Volume 4, Issue 1

CIDS Newsletter

January 2017

CLINICAL INFECTIOUS DISEASES SOCIETY

Editor's note

Dear CIDS members

Wishing you all a Happy New Year.

Please note the dates of CIDSCON: 25-27 August.

Sincerely

Ram Gopalakrishnan

Photo quiz

A 33/F, a kidney transplant recipient in 2014, who was on tacrolimus, MMF and prednisone 5 mg with a baseline creatinine of 1.4 mg%, developed disseminated TB six months post transplant, diagnosed on FNAC and histochemical stains of mediastinal LNs –AFB +. She was started on HZEL & then kept on HEL, on which patient had symptomatic improvement with a repeat HRCT after 3 months s/o resolution of nodules with few LN.

Two years after transplant, she presented with pain in the right side of the chest for 5 days. HRCT chest showed dense consolidation in the right lower lobe (figure). She had no other constitutional symptoms & no skin nodules and was not on TMP/SMX prophylaxis. Investigations revealed WBC-9630, N-90%, ESR- 60, CRP- 19, LDH-normal. First CT guided biopsy of the lung lesion was inconclusive. A 2nd CT guided biopsy was done: G stain, AFB stain & KOH stain were negative with no growth on cultures. Histopathology revealed necrotizing granulomatous lesions with epithelioid cells. ATT was continued for another 3 months without improvement.

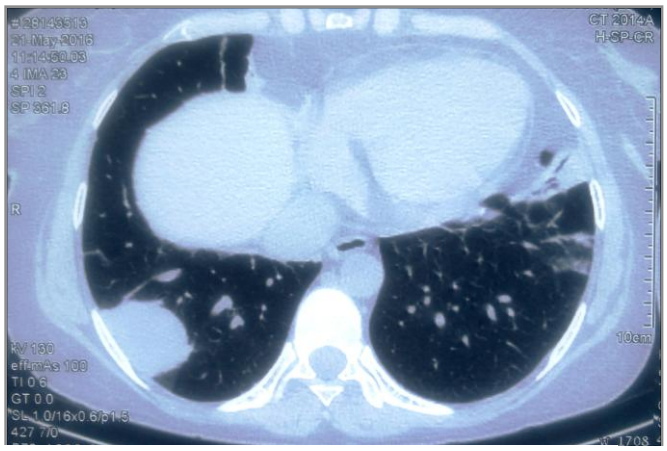


Figure: Dense nodule in the right lung

What is your diagnosis?

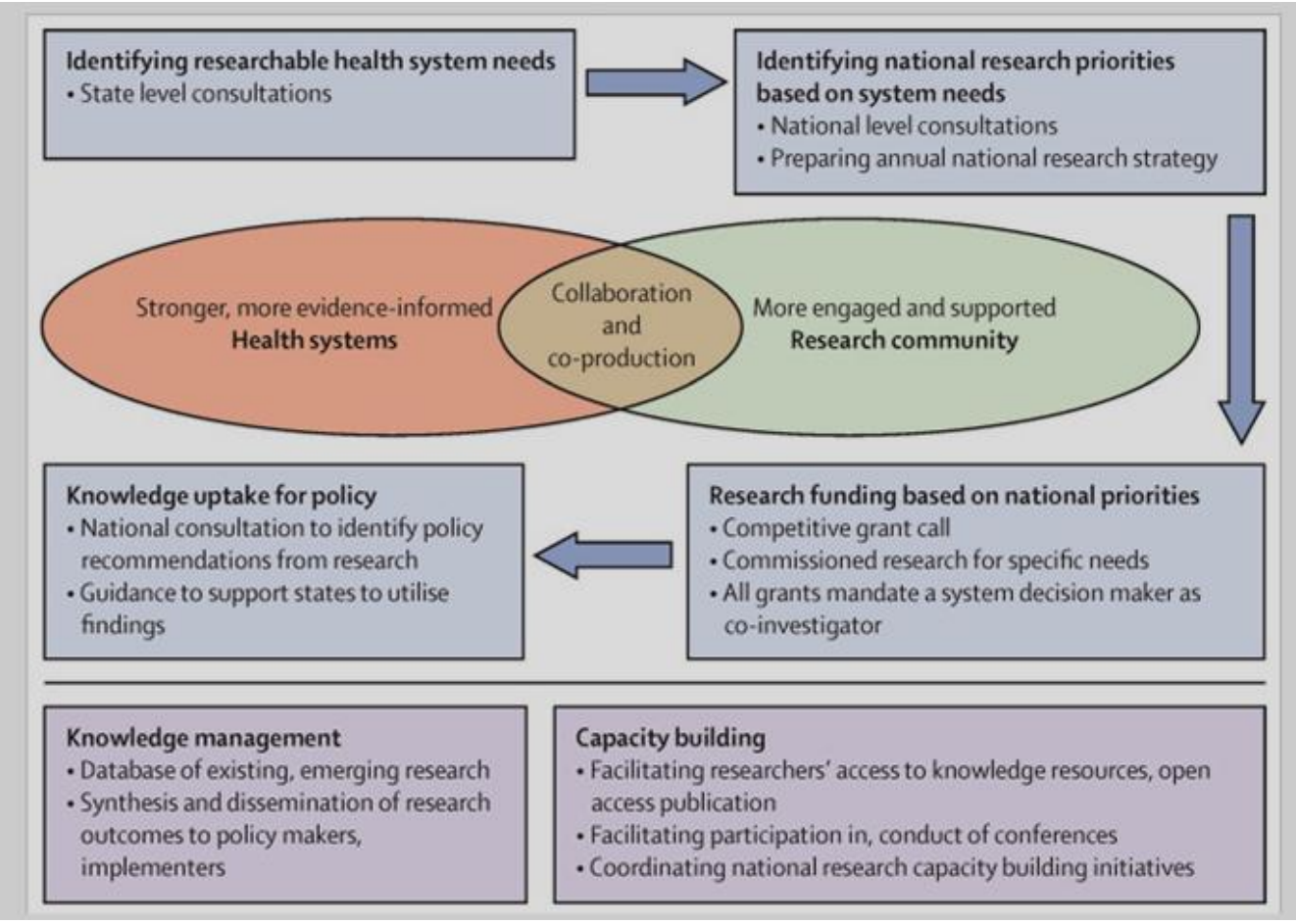
News from the ID world

National Knowledge Platform established

Lancet Volume 388, No. 10061, p2724-2725,3 December 2016

The recent decision by the Government of India's Ministry of Health and Family Welfare to set up the National Knowledge Platform (NKP) for health systems and public health research could be a watershed in how key decisions get made in India's complex, federal health system. The NKP aims to support health systems research and its uptake in policy. It has been established after consultations involving the central government, the Alliance for Health Policy and Systems Research, WHO's country office in India, and national-level technical organisations. The NKP is premised on embedding research in the health system, and facilitating collaboration and co-production of health systems research. The NKP design was built around existing institutions—the Ministry of Health and Family Welfare, the Indian Council of Medical Research, the National Health Systems Resource Centre, and the Public Health Foundation of India—and promotes synergies between them, hence minimising administrative costs.

The platform will support collaborations between health system decision makers and researchers from the conception of new research so that research questions are formulated that meet systemic needs, which will improve uptake of research findings for policy. The NKP will set national priorities for health systems research, and revise them every 2 years, through consultations with state and national stakeholders. The consultations will involve community-based organisations as well as government administrators, so that both perspectives inform research priorities. The NKP will then fund primary research and research syntheses in the priority areas identified, mainly through competitive calls for proposals.



Tenofovir alafenamide approved for chronic hepatitis B

Tenofovir alafenamide (TAF), has been approved for treatment of HIV as part of several combination therapies. TAF enters cells more efficiently than tenofovir disoproxil fumarate (TDF), the previous formulation, so TAF can be given at a smaller dose, resulting in lower plasma tenofovir levels and less toxicity. Phase III randomized trials demonstrated that TAF has comparable efficacy to TDF in hepatitis Be antigen (HBeAg)–positive and HBeAg-negative patients but has less-detrimental effects on bone mineral density and creatinine clearance. Now, the US FDA has approved TAF for treatment of chronic HBV in adults with compensated liver disease. The dose is 25 mg daily with food. There is no dose adjustment for renal insufficiency, but TAF should not be used if the estimated creatinine clearance is <15 mL/min. Testing for HIV should be performed prior to administration; HIV-infected patients should not receive TAF monotherapy. Serum creatinine and phosphorus, estimated creatinine clearance, and urine glucose and protein should be tested before and during treatment. Drugs that strongly affect P-glycoprotein or breast cancer resistance protein activity may alter TAF levels. TAF should not be administered with certain anticonvulsants, rifamycins (e.g., rifampin), or St. John's wort.

HCV drugs may reactivate HBV

The European Medicines Agency warned that some of the most successful hepatitis C treatments on the market could reactivate hepatitis B in patients. The pharmacovigilance Risk Assessment Committee(PRAC), part of the EMA, said it suspected the reactivation of the hepatitis B virus was due to the rapid reduction of the hepatitis C virus, which is known to suppress the hepatitis B virus. The agency recommended that patients be screened to ensure they are not infected with both the viruses before being treated for hepatitis C. It also recommended that a warning be included in the label foe these medicines. The U.S. Food and Drug Administration had issued a similar warning in October, with similar recommendations

Snippets from the literature

Your phone carries not just bacteria but viruses and Candida

Clin Microbiol Infec 2016; 22:456.e1-6
J Occup Environ Hyg 2015:12;D232-5
BMC Infect Dis 2016; 16:238

Chao and colleagues detected bacteria on the phones of 168 of 226 (74%) staff members at a tertiary care hospital [1]. Most organisms represented skin flora such as coagulase-negative staphylococci, but 9%, including coliforms, *Staphylococcus aureus*, *Enterococcus*, and *Acinetobacter* were considered potentially more pathogenic.

Pillet and colleagues, using polymerase chain reaction, examined samples obtained from the surfaces of 109 cell phones belonging to HCWs involved in pediatric and adult care for the presence of viral RNA of metapneumovirus, RSV, influenza, rotavirus, and norovirus. Viral RNA was detected in 42 of 109 (38.5%) samples.

Kordecka et al detected *Candida* on the surfaces of 131 of 175 (74.9%) cell phones of HCWs at a university hospital. The dominant organisms were *Candida albicans*, *Candida glabrata*, and *Candida krusei*. *C.auris*, the recently described species that is multi drug resistant, can also be hand carried.

Time to ban cellphone use in the ICU or on rounds? Or time to pour some handrub on the phone? Doubt both will be popular with doctors.

Can Previous Dengue Infection Exacerbate Subsequent Zika Infection?

Proc Natl Acad Sci USA 2016; 113: 7852-7
Nat immunol 2016; 1102-8

Priyamvada and colleagues examined acute and convalescent serum specimens from 9 patients admitted to Siriraj Hospital in Bangkok (where there have been no known epidemics of Zika virus infection) who had confirmed dengue virus infection. All sera were cross-reactive with Zika virus in both binding and neutralization assays. Of 47 monoclonal antibodies derived from plasmablasts from the 9 individuals, 22 bound to both whole virus and a lysate of Zika, while an additional 4 bound to whole virus; 7 had neutralizing activity. Finally, serum and monoclonal antibody enhanced in vitro infection by Zika virus of cells displaying Fc gamma receptor (FcγR).

Dejnirattisai and colleagues similarly demonstrated serological cross-reactivity of dengue-immune plasma as well as its ability to drive ADE of Zika infection in vitro. Cross-reacting monoclonal antibodies directed to linear epitopes bound Zika virus, but they not only failed to neutralize the virus, they promoted ADE.

The observations reviewed here raise the possibility that preexisting exposure to dengue virus may drive enhanced Zika virus infection. This phenomenon could potentially both exacerbate Zika virus infection (and perhaps increase the risk of transplacental viral transfer) and also increase the likelihood of transmission to biting mosquitoes, thus promoting epidemic effects. India has a high dengue burden and could see just this phenomenon.

Malaria diagnosis: time to switch to PCR?

Am J Trop Med Hyg 2016; 95:58–94.

In Cambodia prevalence of malaria (all species) was 2.74% as determined by microscopy (≥200 fields examined) and 6.31% ($P < .00001$) in the 7718 with PCR—an almost 2.5-fold overall difference. The difference was greatest for detection of *Plasmodium falciparum*—1.81% by microscopy and 4.40% ($P < .00001$) by PCR. Eighteen (0.23%) individuals were inexplicably PCR negative but microscopy positive. Overall, 3.85% of individuals were microscopy negative but PCR positive.

Sensitivities of various tests are: RDT 50–200 parasites/μL, Microscopy 40–100 parasites/μL , QBC and prolonged exam 4/μL and PCR 0.5–5 parasites/μL . PCR seems to be the way forward from a clinical and public health standpoint as we consider malaria elimination.

Global initiative for meticillin-resistant *Staphylococcus aureus* pneumonia (GLIMP): an international, observational cohort study

Lancet ID Volume 16, No.13, p1364-1376, December 2016

The authors did an international, multicentre study of community-dwelling, adult patients admitted to hospital with pneumonia who had microbiological tests taken within 24 h of presentation. They recruited investigators from 222 hospitals in 54 countries to gather point-prevalence data for all patients admitted with these characteristics during 4 days randomly selected during the months of March, April, May, and June in 2015. 3702 patients hospitalised with pneumonia were enrolled, with 3193 patients receiving microbiological tests within 24 h of admission, forming the patient population. 1173 (37%) had at least one pathogen isolated (culture-positive population). The overall prevalence of confirmed MRSA pneumonia was 3·0% (n=95), with differing prevalence between continents and countries. Three risk factors were independently associated with MRSA pneumonia: previous MRSA infection or colonisation (odds ratio 6·21, 95% CI 3·25–11·85), recurrent skin infections (2·87, 1·10–7·45), and severe pneumonia disease (2·39, 1·55–3·68).

Empiric MRSA coverage may be warranted in severe pneumonia in patients with history of previous infection, colonization or recurrent skin infections.

Resistance in M. leprae

Clin Infect Dis. (2016) 63 (11):1482-1484.doi: 10.1093/cid/ciw572

Molecular drug susceptibility testing was performed on skin biopsies from 24 leprosy patients from Guinea-Conakry for the first time. This identified primary drug resistance in 4 cases and a dapsone-resistant cluster caused by the same strain. Primary transmission of drug-resistant *Mycobacterium leprae*, including a rifampicin-resistant strain, is reported.

Perhaps resistance in leprosy is under diagnosed, especially in multi-bacillary disease, and consideration needs to be given to adding additional drugs such as quinolones or macrolides to WHO regimens.

The return of chloroquine-susceptible *Plasmodium falciparum* malaria in Zambia

(courtesy Dr Ashwini Chowdhary)
http://malariajournal.biomedcentral.com/articles/10.1186/s12936-016-1637-3

Plasmodium falciparum resistance to anti-malarial drugs remains a major obstacle to malaria control and elimination. The parasite has developed resistance to every anti-malarial drug introduced for wide-scale treatment. However, the spread of resistance may be reversible. Malawi was the first country to discontinue chloroquine use due to widespread resistance. Within a decade of the removal of drug pressure, the molecular marker of chloroquine-resistant malaria had disappeared and the drug was shown to have excellent clinical efficacy. Many countries have observed decreases in the prevalence of chloroquine resistance with the discontinuation of chloroquine use. In Zambia, chloroquine was used as first-line treatment for uncomplicated malaria until treatment failures led the Ministry of Health to replace it with artemether-lumefantrine in 2003. Specimens from a recent study were analysed to evaluate prevalence of chloroquine-resistant malaria in Nchelenge district a decade after chloroquine use was discontinued.

Parasite DNA was extracted from dried blood spots collected by finger-prick in pregnant women who were enrolling in a clinical trial. The specimens underwent pyrosequencing to determine the genotype of the *P. falciparum* chloroquine resistance transporter, the gene that is associated with CQ resistance. Three-hundred and two specimens were successfully analysed. No chloroquine-resistant genotypes were detected. The study found the disappearance of chloroquine-resistant malaria after the removal of chloroquine drug pressure.

Chloroquine may have a role for malaria prevention or treatment in Zambia and throughout the region in the future. Will it be back to the future?

Effectiveness of Prenatal Tetanus, Diphtheria, and Acellular Pertussis Vaccination on Pertussis Severity in Infants

(courtesy Dr Ashwini Chowdhary)
http://m.cid.oxfordjournals.org/content/64/1/9

The authors used a retrospective cohort study design evaluating whether pertussis-infected infants born in 2011–2015 whose mothers received Tdap vaccine at 27–36 weeks gestation during pregnancy had less severe pertussis, resulting in a lower risk of hospitalization or intensive care unit admission compared with infants born to unvaccinated mothers.

Infected infants of vaccinated mothers were significantly less likely to be hospitalized and had significantly shorter hospital stays compared with infants born to unvaccinated mothers, after adjustment for chronological and gestational age and receipt of diphtheria and tetanus toxoids and acellular pertussis vaccine. Unadjusted and adjusted vaccine effectiveness for preventing hospitalization among infants with pertussis was 72% (95% confidence interval [CI], 49%–85%) and 58% (95% CI 15%–80%), respectively. No infants born to vaccinated mothers required intubation or died of pertussis.

Prenatal Tdap vaccination is a critical strategy for reducing the morbidity and mortality from pertussis. This vaccine and the influenza vaccine should routinely be offered in the third trimester.

Shortened Antimicrobial Treatment for Acute Otitis Media in Young Children

(courtesy Dr Ashwini Chowdhary)
N Engl J Med 2016; 375:2446-2456

The authors assigned 520 children, 6 to 23 months of age, with acute otitis media to receive amoxicillin–clavulanate either for a standard duration of 10 days or for a reduced duration of 5 days followed by placebo for 5 days. Children who were treated with amoxicillin–clavulanate for 5 days were more likely than those who were treated for 10 days to have clinical failure (77 of 229 children [34%] vs. 39 of 238 [16%]; difference, 17 percentage points [based on unrounded data]; 95% confidence interval, 9 to 25). The mean symptom scores over the period from day 6 to day 14 were 1.61 in the 5-day group and 1.34 in the 10-day group (P=0.07); the mean scores at the day-12-to-14 assessment were 1.89 versus 1.20 (P=0.001). There were no significant between-group differences in rates of recurrence, adverse events or nasopharyngeal colonization with penicillin-nonsusceptible pathogens.

Among children 6 to 23 months of age with acute otitis media, reduced-duration antimicrobial treatment resulted in less favorable outcomes than standard-duration treatment; in addition, neither the rate of adverse events nor the rate of emergence of antimicrobial resistance was lower with the shorter regimen. This study bucks the recent trend of studies showing shorter durations are equivalent to longer durations for many infections.

Covalent inhibition of carboxylesterase-2 by sofosbuvir and its effect on the hydrolytic activation of tenofovir disoproxil

(courtesy Dr Surabhi Madan)
Journal of Hepatology (2016), doi:
http://dx.doi.org/10.1016/ j.jhep.2016.11.025

Sofosbuvir can inhibit hydrolysis of tenofovir disoproxil, by irreversibly affecting the drug-activating carboxylesterase-2 enzyme. Sofosbuvir and some anti-HIV drugs such as tenofovir disoproxil contain ester and/or amide bonds, which are hydrolyzed by carboxylesterases. In humans, there are two major - carboxylesterases: CES1 and CES2. This study reports that sofosbuvir is a potent and covalent CES2 inhibitor. This decreases the therapeutic activation of tenofovir disoproxil, with implications of increased kidney toxicity.

As sofosbuvir and other sofosbuvir-containing drugs are often used in combination with tenofovir disoproxil to treat patients co-infected with HIV and HCV, the authors recommended that patients take these drugs at different times or via different routes of administration until clinical trials are performed to fully analyze the effects of taking them in combination.

Impact of Infectious Diseases Consultation on Mortality of Cryptococcal infection in Patients without HIV

(courtesy Dr Surabhi Madan)
Clin Infect Dis. (2016)doi: 10.1093/cid/ciw786

In a retrospective cohort of 147 consecutive cases of cryptococcosis in patients without HIV, patients with an ID consult had a higher fungal burden but a lower 90-day mortality compared to patients without ID involvement (27% vs 45%, p<0.001), with an adjusted hazard ratio of not receiving an ID consult of 4.1 (95% CI: 2.2, 7.6). The ID consult group was more likely to receive an indicated lumbar puncture (86% vs 32%, p<0.001), and more likely to be treated with amphotericin B (87% vs 24%, p<0.001) and flucytosine (57% vs 16%, p<0.001) when indicated. The duration of therapy with AmB (14 vs 11 days, p=0.05) and 5-FC (7.5 vs 1 days, p<0.001) was longer in the ID consult group.

These data suggest that an ID consult should be an integral part of clinical care of patients with cryptococcosis. Similar data exist for Staphylococcal bacteremia and other serious infections.

Guideline watch

WHO guidelines on Infection Prevention and Control Programmes

http://www.who.int/gpsc/ipc-components/en/

WHO has published new guidelines on Core Components for Infection Prevention and Control Programmes. An evidence based document, the guidelines cover eight areas of IPC and comprise 14 recommendations and best practice statements.

WHO recommendations on preoperative measures for surgical site infection prevention

For the first time, WHO has recommended and rated SSI prevention measures.

http://www.thelancet.com/journals/laninf/article/PIIS1473-3099(16)30398-X/fulltext

http://www.thelancet.com/journals/laninf/article/PIIS1473-3099(16)30402-9/fulltext?elsca1=etoc

ATS/IDSA/CDC guidelines for diagnosis of Tuberculosis in Adults and Children

(courtesy Dr Ashwini Chowdhary)

http://m.cid.oxfordjournals.org/content/early/2016/12/08/cid.ciw694.full.pdf

Upcoming meetings and conferences

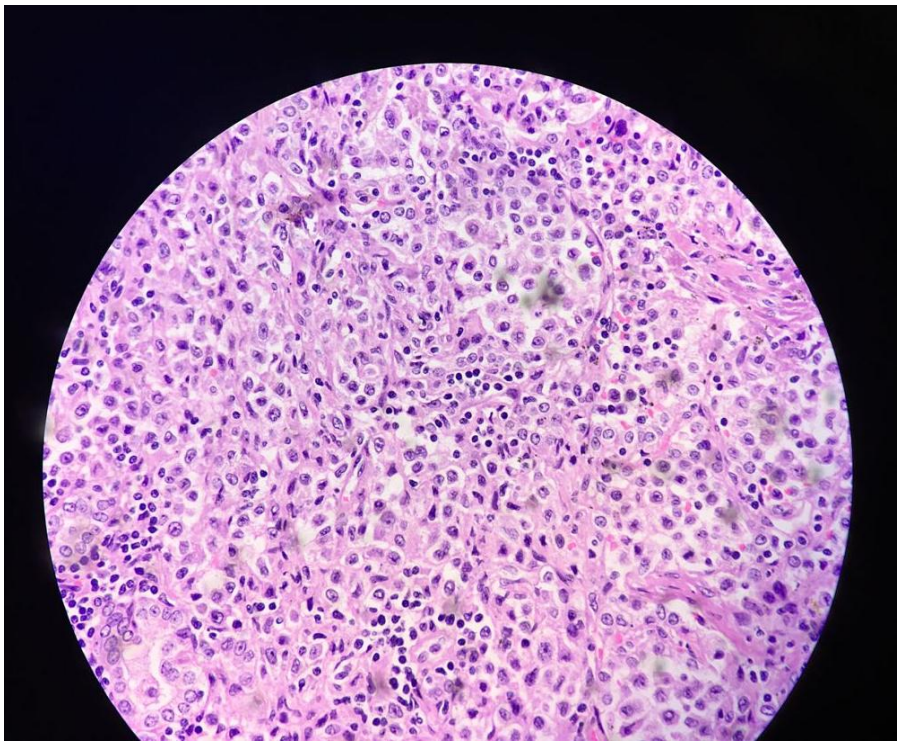
14th HISICON 2017 (XIV th National Conference of Hospital Infection Society India)

9th-11th February 2017, Guwahati

www.hisicon.com

Answer to photo quiz

VATS guided biopsy revealed post transplant lymphoproliferative disorder (PTLD) (Figure) . The incidence of PTLD post kidney transplantation is 1%. Most cases are due to Epstein Barr virus and most patients who develop PTLD are EBV seronegative recipients who get an organ from a seropositive donor
.



Final diagnosis: PTLD

(case provided by Dr Neha Gupta)

CIDSCON 2017

7th Annual Conference of
Clinical Infectious Diseases Society, India

25th | 26th | 27th August, 2017

Venue : Le Méridien Nagpur, Maharashtra

Dr. V Ramasubramanian
Organizing Chairman

Dr. Ashwini Tayade
Organizing Secretary

Dr. O C Abraham
Scientific Committee Chairperson

www.cidscon.in