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CIDS Newsletter

December 2015

CLINICAL INFECTIOUS DISEASES SOCIETY

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Editor's note

Dear CIDS members

The Annual CIDS PG CME at Vellore went off well and was attended by 54 postgraduates; this was very creditable as several faculty and delegates could not attend due to the Chennai floods at the same time. Congrats to Dr George M Varghese and his colleagues who organized the CME.

If any of you have had papers published in peer reviewed journals recently, please send me the details and I will be happy to mention it in the newsletter: this will be of great help for members to know of work going on in India and update themselves on issues relevant to their practice in India.

Similarly any quality paper you come across in the literature on ID issues in India can be brought to my notice, for being summarized in the Snippets from the Literature section.

Looking forward to your help to enhance the quality of our newsletter!

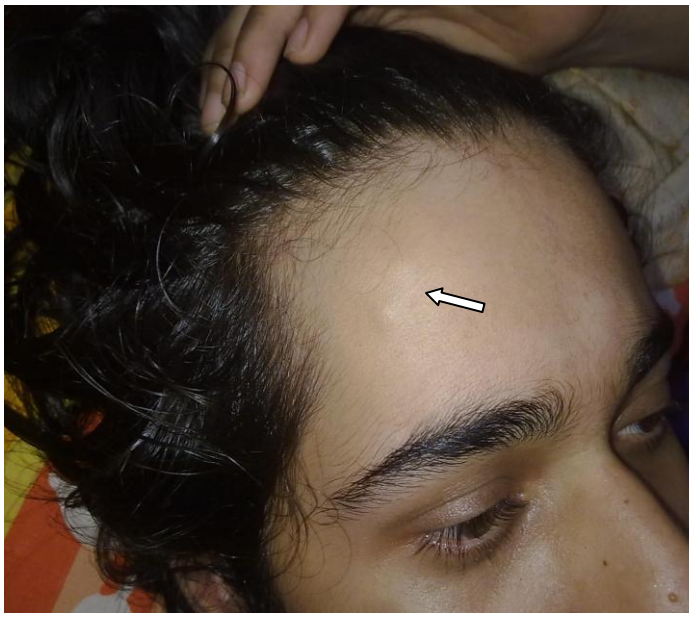
Sincerely

Ram Gopalakrishnan

Photo quiz

A 20/M presented with polyarthralgia, dyspnea on exertion and orthopnea for 15 days. WBC count was 27,000 (P88) and ESR was 100. Echo of the heart showed moderately severe mitral regurgitation.

A nodule was noticed on his forehead (photo).



What is your diagnosis?

New members

We welcome the following new members:

CIDS New members	
Dr. Preeti M Pillai	Maharastra
Dr. Mani Ram Kumhar	Rajasthan
Dr. Deepak Jeswani	Maharastra
Dr. R. Arul	Coimbatore
Dr. Veluri Gayathri	Visakhapatnam
Dr. Mukund Kulkarni	Karnataka
Dr. Falguni S Parikh	Maharastra
Dr. Sindhu Kaza	Karnataka
New Trainee Member: Dr. Vidya Krishna – Chennai	

News from ID world

Global fight against tuberculosis hinges on India stepping up funding: WHO

India is critical to the global fight to end an epidemic of tuberculosis by 2030 and must step up funding to control the disease, the World Health Organization said, citing concerns over broader cutbacks in government health programs. India is the world's TB hotspot as it accounts for 23% of global cases and the most deaths - 220,000 last year. An internal - assessment report in July showed India's TB program was off track due to funding problems New Delhi approved $243 million for TB control during 2012-2015, lower than the requested $432 million. India also needs to upgrade laboratories to better detect the disease - the government last year tracked down 25,000 of the WHO's estimated 47,000 multi-drug resistant TB cases.

GeneXpert available for children free of cost

(provided by Dr Madhukar Pai)

Clinicians can send pediatric (pulmonary and extrapulmonary) samples to one of the labs listed below, and get a GeneXpert TB test done free of cost.

NDTBC Delhi:

New Delhi Tuberculosis Centre,
Jawaharlal Nehru Marg,
Delhi Gate,
New Delhi – 110002
Contact No: 9899249176; 9990084944

IRL Hyderabad:

CBNAAT Lab
State TB Demonstration & Training Centre
Irramnuma, Beside Govt. General & Chest Hospital,
S.R Nagar, Hyderabad-500038
Contact No: +91-9985066444; +91-9160729988; +91-8886004786; +91-966632089

IRL Kolkata:

Intermediate Reference Laboratory, Kolkata
2nd Floor of Dr. B.C. Roy Post Graduate Institute for Paediatric Science,
38, Badan Roy Lane, Kolkata-700010
(Behind Beleghata ID Hospital Emergency Gate)
Contact No: Lab Coordinator, Mob : +91-9831282429

NIRT Chennai:

National Institute for Research in Tuberculosis,
(formerly Tuberculosis Research Center)
No.1, Sathyamoorthy Road, Chetput,
Chennai-600 031
Contact No: +91-9884408955

Intravenous minocycline now available in India

The US FDA recently approved a new formulation of intravenous minocycline for the treatment of Gram positive and Gram negative infections, including MDR Acinetobacter.

A generic version of the drug is now available in India as well.

Ledipasvir-sofosbuvir around the corner

A generic version of this combination regimen, which is superior to sofosbuvir alone, has been approved by the DCGI for marketing in India and should be available soon. This should further facilitate the treatment of hepatitis C infection.

First Dengue fever vaccine approved by Mexico

(provided by Dr Surabhi Madan)

A dengue fever vaccine has been approved for use by Mexico, for prevention of dengue in people in people 9-45 years old, living in endemic areas. In clinical trials, the vaccine reduced the risk of developing dengue by about 60%. The vaccine seems least effective in children younger than 9 (particularly those younger than 6), and may even increase their risk of having more serious disease in the long run (see CIDS newsletter November 2015). In one trial involving children 9 to 16 years, the vaccine reduced the risk of hospitalization from dengue by 80%

Snippet from literature

Are we under-dosing colistin?

Clin Infect Dis. (2015)doi: 10.1093/cid/civ964
First published online: November 25, 2015

The US Food and Drug Administration (FDA) and European Medicines Agency (EMA) have approved updated dose recommendations for intravenous colistin in patients with various degrees of renal function. This study assessed and compared both sets of recommendations in relation to their ability to achieve clinically-relevant plasma colistin concentrations. For patients with creatinine clearance <30mL/min, 100% of patients receiving the EMA dose achieved a colistin $C_{ss,avg}$ ≥1mg/L but attainment rate was as low as 53.1% for patients receiving the FDA-approved dose. For colistin $C_{ss,avg}$ ≥2mg/L, the attainment rates were 87.5% with the EMA dose but only 6.3-34.4% in patients receiving the FDA dose. For patients with creatinine clearance ≥80mL/min, only ~65-75% of patients achieved a colistin $C_{ss,avg}$ of ≥1mg/L with either set of recommendations.

Colistin is widely used in India. It appears that we may be under dosing colistin both in patients with creat cl<30 and >80 ml/mt, even following the higher doses suggested by the EMA. However nephrotoxicity may be an issue with higher doses (see below).

Table 1. Recently Updated EMA- and FDA-approved Daily Maintenance Dose Suggestions for Colistimethate in Patients with Various Degrees of Renal Function

Creatinine Clearance (mL/min)	EMA-approved Daily Dose[a]	FDA-approved Daily Dose[c]
≥80	9 MIU[b] (~300 mg CBA)	2.5-5 mg CBA per kg
50 - <80	9 MIU[b] (~300 mg CBA)	2.5-3.8 mg CBA per kg
30 - <50	5.5-7.5 MIU (~183-250 mg CBA)	2.5 mg CBA per kg
10 - <30	4.5-5.5 MIU (~150-183 mg CBA)	1 mg CBA per kg[d]
<10	3.5 MIU (~117 mg CBA)	Not stated

Colistin-associated Acute Kidney Injury in Severely Ill Patients: A Prospective Cohort Study

Clin Infect Dis. (2015) 61 (12):1771-1777.

This study used a loading dose of 12mu followed by 9mu daily, targeting a concentration of 2.5 mg/L even though the (MIC_{50}) and MIC_{90} was 0.5/2 mg/L for *Acinetobacter baumannii*, 2/2 mg/L for *Pseudomonas aeruginosa*, and 1/1.5 mg/L for *Klebsiella pneumonia*e. The clinical success rate was 77% but the incidence of AKI was high (44%). Intravenous ascorbic acid was highly protective against nephrotoxicity (odds ratio, 0.27).

Even the modest doses, in relation to the high MIC of the target organisms, caused a high incidence of nephrotoxicity.

Plasmid-Mediated Colistin Resistance in Animals and Humans in China

Lancet Infect Dis 2015 Nov 18

Prompted by an observed increase in colistin resistance in isolates from food animals in China, investigators sought the mechanism. They ultimately identified plasmid-mediated colistin resistance (MCR-1) in *Escherichia coli* from a pig. Upon screening isolates from five Chinese provinces, they found the *mcr-1* gene in 21% of 804 *E. coli* isolates in pigs at slaughter; in retail meat (22% of pork and 28% of chicken isolates in 2014); and in 1% of 1322 *E. coli* and *Klebsiella pneumoniae* clinical isolates from human inpatients in southern China. Laboratory studies documented the transfer of colistin resistance from one *E. coli* strain to another and, also, to *K. pneumoniae* and *Pseudomonas aeruginosa*.

Previously, colistin resistance was attributed to chromosomal mutations and was not known to disseminate widely. The authors postulate that *mcr-1*–mediated colistin resistance originated in animals and then spread to humans. China is one of the world's highest agricultural users of colistin, and this clearly needs to be curtailed. Just like NDM-1 spread worldwide from the Indian subcontinent, the implications for India, if this mechanism of resistance spreads here, are truly frightening.

Asymtomatic bacteriuria in pregnancy: treatment needed?

Lancet Infect Dis. 2015;15(11):1324–1333

The current study used a prospective cohort design with an embedded randomized controlled trial and enrolled 5621 women into the screening cohort, of whom 5132 were eligible for screening. In the randomized trial, 40 pregnant women with asymptomatic bacteriuria self-administered 100 mg of nitrofurantoin, and 45 women were given placebo, both for five days. Actively treated women had a similar outcome compared with placebo-treated or untreated women (2.5 percent vs. 2.9 percent). All women who developed pyelonephritis had a mild and uncomplicated disease course.

Results showed that asymptomatic bacteriuria was not associated with preterm birth. Asymptomatic bacteriuria showed a significant association with pyelonephritis, but the absolute risk of pyelonephritis in untreated asymptomatic bacteriuria was low (2.4%).

These findings question a routine screen-treat-policy for asymptomatic bacteriuria in pregnancy, a long held dogma.

Subclavian site best for central venous catheterization?

N Engl J Med. 2015;373:1220-1229

The multicentered trial randomized patients on a 1:1:1 basis for the subclavian, jugular, or femoral vein; or 1:1 basis if one of the sites was deemed not suitable. The primary endpoint was a composite of catheter-related bloodstream infection and symptomatic deep vein thrombosis and occurred with the subclavian group at a lower hazard ratio

compared to either the jugular site (2.1, P=0.04) or the femoral site (3.5, P=0.003). Mechanical complications were noted to a greater extent in the subclavian arm, 18 vs. 12 in the jugular arm, and six in the femoral arm.

If you can avoid a pneumothorax, the subclavian site seem to be the way to go.

Artefenomel: a promising new antimalarial drug

Lancet Infect Dis. 2015; (published online Oct 5.) http://dx.doi.org/10.1016/S1473-3099(15)00320-5.

This phase 2a exploratory, open-label trial was done on adult patients with acute, uncomplicated *P falciparum* or *P vivax* malaria received artefenomel in a single oral dose (200 mg, 400 mg, 800 mg, or 1200 mg). All doses were equally effective in both *P falciparum* and *P vivax* malaria, with median parasite clearance half-lives of 4·1 h (range 1·3–6·7) to 5·6 h (2·0–8·5) for *P falciparum* and 2·3 h (1·2–3·9) to 3·2 h (0·9–15·0) for *P vivax*.

Key advantages of artefenomel are its lack of reliance on natural product starting materials, ease of synthesis, excellent absorption, distribution, metabolism, and excretion (ADME) properties, and, in limited studies, apparent safety and antimalarial efficacy. Patients infected with artemisinin-resistant parasites (based on genotypes) cleared parasitaemia slightly (but not significantly) more slowly than did those infected with sensitive parasites, a result that is better than would be expected for artemisinins. However, with limited available data it remains uncertain whether artefenomel will circumvent artemisinin resistance.

Guideline watch

IDSA guidelines on Candidemia published

http://m.cid.oxfordjournals.org/content/early/2015/12/15/cid.civ933.full?papetoc

Upcoming ID conferences and CME programs

CIDS endorsed ID CME

Jan 23-24, Nagpur
Contact Dr Ashwini Tayade drashwini.tayade@gmail.com

17th International Congress on Infectious Diseases (ICID)

March 2-5, 2016, Hyderabad
http://www.isid.org/icid/

Miscellaneous

A message from Dr PH Chandrasekar

Dr Chandrasekar says *"It has become routine for many journals to charge authors to publish their work. Below is a typical example. Almost every week, like me, am sure you're getting these requests, many from India. Investigators/authors, particularly junior ones, get trapped in this game, and desperate to get their paper published, are prepared to pay money to sub-standard/unknown journals. It may be worthwhile to let our members know to avoid this trap."*

INTERNATIONAL JOURNAL OF ADVANCES IN CASE REPORTS
http://www.mcmed.us/current/ijacr

Book available

(provided by Dr Madhukar Pai)

Let's Talk TB: book on tuberculosis, available online

Please see this website: http://www.letstalktb.org/

This book is a supplement to GP Clinics, an effort to engage and educate GPs and private practitioners, and to share with them the current best practices on TB diagnosis and treatment.

Several authors have contributed to this effort, and several partners have collaborated to produce this book.

Answer to photo quiz

The photo shows the subcutaneous nodules of rheumatic fever. His ASO titer was 15,000 Todd units. He fulfilled Jones criteria for acute rheumatic fever.

Diagnosis: Acute rheumatic fever.

(case provided by Dr Senthur Nambi).