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CIDS Newsletter

December 2016

CLINICAL INFECTIOUS DISEASES SOCIETY

Editor's note

Dear CIDS members

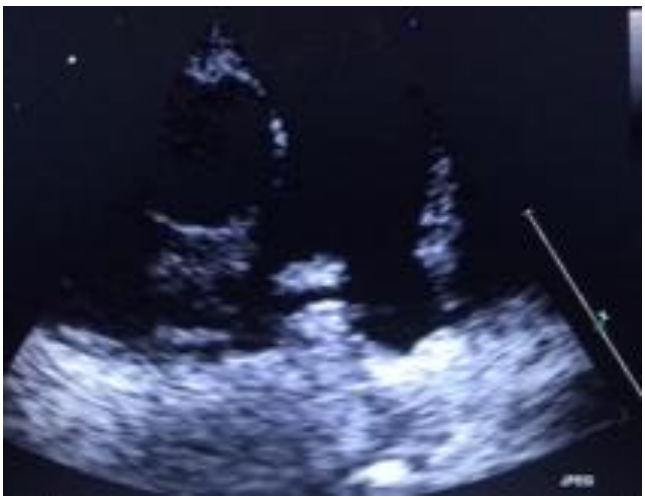
Please encourage your postgraduates and physicians within 3 years of graduation to attend the annual CIDS PG CME at CMC, Vellore on Dec 8-10.

Sincerely

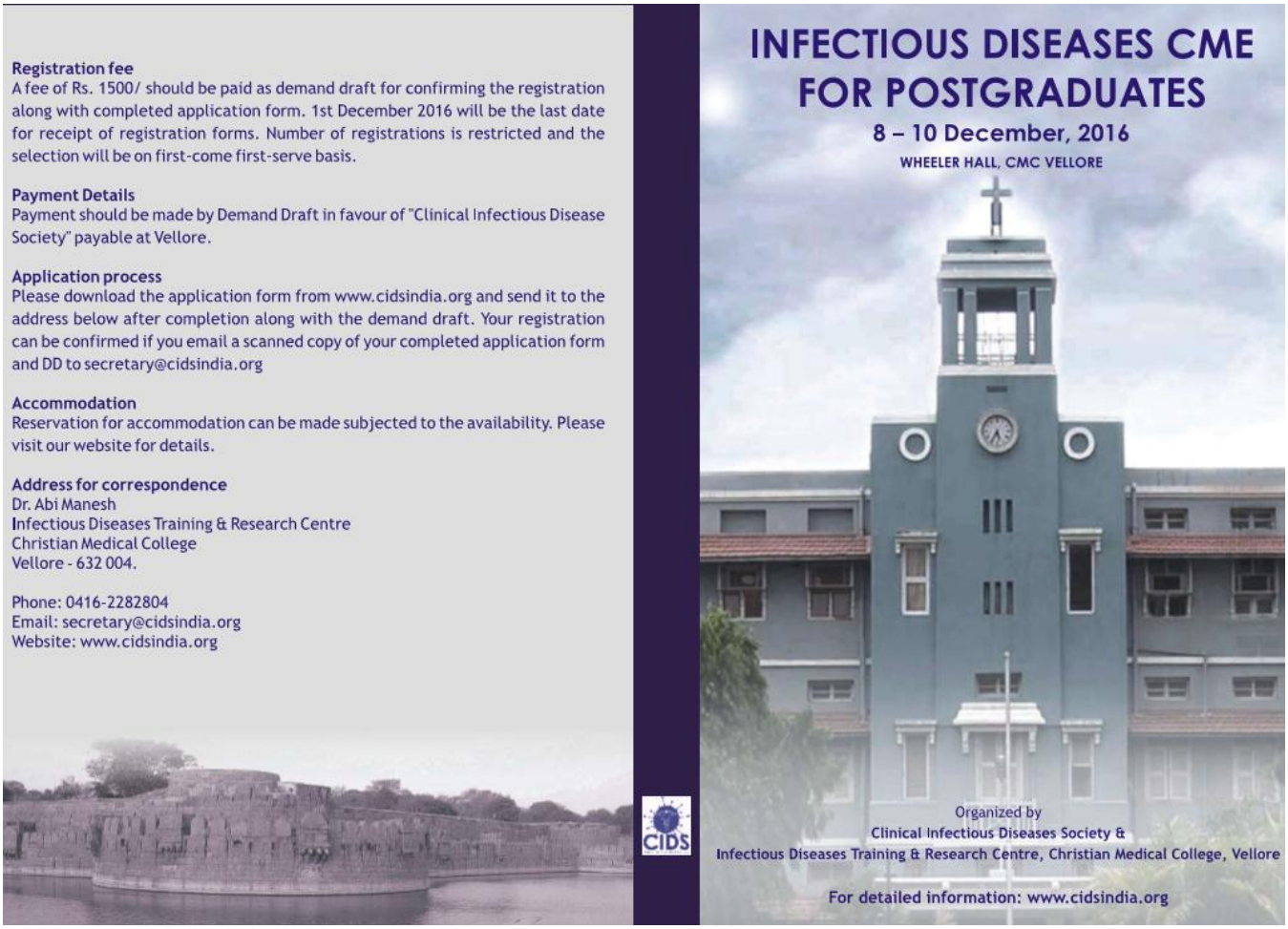
Ram Gopalakrishnan

Photo quiz

A 14 year-old boy from Haryana presented with gradual onset fever and mild myalgia of one month duration. The patient on enquiry had a history of very close contact with cattle at home. He was admitted elsewhere where there was no response to ceftriaxone which was administered for 7 days. On examination-there was hepato-splenomegaly. Investigations revealed Hb-1.6 gm%, WBC-2,210 (with Platelets- 1, 55,000 on admission. Echo revealed vegetation at the bifurcation of the pulmonary artery (Figure 1). His Weil Felix test revealed OX 2-1:160 while OX K and OX 19 were non reactive



What is your diagnosis?



News from the ID world

Pneumococcal vaccine introduced in children

Union Health Minister J.P. Nadda approved the introduction of the Pneumococcal Conjugate Vaccine (PCV) under the Universal Immunization Programme to be implemented in five states, in a planned manner from 2017. The states, where it will be introduced, are Bihar, Uttar Pradesh, Rajasthan, Himachal Pradesh and Madhya Pradesh.

This vaccine should have been a part of the UIP throughout the country as a 7 valent formulation many years ago, as per WHO guidelines. Better late than never, even if only in five states.

Bezlotoxumab, a monoclonal antibody for treatment of *Clostridium difficile*

Zinplava (bezlotoxumab) was approved October 2016 by the US FDA for recurrent *Clostridium difficile* infection (CDI) in patients receiving antibacterial treatment. Bezlotoxumab is a monoclonal antibody that binds *C. difficile* toxin B and neutralizes its effect. The goal of this medication is to reduce recurrence of CDI who are 18 years or older and receiving antibiotics for CDI and at high risk for CDI recurrence. Two phase III trials led to the drug's approval: MODIFY I and II. 1,452 patients from 19 countries were enrolled in MODIFY I, and 1,203 patients from 17 countries in MODIFY II. In each study, patients receiving stand-

-ard antibiotics for CDI were randomized to receive a single one-time infusion of bezlotoxumab, bezlotoxumab and actoxumab, or placebo (the actoxumab arm was stopped for efficacy and safety reasons).In both studies, the rate of CDI recurrence through week 12 was significantly lower in the bezlotoxumab arms (17.4%, p<0.0003 and 15.7%; p=0.0003) and the combination bezlotoxumab and actoxumab arms (15.9%, p<0.0001), compared to the placebo arms (27.6% and 25.7%), respectively. Potential adverse effects include nausea, pyrexia, and headache; the medication should be used cautiously in patients with a history of heart failure.

Bezlotoxumab provides another treatment option for patients at high risk for, or experiencing, recurrent *C difficile* infection.

Meningococcal conjugate vaccination for HIV-infected patients

(courtesy Dr Surabhi Madan)

Growing evidence has suggested that HIV-infected individuals have a disproportionate incidence of invasive meningococcal disease, with an estimated risk 5 to 13 times that of the general population. Because of this, the Centers for Disease Control and Prevention in the United States now recommends meningococcal conjugate vaccination (with MenACWY-CRM [Menveo] or MenACWY-D [Menactra]) for all HIV-infected individuals older than two months. This includes a primary vaccine series for those who have not previously received it and interval booster doses every several years; the precise schedule depends on the age of the patient.

Snippets from the literature

Benefits and Risks of Antiretroviral Therapy for Perinatal HIV Prevention

(courtesy Dr Surabhi Madan)
N Engl J Med 2016; 375:1726-1737

The PROMISE trial randomly assigned HIV-infected women at 14 or more weeks of gestation with CD4 counts of at least 350 cells per cubic millimeter to zidovudine and single-dose nevirapine plus a 1-to-2-week postpartum "tail" of tenofovir and emtricitabine (zidovudine alone); zidovudine, lamivudine, and lopinavir–ritonavir (zidovudine-based ART); or tenofovir, emtricitabine, and lopinavir–ritonavir (tenofovir-based ART). The primary outcomes were HIV transmission at 1 week of age in the infant and maternal and infant safety. Antenatal ART resulted in significantly lower rates of early HIV transmission than zidovudine alone but a higher risk of adverse maternal (anemia, renal injury) and neonatal (pre-term delivery and early neonatal death) outcomes.

WHO recommended efavirenz based regimens are not associated with the neonatal adverse effects seen with PI based regimens in pregnancy.

Isolated orbital aspergillosis in immunocompetent patients

Am J Ophthalmol 2016; 165:125–132.
doi:10.1016/j.ajo.2016.03.007.

The authors identified 8 apparently immunocompetent patients with orbital aspergillosis in the absence of a contiguous source over a 10-year period at 5 centers in India and one in Singapore.

Infection was unilateral in all. Symptoms were present for 0.5–18 months prior to presentation with, in 4 each, either swelling of the upper eyelid or proptosis. One had swelling of the lower as well as the upper eyelid, 2 also had diplopia, and one had ptosis. Mild to severe restriction of ocular motion was present in all 8 patients and a nontender, nonreducible, noncompressible mass was present in 2. All 8 had intact visual acuity, color vision, and pupillary reactions. The paranasal sinuses and nasal cavity were uninvolved in all 8. Culture was performed only in the single patient in whom fungal infection was clinically suspected, yielding *Aspergillus fumigatus*. The 2 patients who underwent excision did not receive antifungal therapy. The other 6 received therapy for

at least 2 months; all received an azole with one also initially receiving amphotericin B for 3 weeks. All patients had resolution of proptosis and ocular dysmotility.

Effect of Cranberry Capsules on Bacteriuria Plus Pyuria Among Older Women in Nursing Homes: A Randomized Clinical Trial

(courtesy Dr Surabhi Madan)
JAMA. 2016;316(18):1879.

Numerous clinical studies on the effects of cranberry products on recurrent urinary tract infection (UTI) in women have failed to clearly demonstrate a preventive benefit. In a year-long randomized trial among female nursing home residents, cranberry capsules similarly did not reduce adjusted rates of bacteriuria plus pyuria or symptomatic UTI compared with placebo. On the other hand, there was likely little harmful effect.

Cranberry juice appears to be a breakfast drink only!

Prognostic Value of Transient Elastography in Human Immunodeficiency Virus-Infected Patients With Chronic Hepatitis C

(courtesy Dr Amarjit Singh Vij)
Open Forum Infect Dis 2016;3(4):ofw212.

The prognostic value of liver stiffness (LS) in HIV-infected patients with chronic hepatitis C (CHC) has been studied HIV-infected patients with compensated CHC and at least 1 determination of LS were analyzed.

The primary outcome was the occurrence of liver-related events (LRE), namely, decompensation or hepatocellular carcinoma, whichever occurred first. The patients without sustained viral response (SVR) or end-of-treatment response (ETR) during follow-up were selected for this study and allocated to an estimation cohort (EC) and a validation cohort (VC).The study population comprised 1292 patients. After a median follow-up of 5.8 years, 90 patients experienced LRE and 73 died. In the subgroup of 957 patients without SVR or ETR, the area under the receiver operating characteristic curves (AUROCs) (95% confidence interval [CI]) of LS for prediction of LRE in the EC (n = 634) and the VC (n = 323) were 0.87 and 0.88, respectively. The best cutoff value of LS to rule out LRE in the EC was 12 kPa, with a negative predictive value of 98.3% in the EC and 98.2% in the VC. Per each 1 kPa and 5 kPa increase above 12 kPa, the hazard ratio of LRE (taking into account death as a competing risk) was 1.07 (95% CI, 1.05-1.08) and 1.38 (95% CI, 1.31-1.46), respectively.

This study concludes that liver stiffness is very accurate for predicting LRE in coinfected patients. Patients with an LS <12 kPa had a 98% probability of not developing LRE after a median follow-up of almost 6 years. Above the 12-kPa cutoff, the hazard of LRE increases proportionally with LS.

Guideline watch

Diagnosis and Treatment of Leishmaniasis: Clinical Practice Guidelines by the Infectious Diseases Society of America (IDSA) and the American Society of Tropical Medicine and Hygiene (ASTMH)

(courtesy Dr Surabhi Madan)

http://cid.oxfordjournals.org/content/early/2016/11/03/cid.ciw670.full

Chandra's Corner

(courtesy Dr PH Chandrasekar)

Notes from the United States

Colleagues,

Warm greetings.

I was hoping to see a positive or negative response from the leadership/readership to my comments on the status quo of the CIDS Annual Meetings. Of course, silent majority prevailed – there was no comment despite the urging from the CIDS President. Active participation is a sign of healthy ownership, let us build together a community of interested and motivated Infectious Diseases activists/physicians in India.

2016 is wrapping up fast. We have moved past ICAAC and IDSA. Diwali and Thanksgiving are over, Christmas is just around the corner. At the IDSA, I was impressed to see the quality and number of presentations/participants from India. This is a palpable change from just about five years ago. I hope the trend continues to improve. At the Meetings, many hours were spent on Zika infection attracting a great deal of attention. The promise of three forms of vaccine in such a short period is truly amazing. I wonder if the speed of progress would have been the same, had the epidemic primarily hit less affluent parts of our world. Zika may have already hit India. Perhaps one of the readers of this column should start looking for serological changes in a systematic manner in appropriate clinical settings?

Looking back as 2016 folds, there have been eight new antibiotics approved by the US FDA since 2010, well on our way towards the goal "10 x 20 initiative" by the IDSA that called for the release of 10 new antibiotics by 2020. Four new drugs have been approved for skin infections (ceftaroline, dalbavancin, oritavancin and tedizolid), two for complicated intraabdominal and urinary tract infections (ceftolozane-tazobactam, ceftazidime-avibactam), one for Clostridium difficile infection (fidaxomicin) and one for drug-resistant tuberculosis (bedaquiline); ceftaroline was also approved for community-acquired pneumonia. All except bedaquiline are members of established drug classes. Almost all the drug approvals were based on non-inferiority trials in fewer than 1000 patients, certainly not ideal studies. Prices of these drugs are much higher than the comparator drugs. A recent article in the Annals of Internal Medicine (2016, May 31) nicely summarized the data –"recently approved antibiotics generally have been lacking in biological innovation or public health importance". They criticized the "me-too" pattern of drug development. I hope the Indian authorities will take note and evaluate these drugs before approval and widespread adoption.

A book I highly recommend is, "When Breath Becomes Air". I purchased the book at one of the Indian airports for Rs 600; this is a book that cannot be forgotten anytime soon. Dr OC Abraham and I, while waiting at the New Delhi airport after 2016 CIDS, were offering high praise for this book. The writing is superb with an introduction by the well-known ID physician, Dr. Abraham Varghese. It is the biography of a neurosurgeon named Paul Kalanithi who at the young age of 36 years, during the final year of his residency, is diagnosed with stage IV lung cancer. The subject matter is compelling enough and gut wrenching, but the masterful use of the English language by Paul is pure gold. It is a must read for every physician, no, every human. I plan to give a copy to my daughter on her birthday.

I wish you all a Happy Holiday Season.

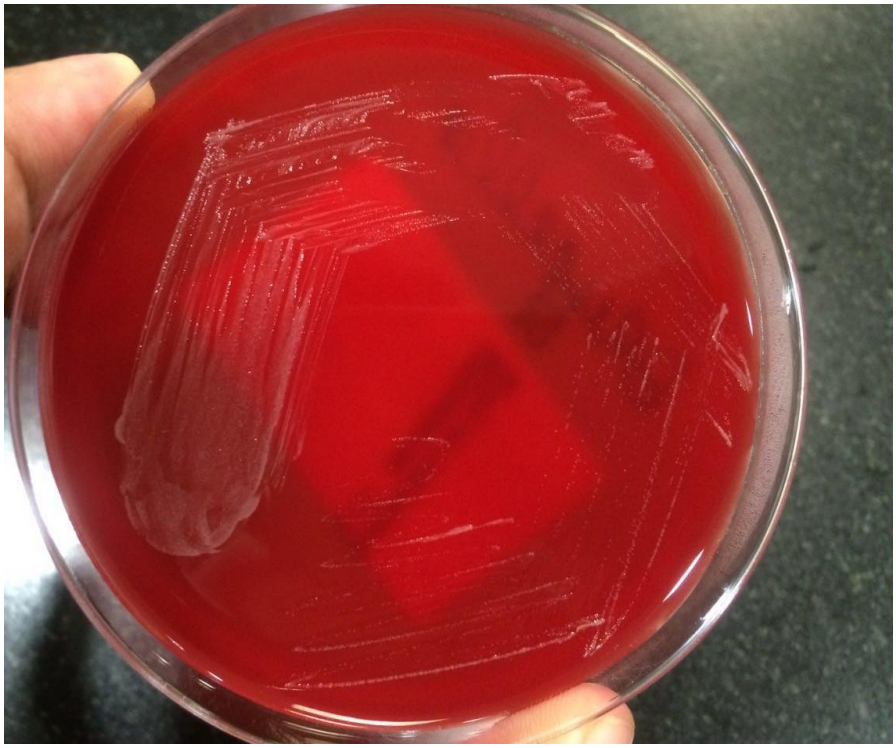
Upcoming meetings and conferences

CIDS Annual PG CME
8-10, December, Vellore
Contact secretary@cidsindia.org

NATCON 2016
16-18 December, PGI, Chandigarh
71st National Conference on Tuberculosis and Chest Diseases (NATCON 2016), under the joint auspices of the Tuberculosis Association of India and the Tuberculosis Association of U.T. Chandigarh along with the Department of Pulmonary Medicine, Postgraduate Institute of Medical Education & Research (PGI, Chandigarh) and the Academy of Pulmonary Sciences (APS)
http://www.natcon2016.in/

Answer to photo quiz

All three sets of blood cultures were positive for Brucella melitensis (Figure). The patient was started on doxycycline, streptomycin and rifampicin and was doing well on follow up.



Final diagnosis: Infective endocarditis caused by Brucella melitensis
(case provided by Dr Neha Gupta)