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Editor's note

CIDSCON 2018 will be from August 16th to 18th 2018 (Thursday to Saturday). Please block your dates.

The annual ID CME at Vellore for postgraduates will be from 20-22 December 2017. Please recommend this popular program to all medicine and pediatrics postgraduates.

We welcome Dr Anup Warrier (Kochi), Dr Neha Gupta (New Delhi) & Dr Vasanth Nagvekar (Mumbai) to the CIDS executive committee, and are confident that CIDS will benefit from their relative youth and energy.

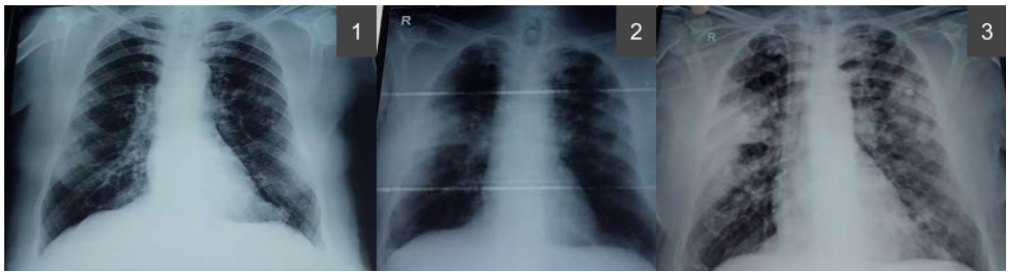
Our website has been updated, please check it out and encourage colleagues and postgraduates to do so. A complete revamping of the website is also being planned. You can access newsletter material directly from the website as open access material. Please send me your feedback and material for website/newsletter.

Photoquiz

An 85-year old male with diabetes, hypertension, IHD, COPD, hypothyroidism was admitted with two days of fever, cough with expectoration and severe breathlessness. On admission patient was alert, had tachycardia 106/min, tachypnea 26/min, saturation on room air 87%, temp-100.50F, bilateral wheeze.

His chest x-ray on admission- prominent interstitialmarkings (Fig 1). Baseline labs showed leukocytosis and respiratory alkalosis. Sputum gram stain -gram positive cocci, he was started on empirical piperacillin tazobactam and clarithromycin and bronchodilators and steroids for bronchoconstriction. Subsequently culture grew ESBL E. coli and MSSA for which meropenem and linezolid were given. He improved marginally and was discharged on request

He was readmitted in a day with high grade fever, leukocytosis and bronchoconstriction, chest x-ray showed rt middle one opacities (Fig 2). He had significant clinical and radiological worsening, for which he required intubation and progressively worsened and expired on day 15 (Fig 3).



What is your diagnosis?

ID NEWS

Mass vaccination against H1N1 not recommended: Health Ministry panel

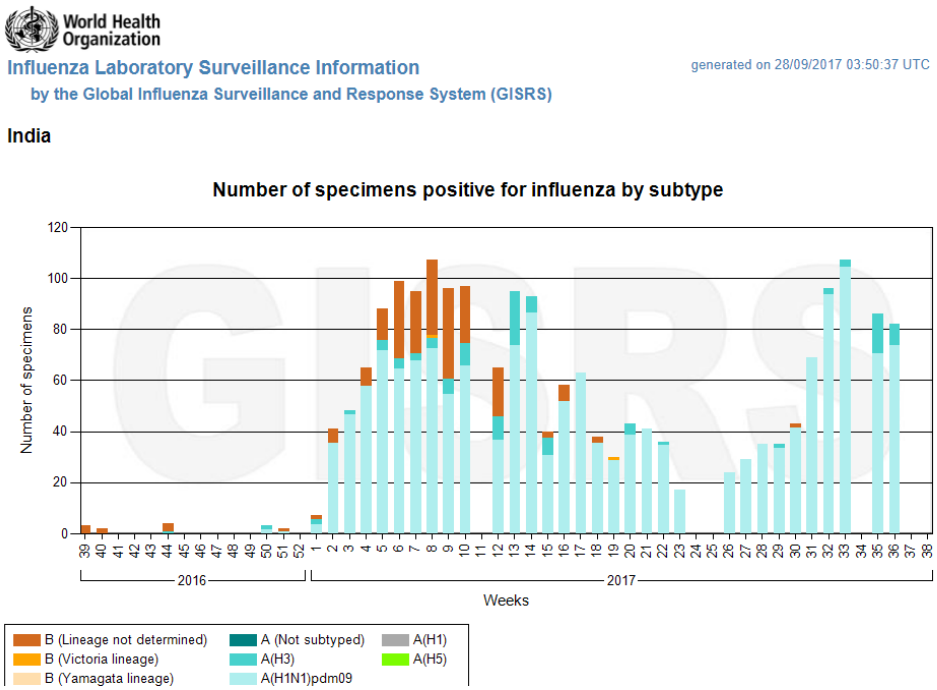
Contributed by Dr Nitin Bansal

A committee set up by the Health Ministry to review its guidelines on seasonal influenza vaccination (H1N1) has said there is “no need” for mass vaccination. The committee, headed by the Director of the National Centre for Disease Control (NCDC), has also suggested vaccinating people aged over 65 and children six months to eight years on a “case-by-case” basis.

H1N1 influenza has killed 1,714 people this year, six times the fatalities recorded last year, with a total of 34,009 cases reported across the country till September 17. According to existing guidelines, vaccination is recommended for pregnant women, persons with chronic illnesses and co-morbid conditions such as chronic obstructive pulmonary disease, heart disease, diabetes, cancer, and an impaired immune system, health care workers in hospitals and institutional settings with a likelihood of exposure to influenza virus.

Focussing on H1N1 alone, as the government has apparently done, may seriously underestimate influenza morbidity and mortality as there is A(H3N2) activity as well, a strain that will also be covered by the trivalent influenza vaccine (see WHO data for India below).

One hopes that vaccination will be rolled out on a population basis at least for adults over 65 and children, rather than on a “case by case” basis, in addition to patients with risk factors. This would seem to make more public health sense rather than current government protocol of contact tracing or focusing on antivirals like oseltamivir, which the WHO has recently downgraded to be used only in ICU patients.



ID NEWS

Dengue vaccine for India? Not now

Contributed by Dr Nitin Bansal

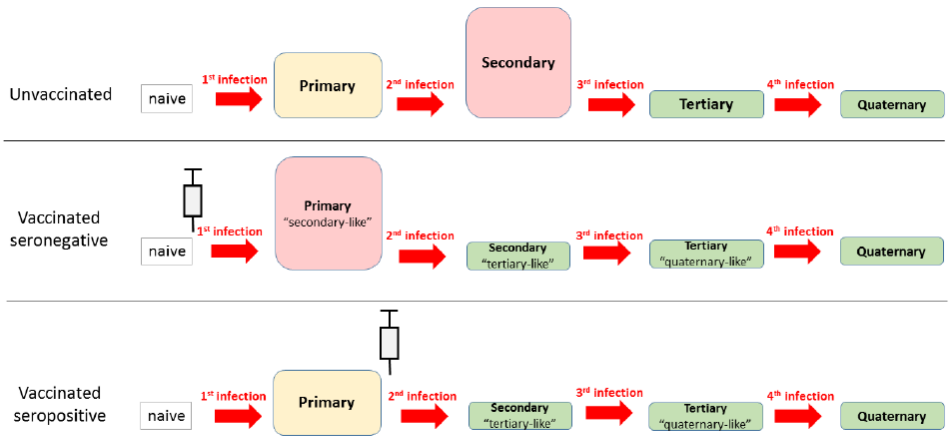
Dengue deaths are in the news daily and dengue vaccine CYD-TDV(Dengvaxia) is a live attenuated (recombinant) tetravalent vaccine that is not planned for introduction in India despite WHO approval and introduction in Mexico other countries. This paper helps shed light on this decision. Dengue vaccine has complicated immune considerations, unlike vaccines for other infections:

- Following a primary infection with one dengue virus serotype, protection against the infecting serotype (homotypic protection) is considered long-lasting.
- Temporary cross-protection is induced to the other serotypes (heterotypic protection), lasting 2 years on average
- Severe illness is more likely to occur with a second dengue virus infection than with the first dengue virus infection [relative risk (RR)~7].
- Antibody-dependent enhancement, cytokine storm, or cross-reactive T cells have been implicated in the pathogenesis
- The vaccine may act as a silent natural infection that primes seronegative vaccinees to experience a secondary-like infection upon their first exposure to dengue virus.
- Even in high transmission settings there may be increased risk among seronegative persons despite a reduction in dengue illness at the population level
- With an assumed vaccine coverage of 80% for the 3-dose series and vaccination at 9 years of age, all models found that deployment of CYD-TDV would result in an overall reduction in dengue illness in settings with moderate to high transmission intensity (seroprevalence ≥50% at 9 years).
- All models predicted that in very low transmission intensity settings vaccination of 9 year-olds was likely to increase dengue hospitalization rates

The WHO position paper suggests:

- Seroprevalence > 70% in target population: WHO recommends
- Seroprevalence 50-70% : WHO says consider
- Seroprevalence is < 50%: WHO says avoid

ICMR does not currently recommend the vaccine, presumably because of absence of sero-prevalence data in the 9-15 year population that is the target for the vaccine, need for 3 doses and modest efficacy of 56-60%.



ID NEWS

TDF/3TC/DTG to be launched in 90 low/middle income countries at reduced price

A breakthrough pricing agreement has been announced which will accelerate the availability of the first affordable, generic, single-pill HIV treatment regimen containing dolutegravir (DTG) to public sector purchasers in low- and middle-income countries (LMICs) at around US$75 per person, per year. The agreement is expected to accelerate treatment rollout as part of global efforts to reach all 36.7 million people living with HIV with high-quality antiretroviral therapy. This one pill, once-a-day generic fixed-dose combination of tenofovir disoproxil fumarate, lamivudine, and dolutegravir (TLD) was developed by generic drug makers under licensing agreements from the original developer of DTG. The generic companies both recently received tentative approval from the U.S. Food and Drug Administration (FDA) for their products under the United States PEPFAR program. Clinical studies demonstrated that treatment regimens that use DTG result in more rapid suppression of viral load, fewer side effects, and greater potency against drug resistance than current regimens used in LMICs.

Hopefully NACO will change to this regimen.

JOURNAL REVIEW

Environmental Pollution with Antimicrobials in Hyderabad, India

Infection. 2017 Aug;45(4):479-491

Researchers collected 5 tap and borehole water samples and 23 aquatic samples from the direct and greater environment of bulk drug manufacturing facilities in South India. The researchers used liquid chromatography–tandem mass spectrometry to analyze the samples for anti-infective pharmaceuticals, selective culture media for multidrug-resistant gram-negative bacteria, and polymerase chain reaction for extended-spectrum beta-lactamase (ESBL) genes.

All environmental specimens contained antimicrobials: 13 contained fluconazole, 12 voriconazole, 9 moxifloxacin, 8 linezolid, 6 levofloxacin, 6 clarithromycin, and 5 ciprofloxacin. Concentrations exceeded the suggested environmental regulation limit for fluconazole, moxifloxacin, ciprofloxacin, ampicillin, clarithromycin and levofloxacin/ofloxacin by up to 950,000 times (more than 20 times the therapeutic blood level), 5500 times, 700 times, 115 times, 110 times, and 50 times, respectively. Tap water from villages was not contaminated with pharmaceuticals, but some samples contained bacteria, including one sample with a drug-resistance gene. All 23 environmental samples contained ESBL- and carbapenemase-producing bacteria; 22 tested positive for the resistance gene *bla*OXA-48, 10 for *bla*NDM, 7 for *bla*KPC, 5 for *bla*VIM, and 5 for *bla*IMP-1.

This study shows why it should not surprise clinicians when they encounter resistant infections from the community. Urgent regulatory action by the authorities is needed.

JOURNAL REVIEW

Dolutegravir compared to lopinavir/ritonavir (LPV/RTV) in second-line treatment: DAWNING study interim data

Infection. 2017 Aug;45(4):479-491
Contributed by Dr Vishnu Rao

DAWNING is a non-inferiority study conducted to compare a PI-sparing regimen of DTG+2NRTIs with a current WHO-recommended regimen of LPV/RTV+2NRTIs in HIV-1 infected subjects failing first-line therapy of 2NRTI + 1/ NNRTI. Adult subjects failing first-line therapy, with HIV-1 RNA ≥400 copies(c)/mL, were randomized to 52 weeks of open-label treatment with DTG or LPV/RTV combined with an investigator-selected dual NRTI background, including at least one fully active NRTI. An IDMC review was performed, which included data from 98% (612/627 randomised) of subjects through 24 weeks on therapy.

At Week 24, 78% of subjects on DTG versus 69% on LPV/RTV achieved HIV-1 RNA < 50 c/mL (adjusted difference 9.6%, 95% CI: 2.7% to 16.4%, p=0.006 for superiority).The difference was primarily driven by lower rates of virologic non-response in the DTG group. The safety profile of DTG+2NRTIs was favourable compared to LPV/RTV+2NRTIs with more drug-related adverse events (AEs) reported in the LPV/RTV group, mainly due to higher rates of gastrointestinal disorders. The IDMC recommended discontinuation of the LPV/RTV arm due to superior efficacy of DTG+2NRTIs and the potential to harm subjects on LPV/RTV based on available data.

DAWNING provides important information to help guide second-line treatment decisions in resource-limited settings. Perhaps DTG based regimens might be appropriate for patients with just M184V or NNRTI resistance mutations alone.

JOURNAL REVIEW

Antibiotics do not benefit pediatric diarrhea in a high-resistance setting

Clinical Infectious Diseases 2017, cix844

The authors conducted a prospective multi-center cross-sectional study of pediatric patients hospitalized with diarrhea containing blood and/or mucus in Ho Chi Minh City, Vietnam. Clinical parameters, including disease outcome and treatment, were measured. Among 3,166 recruited participants (median age 10 months, IQR 6.5-16.7 months), one-third (1,096/3,166) had bloody diarrhea and 25% (793/3,166) were culture-positive for Shigella, NTS, or Campylobacter. Over 85% (2,697/3,166) of patients were treated with antimicrobials; fluoroquinolones were the most commonly administered antimicrobials. AMR was highly prevalent among the isolated bacteria, including resistance against fluoroquinolones and third generation cephalosporins. Antimicrobial treatment and multidrug resistance status of the infecting pathogens were found to have no significant effect on outcome. Antimicrobial treatment was significantly associated with an increase in the duration of hospitalization in particular groups of diarrheal diseases.

In a setting with high antimicrobial usage and high AMR, these results imply a lack of clinical benefit for treating diarrhea with antimicrobials; adequately powered randomized controlled trials are required to assess the role of antimicrobials for diarrhea.

JOURNAL REVIEW

Thumbs up for conjugate typhoid vaccine

Lancet. 2017 Sep 28. pii: S0140-6736(17)32149-9

In this human volunteer study, participants were randomly assigned (1:1:1) to receive a single dose of Vi-conjugate (Vi-TT), Vi-polysaccharide (Vi-PS), or control meningococcal vaccine with a computer-generated randomisation schedule (block size 6). Investigators and participants were masked to treatment allocation, and an unmasked team of nurses administered the vaccines. Following oral ingestion of STyphi, participants were assessed with daily blood culture over a 2-week period and diagnosed with typhoid infection when meeting pre-defined criteria.

103 participants completed challenge (31 in the control group, 35 in the Vi-PS group, and 37 in the Vi-TT group) and were included in the per-protocol population. The composite criteria for typhoid diagnosis was met in 24 (77%) of 31 participants in the control group, 13 (35%) of 37 participants in the Vi-TT group, and 13 (35%) of 35 participants in the Vi-PS group to give vaccine efficacies of 54·6% (95% CI 26·8–71·8) for Vi-TT and 52·0% (23·2–70·0) for Vi-PS. Seroconversion was 100% in Vi-TT and 88·6% in Vi-PS participants, with significantly higher geometric mean titres detected 1-month post-vaccination in Vi-TT vaccinees.

Conjugate typhoid vaccines are made in India and there seems no reason not to use them in place of polysaccharide vaccine on an individual or public health basis, similar to other conjugate vaccines which are more immunogenic than polysaccharide vaccines.

JOURNAL REVIEW

Predictors of increased mortality in TBM

Clinical Infectious Diseases 2017, cix849

The authors included 1699 subjects from four randomized clinical trials and one prospective observational study conducted at two major referral hospitals in Southern Vietnam from 2001-2015. Predictors for increased mortality were higher MRC disease severity grade and lower cerebrospinal fluid lymphocyte cells count, older age, previous tuberculosis, not receiving adjunctive dexamethasone, and focal neurological signs. The model was superior to the MRC scale alone.

The developed models showed good performance and could be used in clinical practice to assist doctors in identifying TBM patients at high risk of death and at increased need of supportive care.

JOURNAL REVIEW

Tuberculosis: obesity protects, diabetes predisposes, treatment of diabetes protects

Clinical Infectious Diseases 2017, cix852

Also CID 2017 cix819, CID 2017 cix632.

In the first study, the authors conducted two population-based cohort studies involving 167,392 participants. The main exposure was BMI and diabetes ascertained at baseline. Occurrence of incident tuberculosis was ascertained from the national Tuberculosis Registry. During a median of over seven years of follow-up, 491 individuals developed incident tuberculosis. Compared with individuals with normal weight, obese individuals (>30 kg/m2) had a 67% (95% CI: -3%-90%) and 64% (95% CI: 31-81%) reduction in tuberculosis hazard in the two cohorts respectively. In the causal mediation analysis, obesity had a harmful effect on tuberculosis mediated through diabetes (0.8% and 2.7% increased odds in the two cohorts) but had a strongly protective effect not mediated through diabetes (72% and 67% decreased odds respectively). Individuals who were simultaneously obese and diabetic had a lower but statistically insignificant risk of tuberculosis (adjusted hazard ratio: 0.30, 95% CI: 0.08-1.22) compared with non-diabetic individuals with normal weight.

In the second retrospective study, among 2,416 patients undergoing TB treatment, after adjusting for age, sex, chronic kidney disease, cancer, hepatitis C, tobacco use, cavitary disease, and treatment adherence, patients with DM had 1.91 times higher odds (95% confidence interval [CI] 1.51-2.40) of death during TB treatment than patients without DM, and 1.72 (CI 1.25-2.38) times higher odds of remaining culture-positive at two months. Metformin use in patients with DM was significantly associated with decreased mortality during TB treatment (hazard Ratio 0.56, CI 0.39-0.82), and metformin users had similar mortality as patients without DM.

In the third study, in a linear dose–response analysis, increasing values of FPG (AOR, 1.02 per 1-mg/dL; 95% CI, 1.01–1.03), PG (AOR, 1.02 per 1-mg/dL; 95% CI, 1.01–1.04), and HbA1C (AOR, 1.13 per 1%; 95% CI, 1.04–1.22) all predicted tuberculosis infection.

JOURNAL REVIEW

Ceftazidime plus Avibactam: A New Treatment for TB

Sci Adv. 2017 Aug 30;3(8):e1701102
Contributed by Dr Vishnu Rao

The investigators identified all current antibacterials with high intrapulmonary concentrations and screened them for potential activity against MTB. Although neither ceftazidime nor avibactam alone demonstrated bactericidal activity, a combination of the two was highly bactericidal in vitro against MTB strains, either in log-phase growth in broth or intracellularly in human-derived monocytes. The bactericidal activity of CAV was greater than that of pyrazinamide and isoniazid, and most South African XDR MTB strains appear susceptible to CAV. Further studies of MTB-infected human-derived monocytes exposed to CAV showed that intracellular concentrations of both ceftazidime and avibactam were higher than extracellular concentrations.

This work shows that when *Blac*, the single gene that encodes MTB beta-lactamase, is inhibited, a cephalosporin can be active against the pathogen, suggesting that other beta-lactam beta-lactamase inhibitor combinations might be active against MTB (similar to meropenem-clavulanate which is currently being used). Clinical trials are awaited.

JOURNAL REVIEW

Predictors of Dengue-Related Mortality and Disease Severity

Open Forum Infect Dis. 2017 May 5;4(2):ofx056
Contributed by Dr R Surendran

This prospective observational study included confirmed adult dengue patients hospitalized between August and November 2015 in AIIMS, New Delhi. Data of 369 patients were analyzed (mean age, 30.9 years; 67% males). Of these, 198 (54%) patients had dengue fever, 125 (34%) had dengue hemorrhagic fever (grade 1 or 2), and 46 (12%) developed dengue shock syndrome (DSS). Twenty-two (6%) patients died. Late presentation to the hospital (≥5 days after onset) and dyspnea at rest were identified as independent predictors of severe disease. Age ≥24 years, dyspnea at rest and altered sensorium were identified as independent predictors of mortality. A clinical risk score was developed (12*age* + *14*sensorium + 10*dyspnea), which, if ≥22, predicted mortality with a high sensitivity (81.8%) and specificity (79.2%). The predominant serotypes in Delhi (2015) were dengue virus DENV2 and DENV4.

10% of patients had bleeding manifestations in the absence thrombocytopenia (median = 130000/mm3). In contrast, 15 patients had no bleeding even with platelet counts below 10000/mm3 (median = 5000/mm3). Although not advocated by the WHO, national guidelines (National Vector Borne Diseases Control Program) still recommend transfusion of platelets to asymptomatic patients with platelet counts below 10000/mm3, an arbitrary cutoff not supported by scientific evidence. Thus, the authors concur with the recommendation against prophylactic platelet transfusion.

Age ≥24 years, dyspnea at rest, and altered sensorium were identified as independent predictors of mortality. Platelet counts did not determine outcome in dengue patients, and prophylactic platelet transfusion is not indicated regardless of the count. Timely referral/access to healthcare is important.

JOURNAL REVIEW

Carbapenems compared to BL/BLIs for treatment of bloodstream infections

Open Forum Infect Dis. 2017 May 16;4(2):ofx099

In this analysis of 14 studies, there was no statistically significant difference in mortality of patients with ESBL-PE BSI that were treated empirically with carbapenems (22.1%; 121 of 547), compared with those that received empiric BL/BLIs (20.5%; 109 of 531; relative risk [RR], 1.05; 95% confidence interval [CI], 0.83–1.37; I2 = 20.7%; P = .241). In addition, 7 studies reported data on definitive therapy. In total, 767 patients (79.3%) received carbapenems and 199 patients (20.6%) received BL/BLIs as definitive therapy, and there was again no statistically significant difference (RR, 0.62; 95% CI, 0.25–1.52; I2 = 84.6%; P < .001). Regarding specific pathogens, the use of empiric BL/BLIs in patients with BSI due to ESBL-Escherichia coli was not associated with a statistically significant difference in mortality (RR, 1.014; 95% CI, 0.491–2.095; I2 = 62.5%; P = .046), compared with the use of empiric carbapenems.

More support for using carbapenems only for the most severely ill patients, and BL-BLIs for all others.

JOURNAL REVIEW

Systematic review and meta-analysis of mortality of patients infected with carbapenem-resistant Klebsiella pneumonia

Ann Clin Microbiol Antimicrob. 2017 Mar 29;16(1):18
Contributed by Dr Mohan Gurjar

Carbapenem-resistant Klebsiella pneumoniae (CRKP) infection doubles the risk of death in comparison to Carbapenem-sensitive Klebsiella pneumoniae (CSKP). A recent systematic review and meta-analysis by Xu et al. includes 22 studies (moderate heterogeneity, I2 39.3%), in which mortality compared between patients infected with CRKP and CSKP, had found that there is significant higher mortality in patients with CRKP than those having CSKP (pooled crude OR 2.80; 95% CI 2.15 – 3.65). In the pooled analysis (from 62 studies) for mortality in different patient conditions, the mortality was found highest with BSI 54.30% (95% CI 47.51–61.02), while ICU-admission 48.9% (95% CI 44.47–53.46), SOT patients 43.13% (95% CI 32.40–54.16), and UTI 13.52% (95% CI 7.50–20.92). In sub-group analysis for mortality of patients infected with KPC-producing K. pneumonia (302 patients) were 47.66% (95% CI 38.61–56.79) and in VIM-producing K. pneumoniae (73 patients) were 46.71% (95% CI 35.81–57.73).

The rate of mortality according to different geographical location revealed highest mortality rate in Europe 50.06% (95% CI 41.45–58.62) of 860 patients, followed by South America 46.71% (95% CI 39.83–53.66) of 191, Asia 44.82% (95% CI 37.83–51.91) of 431, and least mortality rate in North America 33.24% (95% CI 25.08– 42.00) of 980 patients.

This paper had few patients with NDM type carbapenamases found in India. Besides it is unclear whether mortality would be the same if appropriate antibiotic therapy eg colistin was started empirically rather than after receipt of sensitivities, as was seen in the INCREMENT study.

JOURNAL REVIEW

A mini-review of Bunyaviruses recorded in India

Indian J Med Res. 2017 May;145(5):601-610
Contributed by Dr Ashwini Tayade

Newly emerging and re-emerging viral infections are of major public health concern. Bunyaviridae family of viruses comprises a large group of animal viruses. Clinical symptoms exhibited by persons infected by viruses belonging to this family vary from mild-to-severe diseases i.e., febrile illness, encephalitis, haemorrhagic fever and acute respiratory illness. Several arthropods-borne viruses have been discovered and classified at serological level in India in the past. Some of these are highly pathogenic as the recent emergence and spread of Crimean-Congo haemorrhagic fever virus and presence of antibodies against Hantavirus in humans in India have provided evidences that it may become one of the emerging diseases in this country. For many of the discovered viruses, we still need to study their relevance to human and animal health. Chittoor virus, a variant of Batai virus; Ganjam virus, an Asian variant of Nairobi sheep disease virus; tick-borne viruses such as Bhanja, Palma and mosquito-borne viruses such as Sathuperi, Thimiri, Umbre and Ingwavuma viruses have been identified as the members of this family. As Bunyaviruses are three segmented RNA viruses, they can re-assort the segments into genetically distinct viruses in target cells. This ability is believed to play a major role in evolution, pathogenesis and epidemiology of the viruses.

Guideline watch

- 2017 Infectious Diseases Society of America Clinical Practice Guidelines for the **Diagnosis and Management of Infectious Diarrhea** Clinical Infectious Diseases, cix669
- **US DHHS HIV guidelines** updated: The guidelines recommend only INSTI as part of first line regimens, and have moved NNRTIs and PIs to situations where INSTIs cannot be used.

Recommended Initial Regimens for Most People with HIV
Recommended regimens are those with demonstrated durable virologic efficacy, favorable tolerability and toxicity profiles, and ease of use.
INSTI + 2 NRTIs: • DTG/ABC/3TC[a] **(AI)**—if HLA-B*5701 negative • DTG + tenofovir[b]/FTC[a] (**AI** for both TAF/FTC and TDF/FTC) • EVG/c/tenofovir[b]/FTC (**AI** for both TAF/FTC and TDF/FTC) • RAL[c] + tenofovir[b]/FTC[a] (**AI** for TDF/FTC, **AII** for TAF/FTC)
Recommended Initial Regimens in Certain Clinical Situations
These regimens are effective and tolerable, but have some disadvantages when compared with the regimens listed above, or have less supporting data from randomized clinical trials. However, in certain clinical situations, one of these regimens may be preferred (see Table 7 for examples).
Boosted PI + 2 NRTIs: (In general, boosted DRV is preferred over boosted ATV) • (DRV/c or DRV/r) + tenofovir[b]/FTC[a] (**AI** for DRV/r and **AII** for DRV/c) • (ATV/c or ATV/r) + tenofovir[b]/FTC[a] **(BI)** • (DRV/c or DRV/r) + ABC/3TC[a] —**if HLA-B*5701—negative (BII)** • (ATV/c or ATV/r) + ABC/3TC[a] —**if HLA-B*5701—negative and HIV RNA <100,000 copies/mL** (**CI** for ATV/r and **CIII** for ATV/c) NNRTI + 2 NRTIs: • EFV + tenofovir[b]/FTC[a] (**BI** for EFV/TDF/FTC and **BII** for EFV + TAF/FTC) • RPV/tenofovir[b]/FTC[a] **(BI)—if HIV RNA <100,000 copies/mL and CD4 >200 cells/mm^3** INSTI + 2 NRTIs: • RAL[c] + ABC/3TC[a] **(CII)—if HLA-B*5701—negative and HIV RNA < 100,000 copies/mL** Regimens to Consider when ABC, TAF, and TDF Cannot be Used:[d] • DRV/r + RAL (BID) **(CI)—if HIV RNA <100,000 copies/mL and CD4 >200 cells/mm^3** • LPV/r + 3TC[a] (BID)[e] **(CI)**
[a] 3TC may be substituted for FTC, or vice versa, if a non–fixed-dose NRTI combination is desired.

Chandra's Corner

(Dr PH Chandrasekar)

At the recent CIDSCON, I was narrating a true story to Neha Gupta, a young ID star practicing in New Delhi. The story is compelling that I think it is worth sharing with everyone through this column.

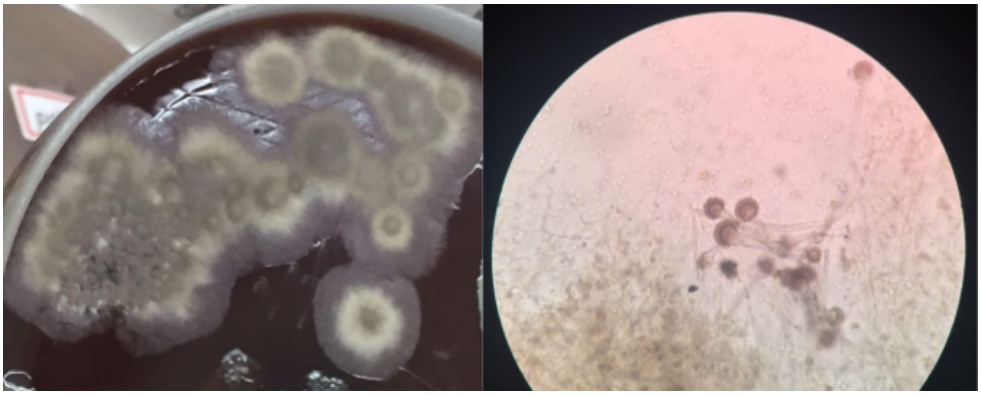
Opioid addiction is huge news in the U.S. It has become a common cause of death, consuming big dollars. Ever since pain was upgraded as the 'fifth vital sign', doctors have been urged to pay attention to this symptom. In the past, the prescribers, including physicians, dentists and others have been generous or more accurately, cavalier with their narcotic prescription habits. Such indiscriminate practice led to widespread physician-enabled opioid addiction, not just in the inner city regions, promoting drug seeking habits but also in the affluent suburbs, particularly affecting white women. The classic profile one conjures of a drug addict has changed. I saw one such person recently. This was a 37-year-old Caucasian woman (Mrs.Diaz) with acute shortness of breath and fever. Blood cultures were positive for MRSA. On examination, she had florid tricuspid valve regurgitation (TR) with engorged neck veins, congestive pulsating, swollen, non-tender liver and edema up to her knees and the classic right heart murmur. Every sign of severe TR described in Hutchison's was bountiful in this poor woman. Chest x-ray was impressive with 10-12 cavitary septic emboli scattered bilaterally. Careful examination of right handed Mrs. Diaz's neck (left side) revealed multiple puncture sites. She readily admitted to IV heroin use. Mrs. Diaz is an atypical drug addict encountered in Detroit-she told us the story. Mrs. Diaz had chronic low back pain for which her physician had been administering narcotics, without much hesitation, for several years when suddenly her physician's narcotic prescribing habits came under closer scrutiny. Alarmed, her physician backed off leaving our patient desperate. With no choice, she turned to cheap, readily available narcotic (heroin) on the street. Gradually, this woman from a respectable suburban family background, transformed into a confirmed drug addict living in a drug haze that led to indiscriminate injections and life threatening staphylococcal cardiac valve infection with metastatic complications and congestive heart failure. Thankfully, her condition gradually improved after several weeks of IV antibiotics in the hospital.

Take home messages are: a) narcotic prescriptions must be initiated with great care and trepidation and, b) continuation or termination of the narcotic prescription must be handled with even greater care combined with a heavy dose of compassion. Man-made monster of opioid addiction in the US often arises from callous and insensitive medical care.

Answer to the photoquiz

Sputum subsequently BAL culture grew Aspergillus niger (Fig 4 and 5). Influenza PCR was negative and BAL galactomannan was 2.6. He was started on voriconazole and brood spectrum antibiotics but progressively worsened and expired.

Invasive pulmonary Aspergillosis outside the immune compromised host has been reported in patients with COPD hospitalized in the ICU, as well as a complication of influenza pneumonia.



Final diagnosis: Invasive pulmonary Aspergillosis

Case provided by Dr Ashwini Tayade