry the consequences of envenomation leading to extensive tissue destruction or an infected wound. In respect of the common bacteria of Cobra bite wound, we can choose antibiotics more wisely.

PBI-030

A nation-wide multicentric study on community acquired urinary tract infection among children from a developing country

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First episode of acute urinary tract infection (UTI) in children is treated with empirical oral antibiotics and there is no large scale nation-wide multicentric study from community on antimicrobial susceptibility to formulate national antibiotic policy. Children (2–18 years) seeking medical care at primary and community health centres in Delhi, Bangalore, Jodhpur and Bhubaneswar representing north, south, west and east India were enrolled from 2019 to 2020. The child having symptoms of UTI for less than a week were included and those with UTI in past, disorder of urogenital system and taken antibiotics in the last three months were excluded. Midstream clean catch urine was processed. A total of 310 children were included in the study and 96% were from poor socioeconomic strata. Delhi recruited 58%, Bangalore 23%, Jodhpur 5% and

Bhubaneswar 14%. M: F ratio was 1:1; 21%were below 5 years, 21% were 6–10 years and 57% were >10 years. 30 urine samples were culture positive (9.6%); *E.coli* was the predominant organism (83%) followed by *K.pneumoniae* (13%). The antimicrobial susceptibility of the isolated organisms is shown in Table 1. 50% of isolates were ESBL producers and 10% were carbapenem resistant. This is alarming data coming from large scale nation-wide community study among children indicating the imminent threat of epidemic of antimicrobial resistance in India in future.

Table 1: Antimicrobial susceptibility pattern

Antibiotics	Antimicrobial Sensitivity (%)
Oral Antibiotics	
fluoroquinolones	40
oral cephalosporins	46.7
co-trimoxazole	56.7
oral b-lactam – blactamase inhibitors	56.7
Nitrofurantoin	93.2
fosfomycin	100
IV Antibiotics	
Aminoglycosides	76.7
Carbapenems	90

PBI-031

Research on the characteristics of dominant Staphylococcus aureus clonal population in China

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The purpose of this study is to investigate the population structure and characteristics of Staphylococcus aureus isolated from bloodstream infected patients in China. We retrospectively collected a total of 484 Staphylococcus aureus in 16 large teaching hospitals across the country from 2019 to 2020, and performed genetic and phenotypic comparision of four dominant clones (ST59, ST5, ST398, ST239).

The phylogenetic tree constructed based on the maximum likelihood method shows that each ST is accurately divided into different lineages. Analysis of VFDB, Resfinder and CARD database shows that each ST has specific virulence and drug resistance genes; Scoary-based GWAS shows that ST5 has population-specific genes that is related to enterotoxin and ESAT-6 secretion system, ST59 is mainly related to cell wall synthetic protein, and ST398 is mainly related to oligopeptide transport system. The susceptibility of 142 strains to fluoroquinolone drugs differs the most in each ST; ST398 and ST59 have stronger red blood cell lysis ability, among which ST398-MRSA has stronger protease hydrolysis and red blood cell lysis ability than MSSA, indicating that ST398 is gaining the drug resistance without the adaptive cost, but the protease hydrolysis ability and red blood cell lysis ability of ST5-MRSA is weaker than that of MSSA. This may be related to its specific combination of virulence and resistance genes. ST398's protease hydrolysis ability is obviously stronger than other STs, but the biofilm formation ability is weaker than other STs, which may be caused by ST398-specific oligopeptide transferase.

In conclusion, we have found that the Chinese bloodstream infection of Staphylococcus aureus shows a polyclonal trend, and each ST has different characteristics in genome and in vitro adaptability. Comparative genome and GWAS analysis based on whole-genome sequencing can help us to find key molecules of each ST, thus providing guidance for precise diagnosis and treatment of infectious diseases.

PBT-001

Unraveling the genomic, antibiotic susceptibility, and antioxidant properties of the dairy starter *Streptococcus thermophilus* SMQ-301

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Background: Antimicrobial resistance (AMR) remains a growing global concern. Probiotics, including *Streptococcus thermophilus* strains, have been proposed as viable alternatives to combating AMR. Here, we provide genomic insights and *in vitro* antibiotic susceptibility and antioxidant profiles of the *S. thermophilus* SMQ-301 strain to further validate its multidimensional and therapeutic use.

Methods: Genomic annotations were constructed using the KEGG database. *In vitro* antimicrobial resistance and antioxidant experiments were performed following previously described standard protocols.

Results: We mined the antibiotic susceptibility and antioxidant genes of the *S. thermophilus* SMQ-301 strain (Fig 1A–C). Antibiotic susceptibility and oxidative stress-suppressive properties were confirmed through *in vitro* antimicrobial resistance and antioxidant experiments (Fig 2A–E).

Conclusion: Our findings show that the *S. thermophilus* SMQ-301 strain is safe and suitable f or potential industrial and health-promoting applications like the production of natural antioxidants. Future works should focus on targeted *in vivo* therapeutic interventions.

PBT-002

The prevalence of beta-lactamase-producing *Enterococcus* sp in a tertiary hospital in Malaysia

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Background: In the Microbiology Laboratory Unit Hospital Kuala Lumpur, all ampicillin-sensitive enterococci isolates are routinely tested for beta-lactamase production.

Objective: In this descriptive study from March 2020 to December 2020, we aim to evaluate the role of beta-lactamase testing and its significance in management.

Methods: Enterococcal species identification was performed by MALDI Biotyper (Bruker Diagnostics, Germany). The antibiotic susceptibility testing was determined by Kirby-Bauer disk diffusion method and analysed using the BIOMIC V3 (Giles Scientific USA). Beta-lactamase testing was done using Cefinase discs (BD BBL™). The data was analysed using descriptive statistics.

Results: Out of 569 enterococci isolates, 380 (66.8%) were ampicillin-sensitive and 189 (33.2%) isolates were ampicillin-resistant. All of the ampicillin-sensitive enterococci were tested for beta-lactamase production, as part of the laboratory standard operating procedure. These isolates were recovered from urine, blood, tissue, pus swabs, body fluids and cerebrospinal fluid specimens, with 97.1% (n = 369) were *E. faecalis*, majority causing urinary tract infections. Two beta-lactamase positive *E. faecalis* were isolated, from blood and urine sample each, giving a percentage of 0.54%.

Conclusion: In view of virulent beta-lactamase-producing *E. faecalis* isolated in our setting, the testing for beta-lactamase production may be limited to in vitro ampicillin sensitive *E. faecalis*

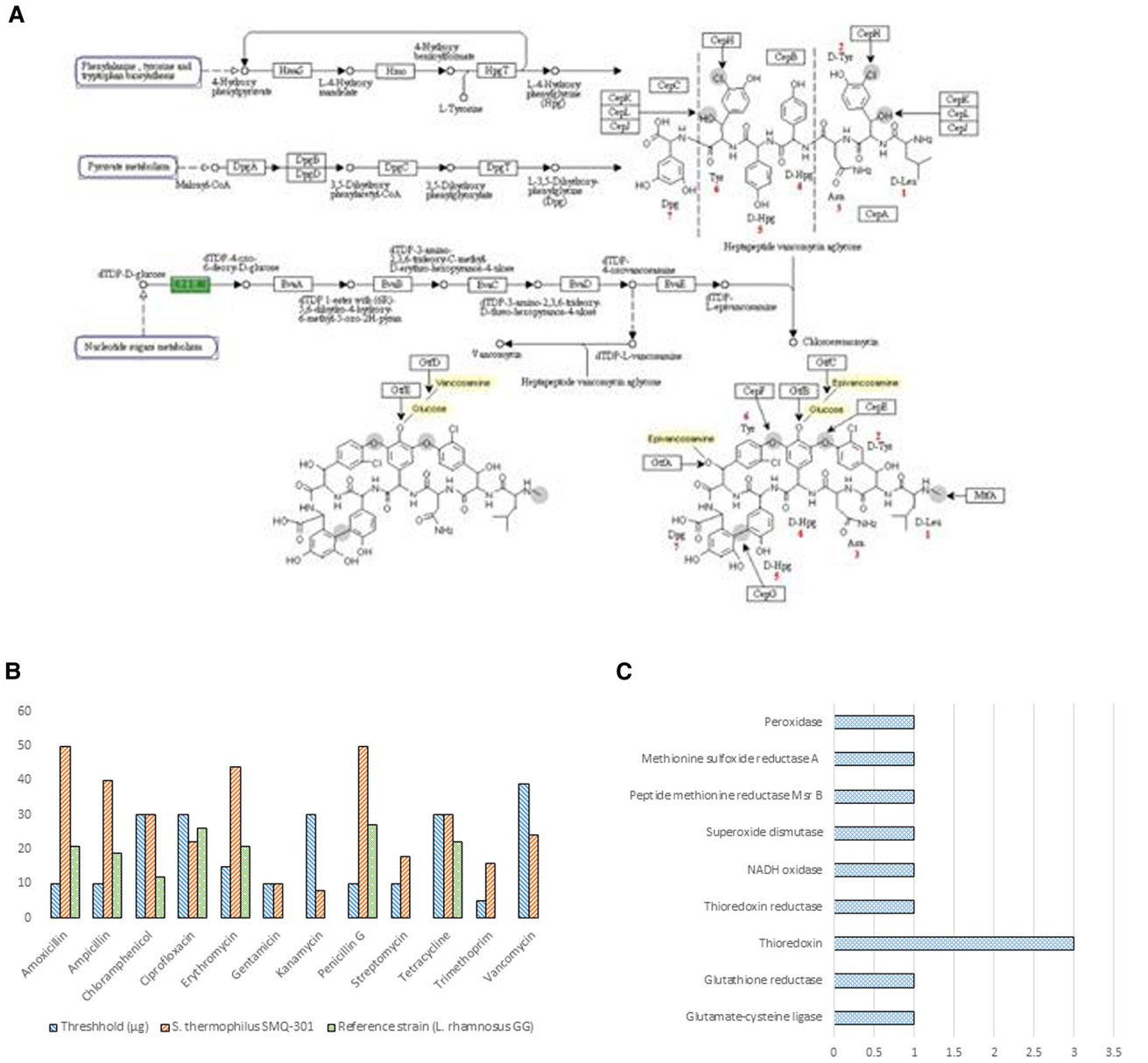

Figure 1: (abstract PBT-001): A – Vancomycin antibiotic biosynthesis pathway model for *Streptococcus thermophilus* SMQ-301, B – Antioxidant genes of *S. thermophilus* SMQ-301, C – Antibiotic susceptibility profiles of *S. thermophilus* SMQ-301.

rather than all enterococci isolates. This may also aid in reducing overutilization of laboratory tests and rising costs of testing.

Keywords: Enterococcus; E. faecalis; beta-lactamase; ampicillin.

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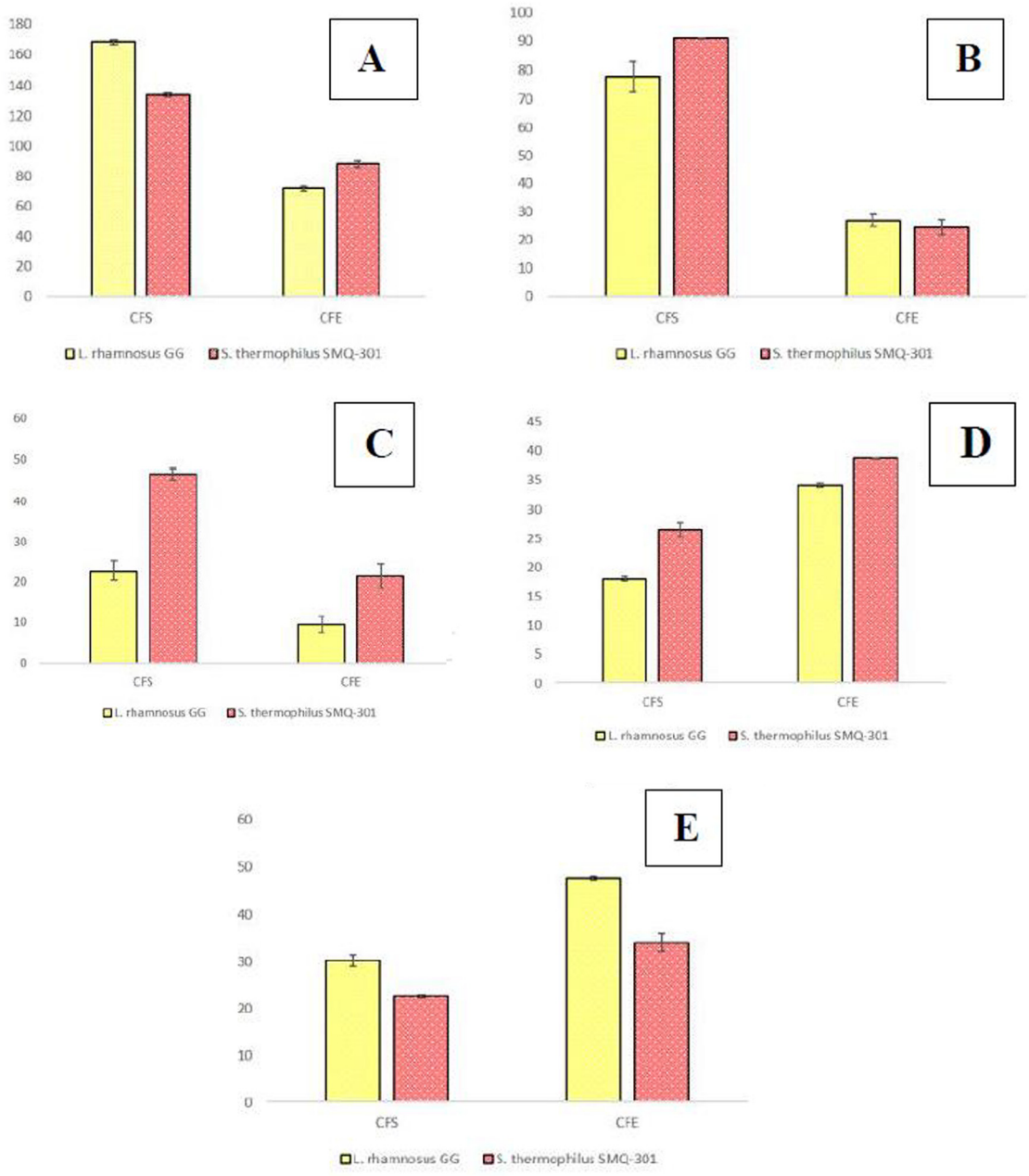

Figure 2: (abstract PBT-001): *In vitro* antioxidant properties of *S. thermophilus* SMQ-301; A – reducing properties; B – DPPH scavenging; C – hydroxyl radical scavenging; D – superoxide scavenging; E – anti-lipid peroxidation; CFS, cell-free supernatant; CFE, cell-free extract.

PBT-004

Construction of a promoterless GFP reporter plasmid for gene expression analysis in carbapenem-resistant *Klebsiella pneumoniae* strain

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In this study, we constructed a GFP fluorescence reporter plasmid, namely pExKP, which can be applied in CRKP strain. Four tandem copies of the T1 terminator from *E. coli* MG1655 were fused to pUC19 plasmid backbone. The T1 terminators were linked through different restriction sites. The GFP gene containing the ribosomal binding site was inserted downstream of the terminators. A single T1 terminator is also inserted downstream of GFP gene. The multiple cloning site (MCS) fragment is inserted upstream of the GFP. The AmpR gene was replaced by the Tetx4 gene by a Gibson assembly reaction, which allows the plasmid to express tigecycline resistance. The plasmid can be successfully introduced by electroporation into CRKP strain with low background fluorescence.

PBT-005

Overexpression of DNA-methyltransferase leads to increasing of persister cell formation in *Acinetobacter baumannii*

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Background: Persisters are a subpopulation within growth-arrested bacterial cells, has transiently tolerant to various harsh environmental pressure or antibiotics. Numerous mechanisms have been reported to associated with persister cell formation, which are Toxin-antitoxin (TA) system, guanosine tetraphosphate (ppGpp), phosphatase metabolism, energy metabolism, SOS response and epigenetic regulation. DNA-(adenine N6)-methyltransferase (Dam) is major type of DNA modification in Gamma proteobacteria, transfers the methyl group to the adenine of the sequence GATC. The DNA methylation is a reversible modification without alter the original DNA sequence, modulates epigenetic functions by regulating protein binding affinity.
Methods: Persister cell formation rate was determined under exposure to various antibiotics or hydrogen peroxide in *Acinetobacter baumannii* strain and isolates. We also evaluated transcriptional levels of *dam* and persister cell-involved genes by qRT-PCR, under exposure to ciprofloxacin, imipenem, and tetracycline, respectively. In three of *Acinetobacter baumannii* strain and isolates, Dam, RecC, UmuD, PhoU and glpD were overexpressed from heterologous promoter, respctively.
Results: Here, we demonstrate that *Acinetobacter baumannii* form persister cell activates transcription of *dam*, *recC*, *umuD*, *phoU* and *glpD* under various antibiotic exposure. Likewise, these genes are transcriptionally activated by overexpression of Dam from heterologous promoter. Our results also show that overexpression of Dam leads to increasing of persister formation rates, slow growth phenotype as a typical persister cell growth. These data strongly support that DNA-(adenine N6)-methyltransferase is associated with persister cell formation as an epigenetic factor.

PCC-001

A case report of *Salmonella enteritidis* subdural empyema in a child

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Background: Salmonella subdural empyema are rarely reported, with mostly being *Salmonella* Typhi infection. We report a case of bilateral subdural empyema in a 6-month-old boy, caused by *Salmonella enteritidis*.
Case report: He presented with an episode of left-sided seizure preceded by four days of fever without gastrointestinal symptoms. He was hypertonic and hyper-reflexic with an episode of vomiting. His head circumference crossed 97th centile, with prominent scalp veins and tensed anterior fontanelle. Other systemic examinations were unremarkable. Full blood count showed leukocytosis (white cell count 26.2×10^9 per L), anemia (hemoglobin 6 g per dL), thrombocytosis (platelet 805×10^9 per L) and raised C-reactive protein (180 mg per L). HIV serology were negative for mother and child. Contrast enhanced computed tomography of brain revealed bilateral subdural collection with left frontal enlarging lesion, likely empyema and early hydrocephalus. He underwent bifrontal craniotomy washout. *S. enteritidis* was isolated from pus specimen, which was susceptible to ceftriaxone, ciprofloxacin, ampicillin and trimethoprim-sulfamethoxazole. His blood culture was negative. He received intravenous ceftriaxone and ciprofloxacin for 6 weeks and discharged home without neurological sequalae.
Conclusion: Focal central nervous system infections are unusual manifestations of salmonellosis caused by non-typhi Salmonella. A large number of non-typhoidal salmonellosis affecting the central nervous system do not present with the common gastrointestinal symptoms as seen in this case. Early detection and prompt diagnosis, along with surgical intervention and proper treatment is mandatory to prevent major sequalae.
Keywords: Salmonella; non-typhi Salmonella; subdural empyema; cerebral infection; meningitis; child.

PCC-002

Severe *Salmonella enteritidis* infection complicated with colonic perforations and abdominal cocoon

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Introduction: *Salmonella enteritidis* is the second most encountered serovar causing invasive nontyphoidal *Salmonella* infections after serovar Typhimurium, accounting for approximately one-third of all cases. Contaminated hen's eggs were the most important vehicle of the infection. Nontyphoidal Salmonella infection can present with diverse clinical manifestations, including gastroenteritis, bacteremia, septic arthritis, osteomyelitis, and endovascular infection.
Case report: An 18-year-old girl, with no prior medical illness presented with a 3-week history of fever, abdominal pain, and diarrhea. Two household members also experienced similar symptoms after they consumed food bought at the market. Upon arrival, she was septic-looking, febrile, and in circulatory shock. Physical examination revealed a grossly distended abdomen with signs of peritonism. Initial laboratory investigation showed pancytopenia, lactic acidosis, and a non-reactive HIV test. Urgent abdominal computed tomography revealed gross pneumoperitoneum suggestive of bowel perforation. She underwent exploratory laparotomy in which multiple punctate perforations were found at the splenic flexure, upper sigmoid, and descending colon. Segmental colonic resection was performed, followed by the creation of a double-barrel stoma. Blood culture revealed *Salmonella enteritidis*; confirmed by Salmonella serotyping. A repeat abdominal imaging in a 2-week interval showed multiloculated intrabdominal and pelvic collections. Percutaneous drainage was performed; however, she did not improve clinically with persistent fever and raised inflammatory markers. She underwent relaparotomy in which an abdominal cocoon was observed with dense adhesion present between the bowel and anterior abdominal wall. A conservative approach was undertaken following a multidisciplinary team discussion. After completing 2 weeks of meropenem, she received ampicillin-sulbactam for another 6 weeks to ensure the eradication of the organism. She recovered well and was scheduled for stoma reversal at a later date.
Conclusion: We present a unique case of *S. enteritidis* infection leading to colonic perforations and abdominal cocoon in a patient who presented late in her illness. Early identification and prompt medical/surgical treatment can be life-saving because of the high mortality and morbidity associated with this disease.

PCC-003

A near miss diagnosis of Granulicatella adiacens infective endocarditis

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Background: This case report depicts endocarditis caused by Granulicatella adiacens, a rare cause of infective endocarditis. Unspecified presentation, rare occurrence and difficulty in laboratory identification of the organism posed significant challenges for this condition to be diagnosed. This case highlighted the role of laboratory in providing significant input in optimizing prompt and accurate patient diagnosis and ultimately optimum patient care and management.
Case report: 58-year-old man with history of mitral valve prolapse presented with vague history of lower back pain and fever for 1-week duration. He had history of motor vehicle accident 5 year prior where he required multiple titanium face implants with exposed plate at lower gum. His blood was taken during admission and sent for culture. In view of his clinical presentation, he was initially treated as pyelonephritis and given ceftriaxone. His condition remained unchanged. In the microbiology laboratory, his blood culture grew Granulicatella adiacens after 7 days. This is beyond standard culture identification, highlighting the significant difficulty and delay in organism identification. The laboratory then referred the case to infectious disease physician in view of possible infective endocarditis. Urgent echocardiogram then was done and revealed large vegetation measuring 2.3 × 0.5 cm at posterior mitral valve. Upon this finding, a diagnosis of infective endocarditis was made, and his antibiotic was then changed to benzylpenicillin and gentamicin. A repeat echocardiogram a month later, revealed the vegetation had shrunken, now measuring 0.2 × 0.5 cm. The exposed plate at his lower gum was removed, and the site cleaned. Patient completed antibiotic therapy of 1 month and 10 days. At the point of this write up, patient is well and scheduled for a mitral valve replacement.
Discussion: Granulicatella adiacens is a nutritionally deficient streptococci (NVS), so called because it needs pyridoxal or other additional agents to be incorporated into standard media for successful laboratory isolation and identification. Because of this Granulicatella adiacens imposed certain challenges in laboratory identification and may have been missed. NVS have been reported to be responsible for around 5% of streptococcal infective endocarditis. Most patient present with unspecified symptoms, imposing further challenge in recognizing the condition.These two factors posed significant challenges in diagnosing endocarditis caused by Granulicatella adiacens.
Conclusion: As highlighted by this case report, a diagnosis was nearly missed because of the unspecified presentation and difficulty in laboratory organism identification. Prompt and close communication between the laboratory and the treating physician play significant role in ensuring optimum care and clinical management can be provided to patients.
Keyword: Granulicatella adiacens, Infective endocarditis.

PCC-004

A case of atypical hemolytic uremic syndrome caused by *Escherichia fergusonii* mimicking *Escherichia coli* in an immunocompetent adult

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Introduction: *Escherichia fergusonii* has been reported to cause infections in human, including hemolytic uremic syndrome (HUS); multidrug resistant strains of this bacteria have also been reported. However, reports on *E. fergusonii* human infections are limited. We report the case of a patient with atypical HUS caused by *E. fergusonii* mimicking *Escherichia coli* in an immunocompetent adult.
Case Description: A 57-year-old man who suffered from fever and myalgia was admitted to our emergency department in January 2021. He had a history of undergoing prostate biopsy at a primary urology clinic 3 days before admission. No other anamnesis was recorded. From day 3, the patient had no fever but renal failure worsened and thrombocytopenia did not improved. A peripheral blood smear revealed schistocytosis. The patient was initially misdiagnosed with *E. coli*–induced bacteremia on conventional blood culture, and secondary HUS caused by *E. coli* was suspected. However, using 16 s ribosomal RNA (rRNA) sequencing, we confirmed *E. fergusonii* in the patient's blood and urine cultures.
Discussion: To our knowledge, this is the first study to report HUS in an immunocompetent adult without any underlying disease. It is essential to further study the techniques for the accurate diagnosis and treatment of newly emerging antibiotic-resistant strains of this bacterial species.
Keywords: Hemolytic uremic syndrome, *Escherichia fergusonii*.

PCC-005

Cryptococcus gattii meningitis with pulmonary cryptococcoma in an immunocompetent patient

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Introduction: Cryptococcosis is a fungal disease caused by *Cryptococcus neoformans* and *Cryptococcus gattii*. By inhalation and subsequent pulmonary infection, it may disseminate to the central nervous system and lead to meningitis or meningoencephalitis. *C. gattii* has been a significant cause of *morbidity* and *mortality* due to increased virulence and the associated high intracranial pressure.
Case report: A 46-year-old hypertensive man presented with headache and difficulty in walking for 1 month. He had no history of fever, migraine, head trauma, or recent travel. On examination, he was alert and cooperative. Detailed neurological examination revealed asymmetrical weakness of bilateral lower limbs; MRC scale: right = 4, left = 3. There was no involvement of the cranial nerves, upper limbs, and sensory system. Blood investigations were unremarkable and the HIV test was non-reactive. Computed tomography (CT) of the brain showed prominent ventricles with communicating hydrocephalus. A diagnostic lumbar puncture was performed where the opening pressure was measured at 40 cmH_2O. The cerebrospinal fluid (CSF) was clear in appearance with *hypoglycorrhachia* and there was presence of encapsulated yeast cells. Cryptococcal antigen was present in high titre (>1:512) and CSF culture revealed *Cryptococcus gattii*. Molecular typing identified VGI. A thoracic CT demonstrated a right lower lobe focal

consolidation which was most likely cryptococcoma. Several sets of blood cultures came back as negative. He was treated with a combination of intravenous amphotericin B and oral flucytosine for 6 weeks duration as induction therapy. Therapeutic lumbar puncture was performed on a daily basis until a ventriculoperitoneal shunt was inserted as management of high intracranial pressure. After 2 weeks, CSF sterilization was achieved with gradual resolution of headache and neurological deficit. Oral fluconazole as eradication therapy was planned for 12 months.

Conclusion: *C. gattii* can affect otherwise healthy, immunocompetent patients and requires prompt diagnosis and treatment in order to prevent severe neurological sequelae. Aggressive CSF drainage to manage intracranial hypertension and early initiation of antifungal therapy have contributed to the favourable outcome in this patient.

PCC-006

Multi-drug resistant trichomoniasis: A case report

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Background: Human trichomoniasis is the most common non-viral sexually transmitted disease globally. Symptomatic patients are traditionally treated with metronidazole or tinidazole, but patients with resistant disease are left with a lack of approved alternative therapies.

Case Presentation: We present a case of a 34-year-old woman with refractory trichomoniasis over a 14-month period. In May 2019, she presented to her primary care provider with pruritic and yellowish discharge and was treated for a urinary tract infection. Her symptoms did not resolve, and she saw her OBGYN who diagnosed her with trichomoniasis. From May to September, she was given six treatments of metronidazole and two treatments of tinidazole, but she was unable to complete the tinidazole after developing heart palpitations and shortness of breath. In October, an infectious disease physician sent a cervical sample to the Centers for Disease Control for resistance testing. While waiting for the results, she was treated with combinations of boric acid and either metronidazole or tinidazole. Again, treatment with tinidazole was discontinued due to adverse side effects. After consultation with the CDC, she restarted tinidazole despite lab results revealing high-level of resistance to both metronidazole and tinidazole, however, the patient preferred to continue with metronidazole due to her history of symptoms with tinidazole. In February 2020, she developed toxicity to metronidazole and continued treatment with boric acid only. After 3 months of treatment with boric acid, the patient's symptoms resolved, and in July 2020 trichomonas vaginalis was undetectable.

Conclusion: For patients with multi-drug resistant trichomoniasis, this case report provides support for boric acid as an alternative treatment.

PCC-007

Meningitis caused by carbapenem resistant *Enterobacter cloacae* after endoscopic third ventriculostomy: A case report

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Introduction and Background: The emergence of carbapenem-resistant *Enterobacter cloacae*, with limited treatment options has posed a serious threat to clinical management. *Enterobacter cloacae* is an opportunistic, facultative anaerobic gram-negative bacteria. An effort is made to present a rare case of meningitis following endoscopic third ventriculostomy caused by carbapenem resistant *Enterobacter cloacae*.

Case Details: A 21-year old female presented with complaints of altered sensorium, irrelevant speech and high grade fever after 25 days of neurosurgery to the out-patient department. She had underwent endoscopic third ventriculostomy and aqueductoplasty for obstructive hydrocephalus. After surgery, the patient was discharged. On examination, purulent discharge was observed at surgical site at right kochers point. She was admitted for further evaluation. Cerebrospinal Fluid (CSF) samples were sent for biochemical analysis and culture. As biochemical analysis of CSF was suggestive of meningitis, intravenous(iv) vancomycin 1 gm q 12 h and iv ceftazidime 2 gm q 8 h were given empirically. Surgery was planned for removal of right CSF reservoir suspected as source of infection and for placement of left side CSF reservoir. CSF and reservoir cultures ordered on day 10, reported *Enterobacter cloacae*. The culture/susceptibility details are presented in Table no. 1.

This prompted a referral call to Drug Information Services at Clinical Pharmacology & Therapeutics department for opinion regarding appropriate antibiotic treatment. As there is no consensus on standard treatment guidelines for XDR *Enterobacter cloacae* meningitis, based on anecdotal reports and culture susceptibility report of isolate, intraventricular treatment with gentamicin 5 mg q 24 h and colistimethate sodium 1.25 lakh units q 24 h was advised along with intravenous colistimethate sodium loading dose of 9 million units followed by maintenance dose of 3 million units q 8 h and 3-hour extended infusion of meropenem 2 gm q 8 h. On day 20, after 10 days of starting intraventricular regimen, patient improved. She was conscious and was responding to verbal commands. The serial cultures of CSF were negative but as the biochemical analysis of CSF reported mild elevation of proteins, iv Gentamicin 80 mg BD was also added to the regimen with monitoring of renal function tests. The treatment regimen was

Table No 1: (abstract PCC-007): Showing the details of culture/susceptibility of the isolate.

Sample	Organism	Sensitive	Intermediate	Resistant
Cerebrospinal Fluid Reservoir of VP shunt	*Enterobacter cloacae* Highly Resistant Isolate	Gentamicin Cotrimoxazole	Colistin	Ticarcillin/clavulanic acid Piperacillin/Tazobactam, Ceftazidime Cefoperazone + Sulbactam Cefepime Aztreonam Doripenem Imipenem Meropenem Amikacin Ciprofloxacin.

advised to be continued till clinical cure of the patient. On day 30, patient had sudden onset of multiple episodes of seizure for which symptomatic treatment was started and she developed hypotension for which ionotropic support was started. On day 31, patient deteriorated on Glasgow Coma Scale and became febrile, patient was later intubated and investigations suggested sepsis. Patient was on ventilator with FiO2 100% and ionotropic support. On day 32, patient had bradycardia and severe hypotension and despite Cardiopulmonary Resuscitation she could not be revived and death was declared.

Discussion: n this case, despite administration of appropriate antibiotic therapy the patient did not attain complete clinical cure. However, in a similar case reported by Cascio et al., a 5-year old boy who was successfully operated for astrocytoma, got admitted to hospital 4 days after the intervention, because of CSF leak from the surgical wound with fever. After wound revision, culture of CSF yielded *E. cloacae subsp. cloacae*, which was sensitive to fosfomycin, tigecycline, and colistin. As definitive therapy, combination of intravenous colistin methanesulfonate 2 million IU/12 h and intravenous rifampin 400 mg/day were started. But, as the patient continued to be febrile and CSF cultures were positive even after 6 days, intraventricular colistin methanesulfonate 10 mg/day was started. The patient became afebrile 48 h after beginning intraventricular colistin and serial CSF cultures were sterile. After 13 days, ventricular drainage was removed. On further follow-up the authors reported that there were no similar complaints. Another case, a 17-year old patient of meningitis by XDR Enterobacter cloacae, after removal of neurocytoma reported by He Z et al., the patient responded to treatment with high dose meropenem along with intravenous and intraventricular amikacin. he treatment suggested by drug information services was based on these two case reports, which reported good outcomes with intraventricular therapy. As in this case, the isolate was sensitive to gentamicin and intermediate to colistin, intraventricular therapy with gentamicin and colistimethate sodium was added to intravenous therapy, which resulted in microbiological cure with serial CSF cultures being negative, but patient deteriorated suddenly.

Conclusion: In this case, despite administration of appropriate antibiotic therapy by both intraventricular and intravenous routes, attainment of microbiological cure and apparent improvement in clinical condition, the patient did not attain complete clinical cure. These carbapenem resistant enterobacteriaceae are threatening public health due to limited treatment options and unfavorable prognosis. There is therefore an urgent need to develop effective treatment regimens to combat such life threatening infections and take necessary precautions to prevent the emergence of resistant isolates with judicious use of antimicrobial agents.

PCC-008

Risk of infection with multiple pathogen in post liver transplantation patient in referral centre in Jakarta, Indonesia

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Introduction: Liver transplantation survival and success rates are increasing due to availability of potent immunosuppressive agents but mortality from infectious diseases complications remains a major problem besides the complication due to the surgical procedure itself. Immunosuppression puts recipients at risk for de novo infection and reactivation of latent infection. The most common types of infection were bacterial (48%), fungal (22%), and viral (12%) but concomitant bacterial, fungal and viral co-infections were rarely reported.

Case report: A 46-year-old male patient with a history of liver transplantation 5 months ago and currently on immunosuppressant therapy came with high fever since 2 days before admission. Physical examination revealed icteric. Chest x-ray revealed paracardial infiltrate. The abdominal MRI shows a septate cyst, intrahepatic fluid collection. Laboratory examinations revealed Hb 10.9 g/dl, Ht 32.8%, leukocytes 7890/ul, platelets 29 000/ul, elevated liver enzymes, galactomannan serum titre >1,0 equal to positive and PCR CMV $4.5.10^4$ copies/ml. The patient was diagnosed with post-liver transplant infection due to biloma, pneumonia, aspergillosis, and CMV infections. The patient received initial empiric Meropenem which then be switched for Tigecycline after ID consultation. The surgical correction for biloma will be performed after the patient clinically stable, definitive antifungal therapy for Aspergillosis was initiated after receiving laboratoty result including the CMV medication.

Discussion: Infected collections of liver fluid (biloma) are one of several major infectious complication of liver transplantation. Opportunistic infections (OI) such as Aspergillus and CMV infections often occur 1 to 6 months post-transplant because of the highest degree of immunosuppression. The screening strategy applied to determine the risk of infection after transplantation and the use of prophylactic antimicrobial therapy can reduce post-transplant infection.

Keywords: post liver transplantation infection, biloma, CMV, aspergillosis.

PCC-009

Aggregatibacter aphrophilus chronic rheumatic heart disease: A case report

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Background: The HACEK group referring to *Hemophillus* species, *Aggregatibacter* species, *Cardiobacterium hominis, Eikenella corrodens* and *Kingella* species are found as part of the normal human oral flora. They are fastidious Gram negative organisms responsible for approximately 3% of cases of native valve infective endocarditis. HACEK infection, although rare, can be extremely serious, but outcomes are generally successful if the organism is identified early and treated appropriately.

Case Presentation: We are presenting a 36 years old lady with chronic rheumatic heart disease presented with typical infective endocarditis symptoms. Transthoracic echocardiography upon admission showed severe aortic stenosis, moderate aortic regurgitation, mild tricuspid regurgitation, and mild mitral regurgitation. No vegetation seen. Blood investigation showed no leucocytosis with raised erythrocyte sedimentation rate and C reactive protein. Blood culture sent was positive with difficult identification and finally came out *Aggregatibacter aphrophilus*. Initially, she was empirically started on iv Ampicillin 2 g 4 hourly and iv Gentamycin 80 mg tds for 1 week. Then was changed to iv Unasyn 3 g qid for 4 weeks. Two weekly transthoracic echocardiography during hospital admission showed no vegetation. Patient improved and had no more of fever in ward. The patient recovered completely and was discharged home.

Conclusion: This case highlights the importance of identifying rare causes of endocarditis and recognizing that treatment may not differ from the standard treatment for typical presentations. HACEK group is known to cause infective endocarditis, however rare and difficult to be identified. Prompt treatment with antibiotic has better outcome.

PCC-010

Atypical presentation of typhoid fever mimicking multisystem inflammatory syndrome in children

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Background: Typhoid, an endemic in South Asian countries, presents in children usually with protracted fever and predominant gastrointestinal symptoms and may get complicated rarely with encephalopathy, myocarditis, hepatitis, bronchopneumonia. MIS-C with concomitant tropical infections like dengue, scrub typhus and leptospirosis is increasingly being reported during the raging pandemic of COVID-19, posing a diagnostic challenge. Typhoid presenting with multisystem inflammatory syndrome features is unheard of, especially when the COVID-19 serology is negative.
Report: We report 9-year-child who presented to our emergency with protracted fever of 2weeks, watery diarrhoea since 4days and bilateral lower limb edema. He had hemodynamic compromise at arrival requiring fluid resuscitation for stabilisation. He had coagulopathy and liver dysfunction. Suspecting MIS-C during this COVID-19 pandemic, RT-PCR and antibodies levels for SARS-CoV2 antibodies were sent, turned out negative. All inflammatory markers were grossly elevated. His blood culture showed Salmonella typhi with in-vitro sensitivity to cephalosporins, but showed no clinical improvement on ceftriaxone. The child dramatically improved on azithromycin and was discharged.
Conclusion: Paediatricians are to be made aware of COVID-19 negative MIS-C concomitant with Typhoid fever, especially during this COVID-19 pandemic; aiding in early initiation of appropriate treatment.
Keywords: Typhoid, MIS-C, Azithromycin, Salmonella typhi, in-vivo resistance.

PCC-011

The transmission mode and epidemiology of *Burkholderia pseudomallei* infection in central Taiwan

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Background: Melioidosis is a disease caused by infection with the bacterium *Burkholderia pseudomallei*, identified in the soil and water. The transmission of melioidosis includes percutaneous inoculation, ingestion, and inhalation. The first case of melioidosis in Taiwan was reported. From 1984 to 2000, 20 patients were reported in Taiwan and were primarily categorized as an imported disease. In 2005, the number of melioidosis cases abruptly increased in southern Taiwan after a typhoon followed by a flood. Since then, clustered cases were reported in south Taiwan after floods. But little data regarding the epidemiology and environmental foci of melioidosis in central Taiwan. Centers for Disease Control (CDC) at the Department of Health in Taiwan reports only 1 to 2 cases per year were isolated in central Taiwan.
Methods: We report a case of pulmonary melioidosis with bacteremia in Nantou County, central Taiwan. And we analyze the route of infection, climatic & seasonal associations, and geographic distribution of this case.
Results: A 62-year-old man was transferred to this hospital because of fever and progressive dyspnea on exertion for seven days. The patient had been well until seven days before this presentation, when fever, chills, cold sweating, malaise, and generalized muscle soreness developed. Two days later, a cough that was productive of terra cotta–colored sputum developed. Three days before this presentation, he had presented to a local hospital with progressive dyspnea on exertion. A chest radiograph was reportedly consolidated over the right lower lung field (Figure 1A). Intravenous ceftriaxone 2 gm daily was administered. The next day, dyspnea progressed rapidly, that he couldn't get off the bed. The oxygen saturation was 88% while the patient was receiving supplemental oxygen through a nasal cannula at a rate of 2 liters per minute. The chest radiograph disclosed progression of right lower lung field opacity. The patient had a history of type 2 diabetes mellitus with HBA1c level 10%, coronary artery disease, and disseminated non-tuberculosis mycobacteria 14 years ago. The patient smoked one pack per day and drank 30 ml of Sorghum every day for 30 years. He didn't use illicit drugs. He lived in Puli Township, Nantou County, for more than 60 years and worked as a chiropractor. He reported having returned from Ren'ai Township, Nantou County, seven days ago. On presentation at the emergency department, the patient reported ongoing fever and shortness of breath. On examination, the temperature was 36.7°C, the blood pressure 111/62 mm Hg, the pulse 134 beats per minute, the respiratory rate 24 breaths per minute, and the oxygen saturation 95% with the administration of supplemental oxygen through a venturi mask with 35% fraction of inspired oxygen (FiO_2). The body-mass index was 24.9. Inspiratory crackles could be heard at the right lung field. Auscultation of the heart was regular, with tachycardia but no murmur. The remainder of the physical examination was nonsignificant. Laboratory test results revealed that multiple hematological and biochemical parameters were deranged and are shown in Table 1. His chest X-ray showed consolidation in the right upper lung field, with progression compared to two days before. Computed tomography (CT) of the chest (Figure 1B), performed without the administration of intravenous contrast material, revealed consolidation throughout the right lower lobe.

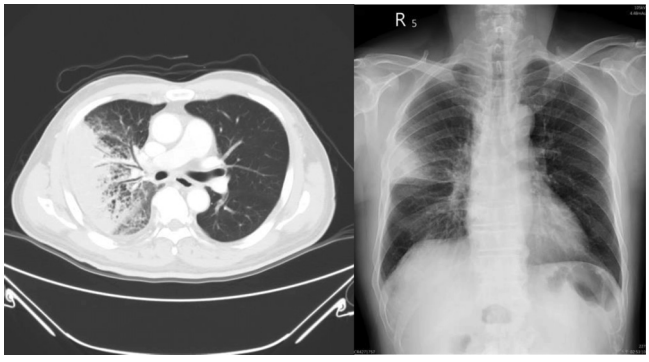

Figure 1. A. Chest radiograph of the patient. B. Computed tomography of the chest during hospitalization.

Table 1: Laboratory Data of the patient during hospitalization

Variable	Reference Range	Hospital Day 1	Day 4	Day 11
White-cell count (per μl)	3900–10600	14 910	20 870	10 520
Differential count (per μl)				
Neutrophils	1800–7700	14 000	19 513	8794
Lymphocytes	1000–4800	284	480	1167
Monocytes	200–1200	626	815	559
Eosinophils	0–900	0	0	0
Basophils	0–300	0	62	0
Hemoglobin (g/dl)	12–16	11.6	11.7	
Platelet count (per μl)	150–400 × 10^3	214 × 10^3	281 × 10^3	418 × 10^3
C-reactive protein (mg/dL)	<0.3	36.9		
Procalcitonin (ng/mL)		>100		
Alanine aminotransferase (Units per liter)	10–50	36	55	44
Creatinine (mg/dL)	0.7–1.4	3.51	1.47	0.85
Sodium (mEq/L)	137–153	129	134	136
Potassium (mEq/L)	3.5–5.3	3.8	3.6	3.8

Influenza real-time PCR tests, pneumococcal urinary antigen testing, legionella urinary antigen testing, and sputum acid-fast stain were negative. Gram-negative bacilli were seen on gram stain. Ceftaroline 600 mg every 8 hours as prescribed. Blood culture grew gram-negative bacilli on day three, and later *Burkhlorderia pseudomallei* was identified by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS). *Burkholderia pseudomallei* was sensitive to imipenem, cotrimoxazole/sulfamethoxazole, ceftazidime, amoxicillin/clavulanate. Based on the sensitivity report, the antibiotic was changed to ceftazidime 2 gm every 6 hours. The patient showed improvement, total counts decreased, his fever subsided on day 4. Antibiotics were continued, and he was discharged on day 33. To identify this case's transmission and epidemiologic risk factor, we review the literature and explore climatic & seasonal associations and geographic distribution of this case.

Conclusion: The occurrence of melioidosis is associate with extreme climate events, such as heavy rainfall and typhoons. Climate change affects the epidemiology of the disease. We identify the climatic & seasonal associations for this case and search the environmental foci in central Taiwan.

PCC-012

Asymptomatic cerebral abscess caused by *Serratia marcescens*: presentation of a newborn case

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Introduction: Cerebral abscess can result from bacterial meningitis, and is often accompanied by clinical symptoms including fever, lethargy, and seizures, and also abnormal laboratory findings related to systemic inflammatory reaction. *S. marcescens* has increasingly known as a causative organism of infection in preterm infant in neonatal intensive care unit (NICU).

Patients and methods: A female infant was born by an emergent Cesarean section because of the fetal distress at the gestational age 31 weeks and 1 day. The birth weight of the baby was 1060 g, and was treated in the NICU. The baby showed regular weight gain and reached full enteral feeding at 24 days. There were no specific findings in periodic brain ultrasonography (US), but on follow-up examination performed on 36 days, a huge hematoma-like mass was observed in the right temporoparietal area (5 × 5 × 4 cm) in the US and non-contrasted CT images. There was still no evidence of distinctive features suggesting the systemic infection in clinical symptoms and laboratory findings, including C-reactive protein and blood culture of the patient. And also, there were no changes in the images according to the time interval in the follow-up US performed 2 weeks later. In the MRI at 50 days of age, a huge necrotic cyst mass (6 × 5 × 5 cm) suggesting abscess or tumor was observed in the right parietal lobe of the brain. So US-guided drainage was performed at the bedside, and pus-like fluid was drained about 10 cc, and *S. marcescens* was isolated in the culture of specimens. In the subsequent lumbar puncture, CSF examination showed a mild pleocytosis (22/μL), an increased protein level (231 mg/dL), and a decreased glucose level (33 mg/dL), but the bacteria did not grow in the culture. Several additional drainages for the abscess were performed and the patient was discharged after 6 weeks of treatment with cefotaxime. Follow-up MRI was showed the improvement of the brain lesion.

Conclusions: I report a case of asymptomatic cerebral abscesses caused by *S. marcescens*, mimicking hematoma and tumor on radiological studies, in the preterm infant.

PCM-001

Unusual cause of gelatinous blobs in the lung

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Background: Hydatid disease is a global public health issue that is more prevalent in the southern and western states of India. Common presentation includes low appetite and abdominal pain with liver cysts.

Objectives: To establish a diagnosis for the case.

Methods: We present the case of a 55-year old man from North East India with an iatrogenic pneumothorax after aspiration of a right lower lobe cyst of unknown etiology. This was managed with a chest drain. Computerized Tomogram (CT) of chest revealed a left upper lobe soft tissue density. Bronchoscopy revealed a contralateral left upper lobe bronchus occluded with yellow gelatinous blobs. Biopsy of the lesion and serology established the diagnosis of Echinococcosis. Liver ultrasound was unremarkable. Patient was successfully treated with Albendazole.

Results: Echinococcosis was diagnosed.

Conclusion: This case highlights an extremely deviant presentation of hydatid lung disease presenting endo-luminally on bronchoscopy and a rare occurrence of bilateral lung involvement, raising a possibility of trans-bronchial spread of previous contralateral ruptured cyst. Direct bronchoscopic visualization with biopsy in our case provided a timely diagnosis and prompt intervention. Rounded cystic opacities in lungs should prompt an investigation for *Echinococcus*. High degree of clinical suspicion with appropriate ancillary imaging and laboratory tests are indispensable, as hydatid disease has varied atypical clinical presentations. Contralateral lesions do not exclude hydatid cysts and bronchoscopy has its utility for diagnosis. This is of utmost importance as early treatment avoids duration related complications of this parasitic infestation.

Keywords: Hydatid cyst, lung, bronchoscopy.

PCM-002

Novel non-invasive point of care sputum test for early identification of *Pseudomonas aeruginosa* airway infection

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Background: Two in three people with lung diseases vulnerable to difficult to diagnose recurrent *Pseudomonas aeruginosa* airway biofilm infections, which eventually leading to higher inflammation and respiratory failure.

Objective and methods: We described novel, non-invasive sputum test for the early identification of airway biofilm infection. The 96 well plate-based test contains nano self-quenched fluorescent dye solution which react with *P. aeruginosa* biofilm substance in sputum, result in solution color change from yellow to green as an indication of biofilm infection. A 240 sputum samples from 81 patients with chronic *P. aeruginosa* lung infection (Mean age; 29.3–56.2 years; n = 33 Females) were used to determine functionality of test.

Results: The population density of bacteria in a sputum biofilm was quantified and correlated to fluorometric response. Over 90% of sputum able to change the color with significant correlation to bacteria density (10^6–10^8 CFU/ml sputum) ($p < 0.01$, $r = 0.983$). A test is accurate, sensitive, and specific for early detection of *P. aeruginosa* biofilm infections in sputum (AUC = 0.94).

Conclusion: Result shows promising used of test as early detection of *P. aeruginosa* airway biofilm infections.

PCM-003

Effect of sustained antibiotic stewardship programme in a tertiary care hospital in Sri Lanka to reduce the threat of antibiotic resistance

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Introduction: Timely understanding of microbial pathogen profiles and introducing antibiotic stewardship programme is important because lack of routine surveillances and limited data describing local AMR patterns in Sri Lanka. We compare antimicrobial susceptibility patterns of *E. coli* and *K. pneumonia* isolates from tertiary care Hospitals in rural (AGH) and urban (SJGH) with National figures (ARSP).

Method: Blood culture isolates from May 2019–April 2020 were tested for identification and antibiotic susceptibility conducted using VITEK®2 Compact. Fisher's exact test (Pairwise) was studied using *rcompanion* package of R (V 4.0.3) software.

Results: From 134-gram (-ve) blood culture isolates 32.8% (44) *E. coli* and 14.9% (20) *K. pneumoniae*. Microbial susceptibility profiles of *E. coli* and *K. pneumoniae* in AGH for Amoxicillin/Clavulanic Acid, Piperacillin/Tazobactam and Amikacin showed a statistically significant susceptibility ($P < 0.05$) with respect to SJGH (2013). Both isolates from AGH maintained similar or statistically better susceptibility compared to National data (2009). Ciprofloxacin susceptibility of *E. coli* from AGH showed no significant change with national data but significantly lower susceptibility than SJGH. However, for *K. pneumoniae* there were no significant change. Meropenem susceptibility of AGH was lower than SJGH for both pathogens, however statistically significant reduction ($P = 0.003$) was only observed in *K. pneumonia*e.

Conclusions: Our results emphasize the importance of enhancing antibiotic prescribing through sustained antibiotic stewardship to improve patient safety and reduce the threat of antibiotic resistance.

Abstract withdrawn

PCM-006

The performance of in-house metagenomics next-generation sequencing with Illumina and Nanopore platform to identify pathogens of pulmonary infection from lung biopsy tissues

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Background: Metagenomic next-generation genomics (mNGS) has a potential to improve the pathogen identification in pulmonary infection. The report on diagnosis performance of Illumina with lung biopsy tissues is rare and nobody focus on the performance of Nanopore in this specimens.
Method: From July 2018 to May 2020, lung biopsy tissues were collected from 140 patients who suspected pulmonary infections or abnormal image finding and applied with clinical microbiological test and mNGS (Illumina and Nanopore) to identify pathogens. The community diversity was calculated based on Illumina result.
Results: We investigated the alpha diversity based on Illumina result, suggesting the significantly lower Shannon's diversity in patients with confirmed pathogen compared with uncertain pathogen patients. The alpha diversity was significantly lower in lower respiratory tract infections (LRTIs) patients than of complications with cancer. The established cutoff value of bacteria and fungi was 239.49 and 263.93 for Illumina RPM (reads per million) ratio, 57 and 31 for Nanopore unique reads. Compared with composite reference standard, Illumina had sensitivity of 77.55%, specificity of 97.62%, with 95.00% positive predictive value (PPV) and 88.17% negative predictive value (NPV). However, sensitivity of 34.69%, specificity of 98.65%, 94.44% PPV and 69.52% NPV for Nanopore. The Illumina/Nanopore could identify more fungi and confirmed by pathological examination, but weakly performance on *M. tuberculosis* complex diagnosis.
Conclusion: We firstly established the cutoff value and investigated the diagnosis performance in Illumina and Nanopore with lung biopsy tissues. Illumina had higher negative coincidence rate, identified more fungal pathogens and demonstrated the changes of community diversity in different diseases. Nanopore should be optimized in wet experimental procedure when applied high background human genome.
Keywords: lung biopsy tissues; mNGS; Illumina; Nanopore; pulmonary infection; alpha diversity.

PCM-007

The impact of procalcitonin testing on antibiotic exposure in an intensive care unit

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Background: Procalcitonin (PCT) is secreted in response to bacterial infection. Compared to C-reactive protein it has a higher specificity, and shorter half- life. Rising incidence of multi-drug resistant organisms, and resulting healthcare costs, are compelling reasons to rationalise antibiotic use. The PRORATA trial demonstrated that PCT testing could safely reduce antibiotic exposure. Our primary aim was to examine the impact of PCT on the duration of antibiotic courses in a London ICU previously naïve to testing. The secondary aim was to determine any potential financial savings.
Methods: The population studied were adult ICU patients admitted for >3 days with a diagnosis of pneumonia. Data from a 6-month period was collected in 2018 (n = 21), when PCT testing was not available, and repeated in 2020 (n = 15) after testing was introduced. Antibiotic type and duration were recorded, and cost was calculated. Median duration of antimicrobial exposure was compared using a Mann-Whitney U test, whilst mean cost was compared using an unpaired t-test.
Results: Median duration of antimicrobial usage in the non-procalcitonin group was 15.6 days versus 14.0 days in the PCT group. The distributions in the two groups differed significantly (Mann-Whitney U = 199, P = 0.04). Mean cost of antimicrobials differed between the two groups but did not reach the threshold for statistical significance (£268.32 (SD = 300.34) vs £307.80 (SD = 183.73), p = 0.65).
Conclusion: PCT testing significantly reduced antimicrobial exposure. This is in spite of the fact that testing had not been used before and nor was an algorithm employed. The lack of a statistically significant difference in cost could be explained by small sample size. We intend to do further larger-scale work on implementing a PCT guided algorithm, and to assess whether this could be of further benefit to reducing antimicrobial exposure and cost.

PCM-008

Study to determine vancomycin susceptibility by different test methods in clinical *Staphylococcus aureus* isolates from the national hospital of Sri Lanka

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Background: Treatment of *Staphylococcus aureus* infections with vancomycin should be guided by minimum inhibitory concentration (MIC). We aimed to determine the concordance between results of different MIC testing methods and to detect creep of vancomycin MIC value..
Methods: A total of 100 clinical isolates of *S. aureus* collected from National Hospital of Sri Lanka were tested simultaneously using agar dilution, BD Phoenix® automated system and E-test method for vancomycin MIC. Results from E-test method was compared with previous study data at the same study setting to detect creep of vancomycin MIC.
Results: All isolates recorded vancomycin MIC ≤2 μg/ml in all three methods as susceptible. Methicillin-resistant *Staphylococcus aureus* isolates had higher vancomycin MIC values in comparison to methicillin-susceptible *Staphylococcus aureus* isolates. E-test method reported higher vancomycin MIC values while agar dilution reference method had the lowest values. Categorical agreement was 100% for both BD Phoenix® and E strip when compared with agar dilution. Essential agreement was 97% for BD Phoenix® while it was 71% for E strip method. According to geometric mean of vancomycin MIC values, a gradual upward trend is seen over the years, but a statistically significant creep was absent.
Conclusions: A gradual upward trend in vancomycin MIC was noted. Higher values were detected for vancomycin MIC by E-test method. Despite having a remarkable categorical agreement, the essential agreement of BD Phoenix® and E-test methods were markedly different.

PCM-009

Clinical metagenomics for complicated skin and soft tissue infections

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Background: A rising variety of infectious illnesses are being studied using metagenomic next-generation sequencing. It is more

sensitive than the usual culture-based approach for detecting diseases since metagenomics sequences all the nucleic acids contained in a material. Next-generation metagenomic sequencing is capable of simultaneously detecting bacteria, viruses, and mycobacterium. Several studies applied metagenomic in various skin and soft tissue infections, such as studying the microbiome of chronic non-healing wounds, infected diabetic foot ulcers, and necrotizing soft-tissue disease. Here, we applied metagenomics sequences in complicated skin and soft tissue infections and review the literature and analyze the pros and cons of metagenomics sequences relative to conventional methods.

Methods: Twelve cases of complicated skin and soft tissue infections were included. The identification of pathogens using clinical metagenomics and culture were compared using tissue specimens, abscesses, and/or interstitial fluids collected during surgical debridement.

Results: Comparing to conventional culture methods, clinical metagenomics identified more pathogens in a greater number of complicated skin and soft tissue infections patients and a significant number of polymicrobial infection. Clinical metagenomics had a greater sensitivity than culture tests for identifying pathogens. Clinical metagenomics carried higher detection rates for viruses and anaerobes comparing to conventional culture. Moreover, clinical metagenomics revealed more polymicrobial complicated skin and soft tissue infections.

Conclusion: Clinical metagenomics is a potential technique for determining the microbiologic diagnosis of complicated skin and soft tissue infections, notably for detecting viruses, anaerobes and polymicrobial infections. Clinical metagenomics is effective at detecting a wider variety of pathogens and identifying anaerobes than conventional culture.

PCM-010

Raman spectroscopy for identification of medically important bacteria – translation from bench to bedside

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Reproducible and robust bacterial identification is key to cutting-edge clinical microbiology. Present approaches for bacterial identification have limitations like poor sensitivity, high cost, slow turnaround time etc. These can be overcome by Raman spectroscopy, as it promises label-free approach and is capable of detecting biochemical signatures from single bacterium. Published studies have confirmed the potential of Raman spectroscopy to identify bacteria. However, focus on medically important bacteria and reproducibility needs to be assessed. We have established Raman database for medically important bacteria, by analysing different bacterial species so that reproducibility can be determined. Raman database was built using 80 clinical isolates of pathogenic bacteria, covering around 95% of ESKAPE pathogens. Isolates were fixed in Paraformaldehyde (PFA) and stored in −4°c. Samples were washed thrice with MilliQ water at 5000 g for 5 mins and bacterial pellets were resuspended in MilliQ. 1.5 ul of diluted bacterial sample was drop-casted on fabricated Raman substrate and dried at room temperature. Raman spectral acquisition was done with 633 nm excitation, mean Raman spectrum was captured and bacterial species was identified with chemometrics. Raman spectra were analysed using multivariate analysis by Principal component analysis (PCA) and neural networks (CNN) profiling. Raman spectra showed clear demarcation of bacterial species (Fig 1). PCA showed good clustering of diverse bacterial species (Fig 2). CNN provided clear distinction of bacterial species ranging in accuracy from 96 to 100% (Fig 3). Raman database for medically relevant bacteria is successfully created. To increase robustness of database, greater number of samples need to be tested. Novelty of the current work is that, database can easily be extended to clinical samples.

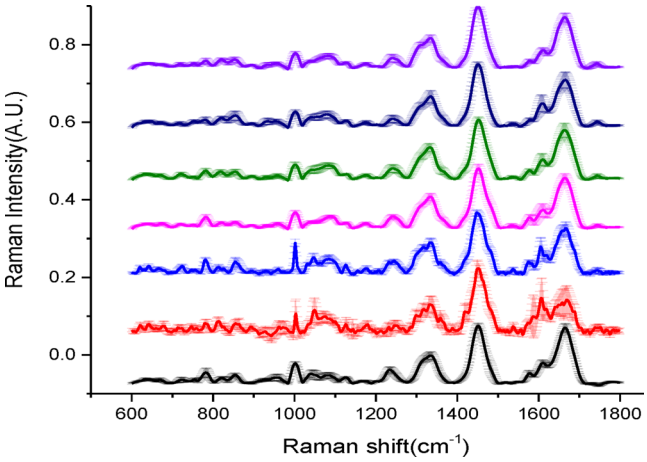

Figure 1

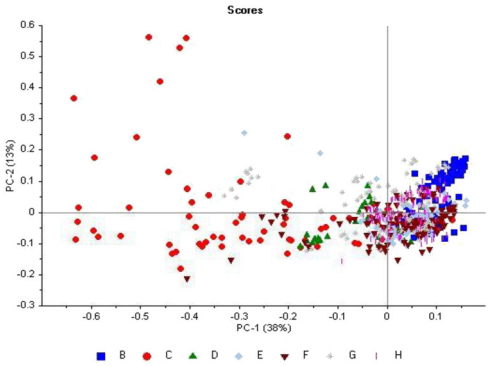

Figure 2

True Label \ Predicted Label	S.aureus	E. coli	K. pneumoniae	Acinetobacter	P.aeruginosa	E. faecalis	E. cloacae	P. vulgaris	Actual Count	Accuracy
S.aureus	6	0	0	0	0	0	0	0	6	100
E. coli	0	13	0	0	0	0	0	0	13	100
K. pneumoniae	0	0	22	0	0	0	0	0	22	100
Acinetobacter	0	0	0	7	0	0	0	0	7	100
P.aeruginosa	0	0	0	0	19	0	0	0	19	100
E. faecalis	0	0	0	0	0	17	0	0	17	100
E. cloacae	0	0	0	1	0	0	21	2	21	100
P. vulgaris	0	0	0	0	0	0	1	26	27	96.2963
Total Predicted percentage	6	13	22	8	19	17	22		28 overall accuracy	99.537

Figure 3

PCM-011

Impact of age and gender on the pathobiology of endophthalmitis in humans

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Purpose: Endophthalmitis is a severe inflammatory ocular disease leading to irreversible loss of vision. The aim of this study was to comprehensively examine the impact of these host biological

factors (age and sex) and corelate it with antibiotic resistance and pathogenesis in patients with bacterial endophthalmitis.
Methods: Sixty vitreous fluids of 60 patients with endophthalmitis and 20 non-infectious controls were included in the study. The patients were divided into 3 groups as A (0–30 years), B (31–54 years) and C (>55 years). Expression of IL-6, IL-10, IL-1β, IL-8, IL-17, TNF-α and LCN-2 were analyzed by multiplex immunoassay (MILLIPLEX, Merck) and correlated with the age and gender of the patients along with the bacterial antibiotic resistance profile.
Results: Group B (age between 31–54) exhibited the highest inflammatory response for all mediators tested except IL-1β. In contrast, IL-10 was found to be significantly higher in younger individuals ($p = 0.04$). Comparatively, LCN-2 was found be higher ($p = 0.01$) in the older age group (group C). Interestingly, only IL-8 was found to be significantly associated with the female group ($p = 0.009$). Additionally, patients infected with antibiotic resistant pathogens exhibited higher IL-1β, IL-8 and TNF-α compared to antibiotic-susceptible group indicating high inflammatory response irrespective of age and sex.
Conclusion: Antibiotic resistance and age, are important biological variables in bacterial endophthalmitis. In future, strategies to differentially engage signaling pathways should be considered in the design of immunotherapeutic approaches to modulate the immune response for better prognosis in aging and drug-resistant endophthalmitis.

PCO-001

The relationship between SARS-CoV-2 antibody titers and the severity of COVID-19

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Background: Severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) antibody titers showed positive correlation with the disease severity in patients with COVID-19 in previous studies. We investigated the cause-effect relationship between the SARS-CoV-2 antibody titers and the disease severity.
Methods: We prospectively enrolled patients who were admitted with the diagnosis of COVID-19 from February to August 2020 at Chung-Ang University Hospital in Seoul, South Korea. We compared the SARS-CoV-2 antibody titers including anti-receptor binding domain (RBD) antibody and neutralizing antibody (Nab) from blood samples and the patients' chest radiographs (CXR) score representing the disease severity of COVID-19.
Results: A total of 40 patients with COVID-19 were finally enrolled in this study. Pneumonia was discovered in more than half of the patients (25/40, 60%). SARS-CoV-2 antibody titers were higher in patients who were more than 60 years old (anti-RBD antibodies $p = 0.003$ and Nab $p = 0.009$), presented with pneumonia ($p = 0.006$ and $p = 0.007$) and applied with oxygen therapy ($p = 0.003$ and $p = 0.004$) than ones who were not. CXR score was positively correlated with both anti-RBD antibody ($p = 0.002$) and Nab titers ($p = 0.001$). In addition, while anti-RBD antibodies showed the peak level in 31–70 days after the onset of symptoms, CXR score showed the peak score earlier in 15–21 days. Similarly, the peak time of CXR score was earlier than Nab titers (15–21 vs 22–30 days).
Conclusions: When we compared the peak time of SARS-CoV-2 antibody titers and CXR score after the onset of symptoms, we suggested that severe clinical manifestations resulted in high titers of SARS-CoV-2 antibodies.

PCO-002

Effect of *Lonicera caerulea* on cytokine production of alveolar macrophages by stimulation with SARS-CoV-2-related proteins

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Background: The SARS-CoV-2 infection is a lethal viral infection that is widespread all over the world, but there is no established drug for the SARS-CoV-2. In fatal cases, cold symptoms worsen to acute respiratory failure. One of the reasons is the cytokine storm due to the overproduction of inflammatory cytokines such as TNF-α, IL-1β, and IL-6. *Lonicera caerulea* has been used in traditional medicine of the Ainu people in northern Japan as a fruit of immortality and longevity. Here, we investigated whether *Lonicera caerulea* extract (LCE) affects the production of cytokines by mouse alveolar macrophages by stimulation with this SARS-CoV-2-related protein.

Figure. SARS-CoV2 antibody titer and chest X-ray (CXR) score according to the days after the onset of symptoms caused by COVID-19. (A) ELISA-based anti-RBD antibody and CXR score, **(B)** Serum virus neutralization assay and CXR score

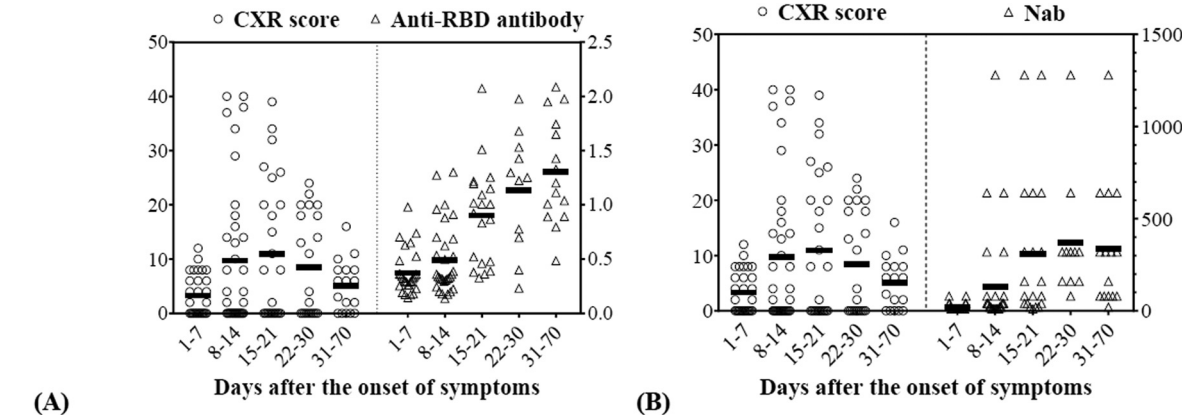

Figure: (abstract PCO-001)

Methods: The LCE was extracted with methanol from fruits from Atsuma Town, Hokkaido. Alveolar macrophages were aseptically extracted from 6 week male ICR mice. Both alveolar macrophage and SARS-CoV-2-related proteins (nucleocapsid, S1 protein, S1 + S2 protein) were cultured in RPMI1640 medium with 5% fetal calf serum at 37°C. and 5% CO2 for 24 hours. After cytokines (TNF-α, IL-1β, and IL-6) in the culture supernatant were measured by the ELISA method.
Results: Cytokine production from alveolar macrophages was significantly enhanced by stimulation with SARS-CoV-2-related proteins. This enhancement was remarkable in the order of nucleocapsid, S1 + S2 protein, and S1 protein. Regarding cytokine production, a significant decrease in cytokine production was confirmed in alveolar macrophages treated with LCE.
Conclusions: Our result demonstrated that LCE suppresses the enhancement of cytokine production from alveolar macrophages by the SARS-CoV-2-related protein. Lonicera caerulea is presumed to suppress the exacerbation of SARS-CoV-2 such as acute respiratory failure.

PCO-003

The estimation of direct hospital costs and Intensive Care Units (ICU) admissions for COVID-19 patients and the assessment of the impact of remdesivir administration in the Saudi Arabian context

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Introduction: Severe Acute Respiratory Syndrome CoronaVirus 2, which causes Coronavirus Disease 2019 (COVID-19) has spread rapidly around the world, with the World Health Organization to declare a pandemic in March 2020. Saudi Arabia was significantly impacted by COVID-19. In March 2021, 381 000 cases were reported with 6539 deaths. This study attempts to quantify the impact that a COVID-19 therapeutic, Remdesivir, could have on preventing ICU admissions, mechanical ventilation, and deaths.
Methods: A forecasting model was designed to estimate the impact of the antiviral Remdesivir (RDV) on the capacity of intensive care and healthcare costs when managing hospitalized COVID-19 patients. The forecasting model was applied in the Saudi context with a 20-week projection between February 1st and June 14th, 2021. Model inputs were collected from published global and Saudi literature, available infectious diseases forecasting resources and expert opinions. Two scenarios were assumed: a pessimistic scenario where the effective pandemic reproduction number (RT) projections will maintain a "1.2" level in the study period and an optimistic scenario where the RT projections will gradually decrease from "1" to "0.8.".
Results: The model estimated that the use of RDV in hospitalized patients in the optimistic and pessimistic scenarios could prevent 1521 and 3550 patient transfers to ICU and mechanical ventilation, prevent 815 and 1582 deaths, and make a potential cost savings of 646 m. SAR and 1393 bn. SAR due to the reduction in ICU capacity, respectively.
Conclusions: The treatment with RDV may improve patient outcomes and reduce the burden on healthcare resources during this pandemic.

PCO-004

Use of personal protective equipment by healthcare workers exposed to COVID-19 patients at a tertiary care hospital in a lower middle-income country

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Background: Evaluating PPE use and Covid-19 transmission within the Sri Jayewardenepura General Hospital, Sri Lanka from 1st October 2020 to 30th January 2021, in healthcare workers (HCWs) who were within 1 m distance to a COVID-19 patient.
Method: This retrospective descriptive study identified HCWs as high or low risk exposures via data collected at a routine risk assessment following the diagnosis of a COVID-19 patient. Those of high-risk were quarantined, monitored for symptoms and polymerase chain reaction (PCR) tested 10 days post-exposure. Those of low-risk continued to work with recommended PPE and were PCR tested only in 7 days post-exposure or if they developed symptoms. Related associations were computed by an online Fisher-Exact Test calculator.
Results:108 COVID-19 positive patients were diagnosed in hospital either by Rapid Antigen Test (RAT) or PCR (as source patient), of which 17 were HCWs. 29 of the 108 (26.9%) were asymptomatic, while 26 (24%) had fever, 15 (11%) had shortness of breath and 23 (21.3%) had cough. Aerosol Generating Procedures were performed in 10 events. 53 HCWs were quarantined for 14-days following exposure but only 4 developed the disease. Of total 946 events, 945 had HCWs exposed within 1 m to COVID-19 positive patients while one event had exposure to the equipment used on a patient. 446 (47.1%) wore N95 masks or equivalent. 17 of the exposed HCWs (whose source was also an HCW) were not wearing any PPE. Among the 945 events exposed within 1 m, the source patient wore a mask only in 717 (75.9%). Only 98 events were for more than 15 minutes. Not having a mask on source ($p = 0.0139$), >15 minutes exposure within 1 m ($p = 0.0298$) and not having eye protection (0.0184) had significant association to COVID-19 transmission.
Conclusion: Not having a mask on source, >15 minutes exposure within 1 m and not having eye protection had significant ($p < 0.05$) association to COVID-19 transmission.

PCO-005

Assessing risk factors for health care associated transmission of SARS-Cov-2 virus infection among health care personnel in a tertiary care hospital, Sri Lanka; a case-control study

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Background: There is a dearth of data regarding the risk factors associated with the transmission of COVID-19. This study aims to find associated risk factors for the transmission of SARS-Cov-2 virus among health care workers (HCW) at Sri Jayewardenepura General Hospital, Sri Lanka.
Method: This is a retrospective case control study. The data was collected from December 2020 to June 2021. A case was defined as either a PCR or rapid antigen test for SARS-Cov-2 virus positive in a HCW, with no known exposure to the disease in the community but had a significant exposure in the health care setting within 14 days. A control was a HCW who had the exposure to the same source patient, but not positive to COVID-19 within 14 days of exposure.

The data collected at risk assessment of 18 cases and 72 controls were analyzed using SPSS_26 software.
Results: Among the cases 77.8% were males. 61.1% of source of infection was a HCW. Source not wearing the mask was high as a percentage (in cases 77.8% vs in controls 59.2%) though not statistically significant. Doctors were significantly at a lower risk of getting the infection than other categories of health care workers (OR = 1.091; 95% CI 1.018–1.170). All the cases and most of the controls have not been fully vaccinated. Being within 1 m distance from the source was a statistically significant risk factor (OR = 8.500; 95% CI 1.067–67.730). Three times higher risk was observed when exposure time was >15 minutes (OR = 3.571; 95% CI 0.949–13.439). The percentages of HCWs who were not wearing any personal protective equipment in the cases was not different to the controls (44.4%vs 43.1%). Among HCWs who were at <1 m distance the percentage of not having any PPE among cases and controls were 47.1% vs 54.2%.
Conclusion: Being within 1 m distance from a positive patient was a significant risk factor to acquire the disease. Doctors were significantly at a lower risk of getting the infection than other categories of health care workers.

PCO-006

Psychological effects of paramedics by experience of managing COVID-19 patients

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Background: During the coronavirus disease 2019 (COVID-19) pandemic, not only medical personnel but also paramedics have faced multiple physical and psychological challenge while carrying out their duties. The aim of this study is to evaluate the difference in psychological effects of paramedics by experience of managing COVID-19 patients.
Material and methods: A survey was conducted during December 2020, targeting paramedics in South Korea. An official letter about participation request that included the link of online-based survey was sent to National Fire Agency. Only one response was accepted from each participant.
Results: A total of 326 paramedics responded to the survey. Of them, 66.3% (216/326) had experience in managing COVID-19 patients. There were no differences in the distribution of sex, age, working area, length of working experience, and underlying comorbidities between those who experienced management of COVID-19 patients (COVID group) and those who were not (non-COVID group). The proportion of person who showed severe Posttraumatic Stress Disorder (PTSD) symptoms was significantly higher among COVID group (11.1% vs. 3.6%, $P = 0.029$). The score of Global Assessment of Recent Stress Scale was significantly higher among COVID group (18.7 ± 11.1 vs. 16.1 ± 9.9, $P = 0.042$). Higher proportion of paramedics in COVID group wanted leave their job if they have a chance to change jobs (24.1% vs. 9.1%, $P = 0.001$). In addition, paramedics in COVID group tended to show concerns about COVID-19 infection.
Conclusion: The experience of managing COVID-19 patients prompted psychological distress for paramedics in South Korea.

PCO-007

Secondary bacterial and fungal infections in COVID-19 patients

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Background: Presence of secondary infections in COVID-19 increases the morbidity and mortality significantly. The ones most commonly seen are multidrug resistant bacteria. These nosocomial multidrug resistant pose a challenge in antibiotic therapy. Whether empirical antibiotics are useful or not is unknown. Increasing reports on invasive fungal infections have been reported all over the world during this pandemic and particularly mucormycosis from India. Risk factors like hyperglycemia, ketoacidosis, iron over load, hypoxia added with prolonged hospitalization, use of mechanical ventilation, and corticosteroid therapy could be the reason behind this rampant spread. Data regarding secondary infections in the ongoing second wave of COVID-19 that affected India from the end of April 2021 is very limited. Here we present our findings regarding the microbial profile of the secondary infections in COVID19 patients admitted to our health care facility during the second wave.
Methods: Retrospective data from hospitalized COVID-19 patients was analyzed from the month of May 2021 to June 2021. Any bacterial growth detected from blood and respiratory samples of COVID-19 positive patients and fungal growth detected in COVID-19 positive and post COVID-19 patients were included in the study. Bacterial growth from non-respiratory and non-bloodstream samples were excluded. Patients included had an RT-PCR test positive for COVID19. Diagnosis of definite mucormycosis/aspergillosis was made on demonstration of hyphae on histopathology of biopsied sample with or without culture confirmation. All data were collated in Microsoft Excel for analysis. Using these data mortality was calculated.
Results: Total number of COVID-19 positive patients admitted to the hospital in this time period were 600. Total 37 bacterial isolates (from 34 patients) were included, of which 16 were from blood culture and 21 from respiratory culture. The mean age of patients was 56.2 years. There was no sex predilection, both males and females were affected equally (M = 17 and F = 17). Among the 37 patients with secondary bacterial infection 24 were in ICU (64.8%) and 13 were in wards (35.1%) at the time of sending cultures. Of the pathogens isolated Gram negative bacteria was predominant (68.75%, 11/16). The most common isolate in blood stream infection was *Klebsiella pneumonia* (4/16), followed by *Enterococcus spp* (3/16). The most common isolate in respiratory tract infection was *Acinetobacter baumanii* (9/21), followed by *Klebsiella pneumonia* (5/21). Out of 34 patients 3 had polymicrobial infection. All *Klebsiella pneumonia* isolates were Carbapenem Resistant and all isolates of *Acinetobacter baumanii* and *Pseudomonas aeruginosa* were Multidrug resistant. The average time between onset of COVID-19 symptoms and development of secondary bacterial infections 8 days. Overall 54 patients had invasive fungal infections of which majority had mucormycosis (45/53), followed by aspergillosis (7/54). The most common species of Mucorales was *Rhizopus spp* (43/45). One isolate was identified as *Cladosporium spp*. Of the 53 cases 2 were pulmonary mucormycosis and the rest Rhino-orbito-cerebral mucormycosis. Total number of deaths was 78. Patients with secondary bacterial infections were 34. Patients with secondary fungal infections was 53. The number of deaths due to secondary bacterial infections was 7. The number of deaths due to mucormycosis was 5. The overall mortality due to COVID-19 was 13% (78/600). The rate of secondary infections in COVID19 patients was 14.5% (87/600). Mortality due to secondary bacterial infections was 20.5% (7/34). The actual mortality rate due to mucormycosis could not be assessed as most cases left the

hospital against medical advice. The outcome of secondary infections is depicted in Figure 1.

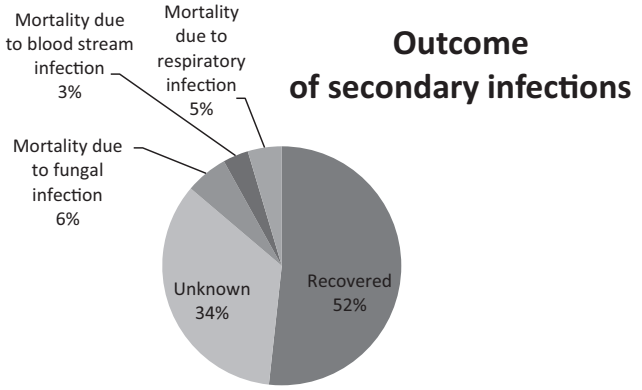

Figure 1. Outcome of secondary infections.

Conclusion: Secondary infections play a vital role in increasing the morbidity and mortality in COVID-19 patients. The common isolates were Carbapenem Resistant *Klebsiella pneumonia* and Multidrug resistant *Acinetobacter baumanii*. Based on the time taken between COVID-19 positivity and development of secondary bacterial infection we can say that these pathogens could be nosocomial. Most of the bacterial isolates identified are multidrug resistant implying that empirical antimicrobial therapy might not be useful in such cases. Adhering to antimicrobial stewardship guidelines and strict infection control practices can help reduce the transmission such resistant pathogens in healthcare settings. The most common fungal isolate was *Rhizopus spp.* The primary reason for dissemination of fungal infection could be improper glycemic control and rampant use of corticosteroids and immunomodulators. Picking up the sentinel signs of mucormycosis early and employing multimodal therapy with antifungals and surgical debridement can play a vital role in reducing this fungal menace.

PCO-008

Identification of daclatasvir as a repurposed drug against Nsp15 of SASR-CoV2 (COVID-19) by using in silico approaches

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Background: In December 2019, SARS-Cov-2 epidemic was reported in Wuhan, China and then it spreads widely affects millions of people around the world. Nsp15 is one of the key members of EndoU family which perform several biological functions like RNA endonuclease activity which generate 2'-3' cyclic phosphodiester termini. In viruses, Nsp15 is conserved among nidoviruses and absent in other RNA viruses which makes it potential target for recent coronavirus outbreak.
Methods: In this study, we have used earlier studied Benzopurpurin B which has inhibition property against Nsp15 protein of SARS virus (0.2 μM). Next, we have developed structure-based pharmacophore model with the help of Benzopurpurin B and crystal structure of Nsp15 endoribonuclease NendoU from SARS-CoV-2 (6vww). For pharmacophore development, we have employed two different software, viz., Discovery Studio 4.0 and Ligandscout. The selected pharmacophore was used to screen FDA approved drugs from DrugBank Database. The hits retrieved were next subjected to molecular docking analysis followed by molecular dynamics studies.
Results: The best pharmacophore model A with 6 features (2 hydrogen bond acceptor, 2 hydrogen bond donor and 2 hydrophobic group, AADDHH) was selected based on highest selectivity score of 11.155. the validated hypo model 1 able to screen out 136 drugs out of 2454 FDA approved drugs from DrugBank Database. These drugs were further filtered out using molecular docking to remove any false-positive hits. Finally, 3 top hits were selected for MD simulation to confirm their binding stability.
Conclusion: Daclatasvir (DB09102), an antiviral approved drug was identified as possible candidate for designing the potent inhibitor against Nsp15 of SARS-CoV-2 virus, although further evaluation via wet lab is required to measure its efficacy.

Abstract withdrawn

PCO-010

Real-time PCR detects 4 rapid transmission variants of SARS-CoV-2

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Background: Currently in the world there are many variants of SARS-CoV-2, among which there are 4 variants: Alpha (B.1.1.7), Beta (B.1.351), Gamma variant (P.1), and Delta variant (B.1.617.2) has a faster transmission rate than the original strain by 82%, 161%, 50% and 198%, respectively. To detect the SARS-CoV-2 variants circulating in a certain endemic area, the method that the researchers are currently using is to sequence the entire genome

of the viruses detected in the samples. However, the sequencing method has the limitation that it cannot be applied in clinical laboratories.

Aim of the study: Design a test kit using multiplex real-time PCR that can be performed in diagnostic laboratories to detect 4 variants Alpha, Beta, Gamma and Delta and two mutations that help the virus to spread rapidly (D614G) and can escape the action of specific antibodies (E484 K).

Material and method: Primers and probes to detect Alpha, Beta, Gamma and Delta variants are designed based on the detection of specific mutations of these variants. The Alpha, Beta and Delta variants were detected based on ARMS Taqman real-time PCR (ARMS: Amplification Refractory Mutation System) with the principle that if a mutation is present, the Taqman probe will not be hydrolyzed and will not have an amplified signal, if there is no mutation the Taqman probe will be hydrolyzed and will have an amplified signal. The Gamma variant and the D614G mutations as well as the E484 K mutations were detected based on the SNP Taqman real-time PCR with the principle that each mutation would be detected by two Taqman probes with different reporters, FAM and HEX or TexasRED and CY5 and depending on the early or late of the fluorescent signal of these two Taqman probes, it can be concluded whether or not there is a mutation. The test kit is designed with three RT multiplex real-time PCR with multiplex A (MPL-A) to detect SARS-CoV-2 based on E gene using primers and Taqman probe (FAM) according to WHO design, variant Alpha (HEX) and the internal control is the RNAseP gene (CY5); MPL-B detects Delta variant (FAM), Beta variant (HEX), and Gamma variant (TexasRED/CY5); MPL-C detects D614G (FAM/HEX) and E484 K (TexasRED/CY5). The multiplex was prepared from AgPath-ID™ One-Step RT-PCR (ThermoFisher, USA). To check the primers and probes, the corresponding DNA sequences for the mutants were also designed as controls [+]. The test kit is then tested on samples that are the RNA extracts positive with SARS-CoV-2.

Results: Testing on [+] controls showed that the detection limit for the E gene and the Alpha variant was 10-6 fm/μl, the Delta variant was 10-5 fm/μl, and the Beta and Gamma variant was 10-7 fm/μl, the D614G and E484G mutations were 10-5 fm/μl. There was no cross-detection of mutations or variants. Tested on RNA extracts that were positive with SARS-CoV-2, the results said that: In HCMC, the strain (1) taken in April 2020 is the wild type, while all strains (12) taken in June 2021 are Delta variants with additional mutations D614G and no mutations E484 K; In Quang Nam, the samples taken in June 2020 are both wild type (2) and have mutation D614G (3), while in June 2021 all strains were variants Alpha (4) and has the D614G mutation. The sample with the wild type, with the Delta variant, with the Alpha variant and the sample with only the D614G mutation were sequenced the whole S gene and the results were completely consistent with the real-time PCR results.

Conclusion: According to the laws of evolution, a rapidly spreading variant will gradually replace the original wild strain, and once community immunity to a variant is achieved, it may be susceptible to another variant and it can therefore replace the old one. Therefore, it is necessary to develop and set-up the multiplex real-time PCR test to detect 4 rapid transmission variants in diagnostic laboratories. With the collected results on the stock samples, we can conclude that at the beginning of the epidemic in Ho Chi Minh City, SARS-CoV-2 was still the original wild strain, but now it has been completely replaced by the Delta variant. In Quang Nam, the beginning of the epidemic was a wild strain but also circulating a strain with a D614G mutation, however the Alpha variant is currently circulating and has a D614G mutation. Particularly, the E484 K mutation has not appeared so far and this is an indication that SARS-CoV-2 has not yet been resistant to specific antibodies that recognize the receptor on the spike protein of the virus.

Keywords: SARS-CoV-2 variants, RT Multiplex real-time PCR.

PCO-011

Assessment of serial monitoring of inflammatory markers in hospital in-patients

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Background: Inflammatory markers such as C-Reactive Protein (CRP) and D-dimer have played a key role in prognostication, triaging of COVID-19 patients. The Ministry of Health and Family Welfare (MoHFW) India has proposed national guidance on the serial monitoring of inflammatory markers as a part of management for hospitalized COVID patients.

Objectives: We aimed to review if the serial monitoring of inflammatory markers adheres to existing national guidance.

Methods: A retrospective review of electronic patient records of 100 hospital in-patients with swab-confirmed COVID-19 was conducted as a baseline audit in which documentation on serial monitoring with CRP and D-dimer on days 1, 4, 7, 10 was checked for patients with moderate to severe COVID disease. Multiple improvement strategies were subsequently implemented and assessed via Plan–Do–Study–Act (PDSA) cycles. A need for more consistent monitoring of markers was emphasized to the treating faculty mainly in form of departmental meetings, in-house clinical seminars. Repeat survey was carried out after a gap of 4 weeks.

Results: Baseline audit highlighted two components were deemed essential: (1) Baseline record of the markers which is up to 4 days of admission; (2) Final record of the markers which is within a period of 4 days prior to discharge. The frequency of these components saw significant improvement by completion of the final PDSA cycle.

Conclusion: The serial monitoring of inflammatory markers did not fall within the existing national guidance. There is a scope for larger studies to validate the serial use of markers, cost benefit and utility of these tests and to determine the frequency of their repeatability in terms of difference it can make in terms of disease outcome.

Keywords: COVID-19, inflammatory markers.

PCO-012

Place of COVID-19 transmission in blood transmission: A case report

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A novel human coronavirus, SARS-CoV-2, has emerged from China in December 2019. It has spread worldwide, conforming to person-to-person transmission. Though the studies have found 15% to 40% of symptomatic patients had detectable RNA-emia, it is not known whether COVID-19 may be transmitted by blood transfusion. Also, according to the worldwide data, only less than 10% do annual blood donations. As Blood and blood components are essential inpatient management it is very important to know whether the SARS-CoV-2 virus is transfusion-transmitted.

Case report: A 33-year-old had donated a whole blood unit at a mobile blood donation campaign on 08/12/2020. The donor was healthy, asymptomatic, and no evidence to suspect COVID-19 infection at the time of donation. He had completed the routine pre-donation procedures including screening questionnaire, temperature check, and short medical review. It concluded without any post-donation complications.

On 19/12/2020, the donor was identified as a COVID-19 confirmed case. 11 days after the contact, all first contacts related to the blood transfusion process, remaining Fresh Frozen Plasma pack, and the

recipient of red cell unit tested for COVID-19 PCR and all were non-reactive. None of the recipients developed any COVID-19 related symptoms post-transfusion

Conclusion: None of the recipients of donor diagnosed with COVID-19 following donation developed COVID-19 related symptoms or tested positive for COVID-19 PCR and remaining blood products were also negative for COVID-19 PCR in this asymptomatic blood donor. Continuous data collection is needed to conclude the possibility of COVID-19 transmission through blood transfusion.

PCO-013

Vaccine-associated disease enhancement: a case report of post-vaccination COVID-19

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Introduction: The COVID-19 pandemic has entered a new phase with the roll-out of several vaccines worldwide at an accelerated phase. Currently, little is known about the potential of vaccine associated disease enhancement (VADE) following COVID-19 immunization.

Case Illustration: We herewith report two patients admitted with confirmed COVID-19 pneumonia with a history of CoronaVac vaccination. The first patient with a relatively milder course of the disease had received two doses of CoronaVac whereas the second patient with a more progressive course of the disease received only one dose before developing symptoms and being admitted to the hospital. Our observations suggest that vaccination could act in boosting the inflammatory process and reveal the previously asymptomatic COVID-19 illness. Theoretically, vaccines could induce VADE, where only suboptimal, non-protective, titers of neutralizing antibodies were produced or pro-inflammatory T helper type 2 response were induced. Secondly, enhanced respiratory disease (ERD) could manifest, where paradoxically, pulmonary symptoms are more severe due to peribronchial monocytic and eosinophilic infiltration can happen during infection after vaccination or previous infection.

Conclusion: We report two cases of patients developing COVID-19 shortly after vaccination with CoronaVac in which VADE is likely. We recommend that current vaccination strategies consider measurement of neutralizing antibody titer as a guide in ensuring the safest strategy for mass immunization. Studies are needed to investigate the true incidence of VADE on vaccinated individuals and on how to differentiate between severe disease unrelated to vaccination and VADE.

PCO-014

Parenteral and oral anticoagulant treatment for hospitalized and post-discharge patients with COVID-19: A systematic review

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Introduction: Coagulation abnormalities are key features of COVID-19 patients and anticoagulants has been endorsed by different thrombosis and hematological societies. Regardless of the recommendations above, evidence on the benefit and risk of both prophylactic and treatment dose anticoagulants in COVID-19 patients are lacking. This study aims to investigate the literature on oral and parenteral anticoagulants treatment for hospitalized and post-discharge patients with COVID-19.

Methods: Systematic search and handsearching was conducted between 22 November and 9 December 2020 in the following databases: Cochrane, EBSCO, Pubmed, and EMBASE. The inclusion criteria are human study, aged 18 years or older, full-text, English, randomized control trial, meta-analysis, systematic review, and observational study.

Results: The search yield 18 studies on in-hospital anticoagulant use and 2 studies with prior anticoagulant use. Four studies were eligible for quantitative analysis. Three case series were on drugs with anticoagulation effects were eligible for appraisal. None of studies are clinical trial. All studies included were high quality studies based on the Newcastle Ottawa Scale.

Discussion: In the absence of clinical trial results, early findings from the studies in this systematic review demonstrate the benefit of anticoagulation in COVID-19 patients, especially in the setting of increased VTE in patients with severe disease. Surprisingly, to date we found no published studies reporting the use of anticoagulants in COVID-19 patients post-discharge.

Keywords: COVID-19, anticoagulant, VTE, thromboprophylaxis.

PCO-015

Human airway epithelial Calu-3 cells as the potential platform to study the pathophysiology of SARS-CoV-2 isolated in Malaysia

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Background: Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has been identified as the etiologic agent for the Coronavirus Disease 2019 (COVID-19) outbreak that started in early December 2019. To date, COVID-19 has caused almost 6000 deaths in Malaysia since its first outbreak in January 2020.

Objective: Understanding the pathophysiology of the virus is important for the researchers to identify the potential targets against COVID-19. For this purpose, the virus must be isolated and propagated in a suitable host that allows the virus to grow well and at the same time would not cause immediate cell death to the host.

Method: In the effort to identify the best host cells for the propagation of SARS-CoV-2, we infected several mammalian cells lines (i.e., Vero, Vero E6, Calu-3, MRC-5, and A549) with different lineages of SARS-CoV-2 that are widely circulated in Malaysia.

Results: We found that SARS-CoV-2 multiplied only in Vero, Vero E6 and Calu-3 cells. Propagation of the virus in these cell lines were

confirmed with real-time RT-PCR. Images from transmission electron microscopy (TEM) revealed multiplication of the virus in various vesicles of these cells. Multiplication of these viruses was accompanied by apoptosis of the host cells (cytopathic effect (CPE)) except for Calu-3 cells.

Conclusion: These findings revealed the potential of Calu-3 as the model cell line to assist scientists into recapitulating the relevant responses of SARS-CoV-2 infection in vitro.

Keywords: COVID-19, SARS-CoV-2, Calu-3, SARS-CoV-2 pathophysiology, SARS-CoV-2 propagation, Malaysia, cytopathic effect, SARS-CoV-2 morphology, viral multiplication.

PCO-016

Community acquired co-infection and trends in antimicrobial use among COVID-19 patients in a referral center in the Philippines

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Background: Antibiotics are often prescribed for patients with COVID-19. This study aimed to describe community acquired co-infection (CAI) and antimicrobial use over time among COVID-19 patients.

Methods: We reviewed electronic medical records of adults ≥19 years with confirmed COVID-19 admitted in our institution from March–August 2020. Clinical, laboratory and outcomes data of patients with and without CAI were compared.

Results: Of 1116 patients included, 55.0% received antibiotics within 48 hours, but only 66 (5.9%) had microbiologically documented CAI, mainly respiratory (40/66, 60.6%). Patients with CAI were more likely to present with myalgia ($p = 0.02$), nausea/vomiting ($p = 0.014$), decreased sensorium ($p = 0.007$), a higher qSOFA ≥2 ($p = 0.016$) and require vasopressor support ($p = < 0.0001$). Patients with CAI also had higher median WBC count (10 vs. 7.6 cells/mm^3), absolute lymphocyte count (1386 vs. 970×10^9 cells/liter), procalcitonin (0.55 vs. 0.13, $p = 0.0003$), and ferritin (872 vs 550, $p = 0.028$). Prescribing frequency ranged from 47.8–72.9% per month, and was highest for critical (92.3%) and lowest for mild COVID-19 (15.1%). Mortality of those with CAI (48.5%) or on empiric antibiotics (13.9%) was higher compared to those without CAI (14.3%) or antibiotics (1%), respectively.

Conclusion: Overall CAI rate was low (6.5%) and antimicrobial use disproportionately high (55.0%), varying little over time. Certain clinical and diagnostic parameters may help identify those with CAI. Antimicrobial use may impact mortality, and stewardship is paramount given low co-infection rates.

Abstract withdrawn

PCO-018

Hospitalization decision model for COVID-19 patients with comorbidities

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Background: The spread of COVID-19 has put a heavy strain on the healthcare system during all over the world.
Aim: Development of a predictive model for making decisions on hospitalization of patients with COVID-19 with comorbidities.
Methods: Observational retrospective cohort study of 74 314 COVID-19 patients with comorbidities based on monitoring data in the first half of 2020. Binary logistic regression, ROC analysis was used.
Results: $P = 1/(1 + e^{-z})$, $z = -1{,}01 + 4{,}22^* X_{SEV} + 2{,}12^* X_{MILD} + 0{,}40^* X_{ONC} + 0{,}41^* X_{OTH} + 0{,}42^* X_{DYS} + 0{,}40^* X_{HOS} + 0{,}45^* X_{ENP} + 0{,}23^* X_{AGE} + 0{,}41^* X_{CVP} + 0{,}36^* X_{BPP} + 0{,}01^* X_{AGE} + 0{,}36^* X_F - 0{,}51^* X_{RIN} - 0{,}38^* X_{LT} - 0{,}378^* X_{CONT} - 1{,}35^* X_{POLIK}$, P is the probability of hospitalization, X_{AGE} –age (years), X_{CVP} - the cardiovascular pathology, X_{ENP} - endocrine pathology, X_{ONC} - oncology, X_{BPP} –bronchopulmonary pathology X_{OTH} - other comorbidities, X_{SEX} –sex, X_{SEV} – severity, X_{MILD} – mild form, X_F -fiver, X_{LT} - loss of taste, X_{RIN} - rhinitis, X_{DYS} - dyspnea, X_{POLIK} - diagnosis in a polyclinic, X_{HOSP}- diagnosis in the hospital, X_{CONT}– contact with COVID-19. The resulting predictive model turned out to be statistically significant ($p < 0.001$). According to Nigelkirk's coefficient of determination R2, predictors account for 46.6% of the factors influencing the dependent variable. The area under the ROC was 0.863 ± 0.001 (95% CI: 0.860–0.866). Patients with a P value of 0.699 or higher were at high risk of hospitalization. At P < 0.699, low risk. The sensitivity of the model for the selected cut-off point value was 77.9% (10941 correct prognosis out of 38484 hospitalizations), specificity - 77.6% (5101 correct prognosis out of 17708 cases of no hospitalization).
Conclusions: The constructed predictive model can be useful for sorting and identifying groups of patients in need of inpatient treatment in patients with COVID-19 and the presence of comorbidities.

PCO-019

Bacterial and fungal secondary infections in COVID-19 patients in a tertiary healthcare center in Malaysia

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Background: Bacterial and fungal co-pathogens are commonly identified in viral respiratory infections and are important causes of morbidity and mortality. This study is undertaken to determine the prevalence of bacterial and fungal secondary infections in patients with COVID-19.
Methods: Clinical records of 2575 COVID-19 patients admitted to Sungai Buloh Hospital, Selangor between 1 February 2020 until 30 April 2020 with complete outcomes were retrieved. Co-morbidities, clinical features, investigations, treatment and complications were captured using REDCap database. Culture and sensitivity test results were retrieved from WHONET database. Univariate and multivariate regression analyses were used to identify associated determinants.
Results: A total of 105 bacterial and fungal infections were found in 36 patients, which make the prevalence of 0.13%. The age ranged of these patients were between 43–78 years old, predominantly male (27/36, 75%) and Malay ethnicity (31/36, 86%). The most common isolation from bacterial infections were mostly gram negative i.e. Pseudomonas aeruginosa (17/88, 19%), Acinetobacter spp. and Klebsiella spp. both 11/88, 12.5%. The most common fungal infections is Candida albicans (7/17,41%). Almost all (30/36, 83%) patients are classified as category 5 i.e. critically ill with or without mechanically ventilation, on dialysis or on inotropes. Patients with higher C-reactive protein values (i.e. 1–10 and >10 mg/dL) has higher risk of getting secondary infections (p-value 0.002 and <0.001 respectively).
Conclusion: Our study illustrated that bacterial and fungal secondary infections in COVID-19 patients are more frequently found in severely ill patients and associated with a higher mortality rate.

PCO-020

Effect of short-term corticosteroid use on reactogenicity and immunogenicity of the first dose of ChAdOx1 nCoV-19 vaccine

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Background: A prospective cohort study was conducted to investigate immunogenicity of healthcare workers (HCWs) with corticosteroid exposure.
Methods: HCWs who took low-dose corticosteroid agents around the first dose of ChAd (ChAdPd group) were recruited and the reactogenicity and immunogenicity were compared with ChAd- (ChAd group) and BNT162b2-vaccinated (BNT group) HCWs without corticosteroid exposure. The immunogenicity was measured 3 weeks after vaccination using quantitative anti-SARS-CoV-2 spike protein (S) antibody immunoassay and interferon gamma (IFN-γ) release assay.
Results: A total of 67 HCWs (24 ChAd, 29 BNT, and 14 ChAdPd) were included. Total corticosteroid dose of the ChAdPd group was 30 mg prednisolone equivalent in median. ChAdPd group experienced significantly milder reactogenicity (total score in median 7.5, IQR 4.0–18.0) compared to those in the ChAd group (median 23.0, IQR 8.0–43.0, P = 0.012), similar with the BNT group (median 5.0, IQR 3.0–9.0, P = 0.067). The S antibody concentrations of the ChAdPd group (62.4 ± 70.0 U/mL) were numerically higher than the ChAd group (3.45 ± 57.6 U/mL, P = 0.192). The cellular immune response was most robust in the ChAdPd group with significantly higher IFN-γ concentration (5.363 ± 4.276 IU/mL), compared to the ChAd (0.978 ± 1.181 IU/mL, P = 0.002) and BNT (1.656 ± 1.925 IU/mL, P = 0.009) groups.
Conclusions: Short-term corticosteroid reduced reactogenicity of the first dose of ChAd without hindering immunogenicity.

PFM-001

Real-time assessment of *Candida* biofilm formation

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Background: *Candida* infections are responsible for increased morbidity and mortality in immunocompromised patients, particularly when the *Candida* biofilm is composed of drug-resistant species. Although the biofilm formation abilities of individual *Candida* species have been described, the real-time interactions between common and rarer *Candida* species are yet to be elucidated.
Methods: In this study an impedance-based biofilm monitoring system was used in comparison with the conventional crystal violet (CV) staining method, for demonstrating the biofilm formation of commonly isolated and less common *Candida* species.
Results: The maximum cell index increased in most mixed biofilms, with the exception of the *C. glabrata*|*C. parapsilosis* and *C. albicans* combinations. Bulk biofilm formation measured by CV staining was the highest in *C. albicans* and *C. tropicalis* combinations and was the lowest for the *C. glabrata*|*C. parapsilosis* combination. Extensive pseudohyphae, which have been associated with increased virulence, were observed in *C. albicans* and *C. glabrata* combinations with *C. tropicalis* or *C. parapsilosis*.
Conclusion: This study appears to be the first to report on the real-time biofilm interactions of *Candida* species using the xCELLigence system and suggests that the presence of specific species influences the biofilm formation of commonly isolated *Candida* species. This is important since biofilms act as reservoirs for disseminated infection and as demonstrated in this study, mixed *Candida* species act in synergy resulting in an increase in biofilm mass and subsequent risk for drug resistance.

PFM-002

Escalation in Non-albicans Candida infection in intensive care unit patients with emphasis on use of automated methods for expeditious diagnosis and management

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Background: *Candida* spp are most common cause of fungemia in ICU setting. These patients are at risk of Candidaemia because of the presence of indwelling catheters, use of immunosuppressive agents and, broad-spectrum antibiotics. *Candida albicans* remains the most common cause of Candidaemia and is generally susceptible to fluconazole, the emergence of non-albicans Candidaemia with reduced susceptibility to fluconazole poses an increasing threat.
Methods: This was a hospital based prospective observational study for a period of two years. All Candida isolates from urine, blood and BAL fluid in ICU patients from January 2019 to December 2020 were collected under aseptic conditions. Conventional identification methods were performed for all isolates, speciation was done by MALDI-TOF and Anti fungal susceptibility pattern is obtained from VITEK-2.
Results: In the present study 45 *Candida spp* were isolated from 484 catheterized urine sample in which *Candida tropicalis* was found to be predominant. Out of 792 blood cultures sent to laboratory, 42 *Candida spp* were reported in which *Candida albicans* was most common. Among 760 Bronchoalveolar lavage samples isolates 31 *Candida spp* were reported in which *Candida tropicalis* was most common. In this study, 27.96% of *Candida* isolates had resistance against fluconazole (33 isolates) out of which 4 isolates were multiresistant to other antifungals. Use of automated machines helped in early identification of these species 24–48 hours less than the conventional methods.
Conclusion: Parallel increase in number of Non albicans Candida beside *Candida albicans* could be because of patients on prolonged antimicrobial therapy, immunosuppressive drugs, varied comorbidities and species selection in the presence of certain antifungals, given the higher level of resistance expressed by NAC. NAC species are emerging as potential threats to cause infection and posing a therapeutic challenge. Early empirical antifungal therapy and further research to improve diagnostic, prevention and therapeutic strategies are necessary to reduce the considerable morbidity and mortality.

Abstract withdrawn

PFM-004

***Fusarium chlamydosporum* fungaemia complicated with ruptured intracranial mycotic aneurysm: a case report**

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Introduction: Invasive fungal infections are an alarming nowadays. Invasive fusariosis can presented with deep cutaneous infections, sinusitis, pneumoniae, disseminated fusariosis and usually happen in immunocompromised patient. However, in immunocompetent patient, it tends to be more subtle and caused localized infections such as onychomycosis or keratitis. Deficit in cellular immunity, neutropenia, induction chemotherapy and hemopoietic stem cell transplantation were considered as risk factors of invasive fusariosis. Herein, we report a fatal case of *Fusarium chamydosporum* bacteremia which leads to subarachnoid hemorrhage most probably due to ruptured intracranial mycotic aneurysm.
Case report: A 39-year-old Malay lady with underlying diabetes mellitus and end-stage kidney disease was hospitalized in a district hospital for 3 weeks. Initially she was diagnosed with *Corynebacterium spp*- catheter related bloodstream infections

which was complicated with infective endocarditis. Serial blood culture during admission grows *Corynebacterium amycolatum*. She was on intravenous vancomycin and subsequently after 2 weeks the blood culture yield no growth. Her chest x-ray interpretated as heterogenous capacity while echocardiography done revealed floppy mass at posterior mitral leaflet. However, her condition deteriorated, she had persistent spike of temperature, become restless and required intubation for ventilatory support. She was continued with intravenous vancomycin and hemodialysis was started. Laboratory tests showed an elevated white cell count (WBC) of 26.77×10^9 g/L with 96% neutrophils. Repeated blood culture from Myco-F lytic bottle sent to our microbiology laboratory isolated *Fusarium chlamydosporum* which was identified by MALDI-TOF MS with a low score of 1.48. Fungal identification was done in Institute for Medical Research (IMR) using conventional polymerase chain reaction (PCR) method for confirmation of the species. During admission in our hospital, she also underwent CT Brain which revealed bilateral subarachnoid hemorrhage with hemorrhagic left parietal lesion with mass effect most probably secondary to ruptured mycotic aneurysm. Unfortunately, she succumbed to death three days later.

Discussion: *Fusarium* species is emerging pathogen and can cause broad spectrum of infections in human including superficial infections and invasive infections, depending on the immune status. The number of patients with fusoriosis is increasing in trend as more patients receive immunosuppressive therapy. In this case, we have illustrated an uncommon cause of sepsis caused by *Fusarium chlamydosporum* of patient with underlying end stage kidney disease complicated with infective endocarditis. Deficit in cellular immunity particularly in end stage kidney and diabetes mellitus patients are probably the risk factors for this patient to develop invasive fusariosis. Patient also had subarachnoid hemorrhage which most probably due to ruptured intracranial mycotic aneurysm. Left sided infective endocarditis is the primary risk factors for intracranial mycotic aneurysm. As in this case, patient had vegetation at her mitral valve that most probably causing septic emboli and lead to intracranial mycotic aneurysm. At that time of event, only *Fusarium chlamydosporum* was isolated from blood culture suggesting possibility of that invasive fusariosis causing intracranial mycotic aneurysm. However, no brain biopsy done to support this evidence. In disseminated fusariosis, most of the cases had 40% positive blood cultures. This is possibly because Fusarium species produce yeast-like structures (sporulation) that facilitate their dissemination and growth in the blood. Although the genus *Fusarium* can be easily identified, species identification is difficult and may require molecular methods. Disseminated disease is the most frequent and challenging clinical form of fusariosis. Generally, the antifungal therapy for fusariosis may include amphotericin B, voriconazole and posaconazole. Lack of clinical trial data and the availability of antifungal sensitivity makes a huge challenge in treating fusariosis. High index of suspicious for invasive fusariosis is a lifesaving actions due to its high fatality rate especially in immunocompromised patients.

Abstract withdrawn

PFM-006

A case report on the first documented case of Candida auris fungemia in a tertiary hospital in Philippines

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Background: Candida auris is a recently emerging nosocomial multidrug resistant pathogen that poses a threat to global health, particularly for hospital infection control in critical care units.
Method: We report the first documented case of C. auris fungemia from a tertiary care hospital in the Philippines.
Case: Patient is a 76 year old male, French national, diabetic, post-coronary artery bypass graft and aortic valve replacement, transferred from another institution after bilateral chest tube insertion due to pleural effusion from heart failure and para-pneumonic process. On further work-up, he was subsequently diagnosed with a biopsy proven-Follicular B-cell lymphoma and received chemotherapy in the form of R-CHOP.
Result/Discussion: On the 104th hospital day, due to febrile and hypotensive episodes, the patient underwent septic work-up revealing Candida auris on two separate blood culture sites, detected by matrix-assisted laser desorption ionization time-of-flight mass spectrometry. Central tunneled catheter was removed and initial empiric antibiotics and antifungal (fluconazole) were shifted to anidulafungin. Repeat blood culture after five days of anidulafungin showed persistence of C. auris.
Conclusion: Nosocomial outbreaks and multiple drug resistance to Candida auris have been reported worldwide despite enhanced infection control protocols in hospital. Our case highlights the importance of an emerging infections other than COVID-19 pneumonia that we should be concerned of because its tendency to be multidrug resistant, difficult to be identified and has caused outbreaks in healthcare.

PFM-007

COVID-19 associated mucormycois – unprecedented experience from a developing country

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Mucormycosis is an aggressive, life-threatening infection requiring prompt diagnosis and treatment. Prevalence of mucormycosis in India was 70 times more than global prevalence, even before COVID-19 and has drastically increased at present. Our hospital is among the largest designated COVID Hospitals and has treated around twelve thousand COVID-19 patients till date. Since May 2021, COVID-19 associated mucormycois (CAM) patients were also admitted, with predominant rhino-orbito-cerebral presentation. Among 198 CAM patients admitted, age ranged from 27 to 83 years, M: F ratio was 2:1. Majority of them hadn't taken COVID-19 vaccination. 45 had severe, 25 had moderate, 22 had mild course of COVID-19. 90% were known diabetic, many were hypertensive, had chronic kidney disease, hypothyroidism. 84 were given steroids for COVID-19, 71 were on oxygen support. Biopsy tissue/ nasal swabs were sent for KOH and fungal culture. Out of 198 samples, 111 were positive for fungal elements by KOH; most of them showed broad aseptate ribbon like hyphae suggestive of mucorales. KOH mount provided rapid diagnosis of CAM. Fungal culture showed growth in 37 samples, of which 14 were Mucorales. Slide cultures identified 10 as Rhizopus species, 02 as Rhizomucor and 02 as Mucor. Rhizopus species were predominant and identified as *R. arrhizus* by MALDI-TOF. Other fungal isolates were Aspergillus species and Candida species, *C. albicans* being commonest and fluconazole resistant. All the cases were treated with Amphotericin B and recovered, except for 02 who succumbed. Study shows that diabetes & steroid therapy can be predisposing factors for CAM. Cost effective, rapid evidence-based diagnosis of CAM by KOH can be useful in resource limited scenarios. Given the expensive therapy, challenges in managing CAM are important concerns in India.

PGN-001

Taking AIM-(1) at carbapenem resistance in *Pseudomonas aeruginosa*

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Carbapenems are potent broad-spectrum β-lactam antibiotics reserved for the treatment of serious infections caused by multi-drug-resistant Gram-negative bacteria such as *Pseudomonas aeruginosa.* The surge in *P. aeruginosa* resistant to carbapenems is an urgent threat as very few treatment options remain. Resistance to carbapenems is predominantly due to the presence of carbapenemase enzymes that deactivate the antibiotic.
Carbapenem resistant isolates of *P. aeruginosa* (n = 32) were screened for carbapenem resistant genes using PCR. Carbapenemase encoding genes were detected in two isolates, the New-Delhi metallo beta-lactamase (bla_{NDM-1}) and the Adelaide imipenemase (bla_{AIM-1}) were detected in a clinical and a waste-water isolate, respectively. The sensitivity profile revealed that AIM-1 conferred much higher (>128 fold increased) levels of resistance to carbapenems when compared to NDM-1.
A further investigation using wastewater samples from various local healthcare and non-healthcare sources as well as water from a river, using probe-based qPCR revealed the presence of the bla_{AIM-1} gene in all the samples analysed. The widespread occurrence of bla_{AIM-1} throughout Adelaide hinted at a possible more widespread

occurrence of this gene than originally thought. The potential of global distributing of the bla_{AIM-1} gene was investigated. A BLAST search revealed the presence of the bla_{AIM-1} gene in Asia, America, and Europe. To elucidate the identity of the organism(s) carrying the gene and to assess the genomic arrangement of the bla_{AIM-1} gene, shotgun metagenomic sequencing was conducted on two healthcare wastewater samples and one non-healthcare wastewater sample to uncover the bla_{AIM-1} gene and surrounding features. Comparison of these nucleotide sequences with that from *P. aeruginosa* isolates revealed that, unlike the genetic environment and arrangement in *P. aeruginosa*, the bla_{AIM-1} gene was not carried as part of a transposon, or on any other mobile genetic elements. A phylogenetic tree assembled with the deduced amino acid sequences of AIM-1 suggested that the potential origin of the bla_{AIM-1} gene in *P. aeruginosa* may be the non-pathogenic ubiquitous environmental organism, *Pseudoxanthomonas mexican*a.

PGN-002

Whole genome sequencing of *Acinetobacter baumannii* clinical isolates from Terengganu, Malaysia indicated predominance of the Global Clonal 2, Sequence Type 2 (ST2) lineage

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Background: *Acinetobacter baumannii* is an opportunistic Gram-negative pathogen that has been the leading cause of hospital-acquired infections especially in patients with prolonged hospitalisation and severe comorbidities. Resistance of *A. baumannii* towards various antimicrobials has become a worldwide public health concern.
Objectives: To determine the whole genome sequences of twenty non-repeat *A. baumannii* isolates obtained in 2017 from Hospital Sultanah Nur Zahirah, the main tertiary hospital in Terengganu, Malaysia.
Methods: Antimicrobial resistance profiles of the *A. baumannii* isolates for 20 antimicrobial agents encompassing 8 different classes were determined by the disk diffusion method. Whole genome sequencing was performed on the Illumina platform and the sequences were assembled using Uni Cycler.
Results: Sixteen of the isolates were categorised as multidrug-resistant (MDR; i.e., resistant towards three or more antimicrobial classes), fifteen of which were typed as Sequence Type 2 (ST2) using the Pasteur multilocus sequence type (MLST) scheme and thus belonged to the Global Clonal 2 (GC2) lineage. Phylogenetic analysis indicated that these 15 isolates were closely related to other ST2 isolates that were obtained from the same hospital in previous years, inferring endemicity of the *A. baumannii* ST2 clones in the hospital environment. The remaining MDR isolate was typed as ST164. Non-MDR isolates had diverse STs (ST103, ST729, ST960 and ST1131) and were phylogenetically distinct from the ST2 clones. Various antimicrobial resistance genes were identified from the Terengganu *A. baumannii* genomes with all isolates harbouring the *Acinetobacter*-derived single-variant cephalosporinase gene, bla_{ADC-25}. All MDR isolates harboured the acquired bla_{OXA-23} carbapenemase gene, which likely contributed to their resistance to carbapenems.
Conclusions: Whole genome sequence data of *A. baumannii* isolates from Terengganu showed the predominance of the GC2-ST2 lineage in its main tertiary hospital, most of which were MDR and harbouring the bla_{OXA-23}-encoded carbapenemase.

Keywords: *Acinetobacter baumannii*, GC2 lineage, multidrug-resistance; carbapenemase.
Funding: FRGS/1/2018/SKK11/UNISZA/01/1.

PGN-003

Colistin-EDTA combination for eradication of colistin-resistant *Klebsiella pneumoniae* catheter related biofilm infections

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Background: Developing an effective therapy to overcome colistin resistance in catheter-related biofilm infections of *Klebsiella pneumoniae* is an important therapeutic challenge that must be addressed urgently. Methods: Checkerboard and time-kill assays, as well as crystal violet and PrestoBlue assays, were used to investigate *in vitro* and *in vivo* synergistic effects of colistin-EDTA combination against planktonic and biofilms of colistin-resistant *K. pneumoniae.* Effects of colistin-EDTA combination on survival and bacterial burden in internal organs of treated animals were determined by survival monitoring and serial dilutions.
Results: According to synergy testing of this study, colistin-EDTA combination was demonstrated to be effective in reversing colistin resistance in planktonic and mature biofilms *in vitro*, as well as eradicating colistin-resistant *K. pneumoniae* catheter-related biofilm infections in subcutaneous mouse catheter model *in vivo*. Colistin-EDTA combination also revealed significant therapeutic efficacies in reducing bacterial load in internal organs and protecting treated mice from mortality.
Conclusion: According to *in vitro* and *in vivo* study, colistin-EDTA combination provide favorable efficacy and safety for successful eradication of colistin-resistant *K. pneumoniae* catheter related biofilm infections.

Keywords: colistin, EDTA, colistin-resistant *K. pneumoniae,* catheter related biofilm infections.

PGN-004

Antimicrobial susceptibility and co-resistance among *Pseudomonas aeruginosa* isolates from hospital-acquired respiratory-tract infections: SMART 2017–2019 Malaysia

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Background: Ceftolozane/tazobactam (C/T), an antipseudomonal cephalosporin combined with a β-lactamase inhibitor, is approved for complicated urinary tract and intraabdominal infections, hospital-acquired (HA) and ventilator-associated bacterial pneumonia. We report C/T and various antibiotics susceptibility and co-resistance profile against *P. aeruginosa* isolates in HA respiratory-tract infections (RTI) across Malaysia.
Methods: From 2017–2019 from five Malaysia SMART sites, a total of 1218 RTI were collected, of which 170 isolates were HA *P. aeruginosa* (≥48 hours from admission date) and susceptibility was reported for C/T, amikacin (AMK), ceftazidime (CAZ), cefepime

(FEP), imipenem (IMI), meropenem (MEM) and piperacillin/tazobactam (P/T). Co-resistance was further analysed by assessing susceptibility of selected antibiotics against MEM-, P/T-, FEP-, CAZ-, C/T-non-susceptible (NS) isolates. MICs were determined using broth microdilution and interpreted with CLSI breakpoints.
Results: *P. aeruginosa* remained the 2nd most common gram-negative pathogen after *K. pneumoniae* isolated in all RTI including HA isolates. Susceptibility of C/T was 96.5%, FEP 87.1%, CAZ 81.2%, IMI 79.4%, MEM 88.2%, and P/T 77.6%. Among all 4 antibiotics (MEM-, P/T-, FEP-, CAZ-NS) tested for co-resistance, C/T remained as most susceptible (range 77.3% to 84.2%). Six out of 170 isolates were C/T-NS; 3 isolates carried metallo-β-lactamases.
Conclusions: C/T exhibited the highest susceptibility among all other beta-lactams tested including the MEM-, P/T-, FEP-, CAZ-NS *P. aeruginosa* isolates demonstrating potential use of C/T for multi-drug-resistant *P. aeruginos*a.

PGN-005

In-silico identification of novel inhibitors for glutamate racemase (MurI) to decipher the subtle of antimicrobial resistance in _Neisseria gonorrhoeae_: A virtual screening and molecular dynamics approach

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Background: *Neisseria gonorrhoeae*, a causative agent of gonorrhea, has developed resistance for most of the drugs and hence recently declared as 'Superbug'. Glutamate racemase (MurI) considered as an important drug target due to its integral role in bacterial cell wall synthesis. Therefore, there is an intense need for identification of novel drugs for the treatment of gonorrhea.
Methods: The amino acid sequence of MurI of *Neisseria gonorrhoeae* (YP_208550; Strain FA1090) was retrieved from NCBI. Based on query coverage, e-score and percentage similarity, 1ZUW (glutamate racemase from *Bacillus subtilis*) was selected as a template after PDB BLAST, homology model was generated by Modeller programme of Discovery Studio 4.0. Best model was selected based on DOPE score and PDF energy score which was further verified by Verify-3D protocol and Ramachandran Plot. Receptor binding site was identified after superimposition of template structure and modelled structure and the co-crystalized ligand of the template was docked into the modeled MurI structure. Based on docking score, best pose was selected and receptor-ligand pharmacophore model was generated. Virtual screening of potent inhibitors against the pharmacophore model was performed, best hits were selected based on ADMET profile and further refined.
Results: The best homology model generated was selected based on the verify score of 107.93 from Verify 3D program of Discovery Studio 4.0. Validation of the selected model by Ramachandran plot showed 214 residues (91.8%) fall in most favored region. Root-mean-squared deviation (RMSD) of 0.2475 A^0 was generated by superimposition of query and template structures. Quality factor of 84% for the protein models was obtained using ERRAT. Six pharmacophores were generated using best docking pose between D-glutamate and MurI. These were subjected to virtual screening with ZINC database. 2214 hits so obtained were filtered by fit value of 1.5 which has resulted in 594 filtered hits. Further refinement done by subjecting these 594 hits to Lipinski and veber filter followed by ADMET, which finally gave 378 hits. These were subjected to energy minimization and docking to obtain the best hits.
Conclusions: The study identifies potential compounds that interact with active site of MurI protein, opening new avenues for the treatment option against multi-drug resistant strains of this pathogen.

PGN-006

Whole genome sequencing of _Acinetobacter nosocomialis_ clinical isolates reveals a tetracycline resistance p_dif_ module in a potentially transmissible 13.5 kb plasmid

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Background: *Acinetobacter nosocomialis* is an opportunistic human pathogen that is a member of the *Acinetobacter calcoaceticus-baumannii* (ACB) complex that has been over-shadowed by the predominance of *A. baumannii* in terms of incidence and antimicrobial resistance rates. However, there is scarce data regarding these bacteria from Malaysia.
Methods: In this study, four non-repeat *A. nosocomialis* wound isolates (designated AC13, AC15, AC21 and AC25) obtained in 2011 from Hospital Sultanah Nur Zahirah in Terengganu, Malaysia, were subjected to whole genome sequencing on the Illumina platform. Sequences were assembled using Unicylcer.
Results: All four isolates were resistant to cefotaxime while three isolates (AC13, AC15 and AC25) were resistant to tetracycline. Core genome phylogenetic analysis showed that the three tetracycline-resistant isolates were nearly identical with an average nucleotide identity of 99.9%, indicating likely nosocomial transmission of the same clone. All four isolates harboured the ADC-255 cephalosporinase gene which is possibly responsible for cefotaxime resistance. The three tetracycline-resistant isolates harboured an identical 13,476 bp plasmid, designated pAC13-1, that encode *tetA(39)* and its associated *tetR(39)* regulatory gene in a 2001 bp fragment flanked by XerC/XerD sites characteristic of a mobile p*dif* module. pAC13-1 is a Rep3-family plasmid that belongs to the GR17 group of *Acinetobacter* plasmids and encode transfer-related genes indicating its potential transmissibility.
Conclusions: Whole genome sequencing of *A. nosocomialis* led to detection of a possible nosocomial transmission event and the identification of the *tetA(39)* tetracycline-resistance gene in a mobile p*dif* module located on a potentially transmissible novel plasmid.
Keywords: *Acinetobacter nosocomialis*, whole genome sequencing, tetracycline resistance, *tetA(39)*, p*dif* module.
Funding: FRGS/1/2017/SKK11/UNISZA/02/4.

PGN-007

Activity of ceftolozane/tazobactam against gram-negative pathogens from pediatric patients in Asia/Pacific – SMART 2017–2019

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Background: Ceftolozane/tazobactam (C/T) is an antipseudomonal cephalosporin combined with a β-lactamase inhibitor approved by FDA and EMA for complicated urinary tract and intraabdominal infections, and hospital-acquired/ventilator-associated bacterial pneumonia in patients ≥18 years. We evaluated C/T activity against isolates collected from pediatric patients (<18 years) as part of the global SMART surveillance program in Asia/Pacific.
Methods: In 2017–2019, 44 clinical labs in Australia, Hong Kong, Malaysia, New Zealand, Philippines, South Korea, Taiwan, Thailand, and Vietnam each collected up to 250 consecutive gram-negative

Table 1: (abstract PGN-007)

Antimicrobial agent	% Susceptible			
	Enterobacterales		*P. aeruginosa*	
	≥48 hours (n = 389)	<48 hours (n = 734)	≥48 hours (n = 131)	<48 hours (n = 102)
Ceftolozane/tazobactam	89.2	97.0	96.2	98.0
Piperacillin/tazobactam	85.6	95.2	77.1	91.2
Meropenem	95.9	99.2	81.7	92.2
Imipenem	87.7	94.1	75.6	81.4
Ertapenem	94.3	98.8	NA	NA
Cefepime	75.3	83.0	83.2	94.1
Ceftazidime	70.2	82.7	80.9	91.2
Ceftriaxone	65.8	75.6	NA	NA
Levofloxacin[a]	70.7	77.2	84.7	90.2
Amikacin	99.0	99.5	97.0	97.1

[a]Data for levofloxacin only available for non-*Salmonella* Enterobacterales from 2018–2019.
NA, not applicable.
C/T maintained activity against 82.1% of 39 piperacillin/tazobactam-NS, 78.1% of 32 meropenem-NS, and 75.0% of 28 cefepime-NS PA isolates. Among 64 C/T-NS Enterobacterales, 62 isolates were molecularly characterized: 15 carried metallo-β-lactamases (MBL), 4 OXA-48-like carbapenemases, 1 KPC, 9 AmpC ± ESBL, and 24 only ESBL; no acquired β-lactamases were detected in 9 isolates, all of which were species with intrinsic AmpC. Among 7 C/T-NS PA, 4 isolates carried MBL and 1 a GES carbapenemase.

pathogens per year from various infection sources. Only isolates from pediatric patients were included in this report. Susceptibility was determined using CLSI broth microdilution and breakpoints. C/T-nonsusceptible (NS) Enterobacterales and *P. aeruginosa* (PA) isolates were screened for genes encoding β-lactamases.
Results: The table shows the activity of C/T and comparators against Enterobacterales and PA stratified by length of hospital stay at time of specimen collection.
Conclusions: C/T is a potential treatment option for pediatric patients in Asia/Pacific with both hospital- and community-acquired infections caused by Enterobacterales and PA.

PGN-008

In vitro activity of imipenem/relebactam against *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* isolates from patients in ICU and non-ICU wards in the Philippines – SMART 2017–2019

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Background: Relebactam (REL) inhibits class A and C β-lactamases and was approved in the USA in combination with imipenem/cilastatin (IMI) for the treatment of complicated intraabdominal and urinary tract infections and hospital-acquired/ventilator-associated bacterial pneumonia. We evaluated the activity of IMI/REL against isolates collected for the SMART surveillance program in the Philippines from patients in ICU and non-ICU hospital wards.
Methods: In 2017–2019, 4 clinical labs in the Philippines each collected up to 250 consecutive gram-negative pathogens from various infection sources. MICs were determined using CLSI broth microdilution and breakpoints. IMI-nonsusceptible isolates were screened for β-lactamase genes.
Results: 320 *K. pneumoniae* (KP) and 189 *P. aeruginosa* (PA) isolates (53.1% and 69.3%, respectively, from lower respiratory tract infections; 19.7% and 13.2% from intraabdominal infections; 14.1% and 7.4% from urinary tract infections, 12.2% and 8.5% from bloodstream infections) were collected in ICU and non-ICU wards. The table shows the activity of IMI/REL and comparators stratified by ward type.

Susceptibility of KP and PA to carbapenems was lower among isolates from ICU than non-ICU wards. Even among ICU isolates, IMI/REL maintained activity against 91.7% of KP and 88.5% of PA isolates, 2-28 percentage points higher than the other tested β-lactams. Among IMI/REL-nonsusceptible KP (n = 14) and PA (n = 20), 13 and 8 isolates, respectively, carried metallo-β-lactamases; no acquired β-lactamases were detected in the remaining isolates.

Antimicrobial agent	% Susceptible			
	K. pneumoniae		*P. aeruginosa*	
	ICU (n = 60)	Non-ICU (n = 260)	ICU (n = 52)	Non-ICU (n = 137)
Imipenem/relebactam	91.7	96.5	88.5	89.8
Imipenem	86.7	95.8	78.9	81.0
Meropenem	88.3	96.2	76.9	81.0
Ertapenem	85.0	93.5	NA	NA
Cefepime	71.7	73.1	86.5	80.3
Ceftazidime	63.3	65.0	80.8	75.9
Ceftriaxone	65.0	65.0	NA	NA
Piperacillin/tazobactam	80.0	81.9	80.8	76.6
Levofloxacin[a]	44.7	66.3	69.2	67.9
Amikacin	96.7	98.9	98.1	97.1

[a]Data for levofloxacin only available for 2018–2019.
NA, not applicable

Conclusions: IMI/REL can provide an important treatment option for patients in the Philippines, including those in ICUs.

PGN-009

Characterization of aminoglycoside resistant profiles in clinical strains in a tertiary care hospital in Sri Lanka

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Introduction: Information is lacking about prevalence of aminoglycoside resistance and the type of aminoglycoside-modifying enzyme (AME) genes involved. The purpose of the study is to understand the implications of aminoglycoside resistant profiles responsible in clinical outcomes.

Method: Blood culture isolates from tertiary care Hospital in Sri Lanka (1 year) was identified and tested for antibiotic susceptibility using VITEK® 2 Compact.
Results: From 142 isolates 94 (66.2%) were detected with Aminoglycoside resistance, which detected by aminoglycosides resisting (AR) enzymes (GEN-NET (5), GEN-NET-AMI (6), GEN-TOB-AMI (5), GEN (5), TOB GEN-NET (5), TOB-NET-AMI (5), TOB-NET (5), AMI (5) and GEN-TOB-NET-AMI (5)) or AME genes (GEN (AAC(3)-I) (14), GEN-TOB (ANT(2")) (13), GEN-TOB-NET AAC(3)-II) (12), GEN-TOB-NET (AAC(3)-IV) (7) and TOB-NET-AMI (AAC(6')) (4)). Aminoglycoside resistance can be categorized under inherited (WILD), acquired (11 combination consists of different AR enzymes or AME genes) and both (inherited and acquired) 56 (59.6%), 31 (33.0%) and 7 (7.4%) isolates, respectively. The highest inheritance pattern was observed in *Escherichia coli* 39 (41.4%) and 11 (11.7%) *Klebsiella pneumoniae*. We identified 3 combinations of AR enzymes or AME genes which were specific for *E. coli* ((GEN-NET-AMI-TOB)-(GEN-NET-AMI)-(GEN-NET)-(GEN TOB AMI)-(GEN)-(TOB-GEN-NET)) and *Acinetobacter baumannii* ((AAC(3)-I)-(ANT(2″))-(AAC(3)-II)-(AAC(3)-IV) and (AMIKACIN)-(TOB-NET-AMI)-(TOB-NET)-WILD).
Conclusion: Our results emphasize the importance of understanding the aminoglycoside resistant profiles in detecting the antibiotic-resistant patterns in clinical isolates.

PGN-010

Superbug *Klebsiella pneumoniae* and emergence of carbapenem resistance

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Background: Carbapenem resistant Enterobacteriaceae (CRE) is a major threat and burden for hospitals throughout the globe. CRE *Klebsiella pneumoniae* has become resistant to all or nearly all antibiotics, including 'last resort drug' carbapenems.
Objective: This study aims to analyze epidemiologic characteristics among CRE *Klebsiella pneumoniae* isolated from patients admitted in Hospital Raja Permaisuri Bainun, Ipoh (HRPB) over a period of one year.
Methods: Fifty isolates of CRE *Klebsiella pneumoniae* were collected from all types of clinical specimens. These isolates were subjected to antibiotic susceptibility testing by disk diffusion method (Kirby Bauer) and further confirmed employing E-test and Modified Hodge Test (MHT). The highest CRE isolates were from rectal swabs. E-test Meropenem was used for further confirmation of antimicrobial resistance. Forty five isolates showed resistant and 5 were intermediate for E-test. Molecular characterization was done using Real-time PCR.
Results: From our study, 44 CRE isolates (88%) were MHT positive. NDM gene was detected in all 50 isolates followed by KPC gene in 45 isolates. IMP, VIM and OXA-48 genes were not detected from all the isolates. PCR products of 25 samples were sequenced for genus confirmation and to study the relatedness among the strains.
Key words: CRE *Klebsiella pneumoniae*, carbapenem, Kirby Bauer, Modified Hodge test.

PGN-011

Antimicrobial susceptibility of Gram-negative organisms from Southeast Asia

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Background: The SENTRY Program monitors the frequency and antimicrobial susceptibility (S) of organisms from various infection types worldwide. We evaluated the S of Gram-negative bacteria (GNB) from hospitals in Southeast Asia (SEA).
Methods: 2,366 GNB were consecutively collected (1/patient) in 2017–2020 from 4 hospitals located in Malaysia (n = 584), Philippines (n = 748), Thailand (n = 667), and Vietnam (n = 367) and S tested by the CLSI broth microdilution method. The most common infections were pneumonia (n = 652), urinary tract (n = 555), and bacteraemia (n = 497). Carbapenem-resistant *Enterobacterales* (CRE) were screened for carbapenemase (CPE) genes by whole genome sequencing.
Results: Ceftazidime-avibactam (CAZ-AVI; 92.0%S overall), meropenem (MEM; 88.0%S), and colistin (COL; 87.3%S) were the most active agents against *Enterobacterales* (n = 1633; Table). CRE rates varied from 9.1% (Malaysia) to 23.1% (Vietnam; 11.9% overall). CAZ-AVI activity against CRE varied from 47.8% (Vietnam) to 0.0% (Malaysia; 32.5% overall). The most active agent against CRE was amikacin, with S ranging from 69.6% (Vietnam) to 93.7% (Philippines). A CPE was identified in 165 of 194 CRE isolates, including NDM-type (123 isolates), OXA-type (39), KPC-type (33), and ≥2 CPEs (29). The most active agents against *P. aeruginosa* (n = 460) after COL (100.0%S) were CAZ-AVI (88.2%S), C-T (88.9%S), and tobramycin (87.2%S). Only 21.2% of *A. baumannii* (from 14.7% [Malaysia] to 46.0% [Philippines]) were MEM-S and 32.2% (from 20.0% [Vietnam] to 50.0% [Philippines]) were amikacin-S.

Table 1: (abstract PGN-011)

	% Susceptible per CLSI criteria (no. tested)				
Organism/antimicrobial	Malaysia (584)[a]	Philippines (748)[a]	Thailand (667)[a]	Vietnam (488)[a]	All (2366)
Enterobacterales	(386)	(568)	(480)	(199)	(1633)
Ceftriaxone	66.1	57.9	51.5	33.7	55.0
Ceftolozane-tazobactam	85.7	83.0	81.7	71.7	81.9
Ceftazidime-avibactam	90.9	93.5	92.7	87.9	92.0
Meropenem	90.9	88.9	89.4	76.4	88.0
Gentamicin	83.7	73.2	73.1	69.8	75.2
Colistin	88.3	86.0	85.7	92.9	87.3
P. aeruginosa	(130)	(130)	(137)	(63)	(460)
Ceftazidime	86.9	91.5	75.7	69.8	82.6
Piperacillin-tazobactam	83.8	87.6	76.5	74.6	81.4
Ceftolozane-tazobactam	93.1	97.7	83.9	73.0	88.9
Ceftazidime-avibactam	92.3	96.9	82.4	74.6	88.2
Meropenem	82.3	91.5	72.1	66.7	79.7
Tobramycin	93.1	95.4	84.7	63.5	87.2

[a]Include *A. baumannii*, which is not included in the table.

Conclusions: GBN from SEA showed high rates of resistance, emphasizing the importance of continued surveillance.

Abstract withdrawn

PGN-013

Genomic characterization of phenotypically carbapenem-resistant *Escherichia coli* isolates carrying unknown resistance genes in Malaysia

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Background: Carbapenem-resistant *Enterobacteriaceae* (CRE) is an urgent public health threat due to rising resistance to most of beta-lactam and carbapenem antibiotics. Institute for Medical Research (IMR) is the national reference center for verification of CRE among Malaysian patients. From 2013 to 2016, 15 of 265 (5.6%) carbapenem-resistant *Escherichia coli* (*E. coli*) were found to be polymerase chain reaction (PCR)-negative for the 5 carbapenemase-encoding genes tested (bla_{IMP}, bla_{VIM}, bla_{OXA}, bla_{NDM} and bla_{KPC}) although phenotypically resistant to carbapenem. This study determined the genomic characteristics of these isolates.
Method: WGS analysis was performed on 15 phenotypically carbapenem-resistant *E. coli* isolates which tested negative for 5 common carbapenemase genes as mentioned before.
Results: 3730 encoding genes were detected and 3223 (86.4%) were similar genes shared by all isolates. 12 different sequence types (ST) were identified and 3 dominant STs were ST3572 (n = 2), ST648 (n = 2) and ST410 (n = 2), suggesting a diverse genetic makeup. In total, 56 known antibiotic resistance genes were detected and each isolate harbored, on average, 11 resistance genes. Carbapenemase genes such as bla_{OXA-1} (n = 4), $bla_{OXA-181}$ (n = 1) and bla_{KPC-2} (n = 1) were present in 5 isolates. Other beta-lactamase genes detected were bla_{CMY-2} (n = 9), bla_{TEM-1B} (n = 7) and $bla_{CTX-M-15}$ (n = 5). The colistin resistance gene mcr-1 was found in 1 isolate.
Conclusion: The study highlights the genetic complexity of the carbapenem-resistant *E. coli* in local population and that transmission was caused by many different STs. WGS analysis has proven to be a critical tool in understanding resistance mechanism among these isolates.

PGN-014

Sequence Type 2 *Acinetobacter baumannii* isolates carrying BlaOXA-23 Carbapenemase responsible for nosocomial infection in a tertiary hospital in Malaysia

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Background: *Acinetobacter baumannii* (AB) is often associated with pneumonia, bacteraemia and is known as a multidrug resistant (MDR) organism. The emergence of MDR AB is worrisome as it limits treatment options. This study characterised the antibiotic resistance genes and their distribution in the clinical setting.
Methods: 128 MDR AB isolates were collected from a tertiary hospital in Malaysia, from August 2017 to August 2018. The location of the isolates includes intensive care unit (ICU), coronary care unit (CCU), neonatal intensive care unit (NICU), high dependency ward (HDW), and general wards from various body sites. Standard identification of the isolates and 16 s rRNA PCR targeting specific *Acinetobacter* spp was performed. Antimicrobial susceptibility tests against IMP, CAZ, AN, GN, AMP CIP and COL were performed. Genes encoding bla_{OXA-23}, bla_{OXA-24}, bla_{ADC}, bla_{VIM}, bla_{IMP} and insertion sequence ISAba1 genes were detected using PCR. Subsequently, 30 distinct isolates were subjected to MLST analysis.
Results: The AB distribution were: HDW (39.06%), general wards (30.47%), ICU (28.13%), NICU (1.56%) and CCU (0.78%). All isolates were resistant to ampicillin and carbapenem, but susceptible to colistin. Bla_{OXA-23} (99.22%), bla_{VIM} (99–100%), and bla_{ADC} (98–99%) genes resided in both chromosomal and plasmid DNA. The insertion sequences; ISAba1 was detected upstream of the bla_{OXA-23} gene in 99.22% of the isolates. None of the isolates harboured bla_{IMP} and bla_{OXA-24} genes. Four sequence types (STs) were common among these isolates; ST2 (76.67%), ST164 (10%), ST642 (10%) and ST643 (3.4%). Our finding suggested ST2 clones to

be responsible and circulating in all wards. ST164 only circulated in general wards and HDW.
Conclusion: The occurrence of the genes and the STs in a clinical setting reflects the mobility of the genes that may contribute to the spread of the organism and its resistance.

PGN-015
Cefiderocol: A new weapon to fight antibiotic resistant *Klebsiella pneumoniae*
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Background: New antibiotics are urgently needed to combat multidrug resistant (MDR) bacteria, that represent a serious threat to human health. We explored the antibacterial activity of cefiderocol (CFDC), a novel siderophore cephalosporin, against a group of *Klebsiella pneumoniae* strains, compared to conventional antibiotics.
Methods: A total of 74 *K. pneumoniae* strains (12 ATCC and 62 clinical isolates from the UAE) were tested for susceptibility to 14 antibiotics. Minimum inhibitory concentrations (MIC) of CFDC were determined using iron-depleted cation-adjusted Mueller-Hinton broth. The strains were tested for the presence of genes encoding ß-lactamases (CTX-M, SHV, TEM and OXA-1) and carbapenemases (KPC, OXA-48-like, NDM, VIM, and IMP).
Results: Majority (95.9%; n = 71) of the tested strains were susceptible to CFDC, including MDR strains (n = 37), strains expressing CTX-M-ESBL (n = 23) and carbapenemases (n = 12). All the strains carrying NDM (n = 4) and KPC (n = 2) were susceptible to CFDC. Strains carrying OXA-48-like carbapenemase (n = 3) were susceptible to CFDC, except one that was intermediately susceptible (MIC = 8 μg/ml). Another strain with VIM carbapenemase was also intermediately susceptible to CFDC (MIC = 8 μg/ml). A single strain with dual carbapenemases (both NDM and OXA-48-like) was highly resistant to CFDC (MIC = 256 μg/ml). The latter strain was considered extremely drug resistant (XDR) as it was resistant to all antibiotics including colistin.
Conclusion: Cefiderocol is a highly promising antibiotic against MDR *K. pneumoniae*. It can be used as a last resort treatment option, when other antibiotics are non-effective. An alarming note that some *K. pneumoniae* strains have developed resistance to CFDC although they were never exposed to the drug before. Further research is required to study the mechanisms of resistance in order to find ways to reduce their spread.

PGN-016
Antibiotic susceptibility pattern in gram-negative uropathogens
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Background: Being the second most common cause of bacteremia in hospitalized patients, urinary tract infection (UTI) has posed a significant public health concern for increased morbidity in developing countries, including Nepal. The rapid and irrepressible increment in antimicrobial opposition of uropathogens is acknowledged as a primary hassle that has been seen throughout the most recent decade.
Objective: This cross-sectional study aimed to determine the current antibiotic susceptibility patterns in gram-negative uropathogens isolated from patients visiting Nepal APF Hospital, Kathmandu, from November 2018 to May 2019.
Materials and methods: A total of 364 midstream urine samples were aseptically collected and subjected to laboratory analysis. Inoculation was performed onto CLED and MacConkey agar simultaneously.Isolated organisms were identified and antibiotic susceptibility patterns were studied by the Kirby Bauer disk diffusion method.
Result: 25.0% (n = 91) of the total 364 patients were infected with urinary tract infection. While the highest infection was among the patients of 20–30 years age group (30.87%), the overall percentage of infection was highest in women (80.2%). *Escherichia coli* was the predominant bacteria (n = 48, 52.7%), followed by *Klebsiella pneumoniae* (n = 19, 20.9%), *Proteus mirabilis* (n = 13, 14.3%), *Citrobacter freundii* (n = 3, 3.29%), *Enterobacter* spp. (n = 3, 3.29%), and *Acinetobacter* spp. (n = 3, 3.29%). Majority of the isolates were found resistant to ampicillin (69.2%), followed by cotrimoxazole (63.7%), and nalidixic acid (61.5%). Nitrofurantoin (60.4%) had a high susceptibility. Among 91 organisms isolated, 31(34.1%) bacterial pathogens were found to be MDR, with *E. coli,* (17.6%, n = 16) being the commonest bacteria.
Conclusion: Nitrofurantoin can be used as the empirical treatment for patients with UTI. MDR uropathogens are prevalent; hence, regular surveillance of susceptibility patterns is of great importance.

PGN-017
Characteristics of one colistin-resistant *Acinetobacter junii* clinical isolate
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Background: The increase of multidrug-resistant Gram-negative bacteria is a serious threat to global health and safety. Older antibiotics such as colistin are increasingly being used to treat infections caused by multidrug-resistant bacteria because of the lack of new antibiotics, especially those that cause hospital-acquired infections that can be transmitted throughout the community, such as multidrug-resistant *Acinetobacter* spp. However, colistin- resistant isolates have emerged rapidly around the world due to the increasing use of colistin antimicrobial agents. However, colistin-resistant *Acinetobacter junii* has been rarely reported.
Methods: We performed whole genome sequencing of 134 *Acinetobacter* spp. isolates. Antimicrobial susceptibility testing was conducted by the agar dilution and broth microdilution to determine the minimum inhibitory concentrations (MICs) of isolates. The morphology of bacterium was observed with transmission electron microscopy. Several known colistin resistance genes were compared with the colistin resistant isolate and one colistin susceptible isolate, including *pmrA*, *pmrB*, *pmrC*, *lpxA*, *lpxC*, and *lpxD*. The growth curve analysis and biofilm formation assay were performed to detect the virulence phenotype of the colistin-resistant isolate.
Results: In our study, one colistin-resistant and carbapenem-sensitive *A. junii* clinical isolate was collected (colistin MIC = 4 mg/L). The colony of colistin-resistant *A. junii* showed dry phenotype, and difficult to form a bacterial suspension. Transmission electron microscopy showed colistin-resistant *A. junii* had a thick outer membrane. The Pacbio sequencing and illumina sequencing data showed that the genome length of colistin-resistant *A. junii* was 3 362 966 bp, with G + C content of 38.7%. Mutations in PmrA, PmrB, PmrC, and LpxA were identified in colistin-resistant *A. junii*, compared with one susceptible *A. junii*. The colistin-resistant *A. junii* did not have plasmids and did not carry the *mcr* gene. The

colistin-resistant *A. junii* showed slower growth rate and stronger biofilm formation ability than colistin susceptible isolate.
Conclusion: One colistin-resistant and carbapenem-sensitive *A. junii* clinical isolate was identified. Mutations in PmrA, PmrB, PmrC, and LpxA may related with the colistin resistance phenotype. The colistin-resistant *A. junii* showed increased fitness cost and virulence.
Keywords: *Acinetobacter junii*, colistin resistance, modification of lipopolysaccharide, biosynthesis of lipid A, *mcr*.

PGN-018
Antibiogram and biofilm formation among multidrug-resistant *Acinetobacter baumannii* clinical isolates at a tertiary care centre in Nepal
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Background: *Acinetobacter baumannii* is an emerging pathogen due to its biofilm-forming ability and resistance to multiple antibiotics. Therefore, the characterization of multidrug-resistant (MDR) *A. baumannii* is crucial to correlate biofilm formation and antibiotic resistance.
Methods: This was a cross-sectional study conducted at 750-bedded Tribhuvan University Teaching Hospital, Nepal. Identification and antibiotic sensitivity test of *A. baumanni* isolates from clinical specimens were done following American Society for Microbiology guidelines. Different β-lactamases were detected by various standard phenotypic tests. Microtiter plate method was used to screen biofilm production by the isolates.
Results: Out of total 104 MDR *A. baumannii* isolates, the majority were obtained from lower respiratory tract specimens (47.1%). All were resistant to cephalosporins and carbapenems; however, susceptibility was seen in all cases with polymyxins, and in some cases with sulbactam-containing antibiotics, viz, cefoperazone-sulbactam (24%) and ampicillin-sulbactam (7.7%). ESBL, MBL, KPC and AmpC production were found in 70.2%, 74%, 75% and 21.2% isolates, respectively. Among all tested isolates, 26.9% and 71.2% possessed moderate and strong biofilm forming ability, respectively. Out of 77 MBL-producers, 71.4% were strong biofilm producers; similarly 64.1% of KPC-producers were strong biofilm producers.
Conclusion: Only polymyxins were effective against all isolates. The study showed carbapenemase producers are strong biofilm producers. The findings of this study can effectively help to understand the antibiotic-resistant mechanism and provide valuable information in the treatment of MDR *A. baumannii* isolates in our setting.

Abstract withdrawn

PGN-020
A study of antibiotic resistance and biofilm formation of *Klebsiella pneumoniae* clinical isolates from a tertiary care Centre at North Kerala, India
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Background: The prevalence of *Klebsiella pneumoniae* infections in community and hospital setting is increasing dreadfully. The bacterial co-infections are more common in viral pneumonia. Predominant co-incidence of *K. pneumoniae* in such viral infections requires much attention in COVID 19 pandemic period. The upsurge incidence of ESBL producing strains and biofilm production is alarming. The present study aimed to correlate the biofilm formation, antibiotic resistance and ESBL production of *Klebsiella pneumoniae* isolates from clinical specimen.
Methods: 325 various clinical samples from tertiary care centre in north Kerala, among this *K. pneumoniae* (N = 108) present. The antimicrobial susceptibility test was performed with different antibiotic disks by the disk diffusion method according to CLSI guidelines. Biofilm formation is identified by tube adherence and congo red agar method.
Result: Among the 108 *K. pneumoniae* isolates, 92.59% were showed resistant to ampicillin, 67.59% to amoxicillin-clavulanic acid, and 47.22% to cotrimoxazole. Forty-nine isolates were ESBLs producers and 59 were non-ESBLs producers. The present study showed a significant association between biofilm formation and resistance to antimicrobial agents such as cotrimoxazole and amoxicillin-clavulanic acid. Among the clinical samples, the highest number of ESBLs producers were detected from urine (53.06%) followed by sputum (22.45%) and pus (16.33%).95.92% of ESBL producing *K. pneumoniae* were biofilm producers.
Conclusion: High level resistance in *K. pneumoniae* have become a great concern. Early detection of beta-lactamase production and knowledge about the biofilm formation is crucial for the control and effective treatment of infection.

PGN-021
Infections caused by extensive drug resistant (XDR) *Acinetobacter baumannii*: An experience of a tertiary care hospital
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Background: The incidence of extensively drug resistant (XDR) *Acinetobacter baumannii* has increased in the recent years and is

Table 1: (abstract PGN-021): Case details of four XDR *Acinetobacter baumannii* infection.

Case Details	Case 1: 19/F	Case 2: 36/M	Case3: 45/F	Case 4: 73/M
Diagnosis	Sepsis with AKI, ARDS, cardiac arrest	Acute necrotizing pancreatitis and retroperitoneal abscess	Sepsis due to pyelonephritis	Ca Rectum
Empiric treatment given	Inj. Meropenem 1 gm IV every 8 h Inj. Clindamycin 600 mg every 8 h	Inj. Meropenem 1 gm IV every 8 h Inj. Metronidazole 100 mg IV every 8 h	Inj. Meropenem 1 gm IV every 12 h Inj. Clindamycin 600 mg IV every 8 h	Inj. Meropenem 1 gm IV every 8 h Inj. Teicoplanin 200 mg IV every 12 h Inj. Metronidazole 100 mg IV every 8 h
Sample	Bone Marrow	Peritoneal fluid	Tracheal aspirate	Blood
Organism	*Acinetobacter baumannii*	*Acinetobacter baumannii*	*Acinetobacter baumannii*	*Acinetobacter baumannii*
Susceptibility	**Sensitive**: Colistin **Intermediate**: Tigecycline	**Sensitive**: Tigecycline **Intermediate**: Colistin Levofloxacin	**Sensitive**: Tigecycline Colistin	**Sensitive**: Tigecycline **Intermediate**: Colistin Minocycline
Regimen advised by DIS	Inj. Colistin 3 MU IV every 8 h Inj. Meropenem 1 gm IV every 8 h	Inj. Colistin 9 MU stat f/b 3 MU IV every 8 h Inj. Meropenem 1 gm IV every 8 h	Inj. Meropenem 1 gm IV every 8 h Inj. Colistin 3 MU IV every 8 h	Inj. Colistin 2 MU IV every 8 h Inj. Tigecycline 100 mg stat f/b 50 mg IV every 12 h Inj. Meropenem 1 gm IV every 8 h
Other concomitant antibiotics continued at clinician discretion	None	None	Inj. Ceftazidime 2.5 gm IV every 8 h Inj. Anidulafungin 100 mg IV once a day Inj. Piperacillin + Tazobactam 2.25 gm IV every 8 h Inj. Amphotericin B 50 mg IV once a day	Inj. Voriconazole 6 mg/kg IV every 12 h f/b 4 mg/kg IV every 12 h Inj. Caspofungin 50 mg every 12 h
Microbiological cure	7 days	5 days	5 days	9 days
Clinical cure	Died	12 days	24 days	Died

associated with high mortality rates owing to high treatment failure. According to recent studies, isolates of *Acinetobacter baumannii* are intermediate sensitive to colistin which is a last resort therapeutic option for carbapenem-resistant *Acinetobacter baumannii*. Currently there is no consensus on optimal treatment for these infections. This is an effort to present the outcomes of treatment in infections caused by XDR *Acinetobacter baumannii*.

Methods: The cases were referred to department of clinical pharmacology and therapeutics for opinion on appropriate antibiotic regimen by the clinicians of different specialties in a tertiary care hospital. Among the cases referred by clinicians for opinion on drug related issues, only records of patients related to infections caused by XDR *Acinetobacter baumannii* were included in the study. Case details related to antimicrobials prescribed, culture sensitivity reports and treatment outcomes are being presented.

Results: In the period between January 2020 to June 2021, twelve cases of infection with XDR *Acinetobacter baumannii* were referred for opinion on appropriate antibiotic regimen. Of which eight cases were excluded because of isolation of other bacteria in addition to *Acinetobacter baumannii*. Case details of four patients whose cultures reported growth of only XDR *Acinetobacter baumannii* isolate are presented in Table 1. As all the four XDR *Acinetobacter* isolates were either sensitive or intermediate to colistin, a combination therapy of colistin and meropenem was suggested as definitive therapy. However, in one of the four cases, tigecycline was also advised. All the four cases with XDR *Acinetobacter baumannii* achieved microbiological cure with mean time to microbiological cure being 6.5 days. Two patients (50%) exhibited a successful clinical outcome with mean time to clinical cure being 18 days. Two patients died despite achieving microbiological cure.

Conclusion: Infections caused by XDR *Acinetobacter baumannii* are difficult to treat and are associated with a high mortality. Of the 4 cases presented, 50% of the patients survived with combination of meropenem and high dose colistin despite the isolates being carbapenem resistant. However, as the same regimen failed in 50% of the cases, there is an emerging need to understand the factors associated with mortality.

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PGN-024

Phenotypic and genotypic characterisation of blaNDM producing *Pseudomonas aeruginosa* in a tertiary care hospital

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Background: *Pseudomonas aeruginosa* is a opportunistic nosocomial pathogen, Carbapenems are final resort of treatment of multidrug resistant *Pseudomonas aeruginos*a.

Methods: 140 isolates of *Pseudomonas aeruginosa* received from various clinical samples were inoculated in culture plates followed by standard biochemical reactions and Antimicrobial susceptibility testing. Phenotypically Carbapenemase production was confirmed by Modified Carbapenem Inactvation Method (mCIM) and EDTA Carbapenem Inactvation Method (eCIM). Conventional PCR was done to identify the presence of NDM gene.

Result: 140 isolates of *Pseudomonas aeruginosa* were obtained from various clinical samples. Levofloxacin, Colistin and Amikacin were found to be most effective antibiotics with sensitivity of 99%, 94.4% and 92.7% respectively.

54 isolates showed resistance to Meropenem and 50 isolates showed resistance to Imipenem.

Metallo beta lactamase production was detected by Modified Carbapenem Inactivation method and EDTA Carbapenem Inactivation method which showed 44 isolates were MBL producers. 38 isolates produced NDM gene by Polymerase Chain Reaction.

Conclusion: The present study showed higher prevalence of Carbapenemase producing *Pseudomonas aeruginosa* and among these more than 90% isolates produced NDM gene.

Infections with carbapenemase-producing organisms are easily transmissible, hence it is very critical to control the spread within institutuion and associated with high mortality rate.

PGN-025

Distribution of colistin and odilorhabdin resistance-regulating gene cluster is independent of genotypes in *Klebsiella pneumoniae*

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Background: *Klebsiella pneumoniae* is a leading cause of hospital-acquired infections. Colistin is one of the last treatment options for multidrug-resistant gram-negative bacterial infections. Modification of lipid A, which is mediated by genetic alterations in the two-component regulatory systems (TCS), is a well-known mechanism of colistin resistance. It had reported that *crrAB* is responsible for colistin resistance by upregulation of *pmrAB* via *crrC*. KexD encoded in the same operon with *crrC*, is the only known resistance mechanism for odilorhabdin antibiotic.

Methods: To evaluate the structural variation of the *crrBAC-kexD* cluster, we explored 59 clinical *K. pneumoniae* isolates and 508 whole genomes of *Klebsiella* sp. Genotypes were determined. Phylogenetic trees of *K. pneumoniae* and *Klebsiella* sp. strains were generated. Significant structural variations in crrBAC-kexD and its surrounding regions were identified among K. pneumoniae genomes.

Results: Within *Klebsiella* genus, the cluster was identified only in *K. pneumoniae*, *K. variicola*, and *K. quasipneumoniae*. An intact *crrBAC-kexD* cluster was identified in 178 isolates, while the cluster was absent in 90 isolates. Some clades, including CC23, lacked the *crrBAC-kexD* cluster. The cluster appears to have been lost and re-acquired repeatedly. The *crrBAC-kexD* cluster was identified in the genomes of other bacterial species, including *Citrobacter freundii* and *Enterobacter ludwigi*i.

Conclusion: The *crrBAC-kexD* cluster is proposed to have been acquired by the ancestor of the *K. pneumoniae* complex from other bacterial species. The cluster may have been lost and re-acquired repeatedly in *K. pneumoniae* strains. The dynamic evolution of the *crrBAC-kexD* cluster suggests that it may have other roles, in addition to colistin resistance, in bacterial physiology.

PGN-026

Demography and antibiotic susceptibility of emerging *Chryseobacterium gleum* among hospitalised patients in Malaysia

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Introduction: *Chryseobacterium gleum* is a lactose nonfermenting Gram-negative bacillus, usually found in the environment. Rarely

implicated as a human pathogen, *C. gleum* has now become an emerging healthcare-associated pathogen. This organism is resistant to numerous broad-spectrum antibiotics and poses diagnostic and therapeutic challenges, but reports of this species are scarcely found in the medical literature. This study describes the demography and the antibiotic susceptibility pattern of *C. gleum* among patients, admitted to public Malaysian hospitals.
Methodology: Retrospective data submitted to the Institute for Medical Research (IMR) as part of the 2020 National Surveillance of Antimicrobial Resistance (NSAR) were retrieved and analyzed using WHONET software. Preset test interpretation with combined disk, MIC and Etest was selected, based on the isolates number. Only data pertaining to *C. gleum* from any specimen types were included.
Results: In 2020, 223 *C. gleum* isolates were reported in 97 patients in Malaysia. Gender distribution was almost equal, affecting 49% male and 51% female, with average age of 47.6 years (±25.1 years). Majority of the organism were isolated from blood (52.5%, *n* = 117), followed by respiratory specimens (27.4%, *n* = 61), urine (11.6%, *n* = 26) and catheter (3.1%, *n* = 7). AST showed that 83.6% isolates were sensitive to trimethoprim/sulfamethoxazole, followed by ciprofloxacin (78.8%), cefepime (71.4%) and ceftazidime (71%). Strikingly, majority of the tested isolates showed low sensitivity towards imipenem (47.4%), amikacin (9.4%), gentamicin (9.4%) and meropenem (6.1%).
Conclusion: Despite of low isolation number, *C. gleum* is an emerging infection that poses significant threat to patients due to their high resistance towards carbapenems and aminoglycosides.

PGN-027

Tigecycline heteroresistance and resistance mechanism in clinical isolates of *Acinetobacter baumannii*

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Background: Tigecycline is regarded as a last-resort treatment for multidrug-resistant *Acinetobacter baumannii*. However, tigecycline resistance in *A. baumannii* has increased worldwide. In this study, we investigated tigecycline heteroresistance in *A. baumannii* isolates from South Korea.
Methods: Antibiotic susceptibility testing was performed on 323 non-duplicated *A. baumannii* isolates. Tigecycline heteroresistance was determined by a disk diffusion assay and population analysis profiling. For selected isolates, an *in vitro* time-kill assay was performed, and survival rates were measured after pre-incubation with diverse concentrations of tigecycline. The stability of tigecycline resistance in resistant subpopulations was investigated by serial passaging in antibiotic-free media. Genetic alterations in *adeABC, adeRS*, and *rpsJ* were assessed, and the relative mRNA expression of *adeB* and *adeS* was compared.
Results: Among 260 and 37 tigecycline-susceptible and intermediate resistant *A. baumannii* isolates, 146 (56.2%) and 22 (59.5%) isolates were heteroresistant to tigecycline. Heteroresistant isolates showed re-growth after 12 h of 2 × MIC of tigecycline treatment, and resistant subpopulations were selected by pre-exposure to tigecycline. The tigecycline resistance in some subpopulations might be due to the insertion of IS*Aba1* in *adeS*, leading to the overexpression of the AdeABC efflux pump. However, tigecycline resistance of resistant subpopulations obtained from heteroresistant isolates was not stable in antibiotic-free media. The reversion of tigecycline susceptibility by antibiotic-free passages might occur by additional insertions of IS*Aba10* in *adeR* and nucleotides in *adeS* in some mutants.
Conclusion: Tigecycline heteroresistance is prevalent in *A. baumannii* isolates, which results in treatment failure. Tigecycline resistance is mainly due to the overexpression of the AdeABC efflux pump, which is associated with genetic mutations, but this resistance could be reversed into susceptibility by additional mutations in antibiotic-free environments.

PGN-028

Two distinct genotypes of KPC-producing *Klebsiella pneumoniae* isolates from South Korea

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Background: We investigated characteristics of carbapenemase-producing *Klebsiella pneumoniae* (CPKp) isolates from a hospital of South Korea. Our previous study showed that KPC was the most associated with two *K. pneumoniae* clones, ST11 and ST307, in South Korea. We compared the characteristics of the two dominant clones of CPKp isolates.
Methods: CPKp isolates minimum inhibitory concentrations were determined by 11 antibiotics and genotypes were identified by Pasteur multilocus sequence typing. To evaluate the virulence of two clones, string test, serum resistance assay and macrophage infection assay were done.
Results: ST11 isolates showed higher MICs of carbapenems than ST307 isolates. While all ST307 isolates were resistant to gentamicin and trimethoprim-sulfamethoxazole, ST11 isolates did not. However, most tigecycline-resistant or colistin-resistant isolates belonged to ST11. The two CPKp clones showed different combinations of wzi type and K-serotype. Plasmids of ST11 CPKp isolates exhibited diverse incompatibility types. Serum resistance and macrophage infection assays indicated that ST11 may be more virulent than ST307.
Conclusion: Along with changes in the prevalent clones of CPKp isolates over time, the different characteristics of the major clones, including virulence, suggests the need for continuous monitoring.

PGN-029

The characteristic of antibiotic susceptibility of *Burkholderia pseudomallei* isolates received in a clinical research centre in Malaysia for 2019–2020

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Background: Melioidosis, caused by *Burkholderia pseudomallei,* is an endemic environmental saprophyte in Malaysia. Clinical manifestation ranges from superficial wound infection to septicaemic shock with multi-organ failure. The treatment regime consists of an intensive phase followed by an oral maintenance phase. Recommended choices of antimicrobials for the maintenance phase is a choice between oral trimethoprim – sulfamethoxazole or amoxicillin-clavulanic acid. However, there are valid concerns for the emergence of antibiotic resistance, likely as a consequence poor adherence to the treatment regime.
Methods: A total of 151 *B. pseudomallei* isolates received within the year 2019–2020 were evaluated. Epsilometer Test (E-test) was performed with the following: amoxicillin-clavulanic acid (AMC), ceftazidime (CAZ), tetracycline (TC), imipenem (IPM) and trimethoprim-sulfamethoxazole (SXT) as per the recommendation of the Clinical and Laboratory Standards Institute M45 3rd edition.
Results: 80 and 71 isolates were analyzed for the year 2019 and 2020 respectively. The majority of the samples (n = 113, 74.8%) were sent from the state of Sarawak. 147 (97.4%), 148 (98.0%) and 149 (98.7%) of

the isolates were susceptible to IPM, AMC and CAZ respectively. 137 (90.7%) of the samples were susceptible to TC and the remaining isolates were intermediate. Only 57 (37.7%) of the isolates were susceptible to SXT; the remaining isolates were resistant. 90 isolates (59.6%) were resistant to at least one type of antibiotic whereas 4 (2.6%) isolates were resistant towards 2 antibiotics.
Conclusion: The rising incidence of antibiotic resistance of *B. pseudomallei*, especially towards SXT, is of particular concern. Alternative choices of antibiotics should be explored and studied for efficacy in treating this disease.
Keywords: melioidodis, antimicrobial resistance, Burkholderia pseudomallei.

PGN-030
Characteristic of *Stenotrophomonas maltophilia* antimicrobial profile in Malaysian isolates 2015–2020
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Background: *Stenotrophomonas maltophilia*, a Gram-negative, rod-shaped aerobe, has been recognized globally as an emerging multidrug resistant organism associated with hospital acquired infections commonly pneumonia or sepsis. Prolonged hospital stay, presence of indwelling devices and poor immune status are known risk factors for infection. The mainstay treatment is trimethoprim-sulfamethoxazole (SXT) but growing concerns about resistance and the potential side effects has many physicians in search of alternative options. Here, we describe the antimicrobial profile of *S. maltophilia* in Malaysian isolates from the year 2015–2020.
Methods: Data was collected from WHONET 2021 specific for Malaysian isolates. Isolates that were identified as *S. maltophilia* from the year 2015–2020 with at least one result towards the following antimicrobial agent were included: ceftazidime (CAZ), levofloxacin (LEV) and chloramphenicol (CHL) E-test and SXT disk diffusion test. Cut-off values for susceptibility were in accordance to the Clinical and Laboratory Standards Institute M100 31st Ed.
Results: A total of 11,607 samples were analyzed. 10,995 samples (94.7%) were tested against at least one of the four antibiotics. Respiratory specimens (n = 5822, 50.2%) were the most common source. Of the 494 sample tested against CAZ; 257 (52.2%) were susceptible and 174 (35.2%) were resistant. 11,381 isolates tested against SXT showed 10,763 (94.6%) as susceptible. Of the 306 isolates tested with CHL, 180 (58.8%) were susceptible and 61 (19.9%) were resistant. Only 60 samples were tested against LEV of which 59 (98.3%) were susceptible.
Conclusion: *S. maltophilia* isolates are still a susceptible organism in Malaysian insofar. Nevertheless, continuous surveillance and awareness is required to monitor any potential changes which may occur in the future.

PGN-031
The origin, phylogeny and spatio-temporal spread of the prevalent clone ST208 of carbapenem-resistant Acinetobacter baumannii on a global scale
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Carbapenem-resistant Acinetobacter baumannii (CRAB) is a common nosocomial bacterial pathogen that has emerged as a global threat. Historically, much of the global spread of CRAB has been due to the dissemination of two major clones, known as global clone 1 (GC1) and global clone 2 (GC2). Oxford sequence type (ST) 208 is one of the most prevalent lineage of A. baumannii GC2. The aim of this study was to utilize bioinformatics analysis to identify the molecular characteristics and phylogeny of globally distributed ST208 A. baumannii. We performed whole-genome sequencing on 45 ST208 isolates collected from 13 provinces of China from 1999 to 2020. Moreover, 191 ST208 genome sequences and their related epidemiological data were downloaded from the GenBank database for comparison. A total of 236 ST208 A. baumannii isolates were subsequently performed the bacterial source tracking analysis. The ST208 A. baumannii isolates distributed widely in sixteen countries. The global ST208 phylogeny showed that ST208 was divided into South Asia sub-clade, North America sub-clade and China sub-clade. Bayesian analysis showed that the most recent common ancestor for ST208 was estimated to have occurred in 1976, with an evolutionary rate of 6.6 × 10-4 substitutions per nucleotide site per year. The antimicrobial resistance was increasing over sampling time, with geographic distribution differences of OXA carbapenemase. In most cases, a few isolates collected from distant geographic regions were revealed to possess smaller genetic distances without an observable epidemiological link. Furthermore, (14/58, 24.1%) plasmids of Chinese ST208 isolates carried OXA-23, and there were isolates in which OXA-23 was localized on both plasmid and chromosome and thought be conjugative. Our study highlights the emerging challenges entailed in the WGS-powered epidemiological surveillance of globally distributed clonal groups. Evolution of resistance elements in ST208 A. baumannii should be paid more attention to and monitored.

Abstract withdrawn

PGN-033

Insertion sequence mediated imipenem resistance in Indian anaerobic bacterial isolates and susceptibility trends in *Bacteroides fragilis*

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Background: In anaerobes, carbapenem resistance is mediated by chromosomal *cfiA* gene, encoding metallo-ß-lactamases (MBL), requiring a mobilizable insertion sequence (IS) element for its expression. The MBLs are emerging as significant resistance determinants in *B. fragilis*; however, limited data is available from the Indian subcontinent.

Methods: In this study we examined 359 clinical anaerobic isolates, belonging to 19 genera and 62 species for imipenem resistance. Phenotypic resistance was determined *via* CLSI break-point agar dilution method. The *cfiA* gene and the flanking regions were analyzed for the presence of IS element immediately upstream of *cfiA* gene. The imipenem susceptibility trends among *B. fragilis* isolates from 2016 to 2020 are presented.

Results: Non-susceptibility to imipenem was 0.3% (1/359) overall, with one intermediate resistant phenotype lacking the *cfiA* gene. The *cfiA* gene was detected in 15% (54/359) of isolates, all *B. fragilis*, thereby making the overall *cfiA* positivity rate of 45% (54/120) among *B. fragilis*. None of the isolates carried IS elements immediately upstream of *cfiA* gene, thus failing to provide a promoter for *cfiA* expression. No trends in changing susceptibilities or *cfiA* prevalence were observed over five years.

Conclusion: In Indian anaerobic isolates the non-susceptibility to imipenem is not a challenge to current treatment options; however, these isolates may act as a reservoir of imipenem resistance. *B. fragilis* harbored a significant repertoire of *cfiA* gene, in contrast to other anaerobes. The absence of IS elements upstream of *cfiA* gene limits its expression and resultant phenotypic resistance. However, the acquisition of mobilizable IS elements from non-adjacent *cfiA* sites may pose threat over time *via* lateral gene transfer.

PGN-034

GC-MS analysis of phytoconstituents from *Artemisia pallens* and molecular docking interactions to identify potential inhibitors against the efflux protein of the multi drug resistant LAC-4 strain of *Acinetobacter baumannii*

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Acinetobacter baumannii is an opportunistic human pathogen with multi-drug resistance. Apart from the presence of native β-lactamase genes, poor permeability and efflux systems, *A. baumannii* LAC-4 strain have gained resistance by undergoing several mutations in the genes present in their chromosomes as well as their plasmids which made them hypervirulent. Efflux pumps contribute to bacterial virulence and its resistance to biocides. *Artemisia pallens, commonly called, Davana* belongs to the *Asteraceae* family is found in India. The plant possesses various medicinal properties like antimicrobial activity. The GC–MS technique was used for detecting and identifying phytochemical compounds present in the *A. pallens* methanolic extract. About 149 compounds were subjected for virtual screening by employing AutoDock Vina software to identify potential inhibitors capable of binding to the efflux protein of the resistant LAC-4 *Acinetobacter baumannii.* From the ten obtained hit's only five compounds were finally selected and prioritized based on protein-ligand interaction. In addition, Molecular dynamics simulations for the five compounds were performed. Their binding patterns, RMSD, RMSF, hydrogen bond calculations and protein-ligand contacts analysis provides deeper insights into the interaction patterns with the efflux protein. Hence these five plant compounds can be considered as potential novel inhibitors. The prospects are to identify similar phytocompounds from *Artemisia pallens* extracts to develop effective plant-based drugs to cure several health issues.

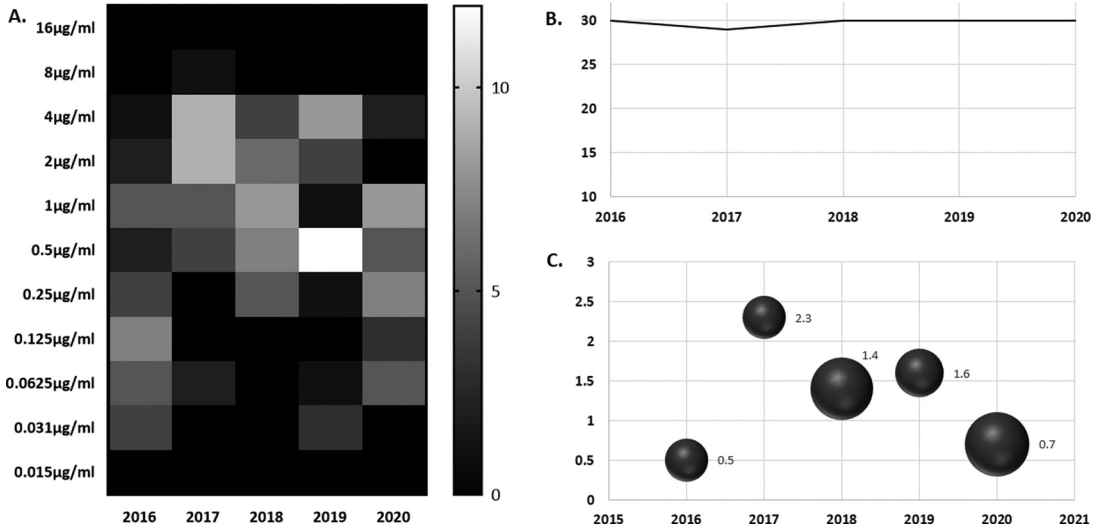

Figure 1: (abstract PGN-033): (A) MIC distribution of *B. fragilis* isolates (n = 150; 30 in each year) to imipenem in five years (B) Trends of susceptibility of all *B. fragilis* isolates to imipenem (C) The geometric mean of MIC values for imipenem in *B. fragilis*; the bubble size represents the number of *cfiA* gene.

Table 1: (abstract PGN-035): (VME) and (ME) rates of Cefiderocol DD compared to BMD.

Organism	N	BMD			DD			VME (%)	ME (%)
		S	I	R	S	I	R		
Acinetobacter baumannii complex	82	61	14	7	72	5	5	14.2	1.6
Klebsiella pneumoniae	81	62	11	8	66	5	10	12.5	1.6
Escherichia coli	63	34	10	19	27	14	22	<3	<3
Pseudomonas aeruginosa	15	13	1	1	13	1	1	<3	<3
Enterobacter spp	5	4	0	1	5	0	0	100	<3
Total	246	174	36	36	183	25	38	8.3	1.1

PGN-035

Analysis of in vitro activity of cefiderocol against carbapenem resistant gram-negative bacilli by broth microdilution and disk diffusion method

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Background: The development of novel antibiotic like Cefiderocol appears to be promising to manage CR-GNB menace. This study was conducted to evaluate the in vitro activity of Cefiderocol against CR-GNB isolates by the reference broth microdilution method (BMD) and disk diffusion (DD).
Materials and methods: 246 clinically significant CR-GNB isolates were included in the study. For MIC determination, Cefiderocol powder was obtained from Chemscene India Pvt Ltd. Iron depleted cation adjusted Mueller hinton broth was prepared as per CLSI recommendations. Cefiderocol 30 μg disc, (Liofilchem) was used for DD. *E. coli* ATCC 25922 and *P. aeruginosa* ATCC 27853 were used as control strains. Investigational CLSI cefiderocol breakpoints were used for categorization of CR-GNB into susceptible (S), intermediate, (I) and resistant ®category.
Results: The distribution of Cefiderocol (S), (I), and (R) CR-GNB isolates by BMD as well as DD is depicted in Table 1. The overall very maior error rates (VME) and major error (ME) rates of DD were 8.3%, 1.1% respectively compared to BMD.
Conclusions: Disk diffusion appears to be the most practical method applied by clinical laboratories with exception of *Enterobacter spp, Acinetobacter spp* and *Klebsiella pneumonia*e.

PGP-001

Risk factors of quinolone-resistant coagulase-negative *Staphylococcus* in conjunctiva

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Background: Conjunctival bacterial flora (CF) are commonly known as causative bacteria of endophthalmitis that occur after cataract surgery (CS) and intravitreal injection (IVI). It is necessary to regularly monitor CF and their changes in antibiotic sensitivity in order to select antibiotics to prevent post-operative endophthalmitis and choose the empiric antibiotics for treatment of post-operative endophthalmitis. In this study, the CF and their antibiotic sensitivity patterns of patients who underwent CS and IVI were evaluated. And the factors related to fluoroquinolone resistance (FR) were investigated.
Methods: One hundred thirty-five patients who underwent CS or IVI at Kosin University Gospel Hospital from April 14, 2014 to September 29, 2016 were studied and a total of 167 samples were collected. The bacterial identification and antibiotic sensitivity tests were performed. The clinical information were reviewed using the medical records. Sixty-eight study subjects with coagulase-negative *Staphylococcus* (CoNS) as CF were classified into fluoroquinolone sensitive CoNS group and FR CoNS group to compare the characteristics of each group.
Results: The number of gram-positive bacteria strains was 192 (73.6%). Among gram-positive bacteria, 87 strains of *S. epidermidis* (33.3%), 49 strains of *Corynebacterium spp.* (18.8%), and 24 strains of CoNS excluding *S. epidermidis* (9.2%) were predominant. Of the 106 CoNS, 65.7% were sensitive to fluoroquinolone. Patients that administered statin within three months prior to sample collection had significantly higher FR in the group of CoNS ($p = 0.016$). Taking statin was a significant risk factor for FR by multivariate logistic regression (OR 6.286 95% CI, $p = 0.023$).
Conclusions: Taking statin was identified as a significant risk factor for the FR, a commonly used topical eye antibiotics. Further large-scale study is needed to confirm the relationship between the use of statin and FR.

PGP-002

Genomic characterisation of a multidrug-resistant *Staphylococcus hominis* ShoR14 clinical isolate from Terengganu, Malaysia

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Background: *Staphylococcus hominis* is an opportunistic Gram-positive pathogen that has been linked to diseases that are potentially fatal. However, there is little information available about its genomic composition, particularly strains from Malaysia.
Objectives: To determine the whole genome sequences of *S. hominis* ShoR14 that was obtained from the blood of a 70-year-old patient warded in Hospital Sultanah Nur Zahirah, Terengganu, Malaysia in 2016.
Methods: Antimicrobial resistance profiles were obtained by disk diffusion for 26 antimicrobial agents comprising 18 different classes. Whole genome sequencing was carried out on the Illumina platform and sequences were assembled using Unicycler.
Results: *S. hominis* ShoR14 is resistant to oxacillin along with 10 classes of antimicrobials and is thus considered a multidrug resistant, methicillin resistant *S. hominis* (MRSHo). Sequence data revealed a genome with a total length of 2,498,464 bp and an average G + C content of 31.33%. *S. hominis* ShoR14 was typed as sequence type 1 (ST1) and is thus likely *S. hominis* subsp. *hominis*. Seven presumptive plasmids were inferred from the presence of plasmid replicase (*rep*) genes in the draft genome contig sequences. Three of them harboured resistance genes for tetracycline (i.e., *tetK*), chloramphenicol (*cat*) and erythromycin/clindamycin (*ermC*). These resistance plasmids were also small, being less than 4 kb in size. The *blaZ*-encoded β-lactamase along with its associated regulatory genes, *blaI* and *blaR1*, were found on a Tn*554* structure in the chromosome whereas the methicillin-resistance *mecA* gene

was located on a SCC*mec* type VIII(4A) element. A ca. 34 kb phage was detected with sequence identities to temperate staphylococcal phages of the *Siphoviridae* family.
Conclusion: Whole genome sequencing led to the finding of seven presumptive plasmids in the multidrug-resistant *S. hominis* ShoR14 with three of these harbouring antimicrobial resistance genes.
Keywords: *Staphylococcus hominis*, multidrug resistance, whole genome sequencing, resistance plasmids.
Funding: FRGS/1/2019/SKK11/UNISZA/02/1.

PGP-003

Study on antibiotic resistance of *Staphylococcus aureus* isolated in Hue University hospital in 2018 and 2019

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Objective: To study the antibiotic resistance of Staphylococcus aureus strains isolated at Hue University Hospital in 2018 and 2019.
Subjects and methods: Investigation antibiotic resistance by the agar disk diffusion method (Kirby-Bauer) on 426 strains of Staphylococcus aureus (S. aureus) in 2018 and 387 strains of Staphylococcus aureus in 2019 that isolated from patients at Hue University hospital.
Results: In 2018, the positive culture rate was 25.3%, in 2019, the positive culture rate was 21.3%, the bacterial isolated strains were Staphylococcus aureus, E. coli, Pseudomonas. aeruginosa, Klebsiella spp and Acinetobacter spp. in which S. aureus strains accounted for the highest proportion. S. aureus strains have markedly increased antibiotic resistance, MRSA (+) increased from 67.3% in 2018 to 85.5% in 2019. Most isolates of S. aureus have increased levels of drug resistance. The most important is S. aureus strains still have a significant percentage that are susceptibility or limited activity to some common antibiotics such as Gentamycin, Doxycycline, Tetracycline, Erythromycin or Trimethoprim-Sulfamethoxazol.
Conclusion: S. aureus tends to increase the level of drug resistance, it is necessary to manage the use of antibiotics and use more rationally, prescribe antibiotics more closely.
Keywords: Hue University Hospital, resistance, antibiotics, infection, S. aureus.

PGP-004

Genomic characterization of vancomycin-resistant *Enterococcus faecium* transmission in hospital by whole genome sequencing

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Background: Since our hospital has diminished vancomycin-resistant enterococci (VRE) screening for admitted patients in 2010, we has observed the increase of the incidence of healthcare-associated VRE bacteremia. We aimed to investigate the relatedness of VREF blood isolates belonging to the major sequence types (STs) between two periods (2006–2009 and 2011–2014) using whole genome sequencing (WGS).
Method: We performed a retrospective study of the genomic epidemiology of 11 ST17 VREF collected in 2006–2009 and 50 VREF blood isolates belonging to ST17, ST78 and ST230 in 2011–2014 from Samsung Medical Center in Republic of Korea. In addition, 10 ST17 VSEF blood isolates in 2006–2009 were included in the analysis. WGS of 71 *E. faecium* isolates was carried out on the Illumina platform and the structure of Tn*1546*-like transposon was characterized using PCR mapping.
Results: The phylogenetic tree, built from sequence alignment of 1945 concatenated core genes, was divided into three groups including ST17, ST78 and ST230 clones regardless of isolation year. a truncated transposon with deletion of *orf*1 (transposase). The ST17 VSEF isolates in 2006–2009 had the genetic relatedness with ST17 VREF isolates in 2006–2009 and 2011–2014.
Conclusion: Given the high genetic relatedness of the ST17 VREF/VSEF clones in 2006–2009 and ST17clones in 2011–2014, it may assumed that the increase of HA-VRE bacteremia following VRE screening policy change occurred through clonal spread and horizontal transfer of the *vanA* gene. In addition, new emerging clone, ST230, also attributed to spread in the hospital. Our analysis showed WGS could provide a better understanding of VREF transmission patterns to assessing the impact of the infection control policy.

PGP-005

Whole genome sequence analysis of methicillin-resistant *Staphylococcus aureus* indicates predominance of the EMRSA-15 (ST22-SCC*mec* IV[2b]) clone in Terengganu, Malaysia

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Background: Methicillin-resistant *Staphylococcus aureus* (MRSA) continues to be an important pathogen especially in the context of antimicrobial resistance (AMR).
Objectives: To perform whole genome sequencing (WGS) on multidrug-resistant MRSA isolates from Terengganu, Malaysia and to compare the phenotypic antimicrobial resistance results with predicted results from the genome sequences.
Methods: Sixty-two MRSA isolates obtained in 2016–2020 from the main tertiary hospital in Terengganu, Malaysia were the subjects of this study. Antimicrobial resistance was determined using the disk diffusion method for 18 antimicrobial classes (26 agents). WGS was performed on the Illumina platform and sequences were assembled using Unicycler.
Results: Genetic diversity was observed among the 62 MRSA isolates with eight sequence types (STs) and 14 *S. aureus* protein A (*spa*) types detected. Nevertheless, the pandemic EMRSA-15 (ST22-SCC*mec* IV[2B]) clone was predominant, making up more than half (67.7%) of the isolates. One isolate had an unknown ST while eight isolates had untypeable SCC*mec*. The most common *spa* type was t032 (50%), followed by t379 and t3841 (both at 8.1%). Methicillin resistance was exclusively mediated by *mecA*. The *lmrS* and *norA* genes encoding multidrug efflux pumps were found in the genomes of all 62 isolates. Resistance phenotype-genotype analysis showed high concordance rates with >95% in most antimicrobial classes except fosfomycin which showed a concordance rate of only 79.0%. The *fosB* gene encoding the fosfomycin-modifying FosB enzyme was found in 13 isolates, but these isolates were susceptible to fosfomycin.
Conclusion: The EMRSA-15 (ST22-SCCmec IV[2B]) clone was predominant in the Terengganu MRSA hospital isolates. Discordances between phenotype and genotype could be due to unexpressed resistance genes or the presence of hitherto unknown AMR genes..

Keywords: Methicillin-resistant *Staphylococcus aureus* (MRSA), antimicrobial resistance (AMR), Whole genome sequencing (WGS).
Funding: FRGS/1/2019/SKK11/UNISZA/02/1.

PGP-006

Impact of vancomycin resistance in *Enterococcus faecium* bloodstream infection on mortality: a retrospective analysis of nationwide surveillance data

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Background: Vancomycin resistance of enterococci has been associated with poor clinical outcome. However, some studies reported that causative species (i.e, *Enterococcus faecium* (Efm) vs. *E. faecalis*), rather than vancomycin resistance, were predictors for poor outcome. We compared the clinical outcome between the patients with VREfm bloodstream infections (BSIs) and those with vancomycin susceptible Efm (VSEfm) BSIs.
Methods: This is a retrospective study of a prospectively identified cohort from a nationwide surveillance for antimicrobial resistance. We constructed a retrospective cohort of consecutive, nonduplicate episodes of monomicrobial BSI caused by Efm from January through December 2016. Electronic health records were reviewed retrospectively to collect clinical information. The primary outcome was all-cause, 30-day, in-hospital mortality. Inverse probability weighting (IPW) was applied using the propensity score for VREfm BSI. Cox proportional hazard model with IPW was used to elucidate independent risk factors for mortality.
Results: A total of 241 episodes of Efm BSI was included, among which 59 (24.5%) were VREfm. Patients with VREfm BSI were younger but had similar comorbidities or Charlson comorbidity index compared to those with VSEfm BSI. Multiple logistic regression revealed that younger age, previous use of piperacillin-tazobactam, and steroid use were significant risk factors for VREfm BSI. In-hospital mortality within 30 days since BSI did not show significant difference between two groups (35.6% vs 23.6%; OR, 1.79; 95% CI, 0.95–3.37; p = 0.101). Cox-proportional hazard model with IPW showed that vancomycin resistance was independently associated with an increased risk for mortality (aOR, 2.35; 95% CI, 1.53–3.58; p < 0.001), along with diabetes, malignancy, prior hospital admission, recent surgery, and renal failure.
Conclusion: In this large cohort of prospectively identified patients with Efm BSI, vancomycin resistance was independently associated with mortality.

PGP-007

Emergence and rapid spread of sequence type 72 methicillin-susceptible *Staphylococcus aureus* following emergence of ST72 community-associated methicillin-resistant *S. aureus* in Korea

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Background: Community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA) is presumed to have emerged as methicillin-susceptible *S. aureus* (MSSA) acquired the SCC*mec* gene. Sequence type (ST) 72 MRSA is a major CA-MRSA clone in Korea. We investigated the time course over the years of the sequence type distributions of MRSA and MSSA in order to understand the molecular evolution of CA-MRSA in Korea.
Methods: *S. aureus* clinical isolates (MRSA 400 isolates, MSSA 400 isolates) collected in Korean hospitals from 1999 to 2018, which were stored in the Asian Bacterial Bank (Asia Pacific Foundation for

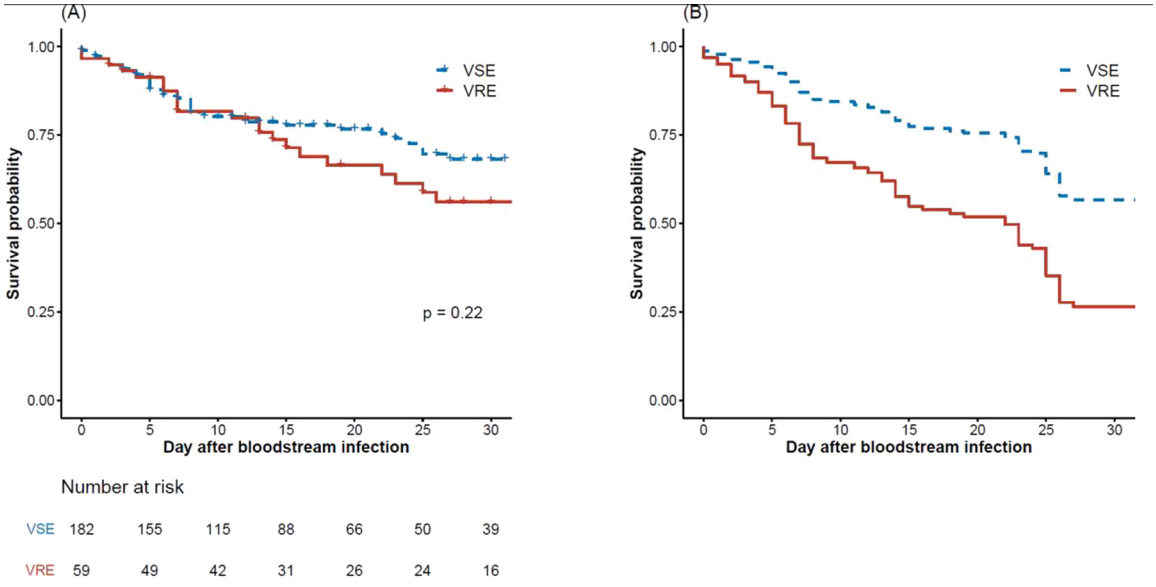

Figure: (abstract PGP-006): Survival curve of patients with VREfm and VSEfm BSI. (A) Observed mortality, (B) survival probability from the Cox proportional hazard model with inverse probability weighting.

Infectious Diseases, Seoul, Korea) were used in this study. All isolates were typed by multilocus sequence typing (MLST).
Results: ST72 accounted for 23.0% of MRSA and 10.8% of MSSA. The most frequent ST among MRSA was ST5 (62.3%), followed by ST72 (23%) and ST239 (6.3%). In MSSA, 47 different STs were identified with ST1 (13.3%) and ST30 (13.3%) being the most frequent, followed by ST6 (10.8%), ST72 (10.8%), ST188 (8.3%) and ST5 (7.3%). Since ST72-MRSA was first found in 2004, it has been the second most common sequence type of MRSA. Interestingly, ST72-MSSA was not identified until 2006, however, ST72 has become one of major STs among MSSA from 2012.
Conclusion: Sequence type analysis for a large collection of *S. aureus* clinical isolates over two decades shows that ST72 MSSA has been rapidly spreading in Korea following the emergence and spread of ST72 MRSA.

PGP-008
Clinical features and outcomes of vancomycin-resistant enterococcal meningitis in neonatal intensive care unit patients: presentation of three cases
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Objective: Vancomycin-resistant enterococcus (VRE) is an emerging pathogen causing invasive infections in newborn infants, but meningitis due to VRE is very rare. I have experienced 3 cases of VRE meningitis in neonatal invasive care unit (NICU) patients over a period of 17 years, and I would like to present clinical features and outcomes of the infection.
Patients and methods: All three patients were in-born preterm infants, two male and one female. In these cases, the onset of infection was 1, 12, and 121 days after birth, respectively. Among the risk factors of infection, chorioamnionitis was present in one case, and central venous catheterization and parenteral nutrition were preceded in two cases. Pre-infection exposure to broad-spectrum antibiotics was prenatal and postnatal in one and two cases, respectively. The pathogenic species was identified as *E. faecalis*, and the causative organism was identified in blood and cerebrospinal fluid samples from all three cases, and indwelling catheter samples from two cases. The VRE genotype was confirmed as vanA in all three cases. Antimicrobial treatment was performed with chioramphenicol or linezolid, and there were no serious adverse effects. All three patients survived, but two of them had brain complications, including hydrocephalus and empyema. At follow-up after 24 months of age, neurological sequelae, including cerebral palsy, epilepsy, and developmental retardation were present in all three cases.
Conclusions: VRE meningitis develops as a disseminated infection in NICU patients with early or late-onset sepsis caused by *E. faecalis*. Patients can survive with appropriate antimicrobial treatment, but they are accompanied by serious neurological sequelae.

PGP-009
Heterogeneous Vancomycin Intermediate *Staphylococcus aureus* infections in tertiary care hospitals in Coastal Karnataka, India
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Background: Heterogeneous Vancomycin Intermediate *Staphylococcus aureus* (hVISA) and Vancomycin Intermediate *S. aureus* (VISA) are emerging as an important healthcare-associated pathogen. Routine antimicrobial susceptibility tests cannot detect hVISA and failure to identify them can result in treatment failure. Special tests required to confirm hVISA are not suited for routine testing in Diagnostic Microbiology Laboratories. The purpose of the present study was to detect hVISA among Methicillin Resistant *S. aureus* (MRSA) isolated from Healthcare-Associated Infections (HAIs) in the four tertiary care hospitals.
Method: Consecutive, non-duplicate isolates of MRSA isolated from HAIs between February 2019 and March 2020 were initially subjected to antimicrobial susceptibility test and agar dilution method/Etest for determination of MIC of vancomycin. Screening and confirmation of hVISA was done using vancomycin screen agar (vancomycin 4 μg/ml) and Population Analysis Profile – Area Under Curve (PAP-AUC) respectively. The results of PAP-AUC were analyzed using Graphpad prism (V.9.0) software. The infections caused and antimicrobial resistance pattern of hVISA was compared with non hVISA MRSA isolates. Statistical analysis of the results was done by chi-square test using SPSS version 25.0.
Results: Out of 220 MRSA strains isolated during the study period, 159 (72.3%) were multidrug resistant. Among 220 MRSA stains, 17 (7.7%) were hVISA by screening and 14 (6.4%) were confirmed as hVISA by PAP-AUC. Majority (78.6%) of hVISA were isolated from skin and soft tissue infections. All MRSA isolates were uniformly susceptible to linezolid, and teicoplanin.
Conclusion: hVISA is an important cause of healthcare-associated infections in tertiary care hospitals. hVISA cannot be identified by routine antimicrobial susceptibility tests, which may lead to treatment failure. MRSA isolates from healthcare-associated deep infections should be checked for hVISA regularly.

PGP-010
Distribution trends of mecA, pvl and SCCmec elements in Malaysian CA-MRSA clinical isolates between year 2017–2018
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Background: Prevalence of SCCmec elements carried by CA-MRSA in Malaysia in recent years is still under reported. This mobile genetic element plays an important role in staphylococci pathogenesis. Moreover, presence of mecA and pvl genes together with SCCmec elements are useful in establishing possible relationships with potential outbreaks. Hence, this study aims to describe population characteristics and distribution of SCCmec types obtained from two consecutive surveillance years of clinical CA-MRSA strains in Malaysia.
Methodology: A retrospective study of 1186 suspected CA-MRSA isolates surveyed between 2017 and 2018 was conducted. The bacterial strains were isolated from various clinical samples and confirmed as MRSA by coagulase and antibiotic susceptibility tests. All isolates were screened for mecA and pvl genes and several isolates (n = 283) were selected for SCCmec typing using multiplex PCR. Statistical analysis was conducted using Fisher's exact test.
Result: The strains were primarily isolated from blood (n = 261; 22%) and most cases belonged to the age group of 17–49 years. Majority of specimens were from male (n = 722; 60.9%) compared to female (n = 646; 39.1%). Only 84% (n = 995) and 34.6% (n = 410) of isolates harboured mecA gene and pvl gene, respectively. Isolates carrying both mecA and pvl genes made up 29.1% (n = 345) of the total. The predominant SCCmec observed was type IV (n = 269; 95%), followed by type V (n = 10, 3.4%), type I (n = 2; 0.68%), and type II (n = 2, 0.68%). No isolate carrying SCCmec type III was found.

Conclusion: Type IV was the most prevalent CA-MRSA SCCmec type surveyed in 2017 and 2018. In contrast to mecA, pvl gene that was previously highly associated with CA-MRSA, was not prevalent among the studied isolates. CA-MRSA without detectable mecA resistant gene warrant further investigation to identify mechanisms of their cefoxitin resistance. This insight will contribute to a deeper understanding on the evolvement of CA-MRSA strains circulating in Malaysia.

Keywords: MRSA, CA-MRSA, SCCmec, mecA, pvl.

Abstract withdrawn

PHI-001

Hand hygiene auditing – Is it a roadway to improve adherence of hand hygiene among health care workers?

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Background: Better standards and reliable service operations are expected from private hospital sectors with better infrastructure. Over the years, there has been an increase in HAIs among patients in India. One of the main reasons is lack of compliance with infection control guidelines, such as hand hygiene. So the present study was conducted to know the rate of hand hygiene compliance among health care workers in a tertiary care private sector teaching hospital in South India.

Materials and methods: The study was conducted in a tertiary care private sector medical college hospital with 1500 beds and 16 ICUs. Prospective study was carried out over a period of 36 months between April 2017–March 2020. During the early months of the study, only five adult ICUs where audited due to constraints in availability of dedicated infection control nurses. Hand hygiene compliance was one of the quality indicators of Hospital infection control department when the organization applied for accreditation process. Realising the importance role of hand hygiene as a measure of quality and patient safety, organization supported the programme with infection control nurses adequate enough to conduct audit in critical areas. By the end of the study, 19 areas were directly observed for HH compliance. At each of the locations, the HH audit was conducted for 1 hour/day for 5 days/month. Thus, in total there were 920 observation periods (each conducted for 1 hour) and 22600 minutes of observation were completed during the entire study period. We evaluated the level of compliance across different units and among different categories of HCWs. HH audit was carried out as a direct observation and filling the HH audit form based on standardized WHO method for HH moments and HH techniques. During the observation period, the observer recorded 3 elements—HH opportunities available, complete HH action performed and partial HH action performed by the each HCWs. Following all 7 steps of handrub (15–30 sec) or handwash (40–60 secs) as recommended by WHO was considered "completely followed" and following fewer than all steps or lesser duration was considered as "partially followed." Profession specific hand hygiene adherence for each of HH Moments were also recorded. The auditing included all HCWs (Doctors including junior residents, nurses and others which includes attendants, students and housekeeping personnel) and conducted as blind audits (HCWs were unaware that they were being audited) to minimize Hawthorne effect and also we have done month-wise rotation of the observers to minimise confirmation bias.

After compiling and analysing the HH auditing, HH report with adherence rate of the overall ICU, Profession specific hand hygiene adherence rate and most commonly missed out HH moment was presented every two months during the regular hospital infection control meeting. Also the report was issued to the respective ICUs on a monthly basis to take necessary arrangements to improve the HH adherence. Institutional ethics committee approval was obtained for the study.

Statistical Analysis: Adherence rate was calculated using the standard formula - HH Complete Adherence rate (HHCAR): No. of times HH followed completely (all 7 steps)/No. of opportunities of HH available × 100; HH Partial Adherence rate (HHPAR): No. of times HH followed partially (less than 7 steps or less duration)/No. of opportunities available × 100; HHMoments Adherence rate: No. of times that particular moment followed/No. of opportunities of HH moments available for that particular moment × 100. Adherence rate among various categories was expressed as percentage.

Results: There were 920 observation periods (each conducted for 1 hour) and 22600 minutes of observation were completed during the entire study period. Overall hand hygiene complete adherence rate was 29.9% (11981/39998); partial adherence rate was 45.3% (18131/39998) and non-adherence rate was 24.7% (9886/39998). Better adherence rate was seen among nurses 44.7% followed by other staff (33.7%) and doctors (33.04%).Moment specific adherence rate showing almost equal adherence rate of 50.7%, 50.75 and 50.1% respectively for moments 2, 3 and 4. Adherence rate was comparatively low for moment 1 & 5 i.e 48.4% & 47.6% respectively.

Conclusion: Despite being an institutional priority in the context of impending final accreditation process, hand hygiene compliance remains low. Hand hygiene is a bundle care approach which needs to consider factors including healthcare staff, clinical, institutional,

environmental and behavioural changes. Multimodal interventions and multidisciplinary commitment is mandatory for sustained compliance. Inadequacy of any of these factors will lead to poor compliance.

PHI-002

Identification of staphylococci contaminating clinical white coats of 4th year medical students, a Sri Lankan experience

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Background: Antibiotic resistant bacteria are a major global problem. Clinical white coats (CWCs) could become a potential reservoir as they get contaminated in hospitals during clinical training. *Staphylococcus aureus* and its antibiotic-resistant variant, Methicillin-Resistant *Staphylococcus aureus* (MRSA), are more frequent species that contaminate the clinical white coats.
Objectives: To determine the prevalence of *S. aureus* and MRSA contamination of CWCs worn by medical students.
Methods: A cross-sectional study was done with the participation of 4th year medical students of the Faculty of Medicine, the University of Peradeniya, Sri Lanka. Swabs were taken from the pockets and sleeves of the CWCs. *S. aureus* was identified using routine microbiological methods. Disc diffusion-based Cefoxitin sensitivity test was used to identify MRSA isolates among the *S. aureus*.
Results: Out of 151 participants, 53 (35.1%) had coats contaminated with *S. aureus* and 15 participants (9.9%) had coats contaminated with MRSA. Factors analyzed, including sex, type of clinical appointment and frequency of washing white coats were not associated significantly with contamination by either of bacteria.
Conclusion: Clinical white coats worn by medical students were found to be heavily contaminated with *S. aureus*. These coats can contribute to spread resistant bacteria between patients. Thus, their use and cleaning need to be streamlined.
Keywords: Bacterial contamination, Clinical White Coats, Sri Lanka, Medical Students.

PHI-003

Knowledge, attitude, and perception on antibiotic usage and resistance of Ayurveda health care staff in Sri Lanka

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Introduction: This study illustrates the knowledge, attitude, and perception (KAP) relate to the antibiotic use and resistance among Ayuruvedic health care staff (AHCS) in Sri Lanka who don't administrate antibiotics in patient management. A self-administered questionnaire was distributed to 100 AHCS including medical and nursing officers.
Method: The questionnaire was comprised of three categories focusing KAP of the subjects towards the antibiotic usage and the threat of resistance. Correct, wrong and unanswered options were analyzed separately to understand the viewpoint of each participant under each category. For the statistical testing (Fishers exact test) lower *P* value was used ($P = 1 \times 10^{-6}$) due to the lower sample size of the study (91).
Results: KAP on antibiotic usage and resistance were correctly answered with averages of 83.99 ± 5.87%, 59.89 ± 20.36% and 62.64 ± 18.12%, respectively. Statistical significance was observed in K compared to A and P. Poor attitude was identified in A5 (prescription containing antibiotics during chest infection?) (30.77%). Poor perception was discovered for the P4 (When doctor does not prescribe antibiotics for respiratory tract infections do you follow doctor's Suggestion?) (10.99%), and P5 (giving antibiotics to friend/family for sickness) (23.08%). Responses for P4 and P5, which were poorly performed were significantly difference than all other questions in the P category ($P = 1 \times 10^{-6}$).
Conclusions: Knowledge of antibiotic use and resistance among AHCS is satisfactory. However, attitude and perception on practical application of antibiotics need be improved.

PHI-004

Effectiveness of ozone generated by dielectric barrier discharge plasma reactor against multidrug-resistant bacteria and *Clostridium difficile* spore

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Background: The contaminated healthcare environment plays an important role in spread of multidrug-resistant organisms (MDROs) and *C. difficile*. Ozone have excellent antimicrobial properties and has been used as an alternative method for the decontamination of healthcare environment.
Objective: To evaluate the antimicrobial effects of ozone generated by dielectric barrier discharge (DBD) plasma reactor on various materials that were contaminated by vancomycin-resistant *Enterococcus faecium* (VRE), carbapenem-resistant *Klebsiella pneumoniae* (CRE), carbapenem-*resistant Pseudomonas aeruginosa* (CRPA), carbapenem-resistant *Acinetobacter baumanii* (CRAB) and *C. difficile* spore.
Methods: Various materials contaminated by VRE, CRE, CRPA, CRAB and *C. difficile* spore were treated with different ozone concentrations and exposure time. Atomic force microscopy (AFM) demonstrated bacterial surface modifications following ozone treatment.
Results: When an ozone dosage of 500 ppm for 15 minutes was applied in VRE and CRAB, about 2 or more $\log_{10}$ reduction were observed in stainless steel, fabric and wood, and 1–2 $\log_{10}$ reduction in glass and plastic. Spores of *C. difficile* were more resistant to ozone than were all other organisms tested. On AFM, the bacterial cells, following ozone treatment, were swollen and distorted.
Conclusions: The ozone generated by DBD plasma reactor can provide a simple and valuable decontamination tool for the MDROs and *C. difficile* spore known to common pathogens of healthcare-associated infections. The ozone may induce structural instability in the bacterial cells.
Keywords: Ozone, multidrug-resistant organisms, *Clostridium difficile*, atomic force microscopy, healthcare-associated infection.

Abstract withdrawn

PHI-008

Device associated infections in intensive care units of a tertiary care hospital–a two-year analytical study

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Background: Centers for Disease Control and Prevention (CDC) defines Health care-associated infections (HAIs) as complications or infections secondary to either device implantation or surgery[1]. HAIs are associated with increasing mortality, morbidity and cost. Device-associated infections constitute the majority of health care-associated infections (HAIs) in ICUs. The prevalence of HAIs is underreported from developing nations due to a lack of systematic surveillance.This study reports a 2 year surveillance of central line associated blood stream infection (CLABSI),ventilator associated event(VAE) and catheter associated urinary tract infection (CAUTI) in intensive care units of a tertiary hospital.

Objectives: To ascertain the incidence of device-associated infections in the ICUs of a tertiary care hospital.

Materials and methods: This was a prospective surveillance study in a tertiary care private medical college hospital with 2100 beds inclusive of 140 bedded ICU (surgical, medical, paediatric, neonatal, coronary, respiratory, neuro). ICUs in the hospital are distinguished from general hospital wards by a higher staff-to-patient ratio. There are specialized medical experts and support staff to handle different ICUs respectively. It is a NABH preaccredited hospital supported with accredited diagnostic laboratory comprising multiple disciplines. The clinical microbiology laboratory performs microscopy, serology, culture identification and sensitivity with conventional as well as automated equipments such as BACTEC blood culture system and Vitek 2 compact identification and sensitivity system. In vitro antimicrobial susceptibility testing of first- and second-line antimicrobials was done according to Clinical and Laboratory Standards Institute guidelines. We have a hospital infection control committee (HICC) with dedicated four infection control nurses (ICNs) and infection control officer. For efficient containment of HAI, all health care workers including newly recruited workers are trained on infection prevention strategies routinely.

Study period: The study was conducted from the period of January 2019–December 2020. The ICU was closed for patient care between June 2020 and July 2020 due to COVID pandemic. The surveillance of DA-HAIs was not performed during this period and is excluded for data analysis. We included all consecutive patients admitted to the ICU.Patients admitted for <48 hours to the ICU were excluded. The surveillance period ends with a patient's discharge or transfer out of the ICU, or death of the patient. Daily surveillance for CLABSI, CA-UTI and VAP in ICUs is done by the ICN with the Hospital acquired Infection surveillance form which is attached to case sheets of all patients on devices. The surveillance definitions for these DA-HAIs were adapted from the CDC's NHSN 2016 surveillance criteria. All the device-associated infections are confirmed by infection control officer. The rates of infection is calculated and compared with benchmark set by the International Nosocomial Infection Control Consortium (INICC). These rates were submitted to individual ICU and Quality department every month. The ICU staffs are routinely trained on urinary catheter, central line and ventilator care bundle. Audit for adherence to bundle care for urinary catheter, central line and ventilator was performed as per the daily check list in the surveillance form.

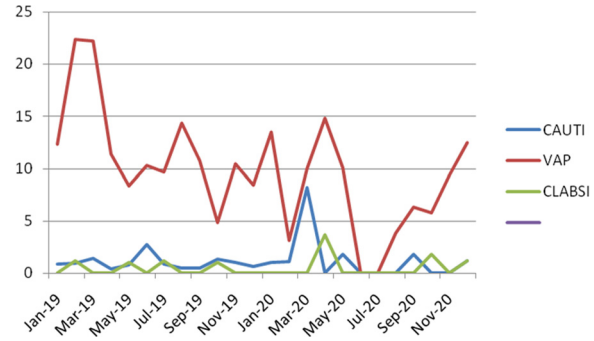

Figure 1. Monthwise trends in DAI rate.

Data analysis: The data were entered into an Excel sheet on a daily basis and analyzed at the end of every month to generate the HAI rates and DU rates [Table 1].

Data collected	Formulae
DAI rate	Number of DAI cases (sum of VAP, CLABSI and CAUTI cases)/total number of device days (sum of ventilator, central line and catheter days) × 1000
VAP rate	Number of VAP cases/total number of ventilator days × 1000
CLABSI rate	Number of CLABSI cases/total number of central line days × 1000
CAUTI rate	Number of CAUTI cases/total number of catheter days × 1000
DU ratio	Number of device days/number of patient days

Ethical considerations: The study was approved by the Hospital Ethics Committee.

Results: The surveillance data was reported over 51 877 patient days. DA-HAI rate of 2.52 per 1000 device days was observed. The device utilization ratios of central line, ventilator, and urinary catheters were 0.31, 0.22, and 0.73, respectively. VAE, CLABSI, and CAUTI rates were 10.5, 0.43, and 0.97 per 1000 device days, respectively. Among 166 DA-HAIs reported, 200 pathogens were identified. *Klebsiella pneumoniae* was the most common organism isolated, accounting 34% for all DA-HAI cases, followed by *Acinetobacter* baumanii (33.7%). The most common organisms causing VAE, CAUTI, and CLABSI were *Acinetobacter baumanii* (53/137, 38.6%), *Klebsiella pneumoniae* (18/55, 32.7%), *Klebsiella pneumoniae* (3/8, 37.5%) respectively. Most of the gram-negative organisms were carbapenem resistant (153/190; 76.5%). Vancomycin resistance rate in Enterococcus was 28.5% (2/7).

Conclusion: Sustained surveillance is an essential tool to reduce the burden of device associated infections. Strict adherence to infection control practices led to a decrease in ventilator associated pneumonia. Central line associated blood stream infection (CLABSI)

and catheter associated urinary tract infection (CAUTI) have been on par with the International Nosocomial Infection Control Consortium (INICC) benchmarks.

PHI-009

Assessment of the knowledge and applications of infection control in Ayurvedic health care staff working in COVID-19 intermediate centres, Sri Lanka

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Introduction: This study identifies the knowledge and practices of infection control in Ayurvedic healthcare staff, proposed to work in the Covid-19 intermediate centres. Since Ayurvedic practice is not related with acute infections evaluating their competence in managing Covid-19 patients is important.
Method: A self-administered questionnaire (comprised of six categories focusing Covid-19 infectivity, vaccinations, standard precautions (SP), hand hygiene and disinfectants) was distributed to 100 Ayurvedic health care staff (5 hospitals).
Results: Only 5.4% could recognize the biohazard sign. Only 55.3% had the knowledge on Covid-19 infectivity while 30.9% didn't know that Covid-19 is not transmitted by skin contact and 58.5% didn't know that N95 masks are not mandatory to prevent Covid-19. Knowledge on SP was satisfactory (84.6%), with 86.2% could clearly understood the definition, 82.9% knew that those are designed to reduce the Hospital Acquired Infections (HAI). Hand washing was recognized by 79.8% as the best method to prevent HAI transmission. But only 26.6% could identify the correct application of my 5 movements. Knowledge on usage of gloves is satisfactory (80.5%). Understanding on glove usage was poor (50.7%), ($P < 0.05$). Knowledge on identifying correct disinfectant for Covid-19 is satisfactory (89.39%). But the application of the disinfectant was poor (50.7%), ($P < 0.05$).
Conclusions: Ayurvedic health care staffs need to be educated on some areas related to basic infection control fundamentals. In addition to that, improvements of their skills and clinical training on the application of infection control practices can be recommended to prevent HAI including Covid-19.

PHI-010

Beating the bugs: the role of microbiology tests in antimicrobial stewardship in spinal cord injury units

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Background: Antimicrobial Stewardship Programs (ASPs) aim to optimize the prescription of antibiotics to combat antimicrobial resistance (AMR), reduce *Clostridioides difficile* infections, and lower antibiotic expenditures. Although ASPs are implemented in Veterans Health Administrations (VHAs) in the US, they are not targeted at the Spinal Cord Injury (SCI) population, which, relative to other patient populations, is more vulnerable to AMR. The goals of the study were to (1) assess the effectiveness of microbiology testing as a strategy to combat AMR and (2) assess the potential for collaboration among ASP leaders and SCI prescribers for implementation of ASPs in SCI units in VHAs.
Methods: We surveyed ASP leaders and SCI prescribers across 23 VHAs. We captured their perceptions regarding level of impact ("high," "mild," "low") and level of implementation ("not," "partially," "fully") of microbiology tests in SCI units.
Results: Of 26 participants, 54% rated "high," 19% rated "mild," 8% rated "low," and 19% rated "don't know" for the perceived level of impact for microbiology tests. There was a positive correlation between ASP leaders' ratings of level of impact and level of implementation of microbiology tests, $r_s = 0.826$ ($p < 0.05$). There was no significant correlation between the SCI prescribers' ratings of level of impact and level of implementation of microbiology tests, $r_s = -0.048$ ($p = 0.903$).
Conclusion: Microbiology tests are perceived to be of high value by the majority of ASP and SCI prescribers for preventing AMR. ASP leaders influence the decision-making process for ASP implementation more than SCI prescribers do. VHAs should strive to create a "deep democracy" in SCI units, where voices of ASP leaders and SCI prescribers are equally valued for ASP implementation.

PHI-011

Current status of hepatitis A virus and measles immunity in secondary hospital workers in South Korea

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Backgrounds: Immunity of healthcare workers to vaccine-preventable diseases is important to prevent hospital outbreak. We evaluated the sero-epidemiology of hepatitis A virus (HAV) infection and measles in secondary hospitals workers in South Korea.

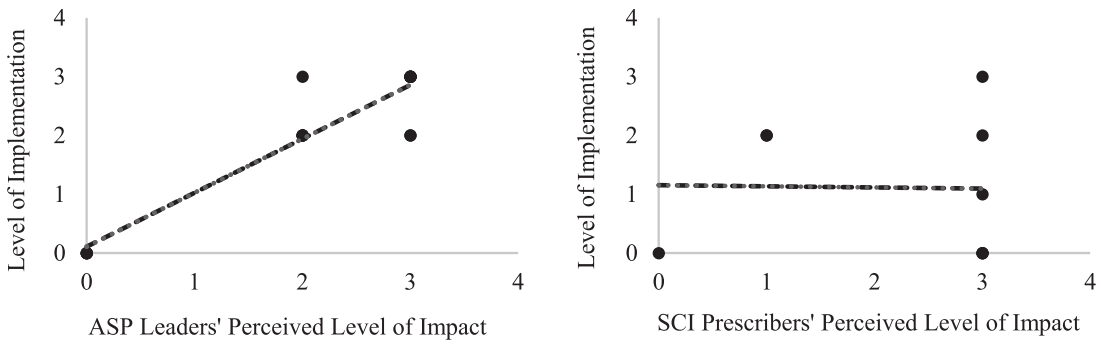

Figure 1: (abstract PHI-010): Trendline for degree of correlation between perceived level of implementation and level of impact of (1) ASP leaders ($r_s = 0.826$, $p < 0.05$) and (2) SCI prescribers ($r_s = -0.048$, $p < 0.05$).

Methods: Serum sample were collected from hospital workers in 28 secondary hospitals with 100–300 beds, located in Jeollanam-do South Korea in 2019. Chemiluminescent immunoassay was used for testing of immunoglobulin G (IgG) antibodies to HAV and measles.
Results: Of total 2573 hospital workers who were tested for HAV Ig G, 7% were physicians, 54% nurses, 19% nurse aides and 20% paramedical technicians. The overall HAV seropositivity rate was 43.3%. There were significant differences in HAV seropositivity between age groups ($P < 0.001$): 37.6% for <25 years, 26.5% for 25–29 years, 25.2% for 30–34 years, 33.3% for 35–39 years, 61.5% for 40–44, and 88.8% for ≥45 years. Among those aged under <40 years old, seroprevalance was significantly lower in nurse aides (23.2%) and paramedical technicians (21.8%) compared to physicians (48.0%) and nurses (33.7%) ($P < 0.001$). Measles IgG test were performed in 2,068 hospital workers (6% physician, 53% nurse, 20% nurses' aides and 21% paramedical technicians). The overall positivity of measles Ig G was 90.9%. The seropositivity for measles significantly increased with age ($P < 0.001$): 75.2% for <25 years, 89.6% for 25–29 years, 98.1% for 30–34 years, 92.4% for 35–39 years, 97.4% for 40–44, and 97.7% for ≥45 years. There were no significant differences in measles immunity between occupations.
Conclusions: Our findings suggest the need to augment appropriate vaccine programs for young hospital workers in South Korea.

PHV-001

Transmitted drug resistance profile of men who have sex with men newly diagnosed with HIV in Hong Kong

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Background: With the extended use of tenofovir (TDF) and emtricitabine/lamivudine (XTC) for HIV prevention, we aimed to examine transmitted drug resistance mutations (DRM) profile and determinants of TDF/XTC-related DRM among newly HIV diagnosed men who have sex with men (MSM).
Methods: Blood samples, behavioural questionnaires and clinical data were collected from HIV clinics' patients in Hong Kong. DRM was determined by HIVdb program from genotypic resistance test (GRT) sequences, following Sanger sequencing. Determinants of having DRM of at least low-level resistance against TDF/XTC were identified by logistic regression after controlling inter-clinic variation.
Results: Of 374 HIV sequences collected between 2016 and 2018, 11 (3%) carried TDF/XTC-related DRM. Seeking partners in gay massage centres ($p = 0.007$), engaging in chemsex ($p = 0.030$) in the year before infection, and recency of infection year ($p = 0.046$) increased odds of having TDF/XTC DRM. Patients' initial health status or treatment outcome were unassociated with DRM. A history of PEP or PrEP used was reported in some resistant cases.
Conclusion: TDF/XTC-related DRM has emerged, which was becoming more prevalent in certain MSM sub-networks in the community engaging in transactional sex and chemsex. Close monitoring of the prescription patterns of antiretrovirals for treatment and/or prevention of HIV in the MSM community is warranted.

PHV-002

Impact of COVID-19 pandemic on HIV care delivery and access in Asia

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Background: The COVID-19 pandemic has threatened general public health services and care delivery worldwide, including but not limited to HIV-related diagnosis, treatment, and care, due to the overburdening of healthcare systems and "lockdown" measures to limit the spread of COVID-19. This study aimed to evaluate the extent of impact on access and delivery of HIV care and identify the barriers faced by the HIV community in Asia-Pacific region during COVD-19 pandemic.
Methods: A descriptive, cross-sectional, web-based study assessing the impact of COVID-19 on HIV care access and delivery was conducted from October to November 2020, among people living with HIV (PLHIV), individuals at-risk of HIV infection, and prescribers. Eligible respondents of PLHIV and at-risk individuals were aged 20 years or older and had provided informed consent. The study populations were recruited across 10 countries/territories in Asia, covering Hong Kong, India, Japan, Malaysia, Philippines, Singapore, South Korea, Taiwan, Thailand, and Vietnam.
Results: A total of 1,398 respondents were recruited – 702 PLHIV, 551 at-risk individuals and 145 prescribers (including infectious disease specialists, HIV specialists and general practitioners). Across the region, a substantial proportion of PLHIV (35.9%) and at-risk individuals (57.5%) experienced disruptions in hospital/clinic visits (decreased frequency or yet to visit the hospital/clinic) during the pandemic. Plasma HIV RNA testing was disrupted in 21.9% PLHIV while routine HIV testing was affected in 47.3% at-risk populations. About one-fifth of PLHIV experienced interruptions in antiretroviral therapy (ART) refills during the pandemic, while decreased and complete stop of preventive medication refills were self-reported by 27.6% and 13.3% at-risk individuals, respectively. Commonest reasons for disruptions in HIV care access perceived by PLHIV and at-risk individuals included travel constraints and concerns of being infected with the SARS-CoV-2. Concomitantly, at least 5 in 10 prescribers across the region reported reduced visits from both PLHIV and at-risk populations, and at least one-tenth delayed or rescheduled patient visits due to clinic closure. About 4 in 10 prescribers observed reductions in both routine HIV/viral load testing and prescription refills (ART/preventive medication) in both PLHIV and at-risk populations during the pandemic. Prescribers perceived travel constraints and patient's willingness/preferences as reasons for reduced prescription refilling during the pandemic. Interestingly, although telemedicine was adopted by 85% of prescribers to deliver HIV healthcare services remotely during the pandemic, many PLHIV (56.4%) or at-risk individuals (64.1%) were not utilizing these services. Prescribers (73.7%) anticipated an increase in telehealth services adoption due to perceived convenience and efficiency, improved workflow, and wider coverage of patients and at-risk individuals.
Conclusions: The COVID-19 pandemic substantially disrupted HIV care access and delivery within the HIV community due to travel constraints, fears of SARS-CoV-2 infection or clinic closure. The findings highlighted gaps in HIV care delivery as HIV telehealth services were not extensively adopted by PLHIV and at-risk individuals. With the future of HIV care delivery progressing towards remote telehealth services, there is an unmet need to

optimize infrastructure and adapt systems to facilitate the continued care of HIV during the COVID-19 pandemic and post-COVID-19 future.

POT-001

Temporal association between Kawasaki disease and infectious diseases: a nationwide observational study in Korea

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Background: Infections are thought to be a triggering factor for Kawasaki disease (KD), although its etiology remains unknown. Recent reports have indicated a 4- to 6-week lag between severe acute respiratory syndrome coronavirus 2 infection and multisystem inflammatory syndrome in children with a similar presentation to that of KD. We explored the temporal association between KD and viral infections.
Methods: Between January 2010 and September 2020, we collected information on KD cases (age: 0–19 years) using big data from the Korean National Health Insurance Service. National databases for infectious diseases were used for time-series analysis of the relationship between viral infections and KD.
Results: Of 14 infectious diseases (respiratory syncytial virus, parainfluenza virus, adenovirus, coronavirus, metapneumovirus, rhinovirus, influenza virus, bocavirus, rotavirus, norovirus, enterovirus, chickenpox, mumps, and scarlet fever) included in the analysis, adenovirus and rhinovirus infections were identified as significant epidemics 1 (Lag 1) and 2 months (Lag 2) before the KD epidemic (adenovirus: $F = 11{\cdot}0$, $p = 0{\cdot}002$ in Lag 1 and $F = 5{\cdot}5$, $p = 0{\cdot}01$ in Lag 2; rhinovirus: $F = 29{\cdot}7$, $p < 0{\cdot}0001$ in Lag 1 and $F = 13{\cdot}4$, $p < 0{\cdot}0001$ in Lag 2). Additionally, chickenpox and mumps were identified as significant epidemics 1 (Lag 1) and 2 months (Lag 2) before the KD epidemic (chickenpox: $F = 6{\cdot}9$, $p = 0{\cdot}01$ in Lag 1 and $F = 19{\cdot}9$, $p < 0{\cdot}0001$ in Lag 2; mumps: $F = 6{\cdot}0$, $p = 0{\cdot}02$ in Lag 1 and $F = 4{\cdot}4$, $p = 0{\cdot}02$ in Lag 2).
Conclusions: Respiratory infections caused by adenovirus, rhinovirus, chickenpox, and mumps were significant epidemics 1–2 months before the KD epidemic.

POT-002

***Panagrellus redivivus* as a model for the study of gram-negative bacteria pathogenesis and antibiotics efficacy**

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Background: *Caenorhabditis elegans* has been widely accepted as a model organism in studying developmental, behavioral, and bacterial infection mechanisms. Unfortunately, *C. elegans* cannot be grown at human physiological temperature of 37°C which makes it less suitable for studying the pathogen infection.
Objectives: In this work, we aimed to develop an easy-to-grow, tropical nematode, *P. redivivus*, as a model organism for investigating gram-negative bacterial infection including, *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Klebsiella pneumonia*e.
Methods: *P. redivivus* were either treated with bacterial cell, supernatants and bacteria with antibiotics including amikacin, imipenem, colistin, sulbactam, ciprofloxacin and ceftazidime.
Results: The results showed that all three bacteria could infect the worms between 10^5 and 10^9 CFU/ml and caused mortality within 24 hours at 37°C. In addition, all three bacterial supernatants of overnight growth also displayed virulent to worms in concentration dependent manner. However, worms were sensitive to some antibiotic treatments such as colistin.
Conclusions: Results from bacterial infection followed by antibiotics treatment showed that *P. redivivus* model could be used to screen the efficacy of antibiotics towards multi-drug resistance bacterial infections. Therefore, we demonstrate the proof of principle and establish *P. redivivus* as a potential model to study the disease caused by multi-drug resistance bacterial infections and antibiotic sensitivity.
Keywords: *Acinetobacter baumannii, Klebsiella pneumoniae*, model organism, *Panagrellus redivivus, Pseudomonas aeruginosa*.

POT-003

Clinical characteristic and outcome of Severe Acute Respiratory Infection (SARI) cases in a tertiary hospital, Malaysia: A descriptive study

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Background: In December 2019, a cluster of cases with 2019 Novel Coronavirus pneumonia (SARS-CoV-2) in Wuhan, China, aroused worldwide concern. The disease causes serious complications and death. The term Severe Acute Respiratory Infection (SARI) is used widely to prevent transmission and early isolation of suspected cases. The aim of our current review is to describe clinical presentations and outcome of SARI cases in a tertiary hospital East Coast Malaysia.
Methods: This was a retrospective study of 96 adults admitted to general medical wards and Intensive Care Unit (ICU) due to SARI from January 2020 until April 2020. Relevant data was extracted and analysed.
Result: 50 (51.2%) were male and 36 (36%) were admitted to ICU. Diabetes mellitus and hypertension were the most common comorbidities ie 39 (40.6%) and 38 (39.6%) respectively. Cough was the commonest reported symptom, observed in 63 (65.6%). Complications of Acute kidney injury were seen in 20 (20.8%) and acute liver injury in 24 (25%). 23 patients (24%) required mechanical ventilation and facemask oxygen ie15 (15.6%) while others either on nasal prong or not on oxygen. Overall mortality was 7 (7.2%). Majority had negative blood culture 86 (89.7%) Others grew klebsiella pneumonia ie 5(5.2%), E.Coli 2 (2.1%) and Staph Aureus 2 (2%) Most sputum culture were also negative ie 72(75%) followed by klebsiella pneumonia in 10 (10.5%). Similarly, most Viral PCR was negative ie 76 (79.2%). Main empirical antibiotic used were Augmentin 36 (37.7%) and ceftazidime 10 (10.5%).
Conclusion: Identification of SARI cases were important in this current pandemic to institute immediate management that is prevention of transmission and appropriate treatment to reduce

morbidity and mortality. This study indeed provides some insight on possible causative organism of SARI cases in our hospital. However, more needs to be done as in most SARI cases the etiology were still unknown.

POT-004

A hospital based prospective observational study on prevalence, genotypes and clinical spectrum of infection with *Trichomonas vaginalis* among women presenting to a rural hospital in South India

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Background: Worldwide *Trichomonas vaginalis* accounts for the highest burden among sexually transmitted infections (STI). In 2015 our rural community prevalence was 6% with OSOM kit-based testing and culture- methods. In this study, coincidently during the national lockdowns, we determined the current prevalence of trichomoniasis as a marker of STI by PCR and the circulating genotypes, which have not been reported earlier from India.
Methods: We enrolled 600 consenting, adult, sexually active women at the rural Obstetrics-Gynecology clinic between July 2020 - February 2021. A vaginal posterior fornix specimen was inoculated into Biomed InPouch TV® Diamond's culture medium. A second specimen for PCR compared the Adhesin, cytoskeleton Beta tubulin 9/2 and Tvk 3/7 gene targets. Genotyping by nested PCR targeting the Actin gene followed by RFLP-PCR using Hind II, RsaI and MseI enzymes was performed.
Results: Nine specimens (1.5%) were positive for *T. vaginalis*. There was a 100% correlation between Biomed InPouch TV® culture and all three primer PCR's. Clinically, 77.7% (n = 7) presented with white-greenish discharge per vagina, 11% (n = 1) with infertility, 22.2% (n = 2) were asymptomatic. Genotyping is currently under completion.
Conclusion: Prevalence of *T. vaginalis* in rural Vellore was 1.5%. The InPouch TV® culture system was equally sensitive to PCR. Molecular assays targeting Adhesin, BTUB 9/2 and Tvk3/7 genes all proved equally sensitive. Genotype determination is a novel finding from India.

Abstract withdrawn

PTM-002

Mycobacterium species on the cutaneous microbiome of very preterm neonates admitted to the NICU in a tertiary health care hospital

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Introduction: The neonatal skin microbiome consists of all the genomes and genetic products of microorganisms harbouring on the skin of babies. This is mainly constituted by bacteria of phyla *Actinobacteria*, *Proteobacteria, Bacteroidetes, Firmicutes,* and *Tenericutes*. Neonatal microbiota helps in angiogenesis, immune function, intestinal T-cell development, gut-associated lymphoid tissue development, etc. Host and the microbiota develop a harmonious environment resulting in symbiosis. Any disruption of this environment could lead to pathological disease.
Methods: The study was conducted to understand the neonatal skin microbiome of very preterm neonates admitted to Neonatal Intensive Care Unit at a tertiary health care setting before and after Kangaroo Mother Care. The study included collection of skin swabs of preterm neonates (n-30) before 32 weeks of gestation and admitted to a Level III NICU in a Tertiary Health Care Hospital. The first swab (Sample A) was collected between the 5th–10th day of postnatal life. A second swab (Sample B) was taken after 7 days of adequate KMC (minimum 6 hours per day). The swabs were sent to the genomics laboratory in sterile water for Next-generation sequencing (NGS). Detection was done using Credence Rapid Infection Detection (credence RIDTM) for Next Generation Sequencing after Polymerase Chain Reaction (PCR). Ethical approval was obtained for the study from Institutional Ethics Committee (IEC - BMCRI/PS/184/2020–21).
Results: Data obtained was in the form of relative abundance with respect to the presence of other organisms in the given clinical isolate. In sample A, the observed average relative abundance for *M. tuberculosis* was identified to be 0.013904093% present in 83.33% (25/30) of samples and for *M. abscessus* 0.116270902% present in 100% (30/30) of samples, while in sample B the values observed for *M. tuberculosis* was 0.01142986% in 66.67% (20/30) and for *M. abscessus* was 0.100288231% in 93.33% (28/30) of samples. We found *Mycobacterium tuberculosis* in 83.33% & 66.67% (p-value, 0.285) and *Mycobacteroides abscessus* in 100% & 93.33%

(p-value, 0.303) on the skin microbiome before and after KMC respectively. The analysis was done using Wilcoxon signed-rank test (IBM-SPSS v.23, New York, USA) with continuity correction at 95%, and significant p-value taken <0.05.
Conclusion: These findings, in our view, are the first findings to be established in such a setting. Mycobacterium species detected incidentally in our study in very high percentages needs exploration with larger cohorts. Although clinically none of the mothers had any history of tuberculosis nor were active cases of tuberculosis, testing all the mothers or any surrounding source would also pose as a limitation of this study. Further larger studies are required to understand the presence of these organisms on preterm skin with long term follow up data including testing both the parents.

PTM-003
Outcomes of isoniazid preventive therapy in a tertiary government hospital HIV/AIDS unit
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Introduction: HIV is the strongest risk factor for developing tuberculosis (TB) disease in those with latent or new TB infection.
Method: This is a retrospective cohort chart review of adult patients aged 19 years and above enrolled from January 2008 until December 2018.
Results: Of the 1038 subjects, 94.6% (982) were male, with mean age of 35 years old. Almost 75% (776) of subjects were started on isoniazid preventive therapy (IPT) but only 66.1% (686) completed IPT. Majority (98.8%) of the subjects who were started on IPT did not develop TB. The incidence of new cases of TB per 100 person-years among those who completed IPT was 0.55 (95% CI, 0.26–1.15) while 1.42 (95% CI, 0.36–5.70) new cases of TB per 100 person-years in those who discontinued. Antiretroviral (ARV) regimen is the only statistically significant factor among the covariates (p-value = 0.014; p-value = 0.007 sub-analysis among those without previous TB), with 5 times higher likelihood [HR: 5.72, 95% CI (1.43–22.93)] among those on second line and 7 times higher likelihood [HR: 7.13, 95% CI (1.70–29.50)] among those without TB history on second line.
Conclusions: There is low incidence of TB after IPT among study population. Those on second line ARV regimen were more likely to develop TB even after IPT, probably due to longer time to achieve viral suppression and immunological improvement, making them prone to TB disease.

PVA-001
Low uptake of seasonal influenza and COVID-19 vaccine in nurses in Hong Kong
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Background: Vaccination of nurse is important both for protecting from viral respiratory infections and as an infection control practice to minimise nosocomial transmission. This study investigated the determinants of non-vaccination against influenza and COVID-19 in nurses in Hong Kong.
Methods: Following the 2021 winter influenza season, an online survey targeting practising and student nurses was conducted in April to examine their uptake and perceptions (on a 5-point Likert scale) of seasonal influenza and COVID-19 vaccine. Determinants of non-uptake and perceptions of the two vaccines were evaluated using logistic and linear regression respectively.
Results: Of 1567 eligible participants, a majority were female (88%) and clinical nurses (80%), with a median age of 39 years (IQR 32–49). Overall, vaccination against influenza and COVID-19 (≥1 dose) was reported in 43% and 33% respectively. Almost half (44%) were unprotected against the two conditions. Determinants of non-uptake between influenza and COVID-19 vaccine were similar: female (OR 1.45 & 1.55), aged <40 years (OR 1.68 & 3.40) and care home nurses (OR 2.45 & 2.09). Nurses refusing influenza vaccination were also more reluctant to get vaccinated against COVID-19 (OR 3.27) and perceived the COVID-19 vaccine to be less effective (B = –0.31) and safe (B = –0.48). "Worry about adverse reactions" was the commonest reason for non-uptake of both influenza (34%) and COVID-19 vaccine (67%).
Conclusions: The relatively low uptake rate of vaccination against both influenza and COVID-19 in nurses posed a dual risk to epidemic control. Strategy for promoting vaccination uptake amidst concerns of adverse reactions is needed.
(The Association of Hong Kong Nursing Staff was thanked for providing logistic support in the survey.).

PVI-001
Delay in influenza treatment in children with false-negative rapid antigen test was in observed in this retrospective single-center study in Korea 2016–2019
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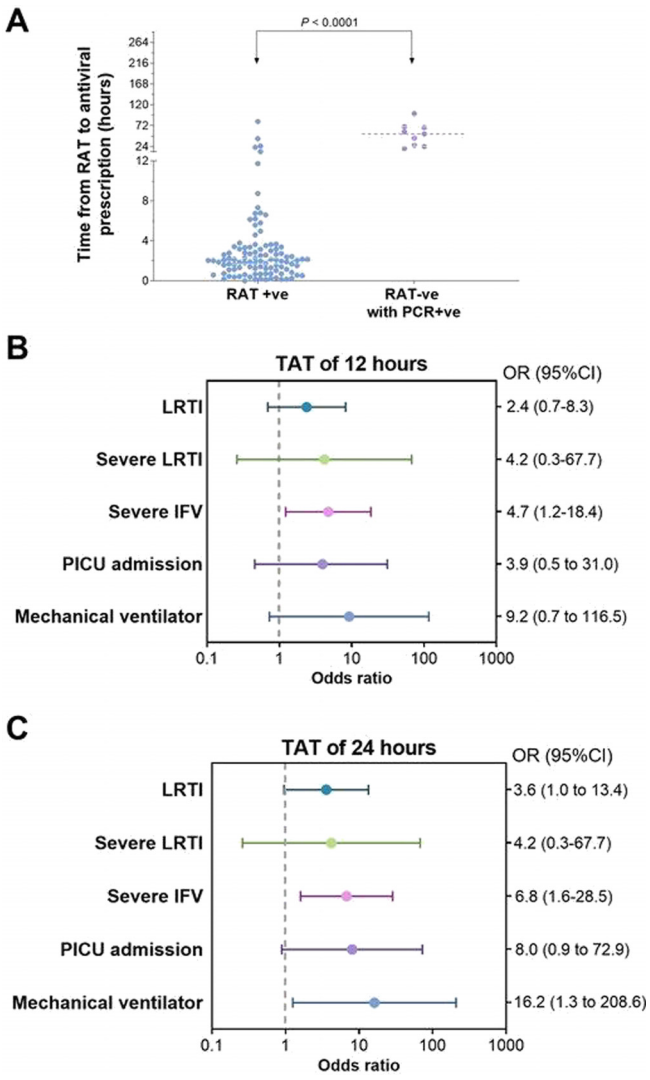
Background: As of March 2021, the National Health Insurance Service of Korea does not cover polymerase chain reaction (PCR)-based assays to diagnose influenza (IFV). Instead, rapid antigen tests (RAT) are still widely utilized in emergency departments (EDs) and outpatient clinics during influenza season. This approach has an advantage that treatment can be started more quickly, but also has the disadvantage of unnecessary antiviral treatment for non-influenza patients and issue of false-negative patients due to low sensitivity of RAT. Therefore, we aimed to examine the delay in antiviral initiation in RAT false-negative children with influenza virus infection and to explore the clinical outcomes. We additionally conducted a medical cost-benefit analysis.
Method: This is a single-center, retrospective study of Severance Children's Hospital during 3 flu seasons (2016–2019) designated by the Korean Center of Disease Control, based on children less than 10 years old, who visited our pediatric ED for influenza-like illness(ILI) and took the RAT then admitted within 48 hours. Severe lower respiratory tract infection (LRTI) in this study was defined as lobar or interstitial lesion on chest x-ray requiring oxygen for more than a day, and severe IFV infection was defined as severe LRTI or progression from upper respiratory tract infection (URTI) to LRTI. The turnaround time to antiviral treatment (TAT) was the time when RAT was prescribed to the time when the antiviral was administered. The medical cost analysis by scenarios was also performed.
Results: 7,377 patients visited the ER during 3 flu seasons from 2016 to 2019. A total of 1,430 patients were included, 7.5% were RAT-positive (n = 107) and 2.4% were RAT-false-negative (n = 20). There were no clinical differences in age, sex, symptoms, and comorbidities between the RAT-positive group and the false-negative group. However, the median TAT of RAT false-negative patients was 52.8 hours, significantly longer than TAT of 4 hours in RAT-positive patients (19.2–100.1, $P < 0.001$). In the multivariable analysis, TAT of ≥24 hours was associated with a risk of severe

influenza infection and the need for mechanical ventilation (OR = 6.8, $P = 0.009$ and OR = 16.2, $P = 0.033$, respectively). The medical cost varied from $11.7–$187.3/ILI patient.



Conclusion: Delayed antiviral treatment was observed in RAT-false-negative, pediatric patients with IFV. Further studies regarding the accuracy and usefulness of rapid PCR-based tests and also cost benefit analysis should be conducted. Until its implementation, our findings support the current guideline that children with IFV, suspected of having severe or progressive infection, should be treated immediately regardless of the RAT result.

*An earlier version of the manuscript was presented by oral presentation at the 70th Korean Pediatric Society Conference, October 22–23, 2020, and was awarded the "Best Abstract Award".

PVI-002

Host-pathogen interactional proteomic atlas of pandemic influenza A virus infection in primary human T cells

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Objective: Respiratory viruses include influenza A virus and SARS-CoV-2 are responsible for the serious epidemics. Decreased peripheral lymphocyte counts have been observed in severe patients with influenza and COVID-19. Among lymphocytes, T cells play a central role in the defense and activation of host response during viral infections, and the longitudinal variation and detailed features of respiratory virus-specific $CD4^+$ T and $CD8^+$ T-cell response remain uncertain. Viruses manipulate host cells to boost their replication, and here we are using quantitative proteomics combined with biochemistry to dissect the lymphopenia and pandemic influenza virus infection in primary human T cells.

Method: Peripheral blood was collected from healthy donors at specific times. What's more, different subsets of T cells were obtained and purified from healthy blood donors and infected with influenza A virus for further research. The protein amount of $CD4^+$ T and $CD8^+$ T cells were dissolved and analyzed by online nano-spray LC-MS/MS on an Orbitrap Fusion Lumos coupled to EASY-nLC 1200 system. The average top three filtered peptides which passed the 1% Q value cutoff were used to calculate the major group quantities. After student's t-test, different expressed proteins were filtered if their Q value <0.05 and absolute AVG log2 ratio >0.58. Raw data of data-independent acquisition were processed and analyzed by Spectronaut X. Proteins were then annotated against GO, KEGG, and COG/KOG database to obtain their functions (q value ≤0.05).

Result: Amongst more than 1000 H1N1-dependent changes, we describe novel T cell-virus interactions. Based on clustering analysis, for $CD4^+$ T cells, the signaling pathways of genetic information processing are up-regulated after infection obviously, such as RNA transport, spliceosome, ribosome biogenesis, and mRNA surveillance. It indicates that influenza A virus has a profound effect on the proteins which contributes to gene transcription and translation. The correspondence is that the Th2 cell differentiation and phenylalanine-tyrosine biosynthesis pathways in $CD8^+$ T cells are up-regulated, shows that influenza A virus may promote the differentiation direction of Th2 cells. Besides, the pathways of complement/coagulation cascades and platelet activation are down-regulated, which suggests the coordination functions of $CD8^+$ T cells can be weakened by the virus. The cell-to-cell atlas of SARS-CoV-2-T cells will be drawn in the future.

Figure: Protein's enrichment loop graph of KO-KEGG (Left, $CD4^+$ T cells; right, $CD8^+$ T cells). 1st lap, top 20 pathways of proteins enrichment; 2nd lap, the number of pathways in the background genes and Q value; 3rd lap, Up-down proteins proportion bar chart (deep purple, up-regulation; light purple, down-regulation); 4th lap, rich factor value (differential proteins divide total proteins in the relevant pathway).

Conclusion: On the one hand, virus is crafty and it can escape from host-immune pathways through virus-host interactions to avoid being wiped out by the host immune system. On the other hand, the initial innate immune responses to pathogens have to restrict virus spread before the adaptive immune responses thoroughly develop. Our unbiased proteomic study provides crucial hetero-genetic insight into primary T-cell responses against infection. We therefore provide a full-coverage host-pathogen interactional proteomic atlas of influenza A virus infection, and some mechanisms of host factors destroyed by virus in lymphocytes.

PVI-003

Complicated varicella zoster virus infection in children

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Background: Varicella-zoster virus (VZV) infection is common in Korea, even in the high 1 dose vaccination rate. The infection is usually self-limited with good prognosis, but complications such as meningitis, pneumonia, hepatitis can occur in children. This study was aimed to evaluate VZV complications.

Method: This is a retrospective study in two tertiary hospitals from January 2015 to June 2021. Hospitalized patients aged ≤18 years old admitted for complicated VZV infection were included. Their demographic characteristics, clinical manifestation and complications were evaluated.

Results: Twenty patients were hospitalized to treat complicated VZV infections. The average age was 8.5 years (range, 0.1–15.9). Two of them (10%) were immunocompromised (acute lymphoblastic leukemia and lymphoma). Eighteen patients (90%) were immunocompetent without chronic underlying diseases. Ten were found to have chickenpox and five had herpes zoster. The average age was younger in the chickenpox group than the herpes zoster group (5.3 vs 12.1 yr, $p < 0.01$). Among ten patients with chickenpox, pneumonia (N = 3), meningitis (N = 4), hepatitis (N = 1), and thrombocytopenia (N = 1) occurred. The patients with herpes zoster had meningitis (N = 4) and hepatitis (N = 1). Five patients were diagnosed with meningitis without skin lesions. Two out of 20 patients (10%) required intensive care unit treatment due to seizure and mental change. No patients died during the hospitalization.

Conclusion: VZV infection can cause complications at 1st infection and reactivation in immunocompromised children as well as immunocompetent children. More discussions about vaccination policies and treatment strategies are needed to reduce the complicated VZV infections.

PVI-004

Respiratory viral infections in adult patients hospitalized in an intensive care unit

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Background: Respiratory viral infection (RVI) for critically ill patients is an important factor in the aspects for treatment and infection control. Yet, recent data on their incidence and occurrence patterns is scarce. The aim of this study was to investigate the epidemiology of RVI in critically ill patients.

Methods: This retrospective observational study was conducted in a tertiary hospital in South Korea from November, 2014 to September, 2020. All adult patients (≥18 years old) admitted in intensive care unit (ICU) with positive multiplex polymerase chain reaction test (mPCR) for RVI were included. Clinical characteristics and outcomes were obtained by reviewing electronic medical records.

Results: Among 22 532 patients admitted in ICU during study period, 2222 (10.1%) patients underwent mPCR test for RVI detection. Finally, a total of 335 (15.1%) non-duplicative RVI positive cases were included for analysis. Incidence rate of RVI in ICU was 308.1 per 100,000 patient-day. Most frequently detected RVI was Influenza A (n = 93, 26.2%), followed by Rhinovirus (n = 85, 25.4%). Six (0.6%) patients were asymptomatic, and 301 (89.9%) cases had pneumonia: community-acquired (n = 193, 57.6%) and hospital-acquired pneumonia (n = 108, 32.2%). All-cause mortality was 27.9%, and 151 (42.5%) patients received mechanical ventilation care. Especially, 151 (45.1%) patients showed bacterial co-infection and presented with longer hospital stay, compared with patients infected only with RVI ($P = 0.001$). Incidence of RVI in ICU patients showed seasonality, with a high incidence in winter season.

Conclusion: The incidence of RVI in ICU patients was not uncommon. Further identification of subjects to be screened for RVI and its clinical implication should be investigated and used as foundation for infection control.

Table 1: (abstract PVI-004): Demographics and clinical characteristics of patients with respiratory virus in ICU.

	Total (335)	CAP (193, 57.6%)	HAP (108, 32.2%)	*p*-value
Age, years (median [IQR])	74 [63–82]	74 [65–83]	73 [63.3–81]	0.537
Male, n(%)	182 (54.3)	103 (53.4)	69 (63.9)	0.077
Coinfection				
Bacterial	151 (45.1)	82 (42.5)	63 (58.3)	**0.008**
Fungal	4 (1.2)	1 (0.5)	3 (2.8)	0.134
Specimen, n(%)				
NP swab	232 (69.3)	145 (75.1)	55 (50.9)	**<0.001**
Tracheal suction	67 (20.0)	33 (17.1)	32 (29.6)	**0.011**
BAL	36 (10.7)	15 (7.8)	21 (19.4)	**0.003**
Underlying Conditions, n(%)				
Heart failure	81 (24.2)	45 (23.3)	21 (19.4)	0.436
Chronic Lung Disease	68 (20.3)	43 (23.3)	21 (19.4)	0.564
Diabetes mellitus	98 (29.3)	61 (31.6)	33 (30.6)	0.850
End-stage renal disease	18 (5.4)	8 (4.1)	10 (9.3)	0.073
Liver Cirrhosis	11 (3.3)	7 (3.6)	3 (2.8)	0.693
Cerebrovascular disease	47 (14.0)	25 (13.0)	17 (15.7)	0.503
Solid Cancer	44 (13.1)	27 (14.0)	16 (14.8)	0.844
Hematologic malignancy	13 (3.9)	6 (3.1)	7 (6.5)	0.236
Solid organ Transplant	4 (1.2)	0 (0)	4 (3.7)	**0.016**
Recent admission	97 (29.0)	33 (17.1)	55 (50.9)	**<0.001**
Receipt of chemotherapy	17 (5.1)	10 (5.2)	7 (6.5)	0.639
Recent surgery	8 (2.4)	2 (1.0)	6 (5.6)	**0.027**
Outcomes				
ICU days, median [IQR]	5 [3–9]	4 [3–8]	7.5 [4–12]	**<0.001**
Hospital days, median [IQR]	21 [12–36]	17 [10–28]	31.5 [16–52.5]	**<0.001**
Mechanical ventilation, n(%)	156 (46.6)	87 (45.1)	64 (59.3)	**0.018**
All-cause mortality, n(%)	103 (30.7)	52 (26.9)	47 (43.5)	**0.003**

PVI-005

The evaluation of surrogate laboratory parameters for predicting the trend of viral loads in patients with severe fever with thrombocytopenia syndrome: cross-correlation analysis of time series

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Backgrounds: Severe fever with thrombocytopenia syndrome (SFTS) has a high mortality rate with average 12% to 30% case fatality rate in endemic areas. This study aimed to demonstrate the laboratory parameters that can predict the dynamic changes of SFTS viral load in SFTS patients and find a specific time point for predicting the clinical course early using serial change of laboratory parameters.
Methods: We carried out a longitudinal panel data analysis using electrical medical records of confirmed SFTS patients at a single tertiary hospital in Jeju Island between 2013 and 2020. The blood samples were collected from the patient at the first visit to the hospital and generally regular intervals. The presence of SFTS virus and SFTSV RNA copies were evaluated by real-time reverse-transcriptase polymerase chain reaction.
Results: A total of 73 SFTS patients were included in the analysis; 11 patients were included in the fatal group (FG), 58 patients to the non-fatal group (NFG). The initial SFTS viral loads were significantly higher in the FG compared to NFG (10 013 974 ± 17 912 878 vs. 228 603 ± 532 862, $p < 0.001$). The mean initial multiple organ dysfunction score (MODS) and MODS on 72-hour after diagnosis were significantly higher in FG than NFG (5.64 ± 4.01 vs 1.91 ± 1.28, $P < 0.001$; 12.09 ± 4.16 vs. 2.90 ± 1.91, $P < 0.001$, respectively). The case fatality rate was also significantly higher in FG than NFG (63.6% vs. 1.7%, $P < 0.001$). The high or low peak time of median value of clinical or laboratory parameters in FG and NFG were as follows; 4 and 2 days in body temperature (high peak); 5 and 4 days in WBC (low peak); 4 and 7 days in ANC (low peak); 2 and 8 days in lymphocyte fraction (high peak); each 7 days in platelet counts (low peak); 10 and 6 days in CRP (low peak), 8 and 4 days in aPTT (high peak), 5 and 8 days in AST (high peak), 8 and 9 days in ALT (high peak), each 8 days in LDH (high peak), 8 and 3 days in CPK (high peak), respectively. Laboratory parameters showed thee type of different correlated patterns; 1) positive correlation (body temperature, aPTT), 2) positive correlation with time lag (body temperature, aPTT), and 3) negative correlation (WBC, ANC, Platelet, CRP). These laboratory parameters show a pattern of decreasing values as the SFTS viral load increases in the early course of disease (1–10 days from the onset of symptoms), and increasing values as the patients enter the recovery phase.
Conclusions: It is difficult to predict the FG of SFTS patients in early stage using initial clinical presentation and laboratory parameters. However, it would be help to predict the severity and prognosis of disease in slow improvement of proportion of lymphocyte, and rapid increment of CRP, aPTT, and AST in FG after day 5.

PVI-006

Seroprevalence of asymptomatic West Nile virus among blood donors in South Indian population

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Background: West Nile virus (WNV) is a member of the Japanese encephalitis antigenic complex of the *Flaviviridae* family. WNV is transmitted by bite of *Culex* mosquitoes. Another significant mode of transmission is blood transfusion. It is crucial to study the prevalence of WNV among south Indian blood donors as WNV cases are being increasingly reported from various states in India and this data will help guide policy.
Materials and methods: Based on the sample size calculation, 500 consenting south Indian blood donors who were at high risk were

recruited for the study. Samples were collected between 2019–2021at the Christian Medical College, Vellore, India. Samples were subjected to both WNV IgM and IgG testing by Euroimmun (Germany) ELISA and further confirmation of positive samples done in InBios International Inc (USA) ELISA. Samples positive in both ELISA were considered as positive for WNV. A subset (n = 100) of negative samples (both IgG and IgM) were subjected to WNV real time PCR.

Results: Based on Euroimmun WNV ELISA, IgM positives were 7/500 (1.4%) and IgG positives were 376/500(75.2%) while 4/500 (0.8%) were IgM borderline and 19/500(3.8%) were IgG borderline, respectively. Real time PCR done on 100 samples were negative. Further confirmation of WNV IgM positive samples was done in WNV IgM capture InBios ELISA which showed 0.2%. Confirmation of IgG is currently under completion.

Conclusion: The high seroprevalence (75.2%) of WNV IgG in our study suggests the circulation of human WNV among the south Indian population and exposure to the virus raising the question as to whether donor screening protocols should include NAT for WNV. However cross reactivity with other flaviviruses has to be ruled out to confirm the seroprevalence of West Nile virus. Shorter viremic period, persistence of IgM, cross reactivity of flaviviruses are the limitations for the diagnosis of asymptomatic individuals.

PVI-007

Prevalence of adenovirus detected from in-patient children with community acquired pneumonia and the distribution of the adenovirus genotype

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Background: Adenovirus is one of the most common viral pathogens detected from many infections including pneumonia in children. Some genotype of adenovirus can also relate to the severity of pneumonia. In Vietnam, due to the lack of laboratory facilities to detect adenovirus, there are very few studies on the incidence of adenovirus causing pneumonia in children as well as its genotype distribution.

Aim of the study: Determine the prevalence of adenovirus detected from in-patient children with community-acquired pneumonia hospitalized at children's hospitals in Ho Chi Minh City and preliminary study of the distribution of genotypes from some detected adenoviruses.

Materials and methods: Use the multiplex real-time PCR with specific primers and probes to detect adenovirus and other respiratory viral pathogens from NTA (Naso-Tracheal Aspirate) samples taken from in-patient children under 5 years old with community-acquired pneumonia and hospitalized the children's hospitals in HCM city during 3 years from 2018 to 2020. From the received results, analyze the prevalence of adenovirus causing pneumonia in in-patient children with pneumonia and also analyze the prevalence of adenovirus co-infected with other viral pathogens. Select a part the adenovirus detected samples in year 2019 and 2020 to do the direct sequencing for adenovirus genotyping then analyze the distribution of adenovirus genotype.

Results: During 3 years, there were 2053 NTA samples were tested by multiplex real-time PCR for adenovirus detection and other respiratory virus. Among these samples, adenovirus was detected in 266 samples (12.96%). Among 266 samples with adenovirus, 96 samples (36.10%) were co-infected with the other respiratory virus. There were 1787 samples (87.04%) without the existence of adenovirus, however among these 1,787 samples, the respiratory virus was detected in 831 samples (46.50%). It means adenovirus and other respiratory virus were detected in 1,097 samples among 2,053 tested samples (53.43%). Eighty-three (83) of adenovirus detected samples were carried-out the direct sequencing for adenovirus genotyping. The received results detected that the most prominent genotype was genotype 7 with 58 samples (69.88%), next was genotype 3 with 13 samples (15.66%), genotype 6 with 4 samples (4.82%), genotype 1 with 4 samples (4.82%), genotype 2 with 2 samples (2.41%), genotype 5 with 1 sample (1.20%) and genotype 8(4) with 1 sample (1.20%).

Conclusions: Thanks to the routine application of multiplex real-time PCR in the laboratory, we were able to detect the adenovirus that accounts for 12.96% of hospitalized children with community-acquired pneumonia. Not only that, up to 36.1% of cases detected with adenovirus were co-infection with other respiratory viral pathogens. Thanks to real-time PCR, we also found that up to 53.43% of community-acquired pneumonia cases in hospitalized children were caused by viral pathogens. Regarding the distribution of adenovirus genotypes, the direct sequencing results allowed us to conclude that the two predominant circulating genotypes are genotype 7 and then genotype 3. The findings in this study are very important for doctors as well as researchers to consider the role of adenovirus in community-acquired pneumonia in children.

Keywords: Adenovirus, Adenovirus genotype, CAP in children.

International Journal of Antimicrobial Agents 58S1 (2021) 106422

Contents lists available at ScienceDirect

International Journal of Antimicrobial Agents

journal homepage: www.elsevier.com/locate/ijantimicag

Abstracts from the 13th International Symposium on Antimicrobial Agents and Resistance (ISAAR) – Late-breaking Abstracts

Abstract withdrawn

PLB-002

Predicting antimicrobial phenotype resistance in *Staphylococcus aureus* by machine learning analysis

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With the reduction in sequencing price and acceleration of sequencing speed, it is particularly important to directly link the genotype and phenotype of bacteria. Here, we collected 472 isolates of *Staphylococcus aureus* from China and selected 20% as the testing set. The minimum inhibitory concentrations of seven antimicrobial agents (clindamycin, cefoxitin, oxacillin, levofloxacin, trimethoprim-sulfamethoxazole, erythromycin, and gentamicin) were predicted by extracting k-mer from isolates combined with machine learning algorithms. For most antimicrobial agents, when considering one two-fold dilution, the accuracies could reach >85%, which can provide important information for clinical treatment. The results suggest that small datasets available in large hospitals could bypass the existing basic research and know antimicrobial resistance genes, accurately predict the bacterial phenotype by constructing machine learning model. Moreover, the k-mer algorithm could dock metagenomics in preparation for faster antimicrobial susceptibility diagnosis in the future.

Keywords: antimicrobial resistance; *Staphylococcus aureus*; machine learning; k-mer algorithm.

PLB-003

Prediction of bloodstream infection in patients with hematopoietic stem cell transplantation by plasma microbial cell-free DNA sequencing

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Background: Bloodstream infection (BSI) is a serious complication of hematopoietic stem cell transplantation (HSCT). After pathogen infection, Microbial cell-free DNA (mcfDNA) is released into the blood. mcfDNA sequencing provides a possibility for pathogen identification and prediction before BSI onset.

Methods: The clinical residual blood samples were collected prospectively within 8 days before the onset of BSI in patients with HSCT, and the plasma was separated and then cryopreserved. The mcfDNA was extracted from plasma and sequenced. The results of sequencing analysis were compared with those of blood culture, and the earliest time of predicting BSI was observed.

Results: From April to June 2021, a total of 16 patients with bacterial positive blood culture undergoing HSCT in Peking University People's hospital were enrolled. 40 blood samples were collected within 8 days before the onset of BSI, and each patient had 1–4 samples. According to the culture results, the prediction rate of mcfDNA sequencing was 58.82% (10/17) within 3 days, and 43.48% (10/23) within 4–8 days. The predicted results of mcfDNA sequencing within 3 days were higher. In addition to early detection of bacterial infection, Cytomegalovirus (CMV) infection was detected in one patient within 1 day before BSI.

Conclusion: Three days before the episodes of BSI in patients with HSCT, mcfDNA sequencing can detect pathogenic microorganisms including bacteria and viruses in advance, and predict the BSI.
Keywords: Microbial cell-free DNA; Hematopoietic stem cell transplantation; Bloodstream infection.

PLB-004

Risk factors and characteristics of multiple concurrent sexually transmitted infection (STI) in Hong Kong

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Background: Understanding characteristics of multiple concurrent STI (simplified as multiple infection as follows) may improve STI screening service. This study aims to identify characteristics and risk factors associated with such infection.
Method: Attendance records between 2009–20 from 7 social hygiene clinics which provide free STI examination and treatment in Hong Kong were retrieved. Male patients with first notification year in 2009–19 who have ever been diagnosed with syphilis, gonorrhoea, chancroid, chlamydia, genital warts and/or genital herpes were included. Diagnosis within 3 months were combined as one episode and multiple infection was defined as episode with >1 STI. Baseline characteristics of each patient were analysed by multivariable logistic regression.
Results: A total of 36434 (61%) male patients were analysed with 2937 (8%) ever had multiple infection. Thirteen percent self-reported as men who have sex with men and 2.3% were HIV-positive. Among 3134 multiple infection episodes identified in total, 41% happened at age 20–29 and 10% had ≥3 concurrent STIs. Episodes with combination of chlamydia and gonorrhoea infection (61%) were most commonly observed. In the final model, risk of having multiple infection decreased with 1-year increase in age at first notification (aOR = 0.980). Risk of blacks (aOR = 1.654, Chinese as reference), MSM (aOR = 2.435) and patients who ever had sex with commercial sex workers (aOR = 2.104) was higher, while risk of married patients (aOR = 0.776, single as reference) was lower.
Conclusion: Screenings for a variety of STIs may be needed for patients with high risk of multiple infection.

PLB-005

Clinical evaluation of methicillin-resistant *Staphylococcus aureus* screening software based on MALDI-TOF MS

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Background: Rapid detection of methicillin-resistant *S. aureus* (MRSA) is very important because MRSA is major causes of healthcare-associated infections and surgical wound infection with resistance against general antibiotics and prompt adequate treatment of antimicrobials against MRSA improved treatment outcome. However, traditional MRSA screening tests based on molecular diagnostics and antimicrobial susceptibility tests are time consuming and labor-intensive methods.
Methods: AMRQuest software that compares MALDI-TOF mass spectra of *S. aureus* with database by working on the machine learning technique was successfully used to screen MRSA simultaneously with bacterial identification. First, sample size for statistical analysis was determined by considering of MRSA infection prevalence in Korea and averages of positive prediction value (PPV) and negative prediction value (NPV) from meta-analysis. In the second, MRSA screening was performed using the 537 of *S. aureus* isolates including 231 of MRSA and 306 of MSSA from 3 tertiary-care hospitals.
Results: PPV and NPV of AMRQuest MRSA screening test were estimated as 95% and 78%, respectively. Percent positive/negative agreement, and overall percent agreement were calculated as 65%, 97%, 83%, respectively. Finally, Cohen's kappa for evaluate the clinical performance of AMRQuest was calculated as 0.7.
Conclusion: When the results of AMRQuest MRSA screening were compared with the cefoxitin disk diffusion test as a reference method, the *S. aureus* isolates collected in each hospital were determined statistically significantly as MRSA and MSSA. Finally, the clinical performance of AMRQuest software for MRSA screening was evaluated to be sufficient for use in the laboratory.

PLB-006

Detection of ESBL and carbapenemase in urinary isolates and susceptibility of uropathogens with special reference to fosfomycin

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Introduction: Fosfomycin, although an old antibiotic and been used in many European countries for UTI, not so popular in India. Due to alarming resistance of uropathogens, there is scarcity of an effective oral antibiotic. In this context, we have studied the susceptibility pattern of uropathogens with special reference to fosfomycin.

Table 1: (abstract PLB-006): Susceptibility pattern of Gram negative uropathogens

Antimicrobials	Gram negatives n = 468 (84.4%)	*E. coli* n = 294 (62.8%)	*K. pneumoniae* n = 71 (15.3%)	ESBL producers n = 257 (55%)	Carbapenemase producers n = 60 (12.8%)
Imipenem	395 (84.4)	263 (89.6)	56 (78.6)	245 (95.2)	0
Amikacin	409 (87.5)	294 (100)	28 (40)	227 (88.2)	0
Nitrofurantoin	301 (64.3)	257 (87.5)	13 (18.2)	182 (70.7)	22 (37.5)
Fosfomycin	434 (92.9)	294 (100)	54 (76.9)	243 (94.7)	47 (77.8)
Cotrimoxazole	101 (21.7)	59 (20)	12 (16.5)	37 (14.6)	7 (11)
Ceftriaxone	88 (18.9)	55 (18.8)	11 (15.4)	0	0
Cefepime	141 (30.2)	100 (34.1)	16 (22.2)	39 (15.2)	0
Ciprofloxacin	102 (21.9)	60 (20.6)	13 (18.2)	15 (5.9)	0
Levofloxacin	152 (32.6)	87 (29.6)	15 (21.4)	41 (15.8)	6 (10)
Piperacillin-tazobactam	174 (37.3)	125 (42.6)	11 (15.4)	88 (34.1)	0

Subjects and Methods: Prospective study was carried out in the central clinical microbiology laboratory of a tertiary care hospital located in southern Tamilnadu, India and catering patients mostly from rural areas. The duration of the study was six months from September 2020 to February 2021.Urine samples from all ages and sex were collected under sterile aseptic precautions. Urine culture was done by standard loop method, a semi-quantitative method. The organisms isolated from urine culture were identified by standard methods.[3] The antibiotic sensitivity test was done on Mueller-Hinton agar by Kirby-Bauer disc diffusion test as per Clinical and Laboratory Standard Institute (CLSI) guidelines. Standard strains of *E. coli* (ATCC 25922), *S. aureus* (ATCC 25923), and *P. aeruginosa* (ATCC 27853) were used as control. Antimicrobial susceptibility test results were entered in the laboratory system through WHONET 5 software.

Results: Of the 890 urine samples processed during the study period, 554 showed bacterial growth. Gram-negative bacilli accounted for 468 (84.4%), gram-positive cocci for 72 (12.9%). Among Gram negatives, *Escherichia coli* (62.8%) was the predominant pathogen followed by *Klebsiella pneumoniae* (15.3%). 55% were ESBL and 12.8% were carbapenemase producers. Among Gram positive cocci, 75% were Enterococci. Sixty isolates were resistant to all three carbapenems-imipenem, meropenem and ertapenem by disc diffusion. MIC of meropenem was determined by agar dilution and found to be of high level resistance (>64 μg). None of them were positive for carbapenemase by modified hodge test. Imipenem EDTA combined disc method was positive in 43 isolates. All were negative for imipenemboronic acid inhibition method which suggest that the isolates were MBL producers. Among the oral antimicrobials, nitrofurantoin and fosfomycin show good in vitro coverage against the commonest uropathogens, *E. coli* and *Enterococcus faecalis* (Tables 1 and 2). In ESBL producers and carbapenemase producers, susceptibility to nitrofurantoin was 70.7%, 37.5% and fosfomycin was 94.7%, 77.8% respectively. Linezolid resistance not found with Gram positive isolates. Among the parenteral antibiotics, aminoglycosides and carbapenems show better in vitro activity.

Table 2: Susceptibility pattern of *Enterococcus faecalis*

Antimicrobials	N = 72 (%)
Ampicillin	8 (11)
High level gentamicin	29 (40)
Levofloxacin	9 (12.5)
Fosfomycin	72 (100)
Nitrofurantoin	54 (75)
Linezolid	72 (100)

Conclusion: In the present study, fosfomycin exhibits good in vitro activity against the common uropathogens, *E. coli* (100%) and *Enterococcusfecalis* (100%) tested. It also shows good coverage against ESBL and carbapenemase producers. Therefore, fosfomycin might be considered as a treatment option for urinary tract infections in India; however, clinical trials should first reinforce the in vitro findings.

PLB-007

Aspergilloma of renal pelvis in a diabetic patient

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Background: Upper urinary tract fungal infections are rare and are usually associated with diabetes, chronic renal failure, long term antibiotic usage and terminal malignancy. Diagnosis is based on microscopic examination of urine and specific fungal culture. Histopathological examination of fungal balls will demonstrate the fungus. Appropriate imaging studies of the pelvicalyceal system and ureter and prompt institution of measures to relieve obstruction and antifungal therapy will help in preserving the renal unit.

Case History: Forty-five year old diabetic male admitted with complaints of fever on and off for the past four months, right loin pain and burning micturition. He had taken several courses of antibiotics. There was no history of prior instrumentation/catheterisation of the urinary tract. Investigations showed raised blood sugar, elevated HbA1c level, urine appeared clear and showed traces of ketones. Patient was treated for diabetic ketoacidosis. Urine culture did not show growth. Chest Xray revealed diaphragmatic hump on right side. USG abdomen showed enlarged right kidney with gross hydroureteronephrosis with moving internal echoes suggestive of pyonephrosis and right lower pole renal calculus of 1.7 cm size. Left kidney showed mild hydronephrosis. CT KUB showed right proximal ureteric calculus with upstream dilation of ureter and gross hydronephrosis with thinning of renal parenchyma with lower pole calculus Internal echoes seen in the dilated right renal collecting system and ureter (Figure 1). Broad spectrum antibiotics were started.

USG guided PCN (Percutaneous nephrostomy) of right kidney performed and pus aspirated. Pus culture grew Methicillin resistant *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Antibiotics were started according to sensitivity patterns. PCN was in situ and confirmed by X ray KUB. Blood glucose was controlled and planned for right percutaneous nephrolithotripsy. Patient was taken up for elective PCNL. The previous PCN tract dilated till 26Fr and amplatz sheath inserted. The stone could not be localised due to slough like material filling the collecting system. All such material removed and stone fragmented and retrieved. 14 Fr nephrostomy inserted. 4Fr DJ stent inserted. Slough sent for microbiology on direct microscopy demonstrated mycelia which were dichotomously branching. Histopathological examination of the material showed narrow fungal hyphae. Gram stain showed fungal hyphae and Gram positive cocci. Culture on SDA (Sabaroud's dextrose agar) grew *Aspergillusfumigatus.* After the microbiology report, intrapelvic instillation of Amphotericin B donecontinously for 3 days. The patient was started on oral voricanozole and discharged with stent in situ. After one month of follow-up, patient had recurrence and underwent nephrectomy in another hospital.

Conclusion: To diagnose fungal infections promptly, a high index of suspicion in certain clinical settings cannot be overemphasized. In addition, multiple large-volume urine cultures may be necessary. Cultures drawn by either a percutaneous nephrostomy tube or transurethral ureteral catheters are useful in case of negative urine cultures. Even in cases of a classic pyelonephritis with repeat positive urine cultures for bacteria, refractory to antimicrobials, fungal infection might coexist, especially in diabetic patients. The possibility of fungal ball as an etiology of obstructiveuropathy should be kept in mind.

PLB-008

The diabetic duo – a rare case of disseminated tuberculosis and cryptoccocal meningitis in a diabetic patient

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Background: A 34 year old Malay lady with underlying poorly controlled Diabetes Mellitus diagnosed four years ago presented with lower abdominal pain for 1 week duration, headache intermittently for 3 days, loss of appetite and loss of weight of 40 kg over one year duration. She had history of pulmonary tuberculosis (PTB) contact with her family members a year ago

however she denied chronic cough or shortness of breath. Clinically she was lethargic looking with initial vitals of blood pressure 110/64 mmHg, pulse-108 beats/min, random blood glucose-12 mmol/L, temperature- 37C. Respiratory system examination revealed right sided pleural effusion and per abdomen examination noted presence of ascites however no organomegaly detected. Initial neurological examination was intact.

Investigation: Blood results revealed Hemoglobin 12.4 g/dL, White blood cell- 4.2×10^9/L, Platelet 493×10^9/L, C-reactive protein-11.7 mg/L, Erythrocyte sedimentation rate(ESR)- 52 mm/hr, and both renal profile and liver function test were normal, Retroviral test and hepatitis screening was also negative. Initial Chest X-ray revealed right pleural effusion. Her Computed Topography (CT) Thorax showed features of active PTB and CT Abdomen and Pelvis revealed features of disseminated tuberculosis peritonitis with tubo-ovarian abscess. Patient then undergone bronchoscopy and pleuroscopy whereby Histopathological examination (HPE) of pleural biopsy revealed necroziting granulomatous changes and Bronchoalveolar lavage (BAL) grew cryptococcal neoformans but no evidence of PTB. She was later subjected for Contrasted CT brain (CECT) due to altered behaviour in ward whereby noted rim-enhancing lesion. Lumbar puncture done showed bacterial picture with opening pressure of 42 cm H20 and Cryptococcal Antigen was positive via latex particle agglutination with titer of 1: 320. Her primary immunodeficiency screening also was normal.

Treatment/Outcome: She was subsequently started on intensive phase of anti Tuberculosis medication (Ethambutol, Isoniazid, Rifampicin, Pyrazinamide) and induction phase of anti fungal (Intravenous Amphothericin B and oral Fluconazole). Her intensive phase for tuberculosis treatment was extended to three months and planned for total 18 months of treatment. Cryptococcal treatment then converted to consolidation phase with oral fluconazole 400 mg once daily with observed clinical and radiological improvement. Patient was planned for outpatient follow up and clinical improvement observed with continuation of oral fluconazole 200 mg once daily for life long duration.

Conclusion: Patient with poorly controlled DM predisposed to immunocompromised state whereby clinical suspicion for Tuberculosis infection and other opportunistic infection such as Cryptococcus should be considered. Early detection with prompt treatment of such condition improves overall outcome of the patient.

PLB-009

Impact of rapid molecular detection of respiratory pathogens on antibiotic use among hospitalized children with acute respiratory tract infections

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Background: Detection of respiratory pathogens using conventional methods among children with respiratory infections is often limited and time consuming. Rapid identification of respiratory pathogens might have impact on antibiotic use among hospitalized children.

Methods: Retrospective review of medical records of hospitalized children with respiratory tract infections whom had rapid molecular detection of respiratory pathogens tests done with a matched control cohort, from January 2020 till June 2021 was carried out. Clinical and antibiotics data was analysed.

Results: Total of 283 medical records of hospitalized children with rapid molecular testing and 150 matched control were reviewed. The most common pathogens detected was Human Rhinovirus/Enterovirus 31.6% (84/266), followed by Respiratory Syncytial virus 18.8% (50/266) and adenovirus 15% (40/266). Duration of therapy was significantly longer in test group than control group (median (IQR): 6 (5) days vs 5 (3) days; $p = 0.043$) but with higher ICU admission (3.9% vs 0%; $p = 0.01$). There was no significant difference in length of therapy (median (IQR): 4 (3) days vs 4 (3) days; $p = 0.84$) and duration of therapy (median (IQR): 6 (5) days vs 6.5 (6) days; $p = 0.729$) among those with positive and negative tests.

Conclusion: Length of therapy and duration of therapy showed no significant difference between groups with and without identifiable pathogens using rapid molecular testing, indicating a well implementation of antimicrobial stewardship in our institute.

PLB-010

Rapid antimicrobial susceptibility testing based on EUCAST guideline for *E. coli, K. pneumoniae*, and *S. aureus*

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Bloodstream infections are a leading cause of high morbidity and mortality worldwide. Therefore, early diagnosis and treatment are important for a good prognosis. European Committee on Antimicrobial Susceptibility Testing (EUCAST) provides a rapid antimicrobial susceptibility testing (RAST) based on the standard disk diffusion methodology. It is faster than the conventional method because the blood culture positive samples are directly inoculated into the media and cultured, and are read after 4, 6, and 8 hours of incubation. The aim of this study was to evaluate the AST for *Escherichia coli, Klebsiella pneumoniae*, and *Staphylococcus aureus* from positive blood culture bottles using EUCAST RAST. In this study, a total of 60 strains were tested including 20 strains of each *E. coli, K. pneumoniae,* and *S. aureus*. Antimicrobial susceptibilities were tested for 10 antimicrobial agents in *E. coli* and *K. pneumoniae*, and 4 antimicrobial agents in *S. aureus*. Diameter of the inhibition zone were compared with minimal inhibitory concentration obtained from the Sensititre AST system as a reference test. As results, for *E. coli*, total categorical agreement (CA) was 135 (68%) at 4 hours, 162 (81%) at 6 hours and 174 (87%) at 8 hours. The results varied depending on the type of antimicrobial agent. For *K. pneumoniae,* total CA was very high in 177 (89%) at 4 hours, 191 (96%) at 6 hours and 191 (96%) at 8 hours. For *S. aureus*, total CA was 68 (100%) at 4 hours, 73 (100%) at 6 hours and 73 (100%) at 8 hours. Total CA of *K. pneumoniae* met US Food and Drug Administration criteria at 6 hours, but *E. coli* did not meet up to 8 hours. Therefore, additional experiments are needed for more accurate evaluation. In conclusion, when testing with the RAST method, it can shorten the time by more than a day, so if applied properly according to laboratory conditions, antibacterial agent results can be reported faster.

PLB-011

Their eyes hurt: The culprit and associated risks for microbial keratitis in southern region of Malaysia

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Background: Microbial keratitis is an ocular emergency requiring early diagnosis and effective treatment (Rai et al., 2017; Wong et al., 2012). Many studies have described keratitis as a leading cause of avoidable monocular morbidity and blindness (Al-Shakarchi et al., 2015; Samsudin et al., 2017). The outcome of blindness is troublesome as this may affect someone's ability to continue their social life and eventually may lost their occupation. The study was conducted to determine the proportion, causative agents and associated risk factors for microbial keratitis in Southern region of Malaysia. The baseline data from the recent study may guide the management of microbial keratitis.

Methods: Study was performed at few government hospitals in southern region of Malaysia. Two hundred seventy-six (276) patients were suspected to have microbial keratitis were included. Corneal scrapping samples were sent for microbiological investigations and the associated risks were obtained from medical record.

Results: Of 276 patients, 43.5% (n = 120) had culture proven bacterial and fungal keratitis. A total of 128 eyes were affected. Majority of microbial keratitis were caused by bacteria (74.2%, n = 89) followed by fungal (22.5%, n = 27) and about 3.3% was due to combination of both organisms. Gram-negative bacteria infection dominated the cases (57.8%; n = 74) followed by fungi (25.0%; n = 32) and gram-positive bacteria (17.2%; n = 22). *Pseudomonas aeruginosa* was the most common causative agents (43.8%; n = 56) whereas Fusarium spp. (n = 7) was the common pathogen for fungal keratitis. Among Gram-positive bacteria, *Staphylococcus aureus* was the common causative agents.

Non-vegetative trauma was the common associated risks, followed by underlying medical illness, ocular eye disease or previous eye surgery. Contact lens wearer, vegetative trauma and ophthalmic steroid usage were also the identified risks.

Conclusions: Bacteria was the most common cause of microbial keratitis among suspected patients in which *Pseudomonas aeruginosa* as the most common isolated organism. The proportion of culture-positive fungal keratitis is significantly lower than that of bacterial keratitis. Eye injury and eye related illness were among the factors that poses higher risk for developing microbial keratitis in southern region of Malaysia.

PLB-012

Clinical and laboratory factors in predicting mortality among SARS-CoV-2 RNA positive patients from a tertiary care center in South Tamilnadu – A retrospective observational study

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Background: The pandemic due to COVID 19 is challenging the healthcare system of many countries and imposing unavoidable burden and economic impact throughout the world. Due to the heterogeneous nature of COVID 19, our study was planned to analyze clinical presentation with comorbidities and laboratory factors in predicting mortality among SARS-CoV-2 RNA detected patients.

Material and Methods: This retrospective observational study was carried out in our tertiary care center in adult patients (≥18 years) admitted in COVID Isolation unit of our hospital with positive SARS-CoV-2 RNA detection between June and October 2020. 100 survivors and 100 nonsurvivors were randomly selected after age and sex matching.

Information regarding demographic details, clinical presentations, co-morbid conditions, and biochemical, hematological including coagulation profile, inflammatory markers (CRP, Procalcitonin) along with treatment details, for both groups were collected from the medical records.

Statistical analysis: Data analyses were done using STATA software version 16. To explore the risk factors associated with in-hospital death, univariable and multivariable logistic regression models were used. As this was a matched case-control study using individual matching, conditional logistic regression was used to estimate the association between the predictors of interest with survivors and non-survivors.

Results: Fever (59%), shortness of breath (46.5%), cough (41%), and myalgia (34%) were the most common presenting symptoms in our setup. Diabetes, hypertension, cardiovascular, and neurological conditions were significantly associated with mortality. Cardiac arrest (0.09%, 9/100) and acute kidney injury (0.29%, 29/100) were common complications in nonsurvivors. Analysis of hematological and biochemical profile among non-survivors and survivorsare given in Table 1, and there was a statistically significant difference in polymorphs, lymphocyte, monocytes, eosinophils, basophils, blood urea, LDH, AST, ALT and procalcitonin among the cases and controls.

In univariable analysis, the odds of in-hospital death were higher in patients with neutrophilia, lymphopenia, monocytosis, elevated AST and raised lactate dehydrogenase. In multivariate analysis, neutrophilia and lymphopenia were associated with death (Table 2). Among non-survivors, biochemical and hematological markers taken at the time of admission and 24 hours before death showed statistical significant difference in total WBC count, neutrophil count, lymphocytopenia, eosinophilia, blood urea and serum creatinine The most common cause of death was respiratory failure (84%), ARDS (77%), followed bycardiac arrest (10%) and septic shock(4%). 92% of non-survivors received corticosteroids, 63% needed high flow nasal cannula oxygen therapy, and 29% had Invasive mechanical ventilation, and 29% received Tocilizumab.

Table 1: Distribution of hematological and biochemical parameters among non-survivors and survivors COVID patients at the time of admission

Variables	Non-Survivors n = 100 Mean ± SD	Survivors n = 100 Mean ± SD	p-value
Polymorphs (cells/cu.mm)	9321.76 ± 5356.563	6470.54 ± 4026.159	**0.000**
Lymphocytes (cells/cu. mm)	894.93 ± 500.907	1425.43 ± 809.490	**0.000**
Neutrophil lymphocyte ratio	18.6 ± 30.09	6.2 ± 6.4	**0.0001**
Monocytes (cells/cu.mm)	536.32 ± 328.814	651.68 ± 419.244	**0.014**
Eosinophils (cells/cu.mm)	21.55 ± 129.409	78.50 ± 205.835	**0.000**
Basophils (cells/cu.mm)	17.77 ± 33.006	28.29 ± 33.592	**0.001**
Haemoglobin (mg/dl)	12.72 ± 2.144	12.25 ± 1.918	0.060
Platelet (cells/cu.mm)	235.98 ± 91.679	255.73 ± 106.120	0.179
Blood urea (mg/dl)	47.63 ± 28.988	35.78 ± 21.778	**0.002**
Creatinine (mg/dl)	1.09 ± 0.549	0.943 ± 0.518	0.069
LDH (mg/dl)	1114.44 ± 443.058	747.51 ± 253.438	**0.000**
Albumin (g/dl)	3.69 ± 0.354	3.75 ± 0.424	**0.320**
AST (g/dl)	67.21 ± 45.819	46.46 ± 26.194	**0.000**
ALT (g/dl)	46.09 ± 29.433	37.48 ± 20.395	**0.029**
Procalcitonin (ng/ml)	0.75 ± 2.803	0.49 ± 1.516	**0.004**

Table 2: (abstract PLB-012): Univariate and Multivariate analysis of risk factors associated with non-survivors

Variables	Category	Total	Uni variable OR	p-value	Multi variable OR	p-value
Polymorphs (cells/cu.mm)	1500–8000	115 (62.84)	1.0 (Ref)		1.0 (Ref)	
	>8000	68 (37.16)	2.357	**0.007**	2.368	**0.049**
Lymphocytes (cells/cu.mm)	1000–4800	101 (55.19)	1.0 (Ref)		1.0 (Ref)	
	<1000	82 (44.81)	3.417	**0.000**	3.361	**0.005**
Monocyctes (cells/cu.mm)	285–500	152 (83.06)	1.0 (Ref)		(Ref)	
	>500	31 (16.94)	0.375	**0.040**	0.406	0.165
AST (g/dl)	≤40	60 (35.50)	1.0 (Ref)			
	>40	109 (64.50)	4.143	**0.001**		
ALT (g/dl)	≤40	107 (63.31)	1.0 (Ref)		1.0 (Ref)	
	>40	62 (36.69)	1.846	**0.075**	2.132	0.066
Blood urea (mg/dl)	≤50	127 (70.56)	1.0 (Ref)		1.0 (Ref)	
	>50	53 (29.44)	1.833	**0.091**	1.387	0.476
Creatinine (mg/dl)	≤1.5	155 (86.59)	1.0 (Ref)			
	>1.5	24 (13.41)	1.714	0.257		
LDH (mg/dl)	≤470	11 (7.24)	1.0 (Ref)			
	>470	141 (92.76)	8	**0.050**		
Procalcitonin (ng/ml)	<0.5	117 (81.25)	1.0 (Ref)			
	>0.5	27 ()	1.833	0.232		

Conclusion: Serial monitoring of neutrophils, lymphocytes, AST, LDH and serum creatinine might provide a reliable and convenient method for classifying and predicting the severity and outcomes of patients with COVID-19.

PLB-013

Candidemia caused by *Candida nivariensis*: A rare case report from Malaysia

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Background: *Candida nivariensis* is a rare Candida species which is phenotypically closely related to *Candida glabrata* and *Candida bracarensis*. The 3 species form the *C. glabrata sensu lato complex*. Here, we describe the rare candidemia reported in Malaysia, isolation and characterization of a *C. nivariensis* isolate cultured from the blood culture obtained from a severely ill lady.
Case presentation: 60 years old with underlying diabetes mellitus, came with lethargy, vomiting and abdominal pain for a week. Total white cell in normal range, urine examination showed leukocyte, nitrate and protein detected. Blood culture was sent twice and both grew similar yeast. The yeast isolate was initially tested conventionally by germ tube turn out as negative. The isolate was streaked on chromagar and slide culture was done, both were incubate 30 degree celcius for 48 hours. The result showed creamy coloured on chromagar and no pseudohyphae seen on slide culture. The identification was confirmed by Matrix-assisted laser desorption ionization time of flight mass spectrometry (MALDI-TOF MS) as *C. nivariensis*. Antifungal susceptibility testing was performed by Etest. Antifungal susceptibility testing revealed high minimum inhibitory concentration (MIC) against fluconazole, but low MICs against amphotericin B and echinocandins.
Conclusions: MALDI-TOF MS with updated software and molecular tests are needed to correctly identify *C. nivariensis*. Since *C. nivariensis* may exhibit reduced susceptibility to antifungal agents, accurate identification and antifungal susceptibility testing are important, particularly for isolates from sterile sites, for optimal patient management.

PLB-014

Prevalence of AmpC beta-lactamase and extended spectrum beta-lactamase co-producer in *Escherichia coli* and *Klebsiella* species in a teaching hospital

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Background: Beta-lactamase producing bacteria have been on surge due to selection pressure and injudicious antibiotics usage. Organisms that co-produce AmpC beta-lactamase and extended spectrum beta-lactamase (ESBL) pose diagnostic challenges which may result in inadequate treatment. To date, there is no standardized guideline offering phenotypic detection of AmpC beta-lactamase.
Objectives: The purpose of this study was to determine the prevalence of ESBLs, AmpC beta-lactamase and co-producer organisms in teaching hospital.
Methods: All *E. coli* and *Klebsiella* sp. were identified using conventional laboratory methods and their antimicrobial susceptibilities were determined using disc diffusion method. Isolates with zone of inhibition of ≤22 mm for ceftazidime or ≤27 mm for cefotaxime were included in this study. These isolates were subjected to further testing with ESBL confirmatory test, cloxacillin-containing Muller Hinton confirmatory test, modified double disk synergy test and AmpC disk test.
Results: A total of 304 isolates were collected which included 159 *E. coli* and 145 *Klebsiella* sp. The prevalence of organisms that co-produced AmpC beta-lactamase and ESBL enzymes were 2.96% (9/304). Only 42 isolates (13.8%) were proven to produce AmpC beta-lactamase through AmpC disk test. By using the CLSI confirmatory test, 252 (82.9%) isolates were identified as ESBL producer and additional 2 ESBL organisms were detected when cloxacillin containing Muller Hinton were used. No additional ESBL organisms were detected using modified double disk synergy test.
Conclusion: Distinguishing between AmpC beta-lactamase and ESBL-producing organisms has epidemiological significance and has therapeutic importance as well. Organisms which co-produce AmpC beta-lactamase and ESBLs can lead to false positive and false negative ESBL confirmatory test. Therefore, knowing the local prevalence can guide the clinician in term of treatment.
Keywords: AmpC beta-lactamase, ESBL, co-producer.

PLB-015

Presence of *mcr*-1 in clinical isolates of *Escherichia coli* ST5162 with colistin and carbapenem resistant phenotype

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Background: Colistin is considered as the drug of last resort used against multidrug resistant Enterobacteriaceae. The plasmid-mediated colistin resistance gene, *mcr*-1, represents a significant public health threat. Thus, the present study was designed to investigate the occurrence of *mcr*-1 in colistin resistant *E. coli* isolates in a tertiary referral hospital of India.
Methods: A total of 120 *E. coli* isolates were collected from various wards of Silchar Medical College and Hospital. Phenotypic screening for colistin resistance was done by broth microdilution method and Polymyxin NP Test. Antibiogram profiling was done. Genotypic characterization was done by PCR assay. Co-occurrence of other resistance determinants was determined. Transferability was determined by transformation and conjugation assay. PCR- based plasmid incompatibility typing and Multilocus sequence typing (MLST) was performed.
Results: Out of 120 *E. coli* isolates, 26 isolates were screened positive for colistin resistance. The positive isolates were found to be resistant against imipenem, meropenem and Aztreonam. The *mcr*-1 gene was found in two *E. coli* isolates belonging to sequence type ST5162. Co- occurrence of other antibiotic resistance genes namely *aph(4)Ia*, *ant(2″)-Ia*, *aac(3)-I*, *aac(3)-IIc*, *sul1* and *qep*A were observed. The resistance determinants was found to be horizontally transferable and located within IncFIA plasmid.
Conclusions: This study revealed the presence *mcr*-1 through IncFIA in a single clone of colistin and carbapenem resistant *E. coli* which highlights the risk of dissemination of this resistance causing a grave concern for infection management and therapeutic options in the clinical settings.

PLB-016

Analysis Kaposi's sarcoma of cases in HIV patients identified by endoscopy at the national medical center

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Background: Kaposi's Sarcoma (KS) of internal organs in patients with HIV infection is underdiagnosed and constitutes a problem for specialists.
Aim: to analyze cases of KS of the gastrointestinal tract and respiratory tract detected endoscopically in patients with HIV infection.
Methods: a retrospective analysis of the medical documentation of 602 HIV-infected patients of the National Medical Center in Moscow (from January 2019 to May 2021) was conducted. 376 diagnostic bronchoscopies and 226 gastroscopies were performed. 11 cases of KS were detected in patients with HIV infection. Descriptive statistics were provided.
Results: All patients were diagnosed with acquired immunodeficiency syndrome (AIDS) and epidemic HIV-associated Kaposi's sarcoma with skin lesions.
Men made up 90.9% of cases, and the average age was 43 ± 12 (95% CI 35–51).
The average CD4 lymphocyte count was 140 ± 107 cells/μl (95% CI 58–222 cells/μl). The median HIV RNA viral load was 1 40 000 copies/ml (Q_1 – Q_3: 24 250–2 25 000 copies/ml). 72.2% of patients received HAART before the endoscopy.
Gastrointestinal lesions were found in the oral cavity in 81.8% of cases, esophagus - 45.5%, stomach - 100%, duodenum - 27.3%.
SC elements during bronchoscopy were detected on the oropharyngeal mucosa in 45.5% of all cases, trachea - 27.3%, main bronchi - 36.4%, lobar bronchi - 27.3%, segmental bronchi - 9.1%.
During endoscopic examination, erythematous forms of elements were found in 18.2% of all cases, popular - 45.5%; tumorous form - 36.3%.
Conclusion: The presence of KS skin changes in patients with HIV infection requires an endoscopic examination of the gastrointestinal tract and bronchial tree to exclude their lesion.

PLB-017

Relationship between treatment category and mortality among patients with multidrug-resistant tuberculosis in Russia

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Background: Mortality from the multidrug-resistant tuberculosis (MRD TB) remains high. However, the influence of treatment features on mortality has not been sufficiently studied.
Aim: Analysis of the relationship between the category of treatment and mortality from MDR TB in regions with different levels of medical care.
Methods: A ranking of 85 regions of Russia on the quality of TB medical care was conducted, and an analysis of official statistical data for 2020 was carried out. A correlation analysis of the relationship between the treatment category and mortality according to the Spearman methods was then conducted.
Results: In regions with a high level of medical care, statistically significant direct correlations of the treatment category and mortality were established: with newly diagnosed cases of TB (ρ = 0.811; $p < 0.001$), with relapses of TB (ρ = 0.869; $p < 0.001$), after ineffective courses of treatment (ρ = 0.685; $p = 0.05$), during treatments after discontinuation of therapy (ρ = 0.754; $p < 0.001$). All the identified connections were high or salient on the Cheddock scale.
Statistically significant direct correlations were also established in regions with a low level of medical care: with a newly diagnosed cases of TB (ρ = 0.835; $p < 0.001$), relapses of TB (ρ = 0.942; $p < 0.001$), after ineffective courses of treatment (ρ = 0.904; $p < 0.001$), during treatments after discontinuation of therapy (ρ = 0.767; $p < 0.001$). All the identified connections were very high or high on the Cheddock scale.
Conclusion: Treatment categories and mortality have very high, high, or salient relationships, regardless of the quality of medical care.

PLB-018

Selection of tuberculosis patients with XDR for valvular bronchoblocation using telemedicine

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Background: The complexities of treating XDR-TB patients in the regions of Russia require the use of remote technologies for patient selection for innovative treatment methods.
Aim: Determination of the possibility of selecting XDR-TB patients for valvular bronchoblocation (VBB) using telemedicine.

Methods: The analysis of 387 telemedicine consultations of XDR-TB patients in the National Medical Center from 2019 to 2020 was carried out. 209 patients with cavities in the lungs were selected for the installation of VBB for treatment at the Federal Center for Innovative Technologies. Then, a retrospective analysis of the VBB effectiveness was carried out.
Results: Chronic patients accounted for 71.3% of all patients, first-time TB patients - 7.2%, relapses - 21.5%. VBB was performed on patients with cavities in one lung (3–5 cm – 58.4%) and two lungs (3–5 cm – 10.5%; 5–8 cm – 31.1%).
An improvement of clinical condition as well as the disappearance of bacterial excretion (by microscopy and seeding) was registered among 100% of patients after 9 months. The disappearance of the intoxication syndrome was registered in 100% of cases. In the X-ray control, the cavity disappeared in 83.7% all cases after 9 months.
After 9 months the cavity disappeared among: 93.3% of newly diagnosed patients; 84.4% of patients with relapses; 82.5% of chronic patients. The cavity decreased by more than 2/3 in 12.4% of all cases, and the cavity disappeared in 87.6% of all cases after 12 months. After 12 months the cavity closed among: 100% of newly diagnosed patients; 93.3% of patients with relapses; 84.5% of chronic patients.
Conclusion: Telemedicine allows selecting XDR-TB patients for installing a valve in the bronchus in the presence of a cavity in the lungs. At the same time, high efficiency of the treatment is recorded.

PLB-019

Hepatitis B infection: Seroprevalence and infectivity among perceived low risk patients in a specialist centre in Malaysia

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Background: The Hepatitis B virus (HBV) seroprevalence rate for Malaysia is approximately ranging from 3% to 5%, that categorized Malaysia as an intermediate endemic country for HBV. HBV infection among adult can be asymptomatic for a significant period and this can lead to delayed diagnosis especially among the low-risk population. Among those that are positive for Hepatitis B surface antigen (HBs Ag), presence of hepatitis B e antigen (HBe Ag) denotes viral replication and potential of infecting another potential susceptible person. This is of important to consider among low-risk population as these asymptomatic, low risk population is vital in playing a role to curb the uprising of HBV infection.
Objective: This study aims to provide preliminary data on HBV prevalence among perceived low risk patients in a specialist centre in Malaysia.
Method: A retrospective study was done where data of 5535 patients that were screened for HBs antigen by chemiluminescence immunoassay (CLIA) during the year 2018 until 2020 were examined. These patients undergo HBV screening as a routine either before cardiac procedure or as part of antenatal check-up. There was no high-risk behaviour recorded. Those who are HBs Ag reactive by CLIA had their HBe Ag presence determined.
Result: There were 63 (1.1%) new cases detected during the screening. Three (4.7%) were HBe Ag positive. Fifty two percent of them were male. Majority of them (90%) in the age range of 40–70 year.
Discussion and conclusion: This study showed that screening detects small but significant percentage of new HBV cases among perceived low risk patients and a significant number of them is categorized as infectious. This highlighted the need to recognize that among low-risk population carries potential risk of spreading of disease burden and to be considered when implementing prevention strategies.
Keyword: Hepatitis B seroprevalence, infectivity.