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CLINICAL INFECTIOUS DISEASES SOCIETY

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Editor's note

Dear CIDS members

We in the ID community are waiting anxiously for the arrival of epidemic viruses like Ebola, enterovirus 68, polio and MERS-CoV in India (hopefully we will wait forever!). The infection control aspects of these viruses (especially Ebola) is very challenging and will surely require our expertise and input in both the private and public sectors.

A new resource to stay updated on disease outbreaks in South Asia is available: the International Society for Infectious Diseases has launched ProMED-SoAs, a free Internet-based reporting system for news and information on emerging and reemerging disease events occurring in South Asia.

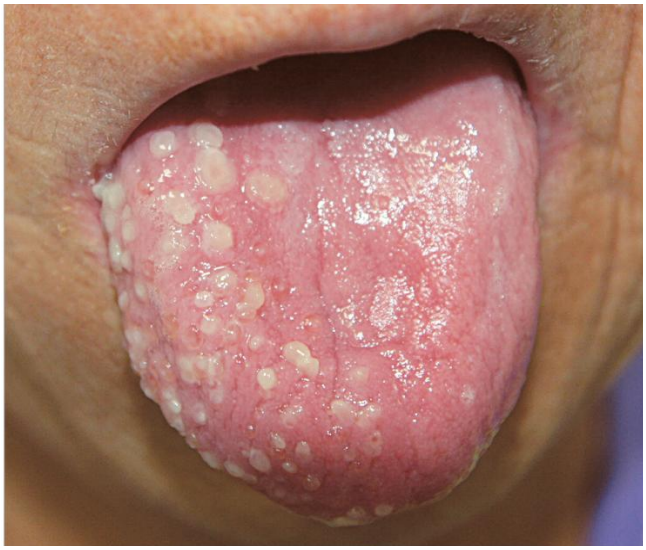
Interested members can subscribe at
http://ww4.isid.org/promedmail/subscribe.php

Sincerely
Dr Ram Gopalakrishnan

Photo Quiz

A 72 year old female presented with pain and lesions over the tongue.

What is your diagnosis?



News from the ID world

Annual dengue incidence in India: 20,000 or 6 million?

Am J Trop Med & Hygiene 2014-0002; Published online October 6, 2014,doi:10.4269/ajtmh.14-0002

Between 2006 and 2012 India reported an annual average of 20,474 dengue cases. Although dengue has been notifiable since 1996, regional comparisons suggest that reported numbers substantially underrepresent the full impact of the disease. Adjustment for underreporting from a case study in Madurai district and an expert Delphi panel yielded an annual average of 5,778,406 clinically diagnosed dengue cases between 2006 and 2012, or 282 times the reported number per year. The total direct annual medical cost was US$548 million. Ambulatory settings treated 67% of cases representing 18% of costs, whereas 33% of cases were hospitalized, comprising 82% of costs. Eighty percent of expenditures went to private facilities. Including non-medical and indirect costs based on other dengue-endemic countries raises the economic cost to $1.11 billion, or $0.88 per capita.

Most of us see a lot of dengue as inpatients and outpatients. The authors conclude that the economic and disease burden of dengue in India is substantially more than captured by officially reported cases, and increased control measures merit serious consideration.

Influenza Vaccine Composition for the 2014–15 Season

For 2014–15, influenza vaccines will contain the same vaccine virus strains as those in the 2013–14 vaccine. Trivalent influenza vaccines will contain hemagglutinin (HA) derived from an A/California/7/2009 (H1N1)-like virus, an A/Texas/50/2012 (H3N2)-like virus, and a B/Massachusetts/2/2012-like (Yamagata lineage) virus. Quadrivalent influenza vaccines will contain these antigens, and also a B/Brisbane/60/2008-like (Victoria lineage) virus: at the present time the quadrivalent vaccine is not being marketed in India.

HCV treatment continues to get easier (but costlier)

The US FDA just approved the first single-pill treatment for hepatitis C genotype 1, a tablet containing 400 mg of sofosbuvir (SOF) and 90 mg of ledipasvir (LDV). No interferon or ribavirin addition is needed even in cirrhotics. For most patients, 12 weeks of therapy will have a 95%+ chance of cure. For treatment-naive patients without cirrhosis who have a pretreatment HCV RNA level < 6 million copies/mL, just 8 weeks is enough. The list price of this combination therapy for 12 weeks will be around $95,000.

No need to isolate MRSA?

JAMA 2014; 312:1395

MRSA is common in US hospitals. Some US hospitals are challenging the conventional dogma that mandates contact isolation for all patients colonized with MRSA, and have recently discontinued contact isolation for these patients. The rationale is that most MRSA infections arise from the patient's own organisms and only 20% of infections can be attributed to patient-patient transmission. Proponents of this approach favor horizontal measures such as increasing hand hygiene

rates and chlorhexidine bathing, rather than contact isolation. There was an interesting debate at the recently concluded ID Week conference on this issue. Indian hospitals will have to figure out their best strategy, given their problems are predominantly gram negative and the relative lack of efficacy of chlorhexidine against gram negative bacteria.

What's new and going around

Currently India is yet to import (hopefully surveillance is accurate!) some of the epidemic viruses going around worldwide:

-Ebola virus: The epidemic continues in Sierra Leone and Guinea but Nigeria and Senegal have been declared free of virus and new cases are fewer in Liberia. Mali has had one case, and the USA and Spain have reported two and one patient-health care worker transmission respectively.

-Enterovirus D68: Between Aug 8 and Oct 8, 2014, 30 cases of respiratory illness with neurological complications in children were reported in nine US states and 13 other cases were reported in three Canadian provinces. During the same period, 628 children who had developed severe respiratory symptoms that needed admission to hospital or paediatric intensive care units tested positive for the virus both in the USA (44 states) and Canada (three provinces). Children with asthma typically are involved, with severe respiratory illness and associated muscle weakness and paralysis.

-MERS-COV: New cases continue to be reported sporadically from Saudi Arabia with one new case from Turkey. 774 laboratory-confirmed cases of MERS-CoV infection, including 329 deaths have been reported in all.

-Polio: Our neighbor Pakistan continues to have cases especially on the border states with Afghanistan, and thanks to intensified surveillance at the border areas and mandatory vaccination for visitors, no cases in India have been reported.

Trichinellosis outbreak in north India

Indian J Med Res 140, September 2014, pp 414-419

Three index cases presenting as acute febrile myalgia syndrome with eosinophilia in a village in Tehri Garhwal district of Uttarakhand state.

Twin outbreak of cholera in rural North Karnataka, India

Indian J Med Res 140, September 2014, pp 420-426

While 101 people (0.38%) were affected in Talikoti, 200 (20.94%) were affected in Harnal. A single clone of toxigenic Vibrio cholerae O1 Ogawa biotype El Tor was isolated from stool samples.

Snippets from the literature

Kawasaki disease due to fungi?

(courtesy Dr Arunaloke Chakrabarti)

Proceedings of the National Academy of Sciences of the United States of America, PMID: 24843117

http://blogs.scientificamerican.com/artful-amoeba/2014/05/25/kawasaki-disease-traced-to-winds-from-northeast-china-carrying-unusual-fungal-load/

This paper describes a connection between unusual loads of Candida in air samples over China and Kawasaki disease. Candida has never been found in environmental samples earlier and changing agricultural practices may be responsible.

An Indian study on inactivated polio vaccine after oral to enhance immunity

Lancet 2014 Jul 11;

Researchers hypothesized that sequential OPV followed by IPV might boost immunity in children older than age 12 months by stimulating immune cells that are already primed to produce anti-polio antibodies. They studied 450 Indian children (age 1 to 4 years) who had received at least five doses of trivalent OPV ending at least 6 months previously. Half of the children were given a dose of IPV; the rest received no vaccine. All received a dose of bivalent OPV (bOPV, serotypes 1 and 3) 28 days later.

Seven days after the challenge dose of bOPV, 12% of IPV recipients shed serotype 1 poliovirus and 8% shed serotype 3; in the no-vaccine group, 19% and 26% shed serotypes 1 and 3, respectively. The differences between the groups were highly statistically significant. In addition, the mean titers of neutralizing antibodies were significantly higher in the IPV group than in the no-vaccine group who later received OPV. Thus, IPV given more than 6 months after the last OPV dose substantially increased both humoral and intestinal immunity to poliovirus.

Orbital aspergillosis in the immune competent host

Br J Ophthalmol 2014; doi:10.1136/bjophthalmol-2013-303763.

This case series of 35 immune competent patients comes from Hyderabad. The infection involved both sinus and orbit in 30 (86%) cases, and intracranial extension was identified in 10 (29%). Cultures yielded *Aspergillus flavus* in 30 (86%) cases and *Aspergillus fumigatus* in the remaining 5 (14%). Patients were managed with a combination of debulking and antifungals (amphotericin followed by voriconazole or itraconazole). Vision improved in 69% of patients.

Short intensified treatment in children with drug-susceptible tuberculous meningitis.

Pediatr Infect Dis J 2014; 33:248–52.

WHO recommends that patients with tuberculous meningitis receive chemotherapy for 9–12 months. In 184 children, the safety and efficacy of a shorter course of treatment in children with tuberculous meningitis in South Africa was assessed. Treatment consisted of 6 months of isoniazid 20 mg/kg (maximum 400 mg daily), rifampin 20 mg/kg (maximum 600 mg daily), pyrazinamide 40 mg/kg (maximum 2 g daily), and ethionamide 20 mg/kg (maximum 750mg daily), all given in a single daily administration, for 6 months' duration. Treatment was extended to 9 months in HIV infected children. Prednisone 2 mg/kg/day (maximum 60 mg/day) was administered for 1 month and then tapered over 2 weeks.

Among the 157 patients who received post treatment follow up, there were no relapses. Overall mortality was 3.8% It should be noted, however, that this regimen differed from the usual recommended regimens with regard to higher doses of some the drugs and in the use of ethionamide in place of ethambutol.

Prednisolone and *Mycobacterium indicus pranii* in Tuberculous Pericarditis

N Engl J Med 371:1121, September 18, 2014

This study from Africa randomly assigned 1400 adults (2/3 were HIV positive) with definite or probable tuberculous pericarditis to either prednisolone or placebo for 6 weeks and to either *M. indicus pranii* or placebo, administered in five injections over the course of 3 months. The primary efficacy outcome was a composite of death, cardiac tamponade requiring pericardiocentesis, or constrictive pericarditis.

There was no significant difference in the primary outcome between patients who received prednisolone and those who received placebo (23.8% and 24.5%, respectively) or between those who received *M. indicus pranii* immunotherapy and those who received placebo. However prednisolone therapy, as compared with placebo, was associated with significant reductions in the incidence of constrictive pericarditis (4.4% vs. 7.8%; hazard ratio, 0.56; P=0.009) and hospitalization (20.7% vs. 25.2%; hazard ratio, 0.79; P=0.04).

Steroids don't seem to be automatically indicated for TB pericarditis, especially if the patient is HIV positive.

Time to bury thrice weekly regimens for TB in HIV infected patients

Clin Infect Dis published 25 August 2014, 10.1093/cid/ciu674
Clin Infect Dis 2014 59: e142-e149

This study from the National Institute for Research in Tuberculosis, Chennai showed that HIV-infected patients with tuberculosis treated with a thrice-weekly antituberculosis regimen are at a 21 fold higher risk of acquired rifampicin resistance in the absence of HAART and an 8 fold higher risk even if HAART started.

Another study from the same group showed that a 5-drug daily regimen of moxifloxacin, rifampicin, isoniazid, pyrazinamide, and ethambutol resulted in significantly higher sputum culture conversion at 2 months compared with thrice-weekly rifampicin, isoniazid, pyrazinamide, and ethambutol in newly diagnosed, sputum-positive, HIV-uninfected pulmonary tuberculosis patients. Late relapse rates were not analyzed.

Hopefully national programs will be changed to conform to WHO guidelines recommending daily therapy for at least the first two months of therapy.

A Four-Month Gatifloxacin-Containing Regimen for TB

N Engl J Med 2014; 371:1588-1598

A standard 6-month regimen that included ethambutol during the 2-month intensive phase was compared with a 4-month regimen in which gatifloxacin (400 mg per day) was substituted for ethambutol during the intensive phase and was continued, along with rifampin and isoniazid, during the continuation phase. The primary efficacy end point was an unfavorable outcome (treatment failure, recurrence, or death or study dropout during treatment). The standard regimen, as compared with the 4-month regimen, was associated with a higher dropout rate during treatment (5.0% vs. 2.7%) and more treatment failures (2.4% vs. 1.7%) but fewer recurrences (7.1% vs. 14.6%). There was no evidence of increased risks of prolongation of the QT interval or dysglycemia with the 4-month regimen.

It appears gatifloxacin is safe but short courses than 6 months carry higher relapse rates. An accompanying editorial attributes relapse with short course quinolones to the fact that concentrations of quinolones are markedly lower in the caseum of caseating granulomas — where persisting bacilli are found to lurk.

Effect of therapeutic lumbar punctures on acute mortality from cryptococcal meningitis

Clin Infect Dis published 23 July 2014

248 individuals with human immunodeficiency virus (HIV)-associated cryptococcal meningitis, screened for the Cryptococcal Optimal ART Timing (COAT) trial in Uganda and South Africa, were observed. Seventy-five (30%) individuals had at least 1 therapeutic LP. Thirty-one deaths (18%) occurred among 173 individuals without a therapeutic LP and 5 deaths (7%) among 75 with at least 1 therapeutic LP. Therapeutic LPs were associated with a 69% relative improvement in survival, regardless of initial intracranial pressure.

Should we routinely do a second therapeutic LP for patients with cryptococcal meninigitis, regardless of clinical status?

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Guideline watch

NCDC guidelines for Ebola Virus Disease in India
http://nicd.nic.in/index1.asp?linkid=265

US CDC guidelines on Antimicrobial Stewardship
http://www.cdc.gov/getsmart/healthcare/implementation/core-elements.html

Upcoming conferences and meetings

Transplant Infectious Disease Conference
6-8 November, Vellore
Contact Dr Priscilla Rupali (prisci@cmcvellore.ac.in)

7th World Workshop on Oral Health and Disease in AIDS.
6-9, Nov 2014, Hyderabad
info@ww7india.com, ww7india@gmail.com

3rd Biennial Conference of HIV Medicine Association of India (HIVMAI)
8th-9th November 2014, India International Centre, New Delhi
http://hivmai.org/hivmai/node/4052

First Conference of Fungal Infection Study Forum (FISF) and Mycology Master Class
Kolkata 14-16 Nov 2014
http://www.fisftrust.com

Antimicrobial Stewardship Course, New Delhi, (endorsed by CIDS) Nov 27-28th
Pre-conference workshop of IAMM Delhi chapter annual conference in November, conducted by BSAC (British Society of Antimicrobial Chemotherapy) GARP and Delhi Chapter of Indian Association of Medical Microbiology

CIDS Annual Postgraduate Course in Infectious Disease
11-13 December, CMC, Vellore.
Contact Dr George M Varghese (secretary@cidsindia.org)

Answer to photo quiz

Herpes zoster (lingual).

The ulcers follow a unilateral distribution and do not cross the midline.