From the Secretary's desk

Another year, another CIDSCON. A wonderful event with distinguished luminaries from the field of Infectious Diseases from all over the world who brought the latest in the subject to our shores. Based on the level of interaction and feedback received, I can confidently say that this year’s edition was a success. The scientific team should be commended for their choices, the organizational team for their planning and the audience for their active participation.

Our society continues to grow. How can we measure growth? By its members. We have added more members year on year. By the impact we have in society. Members of the society have made a mark in many situations, including the recent Nipah outbreak. By being a sought-after academic partner of other societies. We now work with ISOT on a regular basis, and we will be working with Haematocon this year. We hope to increase such collaborations in the future. More academic activities have sought CIDS endorsement, as this represents a mark of quality.

How can we move this forward? This requires a multipronged approach. We need more trained physicians, as this remains an underserved area. In this regard, it is a pleasure to note that 3 new University accredited programs have taken students in the last year. More such programs are likely to start, and it should be the mandate of the society to help such capacity building.

There is still a huge swathe of country with practically no ID service. We need to help generate understanding of need and capacity building. Many centers are approaching members to help them create such a situation. In this regard, our new venture, the visiting Professorship program should create new opportunities.

Increasing the local footprint of ID across the country is important. In this regard, starting local chapters is on the anvil and should be operationalized soon. CIDS will support such local efforts to help disseminate knowledge and create awareness on various challenges facing healthcare. We also need to involve ourselves more with policy making and helping make the right decisions to move the health care scenario forward. We also need to work with more like-minded organizations and involve ourselves in educational activities across the spectrum of infectious diseases.

Finally, mentorship. This is defined as the guidance provided by an experienced and trusted advisor. CIDS has a mandate to mentor juniors through the initial phase of independent decision making to help them become mentors themselves. This is a process, something I learnt from my seniors like Dr Dilip Mathai, Dr OC Abraham and Dr Chandra, among many others. To this end, CIDS will make subcommittees a reality - an opportunity for our younger colleagues to work with the stalwarts in a controlled situation, as equals, unlike their fellowship days, and to help them develop leadership and decision-making skills. This will enable them to get visibility to other organizations and societies, so that they are also sought-after faculty for academic initiatives beyond CIDS. Starting and conducting local chapters of CIDS will also give those in their formative years an opportunity to showcase their potential and develop skills for helping them serve the society in greater roles in the future. This will empower them to one day take over the mantle of leadership in our society and be effective mentors to the next generation of ID physicians in the country.

We are now closing in on a decade of the founding of the organization, and we have weathered difficult times much better than many other similar societies. No doubt, there will be challenges ahead, but with a healthy policies, committed members and guidance from the seniors, we should see sustained growth and opportunities for all.

Dr Subramanian Swaminathan
Editor's note

Dear CIDS members,

After a fantastic CIDSCON in Vellore, you must be getting back to your daily routine! We thank the organizing team of Dr George M Varghese, Dr Priscilla Rupali and Dr OC Abraham for combining a high quality, academic, unbiased scientific program with seamless logistical support. Next year's CIDSCON will be at Kochi, in August as usual.

We congratulate the new office bearers who will assume office from April 2019: Dr V Ramasubramanian (Vice President), Dr Priscilla Rupali (Joint Secretary) and Dr Suneetha Narreddy (Treasurer). We hope to start a CIDS Visiting Professorship program and CIDS city/state chapters soon. While the former will expose medical colleges to an eminent CIDS ID physician, the latter will spur academic activity in between our annual conferences. Suggestions on these programs and participation by members are welcome. CIDS subcommittees in various aspects of ID are already functioning and we welcome all members to volunteer to become part of these subcommittees.

Dr Abdul Ghafur, one of the founder members of CIDS, has resigned from the executive committee. The society thanks him for his contributions, especially in the area of antimicrobial resistance, and looks forward to his continued involvement in this and other areas.

Dr Neha Gupta, Dr Ashwini Tayade and Dr Abi Manesh have volunteered to be more closely associated with putting our newsletter together (most welcome for me personally!). However contributions from each and every one of you for newsletter and website are most welcome.

We have upgraded our website and improved its content, please encourage colleagues and postgraduates to visit; check out the literature review and some of the challenging cases presented at this year’s CIDSCON on the website!
A 40/M presented with fever of over 5 months with loss of appetite and weight. TTE revealed an echogenic mass of 1.4 X 0.4 cm on the aortic valve with aortic regurgitation & mitral regurgitation. Blood cultures grew ampicillin and gentamicin sensitive Enterococcus faecalis. He was initiated on intravenous vancomycin elsewhere. The patient subsequently developed acute kidney injury (AKI) with creatinine increasing to 6.6 mg%.

On admission one month later, the patient had vomiting and fever <99˚F. TTE showed persistent vegetations. Hb- 9 gm%, CRP-49.8, NT Pro BNP -19,100 pg/ml. He was initiated on ampicillin – sulbactam in renally modified doses. However, it had to be discontinued as patient had allergy to this drug. Daptomycin was initiated at 10 mg per kg on alternate days in view of deranged renal function. Subsequently, as the creatinine improved with CrCl> 30 ml/min – the dose was modified to 9 mg/kg/day. After 4 weeks of therapy, during the preoperative evaluation for aortic valvular replacement (AVR)- the chest X Ray revealed bilateral lung infiltrates and CT Chest revealed multiple perihilar bronchovascular opacities in bilateral upper, right middle and lower lobes with bilateral mild effusion (Figure 1 and 2).

On examination, patient was clinically stable, not dyspnoeic (RR:20/min), no cough or expectoration. Hb – 8.2 gm%, WBC -7,900 (N -65.6 %, L 16.8 %, E – 5.7 % & M- 11.1 %). CRP increased to 214, NT Pro BNP 11,900 pg/ml. Echo revealed left ventricular ejection fraction (LV EF) - 40%. Bronchoalveolar lavage (BAL) was negative for G stain, KOH, Xpert Mtb and Aspergillus GM. BAL culture grew Klebsiella pneumoniae (105 cfu /ml) and Candida albicans.

Figure 1: Chest X Ray with bilateral lung infiltrates. Figure 2: CT Chest Interval appearance of multiple perihilar bronchovascular opacities in bilateral upper, right middle and bilateral lower lobes

What is your diagnosis?

**ID NEWS**

**Eravacycline FDA approved**

The US FDA has approved eravacycline to treat “complicated intra-abdominal infections, providing a new option to combat the growing threat from treatment-resistant bacteria.” The company plans to launch the drug in the US in October.

In another development, the FDA's Antimicrobials Drug Advisory Committee has voted in favor of approving omadacycline for the treatment of acute bacterial skin and skin structure infections and community-acquired bacterial pneumonia. Omadacycline is a once-daily, IV and oral, broad-spectrum antibiotic in the tetracycline family. Final approval decision is awaited.
**US-FDA warning: increased risk of Fournier's gangrene with SGLT2 inhibitors**

The US-FDA has issued a warning regarding increased risk of Fournier's gangrene with use of SGLT2 inhibitors in treatment of type 2 diabetes mellitus. This class of drugs includes canagliflozin, dapagliflozin, empagliflozin, and ertugliflozin. SGLT2 inhibitors act on the sodium-glucose cotransporter 2, inhibiting proximal tubular reabsorption of glucose - thus promoting renal excretion. The increased urinary glucose levels however are linked to an increased risk of vulvovaginal candidiasis (~10% patients) and urinary tract infections.

Twelve cases of Fournier's gangrene (necrotizing fasciitis of the perineum) were reported to the FDA adverse event reporting system over a period of 5 years. In contrast, only 6 cases were reported for other anti-diabetic medication classes over a period of 34 years. The SGLT2 linked cases affected both men and women, while the non-SGLT2 cases affected only men. The FDA recommends discontinuation of SGLT2 inhibitors in patients with suspected Fournier's gangrene. The full warning can be accessed at [https://www.fda.gov/Drugs/DrugSafety/ucm617360.htm](https://www.fda.gov/Drugs/DrugSafety/ucm617360.htm)

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**JOURNAL REVIEW**

**Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis: re-thinking one of the mantras of ID?**

*Contributed by Dr Vishnu Rao*

The POET trial was a randomized, noninferiority, multicenter trial, the authors assigned 400 adults in stable condition who had endocarditis on the left side of the heart caused by streptococcus, Enterococcus faecalis, Staphylococcus aureus, or coagulase-negative staphylococci and who were being treated with intravenous antibiotics to continue intravenous treatment (199 patients) or to switch to oral antibiotic treatment (201 patients). In all patients, antibiotic treatment was administered intravenously for at least 10 days. If feasible, patients in the orally treated group were discharged to outpatient treatment. The primary outcome was a composite of all-cause mortality, unplanned cardiac surgery, embolic events, or relapse of bacteremia with the primary pathogen, from the time of randomization until 6 months after antibiotic treatment was completed.

After randomization, antibiotic treatment was completed after a median of 19 days (interquartile range, 14 to 25) in the intravenously treated group and 17 days (interquartile range, 14 to 25) in the orally treated group (P=0.48). The primary composite outcome occurred in 24 patients (12.1%) in the intravenously treated group and in 18 (9.0%) in the orally treated group (between-group difference, 3.1 percentage points; 95% confidence interval, −3.4 to 9.6; P=0.40), which met noninferiority criteria.

In patients with endocarditis on the left side of the heart who were in stable condition, changing to oral antibiotic treatment was noninferior to continued intravenous antibiotic treatment. Avoid MRSA and make sure you pick uncomplicated patients though!

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**Is Ampicillin + Ceftriaxone as safe and effective as Ampicillin + Gentamicin in the treatment of Enterococcus faecalis endocarditis?**

*Contributed by Dr Abi Manesh*

Ampicillin + Ceftriaxone (AC) is an attractive option in the treatment of Enterococcus faecalis endocarditis because of the potential renal safety and prevalent gentamicin resistance. In this retrospective review from Mayo clinic, both the options were equally efficacious with similar 1 year mortality and relapse rates. Also AC therapy was associated with less renal toxicity (greater increase in serum creatinine at end of therapy (median difference, +0.4 [0.2, 0.8] vs -0.2 [-0.3, 0.1] mg/dL, P=.001).

Of course there are no RCTs in this area; but accumulating evidence shows the safety and efficacy of this regimen which is especially attractive in older patients and those on OPAT.
**Six days is what you require for CAP treatment!**

*Antimicrob Agents Chemother. 2018 Aug 27;62(9)*

Contributed by Dr Abi Manesh

In this large meta-analysis including 21 trials, comparing 6 or less days and 7 or more days of antibiotic therapy some things are clear. Clinical cure was similar between the compared groups [4069 patients, RR= 0.99 (95% CI, 0.97-1.01)] irrespective of the severity of pneumonia [RR= 1.05, (95% CI, 0.96-1.14)]. Relapses were similar between short and long-course treatment groups [1923 patients, RR= 0.67 (95% CI, 0.30-1.46)]. Short-course treatment was associated with fewer serious adverse events [1923 patients, RR= 0.73 (95% CI, 0.55-0.97)] Short-course treatment resulted in lower mortality compared to long-course treatment [2802 patients, RR= 0.52 (95% CI, 0.33-0.82)].

Another great example where cumulative results unmask treatment effect that was not identified due to low numbers. One more compelling evidence to stop therapy early in CAP.

**Hepatitis E is more complex than we thought**

*Emerg Microbes Infect. 2018 Jul 5;7(1):125*

Contributed by Dr Abi Manesh

In this interesting study from China, 11747 eligible blood donors were screened for anti-HEV IgM/IgG and HEV RNA and antigen. Twenty-four donors who were positive for both HEV antigen and RNA were followed for ≥ 70 days, and none of these donors reported clinical hepatitis or illness. At least 1 follow-up sample was provided by 17 donors, including 10 with viremia and/or antigenemia for ≥ 70 days and 3 with antigen and RNA positivity for >90 days. Fourteen of the 17 donors did not present with an obvious serologic response during the follow-up period. These donors showed atypical HEV infection progression that differed from that of hepatitis E patients.

This study challenges our concept that Hepatitis E presents as only acute infections. Not only there was an asymptomatic chronic state with viremia, this was also not associated with antibody response as well. These patients are going to pose particular challenge during pre blood donation screening. A compelling evidence that hepatotropic viruses produce multifaceted disease with variable immunological response and clinical disease.

**Severe Manifestations of Chikungunya Fever in Children, India, 2016**

*Emerg Infect Dis. 2018 Sep 24(9):1737-1739*

Contributed by Dr Vinay Devraj

The authors conducted a retrospective, observational study in the pediatric intensive care unit (PICU) and pediatric high-dependency unit of a tertiary care hospital in New Delhi, India. They included patients whose chikungunya infection was diagnosed by positive real-time reverse transcription PCR (RT-PCR) during September–December 2016. The RT-PCR was done using a Gene Finder DENV/CHKV RealAmp Kit (Osang Healthcare, Gyeonggi-do, South Korea) at Oncquest Laboratories (New Delhi, India). This qualitative assay uses a 1-tube RT-PCR technique with internal control for amplification and detection of chikungunya virus RNA.

A total of 49 children had chikungunya fever; 36 had nonsevere disease and 13 had severe disease. All patients with severe disease were admitted to the PICU; 11 had illness consistent with the case definition of severe sepsis and septic shock, and 2 had acute liver failure. Of the 36 patients with nonsevere disease, 16 were admitted to the PICU (11 had seizures, 4 had fluid-responsive shock, 1 had peripheral cyanosis and mottling) and 20 were admitted to the pediatric high-dependency unit (3 had bleeding manifestations, 4 had severe abdominal pain, 2 had underlying cyanotic congenital heart disease, 2 had body temperature >40.3°C with irrelevant talking, 7 had dehydration, and 2 had severe rash).

Although chikungunya usually has a mild course, severe life-threatening manifestations can occur. Clinicians should be aware that these manifestations can develop within 24 hours of the onset of illness, and a high index of suspicion is required to establish diagnosis. In this study, age <1 year and 11–14 years were predictive of severe disease.
**Guideline watch**

**Updated WHO Recommendations on First-line and Second-line Antiretroviral Regimens and Post-exposure Prophylaxis and Recommendations on Early Infant Diagnosis of HIV**

*Courtesy: Dr Kalpesh Sukhwani*

**What to start**

Looks like dolutegravir based regimens are best for all except those of pregnancy potential.

**Key changes to treatment of multidrug- and rifampicin-resistant tuberculosis (MDR/RR-TB)**

*Courtesy: Dr Vidya Devarajan and Dr Rohit Vashisht*

<table>
<thead>
<tr>
<th>Group</th>
<th>First-line regimen</th>
<th>Second-line regimen</th>
<th>Third-line regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Include all three medicines (unless they cannot be used)</td>
<td>Levofloxacin OR Moxifloxacin</td>
<td>Darunavir/ritonavir (DRV/r) + DTG = 1–2 NRTIs (if possible, consider optimization using genotyping)</td>
</tr>
<tr>
<td>B</td>
<td>Add both medicines (unless they cannot be used)</td>
<td>Bedaquiline OR Linezolid</td>
<td>Cycloserine OR Terizidone</td>
</tr>
<tr>
<td>C</td>
<td>Add to complete the regimen and when medicines from Groups A and B cannot be used</td>
<td>Ethambutol OR Delamantidine OR Pyrazinamide</td>
<td>Isoniazid (INH) OR Streptomycin OR Ethionamide OR Pritroxicam OR Pyrazinamide</td>
</tr>
</tbody>
</table>

**Table 1. Grouping of medicines recommended for use in longer MDR-TB regimens**

- It appears that linzolid, bedaquiline and clofazimine have superceded injectables and ethionamide.

**Upcoming conferences**

MYCOCON 4th conference of Fungal Infection Study Forum, New Delhi, Sep 22-23. For details [www.fisftrust.org](http://www.fisftrust.org)
Answer to the photoquiz

Differential diagnoses included

<table>
<thead>
<tr>
<th></th>
<th>Bacterial Pneumonia</th>
<th>Fungal Pneumonia (Invasive Pulmonary Aspergillosis)</th>
<th>Pulmonary edema secondary to congestive cardiac failure</th>
<th>Daptomycin Lung toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+/-</td>
</tr>
<tr>
<td>Breathlessness</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Cough with expectoration</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Peripheral leukocytosis</td>
<td>-</td>
<td>-</td>
<td>+/-</td>
<td>+/-</td>
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<tr>
<td>Eosinophilia</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Lung Infiltrates</td>
<td>Consolidation</td>
<td>Dense consolidation</td>
<td>Intstitial</td>
<td>Intstitial</td>
</tr>
<tr>
<td>BAL Gram stain, Cultures &amp; PCR</td>
<td>Positive Gram &amp; Cultures</td>
<td>Positive KOH, Galactomannan Cultures</td>
<td>Negative cultures</td>
<td>Negative Cultures, May have pulmonary eosinophilic pneumonia</td>
</tr>
</tbody>
</table>

A possible diagnosis of daptomycin lung toxicity was considered and daptomycin was discontinued. Methyprednisolone 40 mg q 8hrly was started and aortic valvular replacement (AVR) was performed. Post discontinuation of daptomycin, repeat CXR showed resolution of infiltrates (Figure 3).

Figure 3: Resolution after discontinuation of daptomycin and steroids

While the exact mechanism of daptomycin toxicity is not known, possibilities include

1. chronic daptomycin administration results in drug accumulation near the epithelial alveolar surface causing epithelial injury and pneumonia
2. the daptomycin-surfactant interaction could alter lipid integrity which may stimulate an inflammatory response.

As use of daptomycin continues to increase, it is important for clinicians to recognize and appropriately manage daptomycin-induced lung toxicity.

**Final diagnosis**: (likely) Daptomycin induced pulmonary toxicity/eosinophilic pneumonia

*Case provided by: Ranjit Shah (ID Fellow), Sony Chawla, R Kasliwal (cardiology), Ahmer (cardiology), Yatin Mehta (critical care), NareshTrehan (CTVS), Neha Gupta (ID)*