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Oral presentations

4 Clinical impact of syndromic molecular point-of-care testing for gastrointestinal pathogens in adults hospitalised with suspected gastroenteritis (GastroPOC): a pragmatic, open-label, randomised controlled trial

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Background

Single-occupancy isolation rooms are a limited resource in UK hospitals but are critical in preventing transmission of infection. Patients with suspected gastroenteritis are nursed in single-occupancy rooms but delays in laboratory testing lead to non-infectious patients remaining isolated for prolonged periods unnecessarily. Rapid molecular test panels for gastrointestinal pathogens have a run-time of around 1 hour but their clinical impact is unknown.

Methods

In this randomised controlled trial, we enrolled adults hospitalised with suspected gastroenteritis in Southampton General Hospital. Patients were randomly allocated (1:1) to receive mPOCT of stool or rectal samples, or to routine clinical care (control) with laboratory testing. The primary outcome was duration of time in single-occupancy rooms. Secondary outcomes included time to results, time to de-isolation, and safety outcomes.

Results

Between March 2017 and March 2020, we enrolled 278 patients, 138 assigned to mPOCT (one withdrawal) and 140 to the control group. The duration (geometric mean) of single-occupancy room isolation was 1.8 days (95%CI 1.5-2.2) in the mPOCT group compared with 2.6 (2.2-3.0) days in the control group (exponentiated coefficient 0.70 [95%CI 0.56-0.87]; p=0.0017). The median (IQR) time to results was 1.7 hours (1.5-2.0) for mPOCT and 44.7 hours (21.2-66.1) for the control group (p<0.0001). Time to de-isolation was 0.6 days (0.3-1.8) in the mPOCT group compared with 2.2 days (1.2-3.2) in the control group, (p<0.0001). There were no differences in length-of-stay, re-admission, or mortality between groups.

Conclusions

mPOCT for gastrointestinal pathogens in patients with suspected gastroenteritis was associated with reduction in single-occupancy room use.

8 The gym, a Spanish holiday and a headache

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46 year old gentleman presented with headache and fever following a holiday to Spain. A diagnosis of suspected meningoencephalitis was made. An LP was undertaken on d3 of admission and showed a low glucose (<0.3), raised protein (5.5) with 146 WBC. No organisms were seen on Gram stain. The following day his blood culture revealed a Gram positive bacillus and Listeria monocytogenes was isolated from his blood and CSF cultures. His antibiotics were changed to Amoxicillin 2g 4-hourly at this point. A history of anabolic steroid use was elucidated.
He had a poor clinical response and Gentamicin was added the following day. He continued to do poorly with hydrocephalus requiring EVD insertion on d8 of admission.
An MRI on d18 of admission showed extensive multifocal intracranial and spinal meningitis, cerebritis and ventriculitis. This prompted us to add high dose cotrimoxazole d19. He continued to require CSF drainage; CSF culture from d20 was negative.
On d24 of admission he required an EVD change for blockage, a sample taken at this time grew Staphylococcus haemolyticus and Candida albicans. Treatment for both these organisms was initiated and patient continued to need CSF drainage.
Following ITU and ward care he was transferred to the rehabilitation ward with lasting cognitive and physical impairments.

Dilemmas

1. Treatment of poorly responding Listeria Meningitis and the use of second agents
2. Treatment of Candida ventriculitis with ongoing need for drainage of CSF

Lessons Learned

1. Duration and dosing recommendations for Gentamicin as a second agent for Listeria meningitis

9 Procalcitonin (PCT) guided proactive antimicrobial review of hospitalized in-patients

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• Background and objectives: Procalcitonin testing has been routinely used in many tertiary centers to improve antibiotic stewardship. This study aimed to evaluate the additional impact of proactive microbiology review of antibiotics along with the use of procalcitonin.
• Methods: An observational study was carried out over a period of 4 months in non-critically ill patients with a PCT value ≤0.25 ng/L. A proactive antimicrobial stewardship approach was implemented in cases which had not been acted upon by clinical team within 24 hours of PCT results. Cases with a negative PCT were discussed with treating physicians via telephone call and during antimicrobial stewardship rounds and decisions made to stop antibiotic therapy if clinically safe and relevant.
• Results: A total of 150 cases were reviewed in a 4-month period, 107 patients were on antibiotic treatment. Antibiotics were stopped or de-escalated for 23/107 (21.4%) patients within 24 hours of the PCT result by the clinical team, however antibiotic treatment was continued for 84/107 (78.5%) cases. The 84 patients who remained on antibiotic therapy were reviewed by microbiology and in 50/84 (59.5%) cases, the decision to continue antibiotics by the clinical team was found to be inappropriate. The microbiology team proactively contacted the clinical team in 40/50 cases. Following discussion, an instant decision to stop antibiotics was agreed for 37/40 (92.5%) cases, while a proposed stop date was agreed for 3 cases. In the remaining 10 cases, where the microbiology team didn't intervene, antibiotics were continued for 6.2 days on average.
Conclusions: Proactive review by microbiology following low procalcitonin values can be an effective strategy to reduce the antibiotic duration in a targeted hospitalized patient group.

21 An unusual case of axillary lymphadenopathy in an 85 year old man

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Case-presentation

An 85-year-old man presented with a 6 week history of painless left axillary lymphadenopathy. A lymph node biopsy showed granulomatous lymphadenitis with visible acid fast bacilli, and culture yielded growth of Mycobacterium avium. He had no past history of mycobacterial infections, warts, zoster or Candida; and he was taking no immunosuppressant medication. His HIV and tuberculin tests were negative, blood lymphocyte subpopulations and immunoglobulins were normal, and a CT CAP showed no evidence of disseminated mycobacterial disease, lymphoma or thymoma. He was treated for 12 months with Clarithromycin, Ethambutol and Moxifloxacin, and the axillary lymphadenopathy resolved completely, with no recurrence at 6 months after completing treatment.

Method/Results

Functional testing of cell-mediated immunity using a whole blood assay showed an absent response to exogenous IL-12. A serological screen for auto-antibodies to cytokines revealed a high-titre IgG auto-antibody to the p40 subunit of IL12 and IL23. A cross-inhibition experiment showed that the patient's serum was able completely to inhibit IL-12 and IL-23 induced IFN-gamma secretion by healthy control PBMCs.

Discussion

IL-12 dependent Interferon-gamma production is crucial for the defence against mycobacteria.
Anti-IL-12 auto-antibodies and associated mycobacterial susceptibility have previously only been reported in patients with thymoma due to the impairment of T-cell tolerance.

Conclusion

This case is distinctive in that an autoantibody selectively targeting IL-12/23 has not previously been associated with non-tuberculous mycobacterial infection in humans. In a patient who presents with an unusual mycobacterial infection in the absence of an obvious immunodeficiency, testing for autoantibodies to IL-12/23 may be informative.

22 An Unusual Case of Necrotizing Fasciitis due to Haemophilus influenzae Serotype a

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Introduction:
We present an unusual case of necrotising fasciitis caused by Haemophilus influenzae in a 76 year old male, managed at Nottingham University Hospitals Trust.

Case history:
The patient had reported a 2 day prodromal illness of shortness of breath, productive cough and right lower leg swelling.
He was admitted to hospital profoundly septic in multi-organ failure with a clinical diagnosis of necrotizing fasciitis made.
Immediate management consisted of emergency surgical debridement and broad spectrum intravenous antibiotics according to local guidelines. Surgical findings included extensive tissue necrosis and large amounts of pus drained with a pyomyositis also evident.
Unfortunately, despite maximal antibiotic therapy, surgical intervention and intravenous immunoglobulin, the patient died of multi-organ failure secondary to necrotizing fasciitis. Culture results from tissue, pus samples and blood cultures revealed Haemophilus influenzae as the causative organism. Reference laboratory genetic sequencing confirmed it as serotype 'a'.

Discussion:
Haemphilus influenzae is an extremely rare cause of necrotising fasciitis even in adults with known immunocompromise. This patient had medical co-morbidities such as hypertension and diabetes which likely increased the risk of invasive disease. As an entity, necrotising fasciitis carries a very high mortality rate. Historically, the majority of invasive infections were attributed to Haemophilus influenzae serotype b (Hib). However with Hib vaccination in the UK national vaccination programme, infections with this serotype are fortunately rare in the UK. However, other serotypes, such as 'a', can cause invasive disease. More awareness is required of this organism as a cause of monomicrobial necrotizing fasciitis.

29 Acute Macular Neuroretinopathy: A Rare Complication of Primary Dengue Fever Infection

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Introduction: Dengue fever is a common viral infection in tropical and subtropical regions and is frequently encountered in travel medicine clinics in the UK. While dengue fever is known to cause a range of systemic symptoms, it can also lead to ocular complications, including acute macular neuroretinopathy (AMN). Here, we present a case of AMN in a patient with primary dengue fever infection.

Case Report: A 21-year-old male cruise ship worker with recent travel to the Mediterranean and Southeast Asia and recent visit to Antigua presented with high fever, headache, neck stiffness, and retro-orbital pain (day 1). Blood work showed negative serology but positive PCR for dengue fever with a high viral load (threshold cycle 16). The patient had a transient thrombocytopaenia, lymphopaenia and transaminitis. After discharge, he represented with bilateral blurred vision and a left paracentral scotoma. Ophthalmological evaluation confirmed AMN with hyperreflectivity of the retinal outer layers on ocular coherence tomography of the macula. IgM and IgG were positive for dengue fever on day 10.

Conclusion: This case highlights the potential for AMN as a rare but recognized complication of dengue fever, even in patients with primary infection, which may develop early in the course of the disease. Ophthalmological assessment should be consider in acute and post-acute presentations of dengue fever. Compared to serology, PCR testing may be more sensitive in detecting acute dengue fever infections that could contribute to earlier exclusion of higher consequence infections and invasive investigations.

33 Fourth dose bivalent mRNA vaccines containing BA.1 significantly augment neutralising antibody titres against SARS-COV-2 Omicron sub-lineages XBB and BQ.1.1 in healthy adults

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Background

As the COVID-19 pandemic continues globally, new variants-of-concern (VOCs) emerge, including XBB and BQ.1.1. These Omicron sub-lineage viruses, have potential for immune evasion and thus consequences for vulnerable patients and healthcare provision.

Methods

We use high-throughput live-virus microneutralisation assays to study the serological responses against VOCs including XBB and BQ.1.1 before and after 4th dose bivalent (BNT162b2+BA1 or mRNA1273.214) vaccination in 174 healthy adults.

Participants were stratified prior to 4th dose by the presence of anti-nucleocapsid antibodies, indicating prior infection (N+/N-). Further, we compare the response to 4th dose bivalent vaccines with previously N- participants, whose 4th Spike protein exposure was a mild COVID-19 infection.

Results

Ancestral/Delta and Omicron BA.1 - BA.5, median post-dose neutralising antibody titres (nAbTs) were above the assay's quantitative range (2560-fold dilutions of serum inhibited >50% of virus infection in vitro). Both BQ.1.1 and XBB titres were substantially increased after bivalent 4th doses (fold change 2.6 (95%CI 1.9-4.8) p=3.24x10-10 and 3.8 (95%CI 3.1-4.7) p=1.35x10-15 respectively). When stratified for anti-nucleocapsid antibody status, N+ adults had significantly higher titres across all VOCs tested than N- adults post dose; pre-4th dose nAbT that were equivalent to N- adults post-4th dose against BQ.1.1 (p=0.21) and XBB (p=0.22). No significant differences between vaccine manufacturer noted.

Furthermore, 4th exposures in previously N- adults after 3 prior vaccine doses generated differing, but equivalent nAbT to 4th dose bivalent vaccines across all VOCs tested

Conclusions

Increasing exposure to SARS-CoV-2 antigens enhances protection conferred by bivalent vaccination against emerging VOCs in healthy adults.

34 COVID-19 caused by either Omicron sub-variants or Delta in non-hospitalised adults associates with similar illness duration, symptom severity and viral kinetics, irrespective of vaccination history

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Background

SARS-CoV-2 variant Omicron rapidly evolved over 2022, causing three waves of infection with sub-variants BA.1, BA.2 and BA.4/5. UK guidance now advises self-isolation based on the presence of fever or illness severity. We characterised symptoms and viral loads throughout COVID-19 infection episodes with these sub-variants in otherwise healthy, vaccinated, non-hospitalised adults, and compared to infections with Delta variant of concern (VOC).

Methods

In a prospective, observational cohort study, healthy vaccinated UK adults who reported a positive PCR/lateral flow test, self-swabbed on alternate days until day 10. We compared symptoms and viral load trajectories between infections caused by Delta and Omicron sub-variants BA.1, BA.2 and BA.4/5, and tested for relationships between vaccine dose, symptoms and PCR Ct value as a proxy for viral load.

Results

555 infections were reported among 483 participants. Symptom burden and duration were similar across VOCs. Anosmia was reported in 7-13% of participants with Omicron sub-variants, compared to 25/60 (42%) with Delta (P= 1.31e-08 or 1.03e-05 or 5.63e-05; χ2 test Delta vs. Omicron BA.1 or vs. BA.2, or BA.5, respectively). Fever was more common with Omicron BA.5 (55%) than Delta (33%, p 0.03) or BA.1 (25%, p 9.98e-05) . Notably, viral load trajectories and peaks did not differ between VOCs, irrespective of symptom severity (including asymptomatic) or vaccination status.

Conclusions

Symptom profiles recommending self-isolation must remain under review with each new VOC.
Our study emphasises the ongoing transmission risk of Omicron sub-variants in vaccinated adults with mild symptoms that may extend beyond current isolation periods.

37 Characteristics and outcomes of patients with COVID-19 at high risk of disease progression receiving sotrovimab, oral antivirals or no treatment in England: a retrospective cohort study

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Introduction: We report characteristics and acute clinical outcomes for COVID-19 patients treated with sotrovimab, nirmatrelvir/ritonavir or molnupiravir, or untreated patients at highest risk per NHS criteria.
Methods: Retrospective cohort study of non-hospitalised patients who received early treatment for, or were diagnosed with, COVID-19 between 1 December 2021–31 May 2022, using the Discover-NOW dataset in London. Included patients were aged ≥12 years, treated with sotrovimab, nirmatrelvir/ritonavir or molnupiravir, or were untreated but expected to be eligible for early treatment per NHS highest-risk criteria at time of diagnosis. Outcomes were reported for 28 days from COVID-19 diagnosis (index). Subgroup analyses were conducted in patients with advanced renal disease, those aged 18–64 and ≥65 years and by period of Omicron BA.1, BA.2 and BA.5 (post-hoc exploratory analysis) predominance.
Results: In total, 696 patients prescribed sotrovimab, 337 prescribed nirmatrelvir/ritonavir, 470 prescribed molnupiravir and 4044 high-risk untreated patients were included. A high proportion of sotrovimab-treated patients had advanced renal disease (29.3%), ≥3 high-risk comorbidities (47.6%) and were aged ≥65 years (36.9%). In total, 5/696 (0.7%) patients on sotrovimab, <5/337 (0.3–1.2%) patients on nirmatrelvir/ritonavir, 10/470 (2.1%) patients on molnupiravir and 114/4044 (2.8%) untreated patients were hospitalised with COVID-19 as primary diagnosis. Similar results were observed across all subgroups and during Omicron subvariant periods.
Conclusion: Patients receiving sotrovimab showed evidence of multiple comorbidities that may increase risk of severe COVID-19. Low hospitalisation rates were observed for all treated cohorts and across subgroups or periods of predominant variants of concern. Funding: GSK (Study 214907)

46 Penicillin allergy delabelling direct provocation test; challenges and outcomes. Retrospective 4 year review

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Introduction
Penicillin allergy is the most commonly reported drug allergy.1 Over 90% of these are mislabelled1. Penicillin allergy is associated with increased broad-spectrum antibiotic use, increased antibiotic costs, and increased length of admission. Recent meta analysis of de-labelling studies showed Drug provocation test (DPT) is a low risk procedure in patients with multiple clinical and financial benefits2

Methods
Retrospective analysis of all patients who had DPT in hospital across one health trust 2019-2022. Hospital and GP electronic records of drug allergies were reviewed. GPs of patients retained an allergy status post-DPT were contacted

Results
46 DPT were documented during this time. PENFAST score was used to identify those suitable for DPT. 1 delayed reaction was recorded. No anaphylaxis was recorded. Infectious diseases was the primary specialty for DPT (67%). 78% were carried out on medical patients. ID consult service was responsible for 100% of DPTs in surgical specialties. 7 patients who received DPT had been relabelled penicillin allergic post-DPT. 2 self reported, 5 from physician review of historic documentation. 56% of patients had not had GP documentation updated.

Conclusion
This review concludes that DPT is safe in an inpatient population and inpatient review of reported penicillin allergy is an opportunity to identify mislabelled allergy. Non infection specialists should be encouraged to use DPT to delabel allergy. Enhanced communication is needed with GPs. Relabeling of penicillin allergy is a risk and further education must be given to patients and healthcare providers post DPT to ensure continuation of delabelled status.

51 Two Unusual Cases of Infectious Mimics of Metastatic Disease

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Some parasites may present with a widespread infiltration of organs. We present two unusual cases of metastatic mimicry.
In the first case, an immunocompetent female presented with eosinophilia (15), crampy abdominal pain, and vomiting leading to perforation of the sigmoid colon. Imaging showed lesions in the liver and lungs consistent with a suspected carcinoma. Colonic and hepatic biopsies sent for histopathological analysis showed a cross section of an Enterobious Vermicularis worm in the colon lumen, with viable ova in the liver parenchyma. She was treated with an end loop ileostomy and course of mebendazole, and recovered satisfactorily.
In another instance, an immunocompetent asymptomatic man exhibited a liver lesion on imaging. He had undergone a right hemicolectomy three years earlier for colonic adenocarcinoma. A three-year surveillance CT scan identified a solitary hepatic lesion in the right lobe of the liver. CT PET showed no uptake at the liver lesion, but malignancy could not be excluded. Biopsy was ruled out to avoid seeding. After a partial metastatectomy of liver, histopathological testing showed no evidence of malignancy, but a necrotic nodule centred on a worm, identified as E. vermicularis. He made a complete recovery with mebendazole.
Haematogenous spread has been postulated in both cases. They show that E. vermicularis, an organism that is usually thought to be localised to the bowel lumen and relatively innocuous, may in some cases cause disseminated disease and mimic metastatic disease. This is an important and easily treated differential in patients presenting with hepatic and pulmonary lesion

54 Cerebral Mycobacterium Avium Intracellulare

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Mycobacterium Avium Intracellulare (MAI) is a recognised opportunistic infection of severely immunosuppressed patients causing pulmonary infection, lymphadenitis and disseminated disease, but is rarely considered as a cause of CNS infection. We describe a 52-year-old male living with HIV (CD4 T cell count of 3 cells/mL, VL 1.4 million copies/ml) presenting with weight loss, diarrhoea, pancytopoenia and extensive lymphadenopathy. Disseminated MAI was diagnosed on mycobacterial blood, sputum and urine cultures and treatment with ethambutol, azithromycin, rifabutin commenced. Treatment limiting drug toxicity, drug interactions, failure to improve and repeatedly positive blood cultures over seven months necessitated switching regimens to include moxifloxacin, amikacin, tigecycline and bedaquiline. Following eleven months of bedaquiline based therapy, CD4 97, culture negative for 5 months, he defaulted from MAI treatment. He presented two months later with fevers, headaches, fluctuating GCS and blood culture positive for MAI. MRI brain/spine showed widespread miliary enhancement in the brainstem, cerebellum, basal ganglia and spinal cord, dilated optic sheathes and oedema throughout the cord. CSF had raised protein and low glucose but negative mycobacterial culture and PCR. Following treatment with aspirin and steroids and re-establishment on bedaquiline based MAI treatment, he made a full neurological recovery. This case presents rare imaging changes caused by cerebral MAI, raising awareness of the risk of CNS involvement and the importance of considering this as a differential in immunosuppressed patients with neurological impairment. It also demonstrates successful treatment of MAI with bedaquiline and highlights complications with toxicity and drug interactions with MAI/HIV treatments.

55 Evaluating the use of cerebral magnetic resonance imaging (MRI) in the management of patients with infective endocarditis (IE)

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Background
There is no consensus on routine use of cerebral MRI in IE; however European Society of Cardiology guidelines advocate its use if the presence of cerebral lesions will impact management (particularly timing of surgery) or aid diagnosis in uncertain cases.

Methods
Electronic notes of patients referred to the IE multidisciplinary team meetings at a tertiary referral centre in London between December 2019 and February 2022 were reviewed. Patient demographics, microbiology, neurological symptoms, and the use of cerebral MRI were noted, as were any adverse outcomes.

Results
104 patients were diagnosed with IE: 80% male, with a median age of 63 (range 24–88). Of these, 31% (32/104) underwent cerebral MRI, with lesions detected in 75% (24/32). 78% (25/32) of those with lesions had neurological symptoms, most commonly confusion (10/24) and limb weakness (5/24). Of the 7 asymptomatic patients, 86% (6/7) had cerebral lesions reported. The most common findings were infarction (15/24) and haemorrhage (9/24). The most common causative microorganisms were Streptococcus viridans spp (6/24) and methicillin-sensitive Staphylococcus aureus (5/24). Adverse outcomes were present in 67% of cases (16/24), with a 25% mortality at 3 months.

Conclusion
Cerebral MRI was performed at clinician request in our centre in one third of IE cases. Most patients in whom cerebral lesions were identified had neurological symptoms, but we additionally found cerebral lesions in 86% (6/7) who were asymptomatic. Two-thirds of patients with radiographic findings had adverse outcomes. Routine MRI may be a valuable tool in IE for risk stratification and managemen

56 Streptococcus pyogenes associated with Lemierre's syndrome

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Background
A previously fit 58-year-old woman presented with sepsis, following 3 days of severe sore throat, neck and back pain treated with ibuprofen. Generalised myalgia, cervical lymphadenopathy, vomiting and diarrhoea, a C- reactive protein of 417, thrombocytopenia lymphocytopenia, and hypotension despite 7 litres of fluid resuscitation, she was admitted to Intensive Care with likely streptococcal toxic shock syndrome. Blood cultures yielded Streptococcus pyogenes, so empirical antibiotics changed to ceftriaxone, clindamycin and doxycycline.

Methods
We describe her stormy course and difficulties in management, with clinical sequelae, highlighting the necessity for anti-exotoxin therapy and aggressive management.

Results
Clinical and radiological examination confirmed pneumonia and right internal jugular venous thrombosis, the final diagnosis being Streptococcal toxic shock and Lemierre's syndrome. Developing reactive arthritis of multiple joints, she was discharged home after two weeks on doxycycline to compete a 6-week course. Six months later, the thrombus had resolved, and she remained well six months later.

Conclusions
Lemierre's syndrome follows pharyngotonsillitis due to Fusobacter spp, with internal jugular vein thrombosis, sepsis and metastatic foci, especially in the lungs. In the setting of severe oropharyngeal infection, neck pain and swelling, thrombosis of the internal jugular vein must be excluded. Clinicians need to be aware that very rarely Streptococcus pyogenes can be the cause. Symptoms and blood markers resulting from exotoxin production let to the early suspicion of streptococcal infection in this case, resulting in appropriate targeted therapy and a successful outcome.

No conflicts of interest to declare

59 The CandiRes study: Candida resistance evolution in the ICU

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Background:
Antifungal resistance is a growing concern worldwide. Frequent empiric antifungal prescribing to at-risk patient groups likely drives resistance emergence in Candida species.
Methods:
CandiRes (ISRCTN14165977) Jan 2022-Mar 2023 is a prospective multi-site observational study enrolling ICU patients on antibiotics at increased risk of invasive candidiasis, with the aim of examining the relationship between antifungal exposure and resistance emergence Twice-weekly patient mouth and perianal swabs underwent selective culture; MALDI-TOF for Candida species identification and MIC testing (YeastOne Sensititre), alongside any invasive Candida isolates. Population analysis profiling (broth microdilution) was performed on serial stored isolates in patients exposed to azoles/echinocandins for >7 days.
Results:
252 participants have completed the study, 80% colonised with Candida at some point, with the top 3 species prior to antifungal exposure being C.albicans (43%), C.glabrata (29%) and C.parapsilosis (12%). Exposure to echinocandins made little impact on species diversity; azole exposure selected for C.albicans: days 14-21 post-azole initiation, 71% of isolates are C.albicans. MICs increased by ≥2 dilutions in 23% of serial isolates in exposed patients. By population analysis profiling (agar microdilution) of serial Candida isolates we can also demonstrate the emergence of heteroresistant subpopulations in azole-exposed and echinocandin-exposed patients, even when the corresponding MIC does not change. These populations reduce when drug is removed.
Conclusions:
Antifungal exposure affects the epidemiology of colonising Candida flora in the ICU. Early in-vivo resistance evolution goes undetected by conventional antifungal susceptibility testing, which may miss minority subpopulations which emerge on therapy and may cause subsequent invasive episodes or transmission events

67 Bridging the gap: linking early post-vaccine events to reactogenicity and later immune responses after viral-vectored and mRNA-based SARS-CoV-2 vaccines

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Adenoviral vector (AdV) and mRNA vaccines were carefully developed to optimise distinct early immune encounters. However, differential mechanisms driving unique early and late immune responses are unclear. We therefore compared the potential drivers and consequences of early human vaccine responses, focusing on “innate-like” lymphocytes known to influence early reactivity and immunogenicity.

Using longitudinal samples from healthcare workers, we profiled the earliest immune responses after homologous prime-boost with mRNA (BNT162b2, n=36) and AdV (ChAdOx1-nCoV-19, n=20) vaccines using a systems immunology approach (FACS, bulk and sc-RNAseq, ELISA) coupled with in vitro functional assays, focussing on mechanisms of innate-like lymphocyte activation.

AdV and mRNA vaccines have opposite patterns of early immune responses to prime-boost. Both modalities induce significant IFNγ via innate-like lymphocyte activation, but the mode of activation dictates the divergent patterns observed. Unique AdV-prime specific early signals (type I IFN, inflammasome) drive innate-like lymphocyte IFNγ, which correlates with spike-specific adaptive responses generated. However, at boost, innate-like lymphocyte-derived IFNγ is dampened with AdV but augmented after mRNA vaccination. Adaptive spike-specific IFNγ transactivates and is amplified by IFNγ-responsive innate-like lymphocyte networks. Reduced adaptive immunity at boost - observed with extended dosing intervals - corresponds to muted innate-like lymphocyte IFNγ, and may underpin robust differences in immunogenicity and reactogenicity.

The integration of innate and adaptive immunity in response to novel vaccines can be bidirectional, acting through bridging innate-like cells at critical early timepoints. These data link manipulable distinct early responses to vaccine-specific patterns of reactogenicity and immunogenicity, with implications for optimising antiviral responses in patients.

77 Malaria cases at a Northern tertiary hospital over a five-year period and potential impact of implementing an ambulatory care pathway

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Background:
Malaria is one of the most common imported tropical diseases in the UK (1) with well-established national guidelines on diagnosis and management (1). With increased bed pressures over the last 10 years (2) there is a need to consider safe ambulatory care where clinically appropriate. This service evaluation aimed to review current practice within our Trust and conduct a preliminary assessment for the implementation of an ambulatory malaria pathway.

Methods:
All positive malaria tests over a five-year period from September 2016 to September 2021 were identified by searching the laboratory database (Telepath). Domains for data collection included demographics, travel history, malaria species, parasitaemia, severity, and timing to presentation, diagnosis, and management.

Results:
129 care episodes were included in analysis. Average age was 35.6 years with a higher proportion of males (59.7%) to females (40.3%). The most common area for recent travel was West Africa (52.7%). All cases were imported except for one case of congenital malaria. 72.1% cases were Plasmodium falciparum, including three cases of mixed species infection. 90.7% (117/129) were treated as inpatients of which 0.05% (6/117) required ICU or PICU admission. There were no recorded deaths. 84 of the 129 patients had uncomplicated malaria appropriate for oral treatment, 72 of these were treated as inpatients.

Conclusion:
Over this 5-year period, had an ambulatory pathway been in place, applying national guidance, 195.5 overnight stays could have been avoided. Further work up to assess the suitability and practicalities of implementing a safe ambulatory malaria pathway locally is needed.

79 Results from TRUNCATE-TB-time for a change in strategy for TB-treatment shortening?

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Background:
The standard management strategy for drug-sensitive pulmonary TB is to treat with multiple drugs for six months, although the majority of patients can be cured with much shorter treatment. TRUNCATE-TB (NCT03474198) evaluates an alternative strategy of treating patients with DS-TB for 2 months with combinations including new drugs or optimised doses of currently available drugs, chosen for their sterilising efficacy.

Methods:
Participants with rifampicin-susceptible pulmonary TB at 18 Asian/African sites were randomised (adaptive design) to receive the standard regimen for 24 weeks or one of four novel 5-drug regimens for 8-weeks (up to 12 weeks).

Results:
674 participants 18 to 65 years of age were randomly assigned to undergo either standard treatment with a 24-week rifampin-based regimen or a strategy involving initial treatment with an 8-week regimen, extended treatment for persistent clinical disease, monitoring after treatment, and retreatment for relapse. Non-inferiority was assessed in the two strategy groups (initial regimens of high- dose rifampin–linezolid and bedaquiline–linezolid (each with isoniazid, pyrazinamide, and ethambutol). The primary outcome was a composite of death, ongoing treatment, or active disease at week 96.

Conclusions:
The TRUNCATE strategy – initial treatment for 8 weeks (with a bedaquiline/linezolid regimen; extended up to 12 weeks for unsatisfactory clinical response); post-treatment follow-up; prompt retreatment (standard regimen) for relapse – was non-inferior to the standard treatment strategy at 96 weeks.

These results have been presented at the TB Union and CROI, and published (https://www.nejm.org/doi/full/10.1056/NEJMoa2212537). This presentation is to highlight the findings to a UK clinical ID audience.

80 Mycobacterium avium infection in a patient with metal-on-metal hip prosthesis

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Background:
Prosthetic joint infection (PJI) due to Mycobacterium avium is particularly rare and associated with profound immunocompromise. A pseudotumour is an adverse reaction of metal-on-metal resurfacing used in hip joint replacement and is only rarely associated with super-imposed infection. We report the first case of pseudotumour complicated by M. avium in a patient without significant immunocompromise.
Case report:
An 80-year-old man presented with pain and discharge from his right hip. He had undergone a metal-on-metal revision of an on original total hip replacement 22 years previously. Medical history included well-controlled type II diabetes mellitus. MRI demonstrated a pseudotumour.
Hip aspiration was negative on routine culture and auramine staining, but grew acid-alcohol-fast bacteria, identified as M. avium. On repeat aspirate, M.avium was detected by PCR and was cultured.
Extensive immunological screening did not demonstrate any abnormalities. An empirical regimen of amikacin and imipenem for two weeks, followed by imipenem and tigecycline for further two weeks was administered. He was continued on azithromycin, linezolid, clofazimine and ethambutol. Linezolid was dropped on receipt of susceptibility results. After three months first-stage revision surgery with an articulating spacer was undertaken, after which rifampicin was added. He became intolerant of clofazimine which was stopped. A sinus developed and a washout with exchange of modular components and femoral stem was undertaken.
The patient continues on oral anti-mycobacterial antibiotics and is well in himself. Continuation of antibiotics for at least 18 months is planned.
Recommendation:
Non-tuberculous mycobacterial infection should be considered, especially in patients with a pseudotumour.

81 Progressing the Clinical Applications of Novel Star-Shaped Antimicrobial Polypeptides for Recalcitrant Infections.

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Objectives
Wound infection management is complex due to antimicrobial resistance, biofilm production, and vasculopathy, which limits achievable systemic antimicrobial concentrations. Topical novel antimicrobials may improve infection management. We recently reported anti-staphylococcal and anti-pseudomonal activity of star antimicrobial peptide polymers (AMPP)s of poly-l-lysine (PLL), against wound isolates. To reduce cytotoxicity, we modified one candidate, 16-PLL10 with trifluoroacetyl (TFA) or poly(ethylene glycol) (PEG) and compared their antimicrobial activity/cytotoxicity.
Methods:
Susceptibility of ESKAPE reference strains (n=10) and clinical isolates (n=9) to 16-PLL10 and TFA-16-PLL10 was evaluated using bactericidal assays and minimum inhibitory/bactericidal concentrations (MIC/MBC). Potential cytotoxicity (IC50 values) of 16-PLL10, TFA-16-PLL10, PEG-16-PLL10 was investigated in human keratinocytes (HaCaT). Haemolytic activity was assessed.
Results:
Log reductions in colony forming units (CFU) (1h incubation, 0.25□M) ranged from < 1 to >5, at 2.5□M log reductions CFU were >2 for all isolates. MBCs for 16-PLL10 ranged from 5µM (E. faecium, S. aureus) to >40µM (E. cloacae). MBCs for TFA-16-PLL10, were 10µM for most Gram-positive strains. Among Gram-negatives, MBCs ranged from 10µM (P. aeruginosa) to >40µM (E. cloacae, K. pneumoniae). At bactericidal concentrations, HaCaT cytotoxicity was greatest for 16-PLL10, IC50 0.89µM (0.73-1.08) compared to PEG-16-PLL10 and TFA-16-PLL10, IC50, 1.14µM (1.03-1.27) and 1.28µM (1.02-1.58) respectively. At 10□M, TFA-16-PLL10 haemolysed 23.1% of erythrocytes Vs 14.5% and 9.6 % for 16-PLL10 or PEG-16-PLL10 respectively. Mean haemolytic concentration (MHC 5%) was 1.25µM for all PLLs.

Discussion & Conclusion:
16-PLL10 demonstrated broad antimicrobial activity for wound pathogens, including AMR bacteria, which was retained in the TFA-16-PLL10. PEGylation or fluorination moderately improved cytotoxicity but further investigation is required.

Poster presentations

2 The need to review the antimicrobial resistance curriculum for preservice medical education in nigeria: evaluation of a nigerian university's amr curriculum

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Introduction
The rise in Antimicrobial Resistance (AMR) is posing a great challenge to the global public health and one of the identified key drivers of AMR is inappropriate prescription of antimicrobial agents by the prescribers. Therefore, the training of undergraduate medical students on AMR-related topics is considered a critical intervention for containment of AMR in Nigeria and globally.

Methods
The qualitative research design was used in carrying out the review of the AMR curriculum for undergraduate medical education in Ahmadu Bello University, Zaria-Nigeria. The approach used in data collection is the document review. The documents reviewed are the ABU students' handbook for medical undergraduate students, the lecture schedules and the lecture notes.

Results
In ABU, the medical students are being exposed to the AMR-related topics in the fourth year. The topics covered include introduction to microbes, antimicrobial agents, IPC, HAI, Vaccination and Immunisation, Antimicrobial Stewardship, Diagnosis of Infectious Diseases, antimicrobial chemotherapy, Sterilization and Disinfection. The teaching methods are didactic lectures, practical sessions, bed side teaching and seminar presentation while assessment methods involve written, oral, practical and OSCE.

Discussion
In comparison with the tripartite (WHO, FAO,OIE) competency framework for pre-service prescribers, the current AMR curriculum in ABU is deficient in some topics such as topics on principles of rational prescribing and monitoring drug therapy, epidemiology of local antimicrobial, surveillance of antimicrobial resistance linked to diagnostic stewardship and importance of ethics, leadership, communication and governance, self-medication, poor adherence and patients' misconceptions about antimicrobial resistance and the importance of 48-to-72-hour review of all antimicrobial prescriptions.

Conclusion
The gaps in the current AMR-related topics in the ABU medical curriculum were identified and there is a need to strategically integrate the lacking topics, mode of assessment and method of delivery into the existing curriculum so as to improve the knowledge, skill and attitude of preservice medical students.

5 An Audit of HIV Testing in patients with Streptococcal bacteraemia at a Tertiary care teaching hospital

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[1]*Hull University Teaching Hospitals NHS Trust*

Introduction:

Human Immunodeficiency Virus (HIV) infection is associated with a wide range of opportunistic infections. Bacterial pneumonia could be the first manifestation of HIV infection and associated with high morbidity and mortality. It is important to consider a HIV test particularly in those with recurrent bacterial pneumonia or with no other risk factors for a bacterial pneumonia.

Methods:

All the blood cultures positive for Streptococcus pneumoniae over a period of 10 months from August 2021 to June 2022 were identified retrospectively using the local microbiology database.
Using hospital electronic records we identified patients who were tested for HIV and we also used our ID advice notes to find out the percentage of patients advised by ID to test for HIV.

Results:

31 patients were identified over a period of 10 months with Streptococcus pneumoniae bacteraemia. Mean age of the patients was 64. Major co-morbidities noted to be malignancy, COPD/Asthma, Diabetes and Heart Failure.
Out of 31 patients, only 3 patients were noted to be tested for HIV. The advice given while liaising these blood cultures by ID/micro team did not include testing for HIV.

Discussion:

Invasive pneumococcal disease is known to be associated with HIV. Therefore, the opportunity to test for HIV that was unfortunately missed in this cohort. BHIVA guidelines recommend that all general admissions should be offered a HIV test.
Since all the blood cultures are liaised by micro/ID team, this is a very good opportunity to advise testing for HIV and to educate the junior doctors on the wards the need for HIV testing in this cohort and to increase awareness of HIV Clinical indicator conditions.

6 Audit of Staphylococcus aureus bacteraemia management at a tertiary care teaching hospital

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Introduction:
Staphylococcus aureus bacteraemia (SAB) is associated with significant morbidity and mortality . The ABS Study group proposed SAB management indicators to investigate quality of care. We compared our current clinical practice for SAB management against the proposed ABS quality indicators.

Methods:
We performed a retrospective audit of 50 adult patients with 51 presentations of SAB at Hull University Teaching hospitals NHS Trust over a 5-month period (May 2022 to September 2022)

The data collected included demographics, timely repetition of blood cultures until negative, methicillin sensitivity, review by the ID team, source of bacteraemia, 30 days mortality and if re-admitted within 2 weeks from the time of discharge.

Patients with positive blood culture with S. aureus were included and patients with multiple episodes were included if there was a gap of 2 weeks or more between episodes.

Results:
An Echocardiogram is recommended within 10 days of positive blood culture in all SABs as metastatic infection develops in approximately one-third of the patients . In our study 35 (70%) patients had an Echocardiogram within 10 days while 9 (18%) patients did not.

The ABS group and BSAC recommends a minimum of 14 days of antibiotic for uncomplicated SAB . In our study 9 patients (18%) received <14 days of antibiotics, 23 patients (46%) completed 14 days, and 18 patients (36%) completed more than 14 days due to deep-seated source of bacteraemia.

Intravenous catheter related SAB is a major cause of healthcare associated infection. In our study 25% of SAB episodes were intravascular catheter related. In 7 (54%) cases the intravascular catheter was removed within 5 days.

Our audit has shown that mortality within 30 days was 9 people, 18% of the population sample.

Whilst 11 people (28%) of patients were readmitted with only 2 (5%) being MSSA readmissions within 14 days.

Conclusion:
Our study showed that the adherence to guideline for management of SAB improved over the time with bedside ID review and highlights the practical value of the quality indicators proposed by the ABS group as an audit tool

7 Gene expression analysis of diseased and control liver tissue to explore pathogenic pathways in inflammation

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Background:

Liver diseases such as Non-alcoholic fatty liver disease (NAFLD) and Non-Alcoholic Steatohepatitis (NASH) are extremely prevalent worldwide and carry a poor prognosis. Gaining insight into the transcriptional profiles of these conditions is therefore crucial for understanding their pathogenesis. We therefore aimed to compare hepatocyte transcriptomic data in control and diseased states using differential expression analysis. We hypothesised that different drivers of inflammation are present in distinct liver diseases, and that gender impacts expression.

Methods:

We made use of data from two large studies which had retrieved liver biopsies. The first study looked at 195 Hepatitis C (HCV) infected individuals, while the second took samples from obese (12), control, (14), NAFLD (15) and NASH-affected (16) individuals. We analysed the second study independently, comparing gene expressions for all states against the controls and then merged the datasets to compare HCV-infected gene expression to control. The impact of gender on gene expression was also compared. Multiple R software packages and Gene-set enrichment analysis (GSEA) were used to analyse the data.

Results and Discussion:

All studied liver diseases (NAFLD, NASH, HCV-infection) resulted in upregulation of inflammatory markers compared to control, with the biggest difference noted in HCV-infection. Meanwhile, obesity did not alter gene expression significantly. GSEA confirmed these findings, further revealing that complement dysregulation is present in all these conditions. We also demonstrated that gender drives differences in gene expression in HCV infection, but not necessarily in the other conditions. Further research is ongoing to delineate the specific pathogenic drivers of each of these conditions.

Conclusion:

Differential expression analysis of diseased and control liver tissue reveals a host of inflammatory markers that are upregulated. Gaining a better understanding of these inflammatory drivers could help in the development of therapeutic targets, for example in the form of complement or IL-2 blockade, which could potentially assist in the halting of hepatocyte inflammation.

10 A case of imported Zika virus infection

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[1]*Nhs Lothian*

Introduction
Here we present a case of Zika infection from a novel location.

Case Description
A female patient presents with 3-day history of fever, joint pain and rash. Symptoms began on day of return travel from Gujarat, India. She had generalised myalgia, arthralgia, widespread maculopapular rash and swollen upper limb joints. On examination there was tender cervical lymphadenopathy, fading maculopapular rash and limited range of movement in the small joints of both hands but no joint swelling or tenderness. The rest of the examination was normal.
Initial blood results were unremarkable aside from reactive lymphocytes on blood film. Malaria investigations, blood cultures and HIV antibodies were negative. Blood samples sent to the Rare and Imported Pathogen Laboratory were positive for Zika virus IgM, IgG and RNA.
The patient fully recovered within 3 weeks. She was advised that she could continue breastfeeding but barrier contraception recommended.

Discussion
Aedes mosquitos are widely distributed geographically, however 61 countries have not yet documented authochthonous Zika vector-borne transmission despite vector presence. At the time of this case there had not been any reported cases of Zika virus in Gujarat. It is likely that there is undetected transmission due to predominantly asymptomatic nature of Zika infection. The non-specific presentation of arboviral illnesses highlights the need for geographical testing panels to determine aetiology. Flavivirus serology can be difficult to interpret due to significant IgG cross-reaction. Detecting RNA provides a definitive diagnosis, as in this case. RNA persists for longer in urine than blood, which aids diagnosis.

12 The Oxford - AstraZeneca COVID-19 vaccine: breakthrough science and collaborative partnership

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Background: In response to the threat posed by the COVID-19 pandemic, AstraZeneca and the University of Oxford formed a unique partnership to drive the clinical development, licensure, manufacturing and global deployment of the AZD1222 (ChAdOx1 nCoV-19) vaccine at unprecedented scale and pace.

Method: This collaboration enabled clinicians and scientists from Oxford to trial the vaccine across 3 continents (Africa, Latin America and Europe), and AstraZeneca to expand the trial portfolio to include North America, Russia and Japan.

Results: AZD1222 is highly effective in preventing COVID-19, with no hospitalisations or severe cases of the disease reported in trial participants receiving the vaccine. The benefit/risk assessment confirmed AZD1222 is well-tolerated and effective, leading to MHRA Emergency Use Authorization in December 2020, just 7 months after the first dose in a clinical trial on 23rd April 2020. The AstraZeneca manufacturing team and partners produced 3.5 billion doses and gained approval for use in >180 countries. The focus on low-cost production and global distribution resulted in lives being saved and a major contribution to vaccine provision for low-and-middle-income countries. In 2022, the World Health Organisation revised its Good Practice Statement on use of COVID-19 boosters to include the use of viral-vectored vaccines, including AZD1222, as first or second boosters as part of any COVID-19 heterologous vaccination schedule.

Conclusion: Interdisciplinary collaboration was a powerful tool in this pandemic response. The model remains critically important for future public health challenges. This transformational arrangement provides a precedent for future academic-industry partnerships, and is a showcase of the strength of life sciences in the UK.

13 Incongruent Serology in Neuroborreliosis

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Lyme disease (Lyme borreliosis) is the most prevalent vector borne illness in the Northern Hemisphere, and incidence is increasing. It is a multisystem disease that can affect the skin, joints, heart and nervous system. Neurological symptoms include headache, lymphocytic meningitis, and cranial neuritis (most commonly resulting in uni- or bilateral facial nerve palsy) in the early stages of the disease. Without treatment, late neurological complications include chronic meningitis, axonal polyneuropathy, encephomyelitis and cerebral vasculitis.

Diagnosis is made with a plausible exposure history, clinical signs and supportive serology. In the US and the UK, peripheral blood serological testing is based on two tiered testing. CSF can be tested for intrathecal antibody production, but results are traditionally interpreted cautiously, and only when paired with serum, to allow for antibody diffusion from blood into CSF.

We present a case of a British man in his 70s with previously treated Lyme borreliosis, who re-presented 5 years later with evolving neurological symptoms. PCR testing for Borrelia was negative, and peripheral serology showed that antibody positivity had fallen since the previous infection. However, CSF serology had a strongly positive IgG immunoblot. This unexpected incongruence between peripheral and central serology has not been widely reported previously.

14 Parvovirus B19 induced severe aplastic anaemia in a patient with well-controlled HIV-1 and no underlying haematological disorder

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Introduction:
Parvovirus B19 (PB19) infection in specific risk groups may result in a spectrum of aplastic anaemias ranging from acute transient aplastic crisis (TAC) to more chronic pure red cell aplasia (PRCA). Classically these have been described in patients with chronic haemolytic syndromes and established immunocompromised states respectively. We present an unusual case of a PB19-induced acute severe anaemia and resulting multi-organ dysfunction in an individual without these risk factors .

Case:
A 25 year old Brazilian tourist was found collapsed following a 5-day history of general malaise. He had a background of HIV-1 infection with excellent adherence to anti-retroviral therapy (ART). On admission he was profoundly anaemic (haemoglobin 18 g/L) and had multi-organ dysfunction requiring intensive care admission. Investigations confirmed acute parvovirus B19 infection with a viraemia of greater than 18 billion copies/ml in blood. He was treated with blood products and 1g/Kg intravenous immunoglobulin (IVIG) to good effect, and has suffered no relapse of anaemia at 6 months post-discharge.

Discussion:
Significant PB19 infection in the era of ART has only been reported in patients with HIV and poor compliance to therapy; a TAC presentation without an underlying chronic haemolytic syndrome is an usual presentation. We consider whether previously under-appreciated aspects of PB19 including extent of viraemia in infection and viral serotype may contribute to this atypical presentation. Furthermore our case serves as a reminder that PB19 remains a differential for aplastic anaemia even in patients that don't fall into the classic risk groups.

15 A man with a painful mouth ulcer

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A 42-year-old man presented with dysphagia, dyspepsia, 10kg weight loss and a 4-day history of a painful mouth ulcer. He was born in Ghana and lived in UK since 2003. Clinical examination revealed cachexia, oral candida, an irregularly-shaped left buccal ulcer with a white base and cervical lymphadenopathy.

HIV antibody-antigen test was reactive (wild-type on resistance testing); CD4 count 12x106/l, HIV viral load 3 million copies/ml. Serum cryptococcal antigen negative.
Treatment commenced: co-trimoxazole for PCP prophylaxis, tenofovir alafenamide/emtricitabine and dolutegravir for HIV treatment and fluconazole for oral candida.

Computed tomography showed cervical lymphadenopathy, left lower lobe 2cm nodule and bilateral adrenal enlargement.

Buccal ulcer histology and lymph node cytology showed mixed inflammatory infiltrate including histiocytes and foamy cells with abundant intra- and extra-cellularly refractile fungal spores of 2-6 microns. Grocott stain was positive with narrow-based single budding.

Contrast MRI brain showed 2 small peripherally-enhancing lesions. Cerebrospinal fluid (CSF) results: white cells 8cells/cmm, red cells <1cells/cmm, protein 0.91, glucose 3.4 (serum glucose 6.2), no bacterial growth on culture.

Serum galactomannan and beta-D-glucan antigen was positive. Urine, serum and CSF Histoplasma antigen was positive (Miravista Lab-USA™).

The patient was treated with intravenous liposomal amphotericin B for 6 weeks followed by oral fluconazole for CNS penetration. The buccal lesion resolved and patient clinically improved.

Histoplasmosis is a frequent opportunistic infection in advanced HIV in the Americas, but is under-recognised and under-diagnosed in other endemic regions. Histoplasmosis has a long latency so should be considered in the differential for oral ulceration in advanced HIV.

16 A particularly prolonged case of chronic meningococcaemia

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Chronic meningococcaemia is a rare manifestation of invasive disease due to Neisseria meningitidis, defined by symptoms lasting over a week and the absence of meningitis. This case of a 45-year-old male is particularly interesting considering his prolonged 8-week history of illness with a 4-week history of purpuric and necrotic lesions on his limbs (documented with serial photographs). His rash had begun on his extremities and extended proximally.

He reported flu-like symptoms, fatigue and relapsing fever over the two months prior to presentation. He complained of arthralgia in both wrists and ankles, which migrated between joints as well as swelling around his ankles and profuse diarrhoea. He had no history of foreign travel, an unremarkable sexual history and believed he had received all routine childhood vaccinations.

He presented to hospital 4 weeks after the rash commenced and was admitted for further investigations. He was intermittently febrile but other observations were within normal ranges. There were no features of meningism and no other focal symptoms to explain the source of his pyrexia. His blood tests were markedly deranged with Neutrophils of 33.01 $x10^9$/L, C-reactive protein of 273mg/L as well as thrombocytopaenia (platelets 53 $x10^9$/L), hypoalbuminaemia (21g/L) and hyponatraemia (124mml/L). Blood cultures grew gram negative diplococci which were identified as Neisseria meningitis (serotype B) and he was commenced on Ceftriaxone 2g once daily. Immunological investigations including HIV testing and functional complement studies were unremarkable. He had an excellent and rapid clinical response to Ceftriaxone and was discharged after a one-week course.

17 A Fishy Cause of Prosthetic Valve Endocarditis

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A 68-year-old man with a transcatheter aortic valve implantation (TAVI) for severe aortic stenosis was seen in haematology outpatients with a 6-month history of weight loss, anorexia, malaise and unexplained anaemia. Physical examination was unremarkable. He had a raised white cell count (12.35x10^9/L) and C-reactive protein (159mg/L). Blood cultures isolated Gram positive cocci ?streptococcus prompting admission to the infectious diseases ward for further management.

Subsequently four sets of blood cultures grew Lactococcus garvieae (penicillin MIC 1mg/l). IV amoxicillin 2g 4-hourly was started. Bedside transthoracic echocardiogram showed elevated velocities across the TAVI. Transoesophageal echocardiogram (TOE) demonstrated vegetations adherent to the TAVI. An MRI brain performed because of transient vertigo showed a small infarct and foci of microhaemorrhage felt likely related to septic emboli. After 12 days he was switched to intravenous ceftriaxone 2g daily because of drug induced liver injury on amoxicillin. He successfully completed 6 weeks of treatment as an outpatient.

Two days after completing antibiotics he re-presented with right-sided weakness and slurred speech. CT brain showed left-sided subacute middle cerebral artery infarct likely due to late embolization of vegetation. Splenic emboli were also seen on CT. There was no evidence of ongoing infection (no systemic features, no bacteraemia and no residual vegetation on TOE).

Lactococcus garvieae is an uncommon cause of infective endocarditis with limited evidence for optimal antibiotic management. Prosthetic valves are most commonly affected and human infections have been associated with ingestion of raw seafood, exposure to fish, presence of colonic polyps and exposure to dairy products.

18 Management of Pyelonephritis in Ambulatory Care

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Introduction:
Pyelonephritis is treated at the Northumbria Hospital in the ambulatory setting and ertapenem is now first-line. This study audited the use of ertapenem in this setting and assessed techniques to optimise the pathway with a focus on switching to oral antibiotics promptly to reduce antimicrobial resistance for this protected antibiotic.

Method:
Data was collected from discharge letters, e-results, and the e-prescribing system. Patients included were managed in Ambulatory Care with the pyelonephritis pathway. There were three cycles, with interventions including one-to-one discussions with team, prompts on the paper proformas, and a presentation to the unit consultants.

Results:
Eighteen patients met inclusion criteria, age range 43-54, and 88.9% female. Each patient had between 2 and 3 appointments and received between 1 and 3 doses of ertapenem. The first cycle found 50% received the appropriate number of doses of IV antibiotics before switching to oral therapy, improving to 67% by the third cycle. Urine cultures collection rose to 100% over the period. By the end an appropriate choice of oral antibiotic was given in 83% of cases.

Conclusion:
In the last two cycles the team maintained 100% adherence to urine culture collection. Growth on culture increased 58% over the three cycles showing the importance of increased cultures, allowing appropriate oral switches. The number of appropriate doses given improved 17% throughout. In summary prompts to remind staff to take cultures and consider oral switches prevents overuse of IV antibiotics and allows for safe ambulatory care for pyelonephritis while maintaining antimicrobial stewardship.

19 A rare case of slowly progressive fatal pneumonia following oral dexamethasone therapy

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Background
Corticosteroids are routinely used in management of cerebral oedema in patients with intracranial lesions. We report a case of slowly progressive pneumonia following three-weeks of oral dexamethasone treatment.

Case report
An 86-year-old Caucasian male presented to emergency following a collapse. He had history of cancer including prostate, urinary bladder and most recently, lung cancer which was managed by lobectomy. CT scan showed a lytic lesion on the skull involving brain. He improved quickly with conservative management and was sent home with oral dexamethasone to treat likely cerebral oedema awaiting MRI.

He re-presented to A&E six weeks later with a three-week history of insomnia, loss of appetite, oral thrush and cough with productive sputum. After reviewing his previous MRI from a different hospital record, his skull lesion was diagnosed as a congenital defect and a decision to wean off dexamethasone was taken. He was treated with co-amoxiclav intravenously for community acquired pneumonia for a week without significant clinical response. Antibiotics were changed to piperacillin-tazobactam and fluconazole for further five days until the blood culture grew a branching gram-positive filamentous bacillus, subsequently identified as Nocardia farcinica. Unfortunately, the patient died within six hours of positive blood culture before appropriate treatment for nocardiosis could be initiated.

Conclusion
Pulmonary nocardiosis is a life-threatening opportunistic infection seen in immunocompromised individuals. Nocardiosis should be considered in cases with slowly progressive pneumonia which remain clinically unresponsive to standard antibiotics. Microbiology team should be involved early for diagnostic and therapeutic intervention of unresolving pneumonia in immunocompromised patients.

20 Impact of COVID-19 Infection Prevention and Control (IPC) restrictions on cardiac arrest (CA) survival rates in pre-hospital practice: a scoping review

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BACKGROUND:
IPC practices are essential in reducing patient care exposure risks. COVID-19 provided unique challenges with no consensus on PPE best-practice.
Prompt response with effective clinical interventions is key in ensuring positive CA outcomes. Existing response delays alongside additional pandemic IPC practices may cause increased patient care delays, and difficulty in performing interventions, which may impact survival likelihood.

OBJECTIVE:
This study aimed to ascertain whether there is a relationship between increased COVID-19 IPC practices and reduced CA survival rates in pre-hospital practice.

METHODS:
A scoping review of peer-reviewed research was undertaken from bibliographic databases using key words.

RESULTS:
Studies note significantly reduced survival rates where time to initiation of CPR was greater than two minutes (14.7%:17.1%; $p<0.002$) with a UK analysis noting that donning COVID-19 PPE takes an additional 66.2 seconds (median) in addition to response time.
This is supported by a study which discovered a relationship between the COVID-19 pandemic and significantly decreased return of spontaneous circulation ($p<0.0001$) and survival to hospital admission ($p=0.0122$) and hospital discharge ($p=0.0004$) rates in Out of Hospital CA compared to pre-pandemic controls.
Endotracheal intubation was also affected with increased intubation times (51.28 ± 3.89s:33.03 ± 2.65s; $p<0.001$) and lower success rates (74.4%:93%; $p <0.001$) associated with increased PPE.

CONCLUSION:
It is reasonable to conclude that delays and impact due to COVID-19 IPC practices contribute to reduced CA survival. Further research is required to determine appropriate PPE levels with the aim of facilitating survival without compromising practitioner safety in preparation for future emerging pathogens.

23 Aminoglycoside genetic testing to prevent ototoxicity – considerations for future practice

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Background

In 2021, the Medicines and Healthcare products Regulatory Agency (MHRA) recommended genetic testing for a mitochondrial variant mt.1555A>G, predisposing individuals to ototoxicity to those who require recurrent or long-term aminoglycosides therapy. This test is now commissioned on the NHS.
Ensuring that appropriate genetic testing is performed to prevent ototoxicity for at-risk patients may be a challenge for healthcare organisations for many reasons.

Objective

To list considerations for stakeholders to contemplate the implementation process of this test.

Methods

The usage of aminoglycosides per specialty was investigated in Define© (NHS Hospitals drug-usage software). A multidisciplinary brainstorming meeting was held to discuss patients' prioritisation and other considerations before implementing the test.

Results

The following specialties were identified as a priority for test implementation: neonatal, paediatrics, respiratory, nephrology, urology, elective surgical, orthopaedics, cardiac, haem/oncology. Key considerations include training and interoperability barriers, a summary of considerations agreed and discussed are listed in Table 1.

Discussion

As the commissioned test is not a point-of-care test (POC), turnaround times imply that only patients who are expected to be on aminoglycosides in the future are the main beneficiaries of this test. Whilst a POC test for mt.1555A>G is making its entry on the market, it is important that healthcare organisations begin a dialogue with affected specialties, pathology providers, audiology department, and patients themselves to ensure successful implementation of this novel commissioned genetic test.

24 Antibiotics Prescribing Practices In Caesarean Section (C-Section): Admission To Discharge In Kawempe National Referral Hospital Uganda, Uganda

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Background: High maternal mortality and morbidity in Uganda, infection is one of the leading Cause1. Antibiotics resistance burden due to inappropriate use of antibiotics in obstetrics2.
Aim: Review of antibiotics prescribing practices through antepartum, intrapartum and postpartum stages in patients admitted for elective or emergency C-section in Kawempe Hospital, Uganda
Method: Retrospective quantitative data was extracted from the notes of 121 patients from 1st-31st May 2022

Results: Of the 121 patient notes reviewed, 59.6% antibiotics use in intrapartum was inappropriate. 61% patients were prescribed prophylaxis antibiotics for C-section procedure as per WHO recommendation. However, majority of the patients were inappropriately prescribed antibiotics postpartum. The high rate of antibiotics prescribed as well as significant lack of information documented showed the need to prioritise antimicrobial stewardship programme, focusing on utilising medication and therapeutic committee and create and implement local guidelines and improve information recording practice.

25 Exploring the views of infectious diseases and microbiology consultants in England on a novel delinked funding model for antimicrobials: the SMASH study

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Objectives

A novel "subscription-type" funding model was launched in England in July 2022 for ceftazidime-avibactam and cefiderocol. We aimed to collect the views of English infectious diseases and microbiology consultants on important aspects of the delinked funding model.

Methods

This was a national online survey of all consultants working in acute hospitals of the National Health Service.

Results

The final response rate was 31.2% (235/753). Most consultants agreed the model is a welcome development (69.8%, 164/235), will improve treatment of drug-resistant infections (68.5%, 161/235) and stimulate research and development of new antimicrobials (57.9%, 136/235). Consultants disagreed that the model will lead to reduced carbapenem use and reported increased cefiderocol use post implementation. Pre-authorisation by infection specialists to access the model antibiotics was universally agreed. Under the new model, 42.1% (99/235) of consultants would use the new antibiotics empirically, if risk factors for antimicrobial resistance were present (previous infection, colonisation, treatment failure

with carbapenems, ward outbreak, recent admission to a high prevalence setting). All consultants felt that infections by carbapenem-resistant bacteria will increase in the future.

Significantly higher insurance and diversity values were given to model antimicrobials compared to established treatments for carbapenem-resistant infections, while meropenem recorded the highest enablement value. Use of both drugs for infection sites outside of their licenced indications was reported. Ceftazidime-avibactam was prioritized for OXA-48 and KPC infections, while cefiderocol for metallo-beta-lactamase infections, infections from Stenotrophomonas maltophilia, Acinetobacter spp, Burkholderia cepacia.

Conclusions.

A “subscription-type” model was viewed favourably by infectious diseases and microbiology consultants in England.

26 Fulminant Primary EBV Infection - Manifestations and Complications in a Host requiring ECMO

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A patient initially presenting with complications of a pilonidal cyst drainage rapidly deteriorates with widespread lymphadenopathy, rash, and acute respiratory distress syndrome (ARDS). They quickly require escalation to a critical care environment for intubation and ventilation and eventually transfer to an extracorporeal membrane oxygenation (ECMO) centre. A diagnosis of primary fulminant Epstein-Barr virus (EBV) infection is made, complicated by disseminated intravascular coagulation (DIC) with haemothorax, progressive spleen and liver necrosis, skin necrotic changes, a pulmonary embolism (PE), pre-renal failure and an Enterococcus faecium bacteraemia.

Unfortunately, the patient develops further significant complications associated with EBV, including haemophagocytic lymphohistiocytosis (HLH) and a possible X-linked lymphoproliferative disease. They are discussed at the national HLH MDT. The extensive complications and superadded infections in this case highlight the complexities of infection in the critically unwell patient and the value of MDT discussion between infectious diseases, virology, haematology, surgical teams and the critical care team.

27 An innovative approach of In-service Education- ''Nip the PDRO* in the bud''(*PDRO-Pan Drug Resistant Organism)

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INTRODUCTION:
Pan Drug Resistant (PDR) is defined as non-susceptibility to all agents in all antimicrobial categories. PDR Gram negative bacteria are associated with high morbidity and mortality.
AIM:
Prevent the cross-transmission of the Pan Drug Resistant Organism (PDRO) through In-service Education (10 minutes' educational sessions) of all Healthcare Staff.
METHODS:
In January 2023 a PDR Enterobacter cloacae was isolated from the screening sample and pus swab of a patient who has had a recent gastric sleeve surgery in Turkey. Immediately strict Infection Prevention & Control measures were implemented to prevent cross-transmission.
Additionally, an innovative approach was used which consisted of the In-service Education of healthcare personnel (24/7) on the concepts of healthcare and patient zones, proper hand hygiene technique and correct technique of personal protective equipment donning & doffing. Dedicated equipment was ensured. A strict Antimicrobial Stewardship Program was also implemented with the help of the Surgeons. Thus, the spread of a PDRO was prevented in-spite of the fact that the patient was visited by several clinical teams and had a prolonged hospital stay.
RESULTS:
In-service education given to nearly 100% of ward Doctors, Nurses, Physiotherapists and House-keeping staff.
Strict layout of Antimicrobial Stewardship Program – antimicrobial dose, route, duration and indication reviewed twice weekly by the Consultant Microbiologist.
CONCLUSIONS:
This innovative approach of In-service Education for all the Staff of the particular area and effective implementation of the Antimicrobial Stewardship Program can prevent the cross-transmission of PDRO and thus nip in the bud an outbreak.

28 Seroprevalence and prevention of strongyloidiasis at a UK transplantation centre

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Background

Strongyloidiasis is a neglected tropical disease caused by Strongyloides stercoralis which is endemic across tropical and sub-tropical regions. Infection can persist for years, and immunocompromised patients are at increased risk of Strongyloides hyperinfection syndrome (SHS), a life-threatening form of the disease. The seroprevalence and optimal strategy for managing S. stercoralis in UK transplant candidates are unknown.

Methods

A cross-sectional observational study was conducted at Imperial College London Healthcare Trust to determine S. stercoralis seroprevalence and feasibility of providing assessment with pre-emptive anthelmintic treatment. All renal transplant candidates (October 2021) and haematopoietic stem cell transplant (HSCT) candidates (June 2018 - July 2020) were tested for antibodies to S. stercoralis using the NovaLisa® ELISA assay. The demographics, epidemiological risk and clinical features of positive cases were described.

Results

Eight out of 133 (6.0%) renal transplant candidates and 0/146 (0.0%) HSCT candidates were seropositive (overall seropositivity = 8/279, 2.9%). 7/8 (87.5%) were either born or had extensive lifetime travel in tropical or sub-tropical countries, 2/8 (25%) had symptoms potentially attributable to chronic strongyloidiasis, and 3/8 (37.5%) had eosinophilia. Seven out of 8 received pre-emptive anthelmintic treatment.

Conclusion

Our study found a significant number of transplant candidates at our centre to be S. stercoralis seropositive and resulted in pre-emptive anthelmintic treatment of
individuals who could have been at risk of SHS. Other UK transplant centres should consider assessment for patients with identifiable epidemiological risks. Larger multicentre studies assessing the management of this pathogen in endemic and non-endemic transplant centres would be beneficial.

30 Overview of Antimicrobial Prescribing Guidance across NHS Trusts in the United Kingdom: Analysis of the Induction(TM) MicroGuide platform

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Background: Effective antimicrobial prescription and stewardship for acute severe infections requires prescribers to use empirical guidance. Many United Kingdom (UK) NHS trusts provide such guidance via the InductionTM MicroGuide platform, using which the availability of antimicrobial stewardship (AMS) and infection principles was explored.

Methods: Acute NHS trusts in the UK (nine commissioning regions) with antimicrobial use guidelines uploaded on MicroGuide were analyzed for inclusion of key sections (sepsis management, AMS, IVOS [IV to oral switch], antifungal guidance, OPAT [outpatient parenteral antimicrobial therapy], and critical care), and time since last update. Guidelines were accessed over 12 days (21st Oct–02nd Nov, 2022). Data were not missing for any trust.

Results: NHS trusts using MicroGuide were non-uniformly distributed across the UK. Four trusts included two hospitals; 111 included one hospital (N=119). Overall, eleven trust hospitals (9.2%) included all key guideline sections; most guidelines included sepsis management (n=117; 98.3%) and AMS (n=112; 94.1%) sections. IVOS sections (n=99; 83.2%) and antifungal guidance (n=83; 69.7%) were also common. OPAT guidance was less common (n=56; 47.1%) and critical care sections were mostly absent (n=27; 22.7%). Four trust hospitals (3%) hadn't updated their guidelines in >1 year; about half (n=62; 52%) updated their guidelines ≤2 months prior to analyses.

Conclusions: NHS trusts are standardizing digital innovations to host antibiotic prescribing guidelines. Achieving consistency in empirical prescribing guidance across trusts may augment AMS efforts and patient outcomes. Guideline sections identified as key to AMS and patient safety are readily available in most NHS Trusts using MicroGuide.

32 Molnupiravir prescribing in the Virtual Hospital (CMDU Pathway)

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Molnupiravir is commissioned by NHS England (NHSE) for the treatment of COVID-19 in non-hospitalised patients at risk of progression to severe disease. Other options are nirmatrelvir/ritonavir , sotrovimab and remdesivir. As of November 2022,NHSE's commissioning policy stated that molnupiravir should only be used if the other 3 options were not suitable treatment options for the patient. This retrospective audit looked at 31 patients prescribed molnupiravir by the virtual hospital team and assessed their appropriateness.
Method: The look back period was between January 1st and September 30th, 2022. Patients were selected at random using random.org. Data collected included confirmation of SARS-CoV-2 infection, nirmatrelvir/ritonavir drug interactions, consideration of sotrovimab and lab results within one year (ALT, ALP, bilirubin, eGFR/CrCl). The data was then analysed and graphs were generated to draw results. All standards were set at 100%.
Results: The results after data collation revealed that 100% patients prescribed molnupiravir had a confirmed SARs-CoV-2 infection. Only 29% patients were eligible for treatment with molnupiravir due to stage 3-5 chronic kidney disease (CKD). 29% patients were eligible for treatment with molnupiravir due to significant drug-drug interactions. Only 22.58% patients had a documented reason as to why they were ineligible for treatment with sotrovimab.
Conclusion: Most patients were inappropriately prescribed molnupiravir and poor documentation meant we could not ascertain why sotrovimab was not considered. Drug-drug interactions were a major reason for prescribing molnupiravir instead of nirmatrelvir boosted with ritonavir, however most of the interactions were not significant and could have been worked around.

35 When the host is late to the party

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Background
Amoebic liver abscess is the most common extraintestinal manifestation of amoebiasis, caused by Entamoeba histolytica.1 Symptomatic cases have been described presenting several years after initial acquisition of infection.2

Case Report
We report a case of a 63-year-old-man presenting with 10 days of lethargy, fevers, a non-productive cough, and diarrhoea. His last episode of foreign travel was 1 year before to Free Town, Sierra Leone. On admission, he had a pyrexia of 39.4°C, and right upper quadrant tenderness. Computed tomography (CT) of the abdomen revealed a right lobe liver lesion, suggestive of an abscess. Ultrasound guided drainage was performed. On review, the fluid contents had an 'anchovy paste' appearance (Figure 1), and subsequent PCR testing was performed on the stool and fluid, both positive for E. histolytica. Amoebic serology results were strongly positive (ELISA OD 6.744). The patient was treated with 3 weeks of metronidazole in addition to oral paromomycin. A repeat ultrasound liver after 4.5 months showed complete resolution. Screening for asymptomatic infection was performed for all household contacts which were negative and there were no identified risk factors for possible UK-acquired infection.

Conclusion
This case represents likely manifestation of disease one year following travel to an endemic area. Given 4-10% of cases with asymptomatic disease go on to develop invasive disease in a one-year period,3 this case reiterates the importance of taking an extended travel history in patients presenting with infective gastrointestinal symptoms.

Appendix:
Figure 1: Liver abscess fluid showing thick, anchovy paste-like appearance.

36 Investigating the utility of hyaluronidase treatment in prosthetic joint fluid analysis, to improve the diagnostic workflow

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1. INTRODUCTION

According to UK SMI, diagnosis of prosthetic joint infection should include total/differential synovial fluid cell count. Viscous samples can impede the ability to perform cell count. On review of EBJIS guidelines (2021), hyaluronidase is suggested as a pre-treatment method to reduce viscosity of synovial fluid and increase the accuracy of optical microscopy.

2. AIMS

The aim of this research was to develop a protocol utilising hyaluronidase, with 2 main objectives:

1. Establish the efficacy of hyaluronidase in reducing viscosity and facilitating a cell count
2. Establish the optimal conditions for sample treatment, including enzyme quantity, and incubation time

3. METHODS AND RESULTS

Samples were analysed before and after treatment with hyaluronidase, using increasing enzyme quantities to establish the optimal reaction conditions. Data were collected to determine the effect of treatment on macroscopic appearance, number of samples on which cell count could be performed, and the quantitative cell count. Optimal reduction in viscosity was achieved by the addition of 10µg hyaluronidase per 50µl of sample, incubated for 5 minutes. Under these conditions, in viscous samples, the percentage on which cell counts could be performed increased from 28% to 100%.

4. CONCLUSIONS

We have shown that the addition of hyaluronidase can improve the microscopic analysis of prosthetic joint fluid, by facilitating a cell count. Further work is required to improve the processing of blood-stained samples, for example, by addition of acetic acid. The final step is to streamline this into the diagnostic pathway.

38 Candidaemia originating from the urinary tract: A retrospective epidemiological analysis

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Background

Candida blood-stream infection secondary to urological source (U-CBSI) is a growing clinical problem, with treatment complicated by antimicrobial resistance. However, its epidemiology and prognosis has not been adequately studied. We aimed to describe the clinical features, microbiology, and outcomes for U-CBSI patients in a large tertiary centre.

Methods

We investigated all Blood culture Candida isolates in NHS Lothian between March 2016 and March 2022. We screened patient EPRs to identify U-CBSI cases, and collected clinical data for these. Data were recorded retrospectively in excel and analysed with R.

Results

Thirty-five patients were identified with an episode of U-CBSI (M=27, 77%). Candiduria was present at diagnosis in 22/35 (63%) patients. Prevalent blood culture isolates were Candida albicans (19/35, 54%) and Candida glabrata (9/35, 26%). Twenty-two (63%) patient isolates were Fluconazole susceptible, 10 (29%) demonstrated intermediate susceptibility, and two (6%) were resistant.

The median number of co-morbidities of U-CBSI patients was 5 (range 1-12), and median age was 75. Eighteen (51%) patients were diabetic. Twenty-six (74%) patients had previous surgical urology intervention, and 18/35 (51%) had ureteric stents in situ at diagnosis. Four inpatient deaths were attributable to a primary episode of U-CBSI. At the end of the data collection period 20/35 (57%) patients had died.

Conclusions

This single-centre retrospective study of U-CBSI featured high rates of previous urological intervention, ureteric stents, candiduria, and diabetes. High all-cause mortality may be related to multimorbidity rates in at-risk patients. Lower rates of Fluconazole resistance may contribute to treatment success rates in this cohort.

39 Mind the CURB! Improving adherence to guidelines for management of community-acquired pneumonia

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Background:
Improving management of community acquired pneumonia (CAP) in the United Kingdom is a national clinical priority in the Commissioning for Quality and Innovation scheme (CQUIN) 2022/23.

Aim:
To evaluate and improve management of acute admissions with CAP in line with national guidance.

Methods:
Data was collected between June 2022 and January 2023 using the CQUIN Data Collection Form. Initial data collection occurred over one month. Subsequent monthly cycles lasted 7 days. Patients on the Acute Medical Unit diagnosed with CAP were included. Outcomes included 1) CURB-65 score documentation and 2) antibiotics prescribed in line with local guidelines. Interventions included re-launching MicroGuide locally, QR code 'CAP Cards' to calculate CURB-65 using MDCalc, and educational sessions.

Results:
Data was collected in 5 cycles. The number of patients with CAP ranged between 6-14 (median 10) per cycle. Only 1/51 patients had been managed fully in accordance with guidelines. Calculation of CURB-65 ranged from 0% to 36%; correct antibiotic choice ranged from 0% to 22.2%.

Conclusions:
Improvements in management of acute CAP admissions may be seen with interventions targeting antibiotic prescriptions and CURB-65 documentation; however, the proportion of patients admitted with CAP who were managed fully in line with national guidance remained largely unchanged despite interventions. An increase in amoxicillin usage in the hospital between January 2021 and December 2022 has been noted, which may reflect more patients being correctly classified as having mild or moderate CAP as a result of greater use of CURB-65 scores, but this requires further analysis.

40 If you hear horses' hooves, look for Yersinia

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Introduction
We present an unusual case of septic arthritis secondary to Yersinia enterocolitica, presenting as breathlessness in a 90-year-old.

Case History
This patient was admitted to hospital with a one-week history of worsening breathlessness. During initial medical assessment, a six-day history of worsening left knee pain was also elicited. Admission bloods demonstrated a moderate inflammatory response, with a deranged INR. Past medical history included severe aortic stenosis, severe tricuspid regurgitation and atrial fibrillation, for which the patient was taking warfarin. In light of a swollen knee and elevated INR, a knee ultrasound was performed, with the working diagnosis of haemarthrosis. Surprisingly, however, a large volume of frank pus was instead aspirated. Yersinia enterocolitica, a Gram-negative bacillus primarily known for gastrointestinal tract infection, was isolated following culture. This patient had no history of recent acute infection, or trauma to the joint. Importantly, there was also no history of undercooked meat consumption, and no gastrointestinal symptoms prior to presentation. Due to significant cardiac impairment, this patient was deemed unsuitable for a general anaesthetic to support a surgical washout of the joint, and was managed with a prolonged course of antibiotic therapy.

Conclusion
Extra-intestinal infections secondary to Yersinia enterocolitica are extremely uncommon, and only a small number of cases of Yersinia septic arthritis have been reported previously. With the added complication of being unable to achieve complete source control, this case provided a new challenge in determining optimal antimicrobial therapy.

41 Generation of a SARS-CoV-2 pseudotyped viral particle system enabling for the study of cell-types of infection and patient sera neutralisation

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[1]*University of Liverpool*

Background: SARS-CoV-2, the virus that causes COVID-19, continues to put pressure on healthcare systems and global socioeconomic balances. The World Health Organization has declared it a global pandemic, with approximately 179 million confirmed cases and 3.87 million confirmed deaths as of June 2021. In vitro viral systems are needed to study viral entry and neutralization of emerging SARS-CoV-2 strains.

Methods: The aim was to generate an HIV-1 pseudotyped virus particle (PVP) system that expresses spike protein (CoV-S2wt) and compare infectivity profiles in two different cells, 293T and 293T-ACE2. We also monitored infection in macrophages (MQ), Dendritic Cells (DCs) and Vero cells. Furthermore, we tested SARS-CoV-S2wt PVP treated with COVID-19 patient's sera to investigate neutralisation capacity.

Results: We generated HIV-1 PVP expressing SARS-CoV-2S2 protein, which infected 293T-ACE2 cells but less efficiently 293T cells, showing the development of a virus mimicking SARS-CoV-2. This virus was successfully neutralised with patient sera generated from acute infected COVID-19 patients. The same viruses were tested for infectivity of MQ, DCs and Vero cells and where it was shown to be infectious, but to far lower levels as on 293T-ACE2 cells. These results indicate that primary cells of the immune system can be infected with SARS-CoV-2 to low levels.

Conclusions: We have demonstrated the successful generation of an HIV-1 PVP expressing SARS-CoV-2Swt protein, which infects cells expressing the ACE2 receptor and can be inhibited with sera from COVID-19 survivors. Utilising these viruses, we demonstrate that MQ, DCs and Vero cells can be infected to low levels.

42 Investigating how host innate immunity potentiates genome adaptation in the human fungal pathogen Candida albicans

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Background:

The opportunistic fungal pathogen Candida albicans harbours a highly plastic genome capable of mediating rapid adaptation to stress through dynamic large-scale genomic alterations, resulting in extensive phenotypic heterogeneity. As host innate immunity drives stress-induced mutagenesis, including loss of heterozygosity (LOH) events and aneuploidy, the resulting genomic instability, albeit unbalanced, is associated with cellular adaptability against diverse stress. However, the mechanistic links between these adaptive phenotypes, genomic changes in C. albicans and host immunity remain elusive.

Here, we investigate how macrophage-associated stress potentiates the genome plasticity of C. albicans by quantitatively measuring real-time LOH and aneuploidy events.

Methods:

Fluorescent proteins (GFP and BFP) are expressed from heterozygotic chromosomal loci. Fluorescence is detected using fluorescence-activated cell sorting (FACS), which reveals signals indicative of chromosome copy number changes.

Results:

We found that temporal exposure to macrophages (J774 and iBMDM cell lines) differentially altered the genome size of euploid C. albicans, resulting in LOH, aneuploidization, and tetraploidization. Importantly, these host stress-induced genomic alterations in C. albicans provide a downstream fitness advantage for tolerating fluconazole. Short-term exposure to macrophage stress (<1 hour) can result in increased frequencies of fluconazole tolerant microcolonies. Interestingly, prolonged co-incubation periods with macrophages reduced the frequency of tolerant microcolonies. However, the level of morphological variation became more substantial, suggesting an expansion of phenotypic variation.

Conclusion:

Together, these results display that antifungal tolerance of C. albicans may arise within the host as subpopulation events due to acute large-scale genomic alterations induced by host-associated stress, which in turn confer universal adaptive capabilities.

43 Invasive fungal infection as an Infective complication of anti-diabetic drugs

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Fungal infections are more common in the diabetic population. Several mechanisms including hyperglycaemia, impaired immune system, and glycosuric effects of anti-diabetic drugs are involved in fungal infection predisposition. Limited literature is available mentioning infective complications of sodium-glucose co-transporter 2 inhibitors, particularly dapagliflozin.

We present a case of a 51-year-old female who presented with dysuria, mild abdominal pain, and fever. She had a past medical history of type 2 diabetes and hypertension. Her regular medications included metformin, dapagliflozin, amlodipine, and Ramipril. She was treated in the community with oral Fluconazole and topical clotrimazole for possible urogenital infection. Her systemic physical examination was unremarkable other than mild hypotension. Initial blood tests showed a significant inflammatory response and acute kidney injury. Her initial treatment included intravenous antibiotics and fluids after taking blood and urine cultures. Later, the blood culture flagged positive showing the growth of yeast identified as Candida glabrata. She was commenced on IV Caspofungin and changed to Amphotericin B based on the sensitivities and resolution of her renal function. Her echocardiography and abdominal imaging were unremarkable. She was given two weeks course of antifungal treatment through OPAT and referred to diabetic services for a review of her anti-diabetic medicines. She had negative surveillance blood cultures and complete resolution of her symptoms.

The infections of urogenital tract caused by candida glabrata or candidemia are particularly prevalent in immunocompromised but can happen in immunocompetent patients. In this case report, diabetes, use of SGLT-2 inhibitor, and azoles are main risk factors.

44 Quantitative PCR demonstrates the underestimated burden of Streptococcus pyogenes as a cause of paediatric pyoderma in The Gambia

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Pyoderma presents a significant public health problem in low-resourced countries where it is commonly associated with scabies. In these settings, skin infections due to Streptococcus pyogenes are increasingly implicated in the development of rheumatic heart disease (RhD). Establishing the true burden of S. pyogenes-related pyoderma is essential to understand the drivers of RhD and design future preventative interventions.

A previous survey in The Gambia demonstrated a high prevalence of pyoderma (17.4%) in 1141 children <5yrs. Staphylococcus aureus was cultured from 80.8% of pyoderma lesions and S. pyogenes from 50.8%. Investigating archived swabs with a newly-developed multiplex quantitative PCR for S. aureus, S. pyogenes and Sarcoptes scabiei, we explored whether the presence of these pathogens was underestimated using clinical and culture-based bacteriology.

In the first 73/250 samples processed, culture identified S. pyogenes mono-infection in 8%, S. aureus mono-infection in 38% and co-infection in 44%. S. pyogenes was identified in an additional 23% (17/73) samples by qPCR, with S. pyogenes mono-infection in 11% and co-infection in 64%. Of these individuals 26 (36%) were clinically diagnosed as having scabies and S. scabiei was detected in 3/73 (4%) samples. Further work using the full dataset will analyse concordance between clinical classification, bacteriology and molecular methods of pathogen detection.

Our results suggest culture-based methods significantly underestimate the burden of S. pyogenes in pyoderma lesions in a setting endemic for RhD. Molecular methods should be used in enhanced surveillance for S. pyogenes in these settings to aid the design and assessment of future interventions against RhD.

45 Delayed transient agranulocytosis associated with long-term ceftriaxone OHPAT administration in patients with complicated pneumococcal infections

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Objective: To report two ceftriaxone-associated agranulocytosis at standard dose during outpatient parenteral antibiotic therapy (OHPAT).
Methods: We described two immunocompetent patient who had complicated pneumococcal meningitis treated with a prolonged course of ceftriaxone. Both patients were admitted with suspected meningitis on clinical and biochemical grounds. Both patients were started empirically on dexamethasone and ceftriaxone.
Results
After microbiological confirmation, ceftriaxone 2gr BD that was continued aiming at a 2-week duration as per BIA guidelines. However, the duration was extended due to complicating mastoiditis in Patient-1 and the development of a subdural collection in Patient-2 which required bur hole evacuation. Following a good initial clinical response, both patients were switched to ceftriaxone 4gr OD to continue IV antibiotic management as outpatients via our OHPAT service. Patient-1 developed neutropenia on the last day of her 21 days treatment with ceftriaxone while Patient-2 developed agranulocytosis 3 days after having completed a 29 days course of Ceftriaxone. One patient developed a neutropenic fever, requiring a short course of antimicrobial cover, but remained clinically well. Both patients responded to transient G-CSF administration(filgrastim) and their neutrophil counts recovered fully.
Conclusion:
These cases illustrate an extremely rare but serious potential complication arising from the use of a standard dose and duration of parenteral ceftriaxone in the community. As OHPAT services expand throughout Europe, outpatient courses of ceftriaxone will increase, with a possible rise in the risk of serious adverse consequences, highlighting to OHPAT practitioners the importance of FBC monitoring, even beyond completion of IVAB's, in the community setting.

47 Definitive treatment of corticosteroid-refractory CNS TB paradoxical reaction: a mini-case series

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Central nervous system (CNS) paradoxical reaction after initial response to anti-tuberculous (anti-TB) treatment causes significant morbidity and mortality. Data pertaining to immunocompetent patients are scarce, however one case series estimated 13% mortality. This mini case-series describes two cases of HIV-negative patients with corticosteroid-refractory CNS paradoxical reactions, and outlines two different paths to definitive management: combination immunomodulatory therapy and surgical resection.

Patient one presented with worsening symptoms after seven months of treatment for fully sensitive culture-positive CNS and pleuropericardial tuberculosis (TB). Patient two presented with new headaches and focal weakness after 13 months of treatment for PCR-positive abdominal and pulmonary TB. MRI imaging identified new cerebral lesions in keeping with tuberculomas, and both patients were therefore diagnosed with CNS paradoxical reactions. Symptoms progressed despite high-dose corticosteroids. Patient one was managed with the addition of infliximab and thalidomide to the steroid regime. Patient two underwent surgical resection of the lesion (histologically confirmed as tuberculoma). Clinical outcomes were favourable and MRI appearances improved in both cases.

Steroids acted as an effective holding measure in each case, alleviating symptoms and minimising progression. However, given the serious side-effect profile of long-term steroids, definitive management is necessary irrespective of disease progression. This mini-case series demonstrates the safety and efficacy of both combination immunomodulatory therapy (infliximab and thalidomide) and surgical resection for management of CNS TB paradoxical reaction refractory to standard treatment with anti-TB agents and corticosteroids.

48 Describing the epidemiological characteristics and treatment patterns of non-tuberculosis mycobacteria (NTM) infections in adults in Liverpool 2010-2022

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Objectives: Non-tuberculosis Mycobacteria (NTM) disease may be increasing in the UK but the true burden remains uncertain. Existing UK clinical guidelines focus on pulmonary NTM disease, particularly Mycobacterium avium complex (MAC),whilst management of rarer species is less evidence-based. We sought to describe the demographics, microbiology, and treatment of NTM at the Liverpool University Hospitals and Liverpool Heart and Chest Foundation Trusts between 2010-2022.

Methods: A retrospective casenote review was conducted based on an audit of samples culturing NTM in Liverpool Clinical Laboratories between 2010 and 2022. A standardised data collection tool was completed by a team of clinicians and descriptive statistical analysis was performed.

Results: NTM were cultured from 80 patients with a median age 61 (range 22-91) and overall mortality of 35% whilst on antimicrobial treatment. From 290 samples identified, 71% were from pulmonary sites. 14 distinct NTM species were isolated, 55% from the MAC group. While 53% of samples cultured positive in the Mycobacteria Growth Indicator Tube (MGIT) system, repeated samples during treatment were sparse, and no clear relationship was identified between length of treatment and time to positivity. The most frequent antimicrobials were ethambutol, rifampicin, clarithromycin, and azithromycin, though regimens varied significantly for non-MAC species. Duration of regimens varied from two weeks to eight years.

Conclusions: Disease burden was dominated by pulmonary MAC and treatment regimens were typically guidance-compliant but patient concordance was variable, likely due to treatment intolerance or co-morbidities. Prospective studies would be valuable to assess the role of MGIT monitoring during treatment.

49 HSV Hepatitis in pregnancy: a rare but serious differential diagnosis missed by current screening guidelines

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Hepatitis secondary to Herpes simplex virus (HSV) is a rare but serious cause of liver failure in pregnancy. HSV hepatitis can occur in pregnancy (1). Recent reviews of the literature (2,3) suggest screening for HSV in pregnant patients with abnormal liver function.

A 30-year-old female who was 22 weeks pregnant presented to hospital with worsening abdominal pain, vomiting and fevers. Her bloods showed inflammation and deranged liver function tests, leading to a presumed diagnosis of cholecystitis. Ultra-sound and magnetic-resonance imaging of her abdomen ruled out cholecystitis or an abdominal collection as the cause for her fevers.

The patient deteriorated: she became pancytopaenic and her liver markers worsened. A hepatitis screen was sent with no positive results. Her lactate increased, and her clotting worsened. A liver centre was contacted. The patient became encephalopathic, she was intubated and transferred. HSV-2 DNA was found on PCR, and the patient made a slow but full recovery when treated with aciclovir.

HSV is an important cause of hepatitis failure in pregnancy that is not screened for routinely. We suggest that clinicians maintain an index of suspicion and consider amending screening guidelines to include HSV. Preventing delayed diagnosis can improve outcomes in this serious, but treatable, virus.

50 Bacterial interactions of Upper Respiratory Tract microbiota

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Background. The microbiome of the upper respiratory tract (URT) has received less research attention than other body sites. This study aims to investigate the microbial ecology of the human URT with a focus on antagonism between the corynebacteria and staphylococci.
Methods. Mucosal swabs were collected from the anterior nares and nasal turbinates of 20 healthy adult subjects. Genomic DNA amplification targeting the (V4) of the 16Sr RNA gene was conducted and analysed using QIIME. Nasal swab isolates were cultured and identified using near full-length sequencing of the 16S rRNA gene. Isolates identified as corynebacteria or staphylococci were typed using (rep-PCR). Antagonism was determined using an agar-based inhibition assay.
Results. Four major bacterial phyla (Actinobacteria, Bacteroidetes, Firmicutes, and Proteobacteria) were identified from all volunteers. The typing of cultured staphylococci and corynebacteria suggested that intra-individual strain diversity was limited. Analysis of generated nasal microbiota profiles suggested an inverse correlation in terms of relative abundance between staphylococci and corynebacteria. Despite the apparent antagonism between these genera, it was limited when investigated on agar. Of 1000 pairwise interactions, observable zones of inhibition were only reported between a single strain of C.pseudodiphtheriticum and S.aureus. Imaging under EM revealed this effect to be bactericidal with clear lytic effects on staphylococcal cell morphology.
Conclusion. Nasal microbiota is complex, but culturable staphylococci and corynebacteria were limited in terms of clone type. Analysis of generated nasal microbiota profiles suggested an inverse correlation in terms of relative abundance between these genera suggesting an antagonism or competition between these taxonomic groups

52 Bolus vitamin D supplementation did not reduce infection risk, re-occurrence, or symptom duration in young male adults undergoing arduous military physical training: D_SAF, randomised controlled trial

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Evidence suggests that vitamin D status and immune function during physical training may be interrelated. We aimed to investigate the effectiveness of bolus vitamin D supplementation in reducing infections in Royal Marines (RM) recruits undertaking arduous 32-week military physical training.

Methods

Recruits (n=1815) were randomly allocated into two groups receiving placebo (CON) or 50,000 IU vitamin D3 (VIT-D) at weeks 1, 6, 15, and 24 of the 32-week programme. Serum vitamin D status (25OHD) concentration was assessed at weeks 1, 6, and 31. Upper-Respiratory Tract Infections (URTI) were defined based on self-reported flu-like symptoms and medical notes, and skin and soft tissue infections (SSTI) from medical notes.

Results

The supplementation regimen increased serum 25OHD (Mean±SD: Baseline CON 62.3±26.5 nmol/L, VIT-D 60.2±23.7 nmol/L; Week 31 CON 54.5±18.6 nmol/L, VIT-D 62.5±15.2 nmol/L), however, sufficiency (≥50nmol/L) was achieved by 74% of study recruits. VIT-D was not superior to CON in preventing the experience (OR=0.76, 95% CI 0.50-1.14), or re-occurrence of URTI during follow-up (OR=0.93, 95% CI 0.75-1.15) or reducing the number of days out of training (B=0.14, 95% CI -0.50-0.77). Similarly, VIT-D showed no superiority over CON in reducing the occurrence of SSTI (OR=0.69, 95% CI 0.44-1.07), or re-occurrence during follow-up (OR=0.72, 95% CI 0.52-1.01), or the number sick days (B=-0.61, 95% CI -1,30-0.09).

Conclusion

In this randomised placebo-controlled trial, we did not find that bolus vitamin D supplementation reduced infectious episodes or sick days compared to placebo in young male adults undertaking arduous military physical training.

53 TRANSLATE TB: Transcriptional Signatures for Latent TB, Sheffield, UK

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Background

Latent tuberculosis infection (LTBI) is complex to diagnose as patients have no clinical signs, no detectable bacilli and may be years from exposure. In low incidence settings, interferon-gamma release assays (IGRA) have increased the yield of at-risk patients who might benefit from tuberculosis chemoprophylaxis. Treatment is not without risk, however, and more accurate detection of patients most likely to benefit might be possible using newer approaches, including the detection of host transcription responses. We evaluated the use of proposed host gene-expression signatures in patients presenting to Sheffield Teaching Hospitals NHS Foundation Trust with LTBI.

Methods

We prospectively recruited patients with IGRA-positive LTBI and four additional comparative cohorts of patients with active TB, IGRA-negative inflammatory disease, other acute infections, and healthy controls. Clinical data and whole-blood samples were collected in PAXgene RNA tubes before, during and after treatment. Extracted RNA was probed for 20 genes (7 signatures of interest) by microfluidic qRT-PCR.

Results

78 patients, including 40 with LTBI, were recruited. No patients with LTBI have developed active TB during 10 months of follow-up. All 7 signatures distinguished LTBI, active TB and healthy control cohorts, but did not distinguish TB cohorts from those with other infections or inflammatory conditions.

Conclusion

Early results show that all 7 signatures were sensitive enough to distinguish between patients with LTBI and healthy controls in a UK cohort. However, the specificity of the signatures for TB versus other infective or inflammatory responses appears low and may be of limited use in clinical practice.

57 Disseminated BCG-osis as a rare complication of intravesical BCG therapy for bladder cancer: a case report

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Introduction
Intravesical Bacillus Calmette-Guerin (BCG) immunotherapy is a commonly used adjunct to transurethral resection in the treatment of high-risk non-muscle invasive bladder cancer. A rare but recognised complication of this is disseminated BCG infection (BCG-osis), although it can be exceedingly difficult to diagnose.

Clinical Case
A 76-year-old male was admitted with dysuria, worsening haematuria and fever 5 days post-BCG instillation. He was established on a 6 monthly maintenance BCG regimen for transitional carcinoma of the bladder, and reported 12kg weight loss despite treatment.

He was presumptively treated initially for a urinary tract infection but also noted to have deranged liver function tests and thus admitted under the hepatologists for possible BCG-induced hepatitis. Workup for both this and his weight loss included ultrasound of his liver, inpatient Oesophago-Gastro-Duodenoscopy and magnetic resonance cholangio pancreatography; all were unremarkable.
Despite several escalations of intravenous antibiotics, he remained pyrexial weeks into admission, with multiple negative blood and urine cultures, normal procalcitonin and echocardiogram.

Diagnosis of likely disseminated BCG infection was eventually reached following computed tomography (CT) of the chest, abdomen and pelvis, followed by a CT PET that showed new apical pulmonary nodules and reactive mediastinal lymphadenopathy. Whilst awaiting bronchoscopy he was empirically commenced on rifampicin, isoniazid and ethambutol; diagnosis later confirmed with positive mycobacterial PCR.
Interestingly, months into treatment he was readmitted for rapidly progressive interstitial lung disease (ILD); cause remains unclear.

Conclusion
This is an unusual case of BCG-osis following intravesical immunotherapy, with co-diagnosis of rapidly progressive ILD of unclear relation to treatment.

58 Antifungal resistance, a hot topic. A case report in co-infection of Mycobacterium avium-intracellulare and chronic cavitary pulmonary aspergillosis

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Introduction:
There is a known association between aspergillus-related pathology and Mycobacterium avium-intracellulare (MAI) infection, both of which are difficult to diagnosis and treat. Alongside this, anti-fungal resistance has become a growing concern globally, due to the limited treatment options.

Case presentation:
A 53-year-old male presented with progressive shortness of breath and worsening consolidation on a chest x-ray after an extended 18-months of treatment for MAI. He had poor adherence to his treatment regime and was lost to follow up.

He was diagnosed with unresectable cavitory pulmonary aspergillosis after high-resolution CT revealed a new myecetoma in his right apical lung, raised serum galactomannan and positive bronchial lavage culture for aspergillus fumigatus.

He was admitted to hospital and trialled on various anti-fungal treatments, including voriconazole, poziconazole and ambisome. His MAI treatment was stopped due to notable interactions between rifambutin/rifampicin and anti-fungal agents, as well as developing aminoglycoside-induced hearing loss.

Prolonged cultures grew a voriconazole-resistant, ambisome-resistant aspergillus. Given limited anti-fungal options, the patient was retrialled on various combinations of anti-fungal agents to which the aspergillus was known to be resistant. He died two months after diagnosis.

Conclusion:
This case highlights difficulties in the diagnosis and treatment of MAI and aspergillosis co-infection, particularly in the context of multi-drug resistance. Earlier diagnosis, developing novel anti-fungal agents and research into anti-fungal resistance are important to improve outcomes in this patient group.

60 Blood Borne Virus Testing in a central London Emergency Department: A Quality Improvement Project Interim Report

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St Mary's Hospital, Paddington, is participating in Blood Borne Virus (BBV) screening during Emergency Department (ED) attendances under an NHS England Standard Operating Procedure (SOP) for high-risk areas, supporting the National HIV Strategy. It provides HIV, Hepatitis B and Hepatitis C screening for all ED attendances requiring blood tests. To February 2023, the scheme across 33 sites has seen 646,299 HIV, 270,601 Hepatitis C antibody and 200,485 Hepatitis B tests, with 268, 299 and 730 new diagnoses respectively. This project aims to improve BBV testing rates at St Mary's Hospital ED.

Following literature and guidance review, an audit of BBV testing was conducted revealing a clear need for quality improvement. Initial problem analysis was conducted using Ishikawa and driver diagrams, with stakeholder analysis and use of a small sample survey of nursing staff and healthcare assistants. Several PDSA cycles were conducted with changes including an MDT education programme, reposition of sample bottles and improved posters/reminders. A run diagram of results was maintained demonstrating moderate progress from 5% of patients in April 2022 to 20% by January 2023.

The project highlights the challenges in implementing BBV screening in a busy ED, including hesitancy of poster informed consent. Multi-site results have demonstrated the advantage of BBV screening on early diagnosis, treatment initiation and transmission prevention. In addition to and continuing the phase 1 MDT education programme, phase 2 of this QIP will include opt-out ordering and exploration of testing using serum separating tubes to increase testing rates within the department.

61 Preliminary Outcomes of Staphylococcus aureus (SA) and Group A Streptococcus (GAS) blood stream infections (BSI) in People Who Inject Drugs (PWID's) and non PWID; a 12 month prospective pilot cohort study

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Background
BSI are a substantial cause of health care utilisation, having a significant impact on mortality and prolonged functional effects. Serious bacterial infections in PWID increased between 2013 and 2019, with 10% of all iGAS and 20% of all SA BSI in England attributed to PWID; this may be an underestimate as surveillance data for SA BSI misses risk information. Studies have failed to quantify the relative risk and outcomes of BSI between these groups; we designed this study to explore the relative risks and outcomes of BSI on mortality, quality of life and cognitive function in PWIDs and non-PWIDs.

Methods
Adult patients with GAS or SA BSI were consented for inclusion. Standardised questionnaires assessing quality of life and functional status were completed at time of consent.

Results

n=46	PWID n = 8	Non-PWID n=38	P-Value
Male	5(62%)	21(55%)	
Female	3(38%)	17(45%)	
Age	37(22-47)	66(23 - 96)	<0.001
iGAS BSI	1	4	
SA BSI	7	33	
30 day mortality	1(12.5%)	1(3%)	
Surgery needed	4(50%)	12(32%)	
Charleson median score	0(0-4)	3(0-8)	
Length of stay (days)	22 (4-47)	22(4-91)	
Critical care	2(25%)	4(11%)	
#EQ-5D-5L health rank	25	47.5	0.353
MOCA+	18	17.5	0.568
HAADS* depression	9	6.5	0.093
HAADS anxiety	15	8	0.002
HAADS total	28	16	0.01

#-EuroQoL questions, +Montreal Cognitive Assessment (V8.1 Blind English), *Hospital Anxiety and Depression Scale

Conclusion

These are early results from this cohort; we observe high rates of anxiety / depression in the PWID cohort, with only marginally improved cognition results compared to the non-PWID cohort.

62 A journey from India to the ICU; when a UTI becomes more than complicated

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A 77-year-old man attended hospital in January with fever and dysuria for 3 weeks. A GP urine culture isolated a NDM CPO producing E.coli. He was pyrexial but otherwise stable, WCC normal and CRP 26. Blood cultures were negative and a CT scan indicated no renal tract abnormality. He had hypertension and was normally well, having travelled in December to Delhi, where he was originally born.

Despite treatment with IV fosfomycin and aztreonam, his fevers persisted and he deteriorated with increasing oxygen requirement and fluid overload. He developed an AKI, deranged clotting and LFTs with ferritin rising to 3510 and LDH at 959. A progressive pancytopenia developed and he was admitted to ICU with multi-organ failure requiring intubation. Repeat CT showed; no intra-abdominal source of infection, bilateral pleural effusions with no lymphadenopathy or organomegaly.

A diagnosis of haemophagocytic lymphohistiocytosis from E.coli infection was suspected with bone marrow biopsy confirming haemophagocytosis. Methylprednisolone and Anakinra were started. Negative results included; EBV, CMV, HIV, Hepatitis, Malaria, Brucella & Leishmaniasis. Histology showed non-necrotising epithelioid granulomas with positive staining on ZN stain. Mycobacterium tuberculosis PCR was positive. ICU BAL samples were PCR and culture positive for TB. An earlier urine sample taken on the ward later cultured TB. Standard TB therapy was commenced and changed to ethambutol and levofloxacin due to worsening LFTs. He clinically improved, with therapy re-introduced as his LFTs improved.

Lesson learnt
Clinicians should consider TB causing HLH in individuals with risk factors despite no indication of TB from history and imaging.

63 Observational overview of the effects of epidemic seasonal respiratory viruses on sepsis, antimicrobial use, and Clostridioides difficile (CDI) rates at an acute hospital

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Objectives:
To evaluate the effects of increasing seasonal respiratory virus activity (RSV, influenza, and SARS-CoV-2) on sepsis alerts, blood culture (BC) positivity, antibiotic prescribing, and Clostridioides difficile (CDI) rates in Acute General Medicine (AGM).
Methods:
A 14-month period, including two winter seasons (December 2021 – January 2023) was reviewed. Antibiotic administrations in AGM, including ambulatory care, for co-amoxiclav, doxycycline, ceftriaxone, and amoxicillin were extracted using the trust's e-prescribing system. The same system recorded trust-wide sepsis alerts. BC positivity for Streptococcus pneumoniae, Escherichia coli, and Staphylococcus aureus was determined from microbiology laboratory e-records. Infection Prevention and Control data were used to ascertain positive samples of C. difficile, Influenza, RSV, and SARS-CoV-2. Trends were reviewed for correlation with increasing respiratory virus rates.
Results:
During the second winter, compared with the first, a surge in influenza cases, correlated with increases in BC positivity and admission to AGM with sepsis. A 55% increase in administrations of antibiotics recommended for sepsis, HAP, and CAP was observed in December 2022 compared to December 2021. A corresponding increase in C. difficile rates was noted over the 2022 winter.
Discussion:
We postulate that the increasing respiratory virus effect, resulted in an increase in patients presenting with sepsis, resulting in increased antibiotic prescribing and CDI rates. Further review of these trends may provide AMS teams with signals to plan for periods of increasing antibiotic use during respiratory virus epidemics, such as promoting POCT for respiratory viruses and prompt review of antibiotics.

64 Threshold Concepts and Implications for Antimicrobial Stewardship Education

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Introduction: Antimicrobial resistance is a major global health threat. Unfortunately, despite antimicrobial stewardship (AMS) education, healthcare practitioners continue inappropriately prescribing antibiotics.In this paper, we explore the need to recognise 'threshold concepts' – concepts which students may initially find counter-intuitive, but once understood, 'transform' student thinking – and techniques to address them according to students' differing Honey&Mumford learning styles, to promote more effective application of AMS theory into clinical practice.

Content: Threshold concepts are transformative, irreversible (difficult to forget once learnt) and integrative (exposing previously concealed inter-subject relationships).They necessitate extended teacher-learner discourse,leading to 'reconstitution of self' where learners let go of previously-held concepts.Unfortunately, the most common AMS education methods in medical schools remain passive,such as didactic lectures.Instead of dictating antibiotic choice,students must be given opportunities to express their own thoughts on the safest,most targeted antibiotic regime(if any). Students may initially face 'troublesome knowledge' as they attempt 'internalising' that narrow-spectrum antibiotics may be adequate/altogether unnecessary,but support for this 'threshold concept' can be provided according to each student's unique Honey&Mumford learning style (such as simulations for 'activists',observations for 'reflectors',case studies for 'pragmatists' and model-based storyboarding for 'theorists').When designing AMS modules,educators should incorporate diverse teaching methods into a Universal Design for Learning (UDL) framework,optimising technology-assisted learning (TEL) to address resource limitations.

Conclusion: We need to shift from didactic AMS teaching methods to more interactive, student-centered TEL methods which recognise students' threshold concepts and address them according to students' different learning styles. Further quantitative studies are required to identify common AMS 'threshold concepts' for students.

65 Administration of Covid-19 vaccines to patients with a high risk of anaphylaxis- update from the NHS Lothian monitored vaccine clinic

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Introduction
Soon after the start of COVID-19 vaccination in the UK, following two reports of serious allergic reaction, the MHRA advised against Pfizer vaccines for any individual with a history of anaphylaxis. To prevent possible unnecessary exclusion from vaccination, we set up a clinic for people considered 'high risk'.
Results
Referrals were triaged by an allergy specialist. High risk individuals were assessed and vaccinated in clinic with resuscitation facilities on-hand. A total of 207 vaccinations were carried out between the 30/03/2021 and 07/02/2023: Astra-Zeneca (87), Pfizer (105), Moderna (14) and Novovax (1). The triaging clinician determined vaccine choice, based on potential allergy to excipients, risk of clot formation, and later availability of vaccines and benefits of a bivalent. Pre-vaccination, antihistamine was given on 52 occasions. There were 41 reactions to the vaccine, typically orofacial tingling, or minor mucosal swelling or skin rashes. 24 people required medical treatment: mainly oral antihistamines (22), as well as oral steroids (4), nebulised adrenaline (2) and paracetamol (2). On only 3 occasions critical care assessment was carried out, with admission to a ward for overnight observation. No patient had a clinically significant change in observations in keeping with anaphylaxis, and IM adrenaline was never given. Most patients were advised they could safely receive future vaccines within community settings.
Conclusions
We demonstrate a way in which vaccines can be given safely to individuals at high risk of anaphylaxis We propose that the format of this clinic could be extended to all vaccination programmes.

66 Procalcitonin-guided antibiotic stewardship in patients with cancer

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Objectives

Antibiotic treatment is common for presumed infections in cancer care. Accurate identification of bacterial infections impacts hospital length of stay, therapeutic cost, antimicrobial resistance, and incidences of hospital-acquired infections.

Procalcitonin rises in bacterial infection and falls in response to antibiotic treatment but evidence for procalcitonin in the diagnosis of infection and monitoring in patients with cancer is limited.

We measured procalcitonin in patients with a clinical suspicion of a bacterial infection, presenting to a Cancer Centre Sept 2021- Nov 2021, The aim was to identify patients who could have their antibiotic therapy discontinued early.

Methods

Procalcitonin was measured at admission and at 48-72 hours. Demographics, disease stage, systemic therapy, central catheter presence, antibiotic use, microbiology samples, neutrophil-lymphocyte ratio, and C-reactive protein were collated.

Results

78 admissions were reviewed. 39 (50%) female; 23 (29.5%) were curative; median age was 64 (range 17-83). 70 (89.7%) received intravenous antibiotics. In 27 (34.6%) admissions, patients had consistently low procalcitonin (defined as <0.25), interpreted as unlikely to have bacterial infection. No objective evidence of bacterial infection was observed in these patients.

Discussion

Over a third of patients received antibiotic treatment despite low procalcitonin and little objective evidence of infection. Although it is yet unknown whether these patients required antimicrobial treatment or not, use of procalcitonin has the potential to improve patient care.

Conclusion

34.6% of the patients admitted to oncology ward received antibiotic treatment despite having persistently low procalcitonin. Further research is required to identify people who do not need antibiotic treatment.

68 Uncommon Culprit: Can Staphylococcus epidermidis be a Cause of Native Valve Infective Endocarditis in an Injecting Drug User?

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Infective endocarditis is a serious condition associated with significant in-patient mortality of up to 26%. A recent study with a large cohort of 1504 patients showed NVE caused by Coagulase Negative staphylococci is 6.6%. Here, we report a case of Staphylococcus epidermidis bacteraemia in an injecting intravenous drug user that was found to have infective endocarditis.

We describe a 41-year-old person who injects drugs with a background of recurrent soft tissue infection, who presented with acute severe back pain, neurological symptoms, peripheral stigmata of infective endocarditis and a new systolic murmur. MRI whole spine revealed degenerative and inflammatory changes at L4/L5. Blood cultures taken 6 hours apart grew Staphylococcus epidermidis with the same antibiogram panel. Transthoracic echocardiography showed no vegetations, but transoesophageal echocardiography confirmed aortic valve endocarditis with a small hole in the cusp and mild aortic regurgitation through the right coronary leaflet. The valve multidisciplinary team recommended to treat as infective endocarditis for six weeks. They were given Teicoplanin (MIC 2µg/mL) and Cotrimoxazole.

Staphylococcus epidermidis, which is usually considered to be a contaminant when isolated from the bloodstream, has the potential to cause significant pathology and should not be ignored when isolated repeatedly in someone with clear clinical features of bloodstream infection. Infective endocarditis should be considered as one possibility if there are clinical signs of concern. Further studies are needed to understand the pathogenesis and risk factors for Staphylococcus epidermidis NVE in active intravenous drug users.

69 Teaching Medical Students About Pneumonias: The Design and Development of an E-Learning Resource

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Background
Undergraduate infectious diseases (ID) teaching is highly variable with only a few specialised centres in the UK. There is currently no dedicated undergraduate ID curriculum. E-learning is an effective and flexible method of meeting educational needs.

Aims
1. Assess undergraduate students' perspectives towards current ID teaching
2. Design an e-learning package and capture feedback

Methods
Clinical years undergraduate medical students were invited to complete a survey on current ID teaching. These were then processed using thematic analysis with computer-assisted qualitative analysis software. A Xerte package on pneumonia was then sent to students with feedback analysed.

Results
32 students completed the initial survey. Analysis revealed that students largely enjoyed their lecture-based ID teaching but felt formal teaching was too sparse and would welcome an online package covering common presentations and high-yield topics.

All 32 students opted to be sent a link to the Xerte package. Feedback analysis showed that students found the e-learning beneficial and enjoyed the multimedia components and integrated assessments. All students rated the package 9/10 or higher. All students stated they would recommend the e-learning to peers and would engage with further packages.

Conclusions
ID is a visual speciality that lends itself well to e-learning. Students were satisfied with the resource and found it helpful in their approach to patients with pneumonia. This resource can be utilised either as a standalone or before starting clinical placements and may prove particularly useful in the current and challenging learning environment where there is an increased shift to digital resources.

70 Use of Co-trimoxazole as Oral Antibiotic Switch for Staphylococcus aureus Spinal Infections

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Spinal infections in our centre, managed through a MDT involving a microbiologist has helped to treat patients with narrow spectrum antibiotics and also to switch to highly bio-available oral agents at an early stage. We audited patients with Staphylococcus aureus spinal infections who were treated in 2021 & 2022 to assess their outcome.

There were 17 patients with spinal infections caused by S. aureus treated during this period. The infections included discitis, epidural abscesses and post-operative metal prosthesis infections. We used a CRP of 20 mg/L as a cut-off to switch from intravenous to oral antibiotics. The oral antibiotic of choice was co-trimoxazole with or without rifampicin, except for 3 patients, 2 of whom were intravenous drug users requiring early oral switch to oral ciprofloxacin and rifampicin. One patient with multi-focal infection passed away while still on IV antibiotics.

The mean number of days for the oral switch was 21 days, while the mean total antibiotic treatment was 56 days. The mean CRP level at the time of the oral switch was 14.8 mg/L. The mean length of in-patient stay was 32 days with 53% <20 days. All 16 patients who were switched to orals recovered from infection and no complications/ re-admission seen within 3 months of completion of treatment.

We can conclude that use of CRP of 20 mg/L as cut-off for oral switch and co-trimoxazole as oral option is safe and effective management strategy for patients with spinal infections.

71 An Atypical, Atypical Pneumonia: Multisystemic Legionellosis Presenting with Encephalopathy

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Case:
We report a case of a 61-year-old gentleman with no significant medical history who presented with pyrexia and multi-system upset 7 days after returning from Thailand. He was confused with slurred, repetitive speech, unsteadiness and falls, a left-sided hemiplegia, hip and eye pain, shortness of breath, cough, and oliguria.
Inflammatory markers were raised with a CRP of 617 and a white cell count of 18.0. He had a new AKI with a urea of 31.0 and creatinine of 892. His neurological status quickly deteriorated requiring intubation, haemofiltration and ITU admission. Blood cultures and malaria screen were negative. His sodium was 148, Liver function test normal, Creatine kinase 42 and highly sensitive troponin T 194 due to possible myocarditis.
CT chest, abdomen and pelvis identified lung consolidation and a renal nodule and urine antigen and subsequent bronchoalveolar lavage PCR was positive for Legionella infection. MRI head showed possible bilateral watershed infarcts, corpus callosum lesions and caudate and pontine signal changes of query encephalitis and possible pontine/ extrapontine myelinolysis. CSF taken on admission and one week later produced normal findings. A tropical encephalitis screen was undertaken, and the case discussed with the imported fever service. Stool PCR for campylobacter was positive.

Discussion:
After 2 weeks he had not shown signs of clinical improvement and was discussed at Queen's Square National Encephalitis MDT. The causes of infectious and metabolic encephalopathy in a returning traveller are discussed with special emphasis on Legionella encephalopathy.

72 Lyme disease in Scotland 2018-2022: pandemic effects?

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Background
Early in the COVID-19 pandemic, travel restrictions reduced visitor numbers to rural areas. The lifting of restrictions potentially caused a rebound effect also altering exposure dynamics.
Aim
To analyse testing data from SLDTRL to examine potential impacts of the pandemic
Method
SLDTRL receives samples from throughout Scotland for Borrelia burgdorferi antibody testing. Data from 2018-2022 was analysed for trends in testing numbers, positivity rates, clinical presentation and age/gender profiles of confirmed cases.
Results
Sample numbers ranged from a high of 9107 in 2019 to 5444 in 2020. The proportion positive rose from 3.5% in 2019 to 5.5%, 7.7% and 7.5% in 2020-22.
2020-22 saw a rise in cases in the 30s-40s age groups and fewer in the 50+ age groups. The proportion of female cases rose from 35% in 2018 to 51% in 2021.
There has been a notable rise in neuroborreliosis cases from 35 in 2018 to a peak of 130 in 2021.
Cases in NHS Highland patients rose in 2021/2022 with a simultaneous reduction in the proportion from Highland.
Conclusions
The interesting trends are likely due to changes in tick exposure, access to GP diagnosis and use of laboratory diagnostics.
The higher positivity rate and rise in neuroborreliosis cases may be a result of delays or barriers to seeking healthcare advice.
Differences in case numbers may be associated with changes in behaviour in certain population groups (females, age 30s-40s and non-NHS Highland patients) allowing greater opportunities for exposure.

73 Preliminary Data PWID Study: Carriage rates of Staphylococcus aureus (SA) and Group A Streptococcus (GAS) in patients with concomitant blood stream infections (BSI) in People Who Inject Drugs (PWID's) and non-PWID; a 12 month prospective pilot cohort study.

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Background

Preventable bacterial infections are a cause of injecting-related harm to people who inject drugs in the UK. In 2020, 38% of PWIDs responding to the "Shooting Up" survey reported having a sore, open wound or abscess at an injection site with possible symptoms of a bacterial infection. The majority (32%) were treated in hospital; with 80% requiring an overnight stay and 56% requiring surgical intervention.

The rise in BSI in PWID, which have increased each year, with 10% of all invasive GAS and 20% of all SA BSI in England and Wales in 2019 attributed to PWID.

Understanding the relationship between carriage of SA and GAS and the development BSI, may help to develop strategies to reduce endogenous BSI in PWID, including skin decolonisation.

Methods

Adult patients with GAS or SA BSI were consented to have swabs taken to determine carriage and source of SA and GAS.

Results

n=46	PWID n = 8	Non-PWID n=38
Male	5(62%)	21(55%)
Female	3(38%)	17(45%)

Community Onset iGAS BSI	1(12.5%)	4(11%)
Community Onset SA BSI	7(87.5%)	21(55%)
Surgical Intervention	4(50%)	12(32%)
Groin Infection /DVT	7 (87.5%)	0%
Confirmed Infective Endocarditis	1 (12.5%)	1 (3%)
Critical Care	2(25%)	4(11%)
Infection Managed by ID Unit	3 (38%)	7 (18%)

Conclusion

These are early results from a novel cohort study; a concomitant groin infection is associated with a SA or GAS BSI in the PWID cohort. Nasal carriage of SA was found in both cohorts, often after antibiotics were initiated, suggesting a role for decolonisation.

74 Treating Cryptococcal meningitis - Can African AMBITIONs find a home in the UK?

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Globally, cryptococcal infection is responsible for 19% of AIDS-associated mortality (1), disproportionately affecting low income countries (2). The AMBIsome Therapy Induction OptimisatioN (AMBITION) Study Group demonstrated that a single high dose of liposomal amphotericin B with flucytosine and fluconazole was noninferior in the induction phase of treatment for cryptococcal meningitis when compared with the 2018 WHO standard of seven days of amphotericin B deoxycholate and flucytosine-based therapy (followed by seven days of fluconazole 1200 mg) (3). The trial was performed in five African countries and focused on populations where the logistics of administering a 7-day course of amphotericin and monitoring toxicities present major challenges. Its findings resulted in a revision of WHO guidelines (3). Such treatment simplification may also have benefits in countries where a 7-day amphotericin course, although more readily completed, remains a cause for prolonged intervention and hospital admission. We present a case of a patient with HIV, poor immune reconstitution and a late relapse in cryptococcal meningitis who was managed at St George's Hospital, London using the AMBITION protocol. He was able to return home more promptly than would otherwise have been the case and had an excellent clinical outcome with minimal adverse effects. Although the AMBITION protocol was designed to address urgent needs in low and middle income settings, its advantages are applicable in better-resourced settings, with reduced cost, the possibility of reduced hospital length of stay for some patients, and reduced toxicity. This approach could be adopted more widely in settings such as the UK.

75 Leptospirosis: A Case Series of Patients Presenting Over 10 Years to A Regional Hospital in Oxford, UK

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Objective and Methods:
Leptospirosis is a bacterial zoonosis that occurs worldwide. No recent case series have summarised the disease in the United Kingdom. We reviewed positive PCR and serology results in the OUH NHS trust from 2012-2022 to identify cases of leptospirosis.

Results:

1087 tests for Leptospirosis were performed in 924 patients with 49 positive results in 42 patients. After exclusion of 3 patients with unobtainable notes and 10 cases with an inconsistent clinical history, 29 Patients were diagnosed with leptospirosis.

Median patient age was 39 (Range 8-72) and 76% were Male. 62% of patients had a history of travel, presenting a median of 2 days (range 0-10) after return. 57% of patients reported recent exposure to freshwater. All UK cases occurred between May and December when average UK water temperature is higher.

All patients reported fever with a median duration of 6 days (Range 1-8 days). Headache was reported in 79% of patients, meningism 14%, myalgia 93%, abdominal pain 41% and vomiting or diarrhoea 38%. Jaundice was present in 31% of patients, conjunctival suffusion in 17%, splenomegaly in 7%, and hepatomegaly in 0%.

All but one patients received treatment with antibiotics. Median duration of antibiotics was 7 days (range 3-28 days). Median duration of admission was 4 days (range 0 to 111). Six patients required ICU admission, five required renal replacement therapy, and one patient died.

Conclusion:

Doctors should be aware of Leptospirosis and its clinical presentation and risk factors. Patients have a good outcome with prompt treatment.

76 An unusual suspected case of disease recrudescence in a patient insufficiently treated for murine typhus

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Murine typhus a widely distributed disease, common in regions of the tropics and subtropics. It is caused by the bacteria Rickettsia typhi, spread predominantly by fleas of rodents, however recently other groups of small mammals over different geographic areas have been incriminated as disease reservoirs. Commonly causing mild disease, however serious complications occur; deafness, meningitis, thromboembolic events with fatality reported in 4% of cases. Due to the non-specific presentation of fever, constitutional symptoms and transient rash it is thought to be underdiagnosed.

This case report discusses a female patient who presented to hospital with an acute fever, headache, myalgia, diarrhoea and transient rash, immediately following her return from 2 weeks of travel to Thailand and Vietnam. Based on these symptoms and travel history a geographic panel of investigations was sent, including Rickettsia species polymerase chain reaction (PCR) and serology which was strongly positive IgG/IgM and positive PCR. Following this oral doxycycline 100mg OD was commenced on discharge. 7 days post discharge the patient represented feeling unwell, with fever, headache and myalgia. The dose of doxycycline was increased to 100mg BD for a further 7 days.

The standard treatment regime for rickettsial infections is doxycycline, 200mg for 14 days. This patient was undertreated and represented with symptoms indicating a recrudescence of disease. Recrudescence is a well-recognised feature of R. prowazekii, also in the typhus group but has not been described in the literature with R. typhi. This phenomenon is noteworthy, in a disease that is underdiagnosed, with potentially life changing complications.

78 Evaluating and Improving the Blood Culture pathway in the Cambridge Microbiology and Public Health laboratory

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In June 2022, NHS England introduced new key performance indicators (KPIs) in the blood culture pathway regarding number of blood culture sets (2 per septic patient), collection volume (10mL per bottle), and maximum time to incubation (TTI, ≤ 4hrs), to improve blood culture yield and patient outcomes in sepsis. The degree to which the Cambridge Microbiology and Public Health Laboratory (CMPHL) adhered to these regulations was investigated, with the aim to monitor current trends against the KPIs to identify areas for improvement. Adult aerobic and anaerobic culture bottles were sampled on morning of February 3rd, 2023, via measurement of meniscal height for volume, and time delta between draw and incubation as TTI. This revealed evidence of underfilling, with ~56% of sampled bottles <8mL, and 16% overfilled above 13mL. This was consistent with a retrospective analysis conducted using the EPICENTRE interface which observed the average blood culture volume over the latest complete 5-month period to be 6.4mL. 8 / 20 sets measured had a TTI exceeding the 4h standard, and only one of the sampled cultures consisted of two sets taken (5.6% of samples). Thus, CMPHL does not reach the level of compliance on any set standards. We propose an educational intervention targeted to poorly preforming departments to improve culture volume and TTI, with monthly feedback to monitor efficacy. We recommend the hospital address resources and instrument space required before targeting improvement in number of blood culture set.