Indexed with IndMED
Indexed with MedIND
Indian Citation Index (ICI)

ISSN 0971-0876
RNI 50798/1990
University Grants Commission 20737/15554

IJCP
A Medical Communications Group
www.ijcpgroup.com

Indian JOURNAL of CLINICAL PRACTICE

A Multispecialty Journal

Volume 31, Number 6 November 2020, Pages 501–600 **Single Copy Rs. 300/-**

Peer Reviewed Journal

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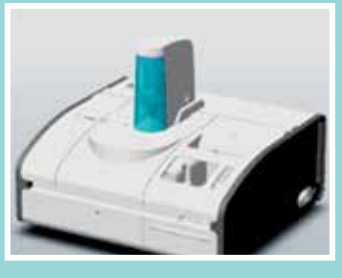

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Indian JOURNAL of CLINICAL PRACTICE
A Multispecialty Journal

Volume 31, Number 6, November 2020

Published, Printed and Edited by
Dr KK Aggarwal, on behalf of
IJCP Publications Ltd. and
Published at
E - 219, Greater Kailash Part - 1
New Delhi - 110 048
E-mail: editorial@ijcp.com

Printed at
New Edge Communications Pvt. Ltd., New Delhi
E-mail: edgecommunication@gmail.com

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Indian Journal of Clinical Practice, Vol. 31, No. 6, November 2020

Dr KK Aggarwal
President, CMAAO and HCFI
Past National President, IMA
Group Editor-in-Chief, IJCP Group

Round Table – HCFI Expert Group on Environment Meeting on "Air Pollution Issues in Winter Months and Its Link to COVID-19"

18TH OCTOBER, 2020, 12-1 PM

PARTICIPANTS:

- Dr KK Aggarwal, Padma Shri Awardee and President, Heart Care Foundation of India and CMAAO.
- Shri Jatinder Singh Kamyotra, Ex-Member Secretary, Central Pollution Control Board.
- Prof SK Singh, Head, Dept. of Civil and Environmental Engineering, Delhi Technological University.
- Prof Meenakshi Dhote, Dept. of Environmental Planning, School of Planning and Architecture, Delhi.
- Dr SK Tyagi, Ex-Additional Director, Central Pollution Control Board.
- Dr Sanjeev Agarwal, Ex-Additional Director, Central Pollution Control Board.
- Shri Radhe Shyam Tyagi, Ex-Member (Drainage), Delhi Jal Board.
- Dr MP George, Sr Scientist, Delhi Pollution Control Committee.
- Shri SK Gupta, Director, Envirotech Instrument, Delhi.
- Shri Pradeep Khandelwal, Chief Engineer, East Delhi Municipal Corporation.
- Shri SA Verma, General Manager (Environment), Delhi Metro Rail Corporation.
- Shri Sharat Kumar, Superintendent Engineer, Delhi State Industrial and Infrastructure Development Corporation.
- Dr M Dwarkanath, Ex-Member Secretary, Puducherry Pollution Control Committee and Ex-Senior Scientific Officer, Dept. of Environment, Govt. of Delhi.
- Dr BC Sabata, Ex-Director, Mahatma Gandhi Institute of Combating Climate Change, Delhi and Ex-Senior Scientific Officer, Dept. of Environment, Govt. of Delhi.
- Dr KK Kalra, Ex-CEO, NABH and Director, Heart Care Foundation of India.
- Dr Uday Kakroo, Director, Heart Care Foundation of India.
- Dr Anil Kumar, Ex-Director, Dept. of Environment, Govt. of Delhi and Director, Heart Care Foundation of India
- Ms Ira Gupta, Advocate, Heart Care Foundation of India.

KEY POINTS FROM THE DISCUSSION

The Meeting was chaired by Shri Jatinder Singh Kamyotra

- Every winter, the air quality reduces due to meteorological conditions and particulate matter (PM) levels exceed the norms by many folds. This is a cause for concern, especially in view of the ongoing coronavirus disease 2019 (COVID-19) pandemic.
- The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus, which causes COVID-19, and particulate matter (PM10, PM2.5 and PM1) have the same pathophysiology; they cause inflammation in the body. There is, therefore, a direct relationship between the COVID virus and the particulate matter.
- If we do not control air pollution, mortality due to coronavirus may be higher during winter.
- Winter air pollution is particularly a problem for senior citizens and children.
- Every winter, there is almost 30% increase in respiratory and allergic diseases in the emergency department due to pollution.
- Government has been working, but things are not improving. There is a need for guidelines on how to keep pollution to a minimum in our vicinity. We should focus on the individual responsibility in the campaign to reduce air pollution.
- A proper health advisory from time to time has to come from an authenticated source, which can be the government health department or a body like the Indian Medical Association (IMA).
- Staggering of academic sessions for schools and other activities can be done in winter.
- Winter break for schools/colleges can be extended depending on the severity of pollution.
- In summer, the major contributors to particulate matter are fly ash, soil, road dust; in winters, the major contributors are vehicular particles and secondary pollutants or conversion of nitrogen oxides (NO_x) and sulfur dioxide (SO_2) emissions to particles combined with biomass burning. We need to control these sources.
- Activities that contribute to air pollution, such as biomass burning or municipal solid waste burning, should be avoided.
- Use private vehicles only when necessary or there is an emergency.
- Switch off the vehicle engines when waiting at red lights.
- Synchronization of traffic signals, so that vehicles do not have to wait much; this saves fuel and reduces pollution.
- With social distancing, the need for public transport has increased manifold, which was already short to begin with. More private vehicles are being used. This is a big challenge.
- An Italian study has correlated nitrogen dioxide (NO_2) and high particulate level (PM2.5) with COVID-19. All steps must be taken to control NO_2 and PM2.5.
- About 25% of contribution is from biomass burning; it is not in our hands to control emissions from stubble burning in neighboring states, but we can at least stop Delhi's local contribution, i.e., local sources of pollution.
- A scenario has to be visualized where closure of power plants and use of GenSets can be controlled.
- Management of solid waste has to be improved. Resident Welfare Associations (RWAs), MTAs can play a leading role in this.
- COVID preparation at construction sites: mandatory thermal screening, sanitization and hand wash at the entry and all over the site, mask check for workers and staff.
- It is important to control dust at the construction site. A total ban on construction activity is not needed. When pollution becomes severe, activities can be divided: Those which are carried out indoors and do not cause any air pollution; some procedures like drilling, etc., where some amount of dust is generated; and thirdly, activities which cause dust. Sprinkling can be done to control dust.
- A blanket ban does not help; some relaxation with stringent measures.
- Diesel cars older than 15 years should be taken off the road by giving some incentive and/or penalty.
- Emission of obnoxious gases (CH_4, NO_2, SO_2) from untreated sewage flowing into the drains also pollutes the environment. More work needs to be done on this.
- Treated effluent water should be used for sprinkling to control dust pollution.
- PM and the virus will remain in the air for some time and aggravate the pandemic, if timely precautions are not taken.

- The main pollutants in the industrial areas are from road dust and burning of garbage. Delhi State Industrial and Infrastructure Development Corporation (DSIIDC) has prepared an action plan to reduce pollution in industrial areas. Regular inspections are being carried out to identify polluting industries. Penalties are being imposed. Repair of roads (potholes) is being carried out, which are sources of dust. Sprinklers (treated water) are being deployed to control road dust.
- More studies need to be done to investigate the association between PM and what is happening inside the body. The medical fraternity has to come forward for this. Populations living around the ambient air quality monitoring stations can be studied for a start. Adequate data is now available on air pollution.
- Burning of waste in landfills adds to air pollution. This needs to be looked at.
- There is an ongoing study investigating the concentration of nanoparticles and microparticles in the ambient air and their impact on health.
- Right architecture is required; micro- and macro-planning is very important.
- Studies have shown a correlation between activity build-up and pollution.
- An environmental revolution is needed similar to the Green and White revolutions in the country. Three issues in pollution - solid waste, air pollution and drainage – which can be solved only by people participation. We need to have micro treatment plants at RWA level or Mohalla level, wherever space is available. This can be done by RWAs and the government can help them either with the budget or give them technical guidance.
- Most of the plantation that has been done in Delhi does not help with oxygen production. The indigenous plants have been virtually replaced by plants which are just for cosmetic purposes and not for providing clean environment.
- We need to have target fixed long-term plans and policies. Every citizen needs to share the responsibility.
- Long-term studies on impact of air pollution are needed. The air quality during the first lockdown can be taken as the baseline.
- Pollutants have changed, from CO, SO_2 in the 90s to NO_2, ozone, PM2.5 now.
- We need some common prevention for corona and PM; one is face mask (0.3 μ). N95 mask (this will take care of PM2.5 up to 95%) is better than surgical mask (this will take care of PM2.5 up to 80%), which is better than fabric mask (this will take care of PM10).
- CDC has said that the coronavirus may be transmitted indoors in poorly ventilated areas; use air purifiers in such areas with 6 exchanges per hour.

With input from Dr Monica Vasudev

■■■■

New Book Urges World Leaders to Unite in Response to Health Threats

On the occasion of the World Health Summit 2020 and the 75th anniversary of the United Nations, a new book was launched that urges world leaders and politicians to unite in their response to the COVID-19 pandemic as well as other threats to health and global economy.

Health: A Political Choice – Act Now, Together is published by the Global Governance Project in association with WHO. The publication calls for unified action in response to COVID-19 and on other major health-related issues. It emphasizes on the following critical areas: Inclusive economics, defined by a new social contract and the pursuit of progress for all; Fundamental requirements for a healthy life and equitable healthcare; Equitable investments and making universal health coverage a reality; Health in the digital age and how technology can have a role in reshaping human rights agenda; Long-term outlook on global health… (*WHO*)

Indian Journal of Clinical Practice, Vol. 31, No. 6, November 2020

Understanding Evolution of Resistant Strains in Recent Decades and Approach Towards Antibiotic Therapy

NEETHU POULOSE*, ANIL ANTONY*, SREELAKSHMI SREEDHAR*, ANIL BABU†

ABSTRACT

Developing resistance to antibiotics is a natural process, and a rising threat to human society. These emergent strains have worsened the burden on existing regimen of antibiotic therapy. Resistance, classified under multidrug resistance (MDR), extensively drug-resistance (XDR) and pandrug-resistance (PDR), is widely seen in hospital setup. Methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *S. aureus* (VRSA), *Escherichia coli* and Klebsiella (Resistant to third-generation cephalosporins), carbapenem-resistant Enterobacteriaceae (CRE) are currently spread infectious agents which call for careful and proper antibiotic management. Antibiotic control programs, better hygiene, antibiogram-based empirical therapy with improved antimicrobial activity are needed to limit bacterial resistance.

Keywords: Antibiotics resistance, mechanisms, biofilm resistance, multidrug resistance, extensively drug-resistance, pandrug-resistance

Discovery of antibiotic was a milestone in the history of medical science, which revolutionized clinical world. The antibiotics are wonder drugs which have immense role in health sector by reducing morbidity as well as mortality. They are the main weapons against infectious diseases which is a serious issue on a global level, and save countless lives. The antibiotic era started in the 1940s, which changed the profile of infectious diseases and human demography. With due course of time, there evolved a large variety of pathogens and discovery of new antibiotics became necessary. However, as antibiotics served as magical bullets, equally infectious agents challenged by rapid appearance of resistance through unbelievable molecular mechanisms emerged. Over a period of 65 years, newer antibiotics were introduced in the market, which was followed by emergence of resistant strains. Due to increased concern of change in resistance, this is an attempt to point out how far our chemotherapy with antibiotics has reached, emerging resistant strains, mechanisms, multidrug resistance (MDR), extensively drug-resistance (XDR) and pandrug-resistance (PDR) and how intense use of reserve antibiotics will affect in future.

EVOLUTIONARY CHANGE OF ORGANISMS AFTER ANTIBIOTIC DISCOVERY

The extensive use and misuse of antibiotics are the major factors driving the high numbers of resistant pathogenic bacteria worldwide, which is a rising threat to the society. The introduction of new antibiotics to counter those pathogens has frequently been closely followed by the emergence of resistant strains. These emergent strains have worsened the burden on existing regimen of antibiotic therapy in both clinical and economical aspects. Some of the examples are *Staphylococcus aureus* isolates resistant to β-lactams due to β-lactamase as well as extensive spectrum β-lactamase and many of these are also resistant to β-lactamase-resistant penicillins. Methicillin-resistant *S. aureus* (MRSA) isolates are one of the most challenging resistant pathogens now-a-days. Evolutionary pattern of resistant strains of *S. aureus* is given in Figure 1. They are usually associated with hospitals and require implementation of appropriate control measures, which usually reduces prevalence

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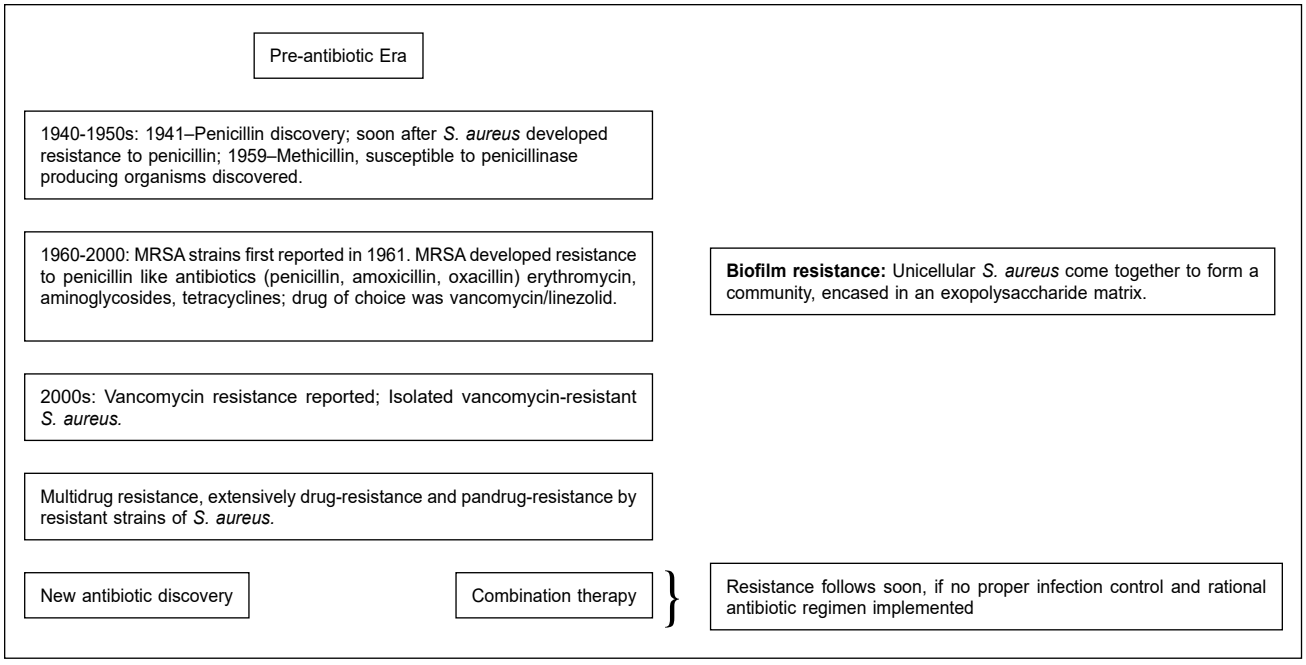

Figure 1. Evolutionary pattern of resistant *S. aureus* strains.

to sporadic levels. Antibiotic resistance often results in failures of empirical therapy. These conditions call for the need for the revolutionary change by either discovery of new antibiotics or combination antibiotic therapy in future. But it is not a rational solution to the problem because resistance follows with these approaches. In short, antibiotic resistance is the major challenge associated with chemotherapy against infectious diseases. Resistant pathogens developed are more virulent, so as a first step, knowledge of etiological agents of infections, antibiotic resistance mechanisms, pattern of developing resistance and sensitivities to available drugs is of immense value for the rational empirical therapy of antibiotics and to slow down the process of antibiotic resistance.

RESISTANT STRAINS IN RECENT DECADES

The susceptible populations of bacteria may become resistant to antimicrobial agents through mutation and selection, or by acquiring from other bacteria, the genetic information that encodes resistance. The infectious agents may get intrinsically resistant to more than one class of antimicrobial agent, or may acquire resistance by *de novo* mutation or via the acquisition of resistance genes from other organisms. These spontaneous mutations may cause resistance by: a) altering the target protein to which the antibacterial agent binds by modifying or eliminating the binding site; b) up regulating the production of enzymes that inactivate the antimicrobial agent; c) down-regulating or altering an outer membrane protein channel that the drug requires for cell entry; or d) up regulating pumps that expel the drug from the cell (Table 1).

However, acquisition of new genetic material by antimicrobial-susceptible bacteria from resistant strains may occur by means of conjugation, transformation or transduction, with transposons often facilitating the incorporation of the resistance genes into the host's genome or plasmids. Some of the important or recently developed resistant strains in our community and its mechanisms are discussed below.

E. coli and Klebsiella: Resistance to Third-generation Cephalosporins

Escherichia coli is a common cause of urinary tract infections (UTI) and bacteremia in humans. It has been observed that there is a generalized decrease in bacterial susceptibility of common oral antibiotics to community-acquired UTI, which is frequently resistant to aminopenicillins, such as amoxicillin or ampicillin and narrow-spectrum cephalosporins. Resistance is typically mediated by the acquisition of plasmid-encoded β-lactamases. But the third-generation cephalosporins are broad-spectrum drugs with intrinsic activity against Gram-negative species. Resistance to third-generation cephalosporins and monobactams (aztreonam) occurs through the acquisition of extensive spectrum beta-lactamases (ESBLs). ESBL are strong bacterial enzymes that raise the burden of resistance to even highly

Table 1. Common Resistance Mechanisms and Examples

Common resistance mechanisms	Example	Antibiotics
a) Altering the target protein to which the antibacterial agent binds	Change in penicillin-binding protein 2b in pneumococci, which results in penicillin resistance	Penicillin G, ampicillin, amoxicillin, ticarcillin, piperacillin, methicillin
b) Up regulating the production of enzymes that inactivate the antimicrobial agent	Erythromycin ribosomal methylase in staphylococci	Penicillins, monobactams, carbapenems and cephalosporins, aminoglycosides (streptomycin, neomycin, netilmicin, tobramycin, gentamicin, amikacin, etc.)
c) Down-regulating or altering an outer membrane protein channel that the drug requires for cell entry	OmpF in *E. coli*	β-lactams, carbapenems, fluoroquinolones, chloramphenicol have specific porins
d) Up regulating pumps that expel the drug from the cell	Efflux of fluoroquinolones in *S. aureus*	Aminoglycosides, ampicillin, ciprofloxacin, chloramphenicol, clindamycin, cephalosporin, erythromycin, fluoroquinolones, macrolides, nalidixic acid, novobiocin, norfloxacin, streptogramin B, tetracycline, tigecycline, trimethoprim, vancomycin

effective antibiotics. The problem of resistance due to ESBL, even though more reported on Klebsiella, now-a-days has a similar pattern for *E. coli*. Different studies showed that ESBL-producers are also resistant to fluoroquinolone, trimethoprim-sulfamethoxazole and aminoglycoside. However, resistance to cephamycins and other β-lactams may arise as a result of changes in the porins in the outer membrane.

Methicillin-resistant *S. aureus*

Methicillin, the first of the semi-synthetic penicillinase-resistant penicillins, was introduced to target strains of penicillinase-producing *S. aureus*. However, resistance to methicillin was reported very quickly after its introduction in 1960s and detection of MRSA has been associated with more severe clinical presentation of community-acquired pneumonia and it is a leading pathogen in skin infection. It was the beginning of global outbreaks of community-associated MRSA infection. MRSA is a common cause of infection among hospitalized patients. Consequently, treatment of these infections has become more difficult and is a healthcare burden. The studies show that MRSA bacteremia is linked with significantly higher mortality rate compared to methicillin-susceptible *S. aureus* (MSSA) bacteremia. Resistance occurs following the chromosomal acquisition of novel DNA, resulting in the production of a new penicillin-binding protein (PBP2a), with a low-binding affinity for methicillin. PBP2a substitutes for all other penicillin-binding proteins, and because of its low affinity for all β-lactam antibiotics, it confers resistance to all β-lactam agents, including cephalosporins. Vancomycin is currently the gold standard for the treatment of MRSA bacteremia, but over the last decade, there has been increasing concern about the development of MRSA strains with reduced susceptibility to vancomycin.

Vancomycin-resistant *S. aureus*

Another major concern after the emergence of MRSA is the vancomycin-resistant strains (VRSA), that is, evolution of strains resistant to vancomycin, which is the typical treatment for MRSA infection. However, the therapeutic failure of vancomycin therapy is explained by the reduced susceptibility of glycopeptides rather than using the term resistance in clinical world and is associated with minimum inhibitory concentration (MIC). *S. aureus* strains with reduced susceptibility to glycopeptides can be divided into three categories - vancomycin-resistant strains (VRSA; MIC, ≥16 μg/mL); vancomycin-intermediate strains (VISA; MIC, ≥4 μg/mL) and heterogeneous vancomycin-intermediate strains (hVISA; MIC <4 μg/mL). Reduced susceptibility versus resistance of vancomycin is controversial, as the term resistance is reserved for those with MIC ≥16 μg/mL. However, the prevalence of hVISA among MRSA is rising.

The exact mechanism of vancomycin resistance remains unclear, but it probably involves thickening of the organism's cell wall due to the accumulation of cell wall fragments capable of binding vancomycin extracellularly, thereby preventing them from reaching their bacterial target. High-level vancomycin resistance occurs because of expression of vanA, which is

associated with alteration of the vancomycin-binding site in the cell wall. Expression of vanA and other genes made the affinity of vancomycin 1,000 times lower than for the native peptidoglycan precursor and resulted in high resistant density.

E. coli, *S. aureus*, *Streptococcus pyogenes*: Biofilm Resistance

Bacterial biofilm is an emerging mechanism of resistance, as it succeeded in explaining the reason of chronic infectious diseases that ends in treatment failure. Biofilms are communities of microorganisms attached to a surface. Bacterial biofilms are formed when unicellular organisms come together to form a community that is attached to a solid surface and encased in an exopolysaccharide matrix. Example-biofilm development in both commensal and pathogenic *E. coli* - the polysaccharide matrix contributes to the development of phenotypic resistance of pathogenic *E. coli* biofilms and leads to persistent infections. Biofilm bacteria show much greater resistance to antibiotics than their free-living counterparts. Its mechanisms is entirely different from familiar mechanisms of resistance such as familiar plasmids, transposons and mutations. This emerging mechanism has grabbed the attention of clinical world and calls the need for potential antibiotic therapies.

It has been suggested that this matrix prevents the access of antibiotics to the bacterial cells embedded in the community. However, *Staphylococcus epidermidis* biofilms formed allowed for the diffusion of rifampicin and vancomycin. These results suggest that inhibition of diffusion cannot always explain resistance to antimicrobial compounds and other mechanisms must be in place to promote biofilm cell survival. Some organisms in biofilms have been shown to express biofilm-specific antimicrobial resistance genes that are not required for biofilm formation. The 38% of the *E. coli* genome is affected by biofilm formation (ompR gene, csgD gene involved in bacterial adhesion). However, the exopolysaccharide matrix does act as an initial barrier that can delay penetration of the antimicrobial agent. Phenotypic and genotypic characteristics associated with biofilm formation of *E. coli*, *S. aureus*, *Streptococcus pyogenes* have been widely studied. Pharyngitis treatment failure has been seen in patients with isolates of *S. pyogenes* having a biofilm-positive phenotype and increased minimum biofilm eradication concentration (MBEC) for all contemporary antibiotics that are used to treat acute pharyngitis cases. *S. epidermidis* infections on indwelling medical devices point towards biofilm formation. *S. aureus* infections, such as osteomyelitis, specifically cases of juvenile osteomyelitis, periodontitis and peri-implantitis, wound infection, endocarditis, are types of biofilm infection. Device-mediated infections are also common and such devices need to be replaced more frequently than those infected with *S. epidermidis*. Biofilm infections must be either prevented from forming or be surgically removed once formed in order to resolve the infection, together with potential antimicrobial therapy.

Carbapenem-resistant Enterobacteriaceae

The difficult situation has not ended with the emergence of broad-spectrum third-generation cephalosporins, carbapenems (example: *E. coli*-resistant to imipenem). These entered the clinical world with extreme potency and broad-spectrum of activity, but are also showing resistance now-a-days. This may have serious public health consequences, resulting in the elimination of many effective antimicrobial drug treatments against the most common human bacterial pathogens. Many studies support the use of carbapenem as an empirical antibiotic for patients with community-onset bacteremia and those with high risk of resistance. Increased consumption of carbapenems after rise of third-generation cephalosporin-resistant *E. coli* and *Klebsiella pneumoniae* may be the reason for emergence of carbapenem-resistant strains of organisms. Resistance density of carbapenem-resistant *K. pneumonia*e is also increasing along with third-generation cephalosporin-resistant *E. coli* and *K. pneumoniae*.

Carbapenemases are powerful enzymes that inactivate carbapenems. Bacterial acquisition of carbapenemases has a role in the emergence of carbapenem-resistant Enterobacteriaceae (CRE). It also led to resistance to all cephalosporins, aztreonam and β-lactamase inhibitors including clavulanic acid and tazobactam. CRE isolates are increasingly reported as multidrug-resistant, extensively drug-resistant or pandrug-resistant. In a short time, isolates of *E. coli*, Klebsiella, Enterobacter, Serratia, and Salmonella species have reported carbapenem resistance and it globally changed the epidemiology of resistance. Combination regimen or monotherapy of agents such as polymyxins (such as colistin), aminoglycosides, tigecycline and fosfomycin are the available therapeutic options.

Multidrug Resistance, Extensively drug-resistance and Pandrug-resistance

Multidrug resistance, extensively drug-resistance and pandrug-resistance have been defined differently in medical literatures. The standardized international

terminology was created by group of international experts that came together through a joint initiative by the European Centre for Disease Prevention and Control (ECDC) and the Centers for Disease Control and Prevention (CDC) defines these terms as follows: MDR is defined as nonsusceptibility to at least one agent in three or more antimicrobial categories; XDR is defined as nonsusceptibility to at least one agent in all but two or fewer antimicrobial categories (bacterial isolates remain susceptible to only one or two categories). PDR is defined as nonsusceptibility to all agents in all antimicrobial categories (no agents tested as susceptible for that organism). The pictorial representation of relation between MDR, XDR and PDR is shown in Figure 2.

Emerging and spreading of MDR (emerged strains are referred as 'super bugs') is a natural phenomenon, followed by the inappropriate use of antimicrobial drugs, inadequate sanitary conditions, inappropriate food-handling and poor infection prevention and control practices. XDR ('extreme drug resistance', 'extensive drug resistance') was the term created initially to describe drug-resistant *Mycobacterium tuberculosis.* Eventually, the condition changed and the resistance profile of non-Mycobacterium that compromised most standard antimicrobial regimens was also described by same term. Pandrug-resistant (pan-'all') means 'resistant to all antimicrobial agents'. The management of pandrug-resistant Gram-negative bacterial infections is very difficult. Only few drugs, including colistin, in combination with β-lactam antibiotics, polymyxins, an old class of antibiotics, are recommended. Now the time has been reached where there are only limited therapeutic options. Even though many antibiotics are in our hand, it's time to focus on careful handling of antibiotics.

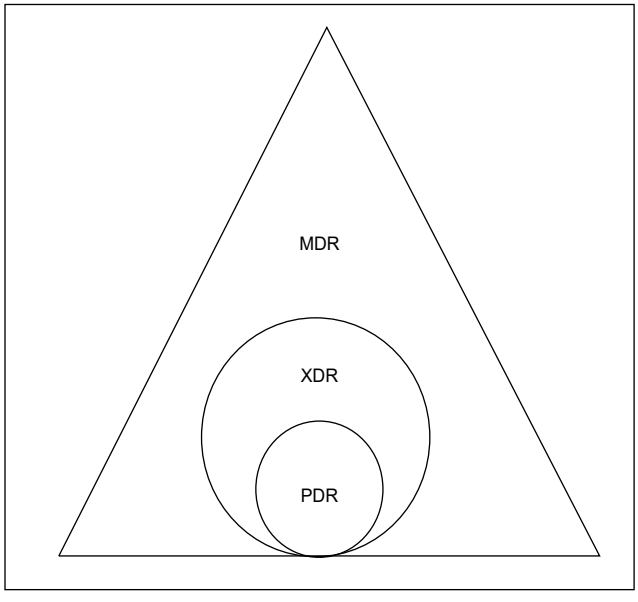

Figure 2. Relation between MDR, XDR and PDR.

MANAGEMENT OF ANTIBIOTIC RESISTANCE

Most of the antibiotic drug resistance is nosocomial or of hospital origin. In India, 1 in 4 patients admitted into hospital acquire nosocomial infection. So, for adequate management of critically ill patients and patients undergoing various operative procedures and other medical interventions, hospital antibiotic policies need to be revisited. In the management of infectious diseases, initially more care should be given in the selection of antibiotics based on hospital antibiogram in empirical therapy. More rational selection of antibiotics based on the most likely pathogens for a given infection and the susceptibility profiles of these pathogens that are specific to each institution will reduce density of resistance in and around institution. Antibiogram considerably helps in proper empirical selection of antibiotics. Each practitioner should have updated knowledge about evolutionary stage of resistant isolates in the hospital, while prescribing each antibiotic. Proper infection control should be employed in hospitals. In short, antibiotic control programs, better hygiene, antibiogram-based empirical therapy and synthesis of agents with improved antimicrobial activity are needed to limit bacterial resistance. In a developing country like India, there is an urgent need to develop and strengthen antimicrobial policy and standard treatment guidelines at the national, community and hospital level.

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Antibodies Against Coronavirus Detectable up to 7 Months After COVID-19 Onset: Study

Antibodies against the novel coronavirus show a rapid rise within the first 3 weeks after symptoms, and are detectable for up to 7 months after contracting the disease, suggests a new study that evaluated 300 patients infected with COVID-19 and 198 post-COVID-19 volunteers.

The research, published in the *European Journal of Immunology*, revealed that the participants had antibodies with confirmed neutralization activity for up to 6 months after the infection with the virus. Nearly 90% of the subjects were reported to have detectable antibodies up to 7 months post contracting the viral disease. Age was not a confounding factor in levels of antibodies produced, though disease severity is, reported the research… (*ET Healthworld – PTI*)

The Americas Facing Risk of Polio Outbreak Due to Disruptions Caused by Pandemic

Health experts are worried about an outbreak of the polio virus in the Americas during the COVID-19 pandemic caused by a delay in vaccinations and surveillance.

Experts at the Pan American Health Organization (PAHO) stated that countries in the region should maintain polio vaccinations and surveillance during the pandemic in order to prevent an outbreak. PAHO Director Carissa Etienne stated that if vaccination coverage rates fall and become too low, there will be a risk for polio circulation in the communities. During the ongoing pandemic, there is a need to work extra hard to not lose what has been gained, said Cuauhtemoc Ruiz Matus, head of PAHO's Immunization Program… (*CNN*)

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Indian Journal of Clinical Practice, Vol. 31, No. 6, November 2020

Can the Concept of a Universal Influenza Vaccination Minimize the Severity of COVID-19?

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ABSTRACT

In view of the uncertainty of when the coronavirus vaccine will finally hit the market and how it is going to yield that protection in terms of efficacy, it is time that we think beyond what is "more than the vaccine". "It is about vaccination" at large. Influenza vaccination is now being extensively talked about as one of the public health measures to cushion the other epidemic, this current coronavirus outbreak.

Keywords: COVID-19, influenza vaccination

As of July 11, 2020, coronavirus disease 2019 (COVID-19) has been confirmed in 12,322,395 people globally, with a case mortality rate of approximately 4.5%.[1] It is well appreciated that COVID-19 mortality rate is higher in the elderly and in those with pre-existing chronic comorbidities like diabetes and cardiovascular disease (CVD), just like seasonal influenza confers increased morbidity and mortality to them.[2] Annual influenza vaccination has been routinely recommended for this population since over a decade to battle it out but till date, the rate of the practice of vaccination is abysmally low. Co-infections, seasonal influenza A and B, are being increasingly reported in COVID-19 patients.[3,4] The absolute risk reduction from the vaccine was 2- to 4-fold higher in the elderly population with chronic comorbidities compared to the healthy population of the same age group, despite a poor match between the vaccine and circulating strains,[5] and also with a low (10%) vaccine effectiveness rate.[6]

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EFFECTIVENESS OF THE VACCINE

The vaccine has been shown to be effective at reducing the rate of hospitalization from pneumonia and mortality in elderly people with chronic lung diseases.[7] Interestingly, an inverse relationship between influenza vaccine coverage in adults aged between 18 and 64 years and influenza-related illness in the older population (≥65 years) has been observed due to reduced transmission in the community.[8] A conjecture is derived that there is a reduction in the complications and deaths associated with COVID-19 when the rate of both acute and chronic respiratory comorbidities in high-risk populations are reduced. Live-attenuated influenza vaccines, by boosting the innate immunity[9] may provide transient protection against COVID-19 which is notoriously known to suppress innate immune response,[10] thereby reinforcing that vaccination could be beneficial to society at large.

In a study on 92,664 patients from Brazil, inactivated trivalent flu shot also offered protection from getting severe COVID-19. The mortality in the nonimmunized group rose from about 14% in the 10 age group to 84% among those aged 90 years, but lower in all age groups in the immunized group, with the risk being 17% lower in the 10-19 years age group and 3% less in those aged 90 years. Those receiving a recent influenza vaccine experienced on average 8% lower odds of needing intensive care treatment and 18% lower odds of requiring invasive respiratory support.[11]

Considering age only as a parameter, flu vaccination was associated with a 35% reduction in the mortality among COVID-19 patients. When compared with

results of patients getting care at the same healthcare facility, the odds of dying of COVID-19 was found lower by 18%.

Another study on the elderly population in the US showed that for every 10% increase in influenza vaccination, flu shot can reduce mortality by 20% when taken before the onset of COVID-19 and about 27% when the vaccine was given after the onset of COVID-19. Overall, with a 10% increase in vaccination coverage, there was a 28% decrease in the rate of mortality from COVID-19.[12]

Memory T cells induced by previous pathogens can drive the susceptibility to, and the clinical severity of, subsequent infections.[13] Flu virus specifically impairs the ability of T cells to kill virus-infected cells; hence it impairs a person's immune system to fight against other pathogens, including the COVID-19. Unvaccinated people are at risk of persistent viral infections that decline their T cells diversity, in a way suppressing their immune system. T cells diversity helps fight infections better as it provides a bigger pool of T cells to fight against a new pathogen and it also provides more flexible T cells receptors to fight the pathogen even if it mutates.

Hence, the vaccination promises to boost the immunity. In Italy, it was found that people who took a quadrivalent flu vaccine had a lower death rate from COVID-19. However, this kind of response is more likely in a live-attenuated vaccine, not in an inactivated vaccine. This study also states that both severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of COVID-19 and the flu virus are RNA viruses for one and they both have similar pathogenesis and transmission. Even though influenza and SARS-CoV-2 display only limited nucleotide sequence similarity, overall CD8+ T-cell epitopes with modest sequence resemblance seem plausible in respect to viral structure, transmission and pathogenic mechanisms, and their binding to viral RNA can then trigger suitable inflammatory and antiviral responses.

A flu shot can be either a live-attenuated vaccine or an inactivated vaccine. The former is given to only healthy people (excluding pregnant women) in the age group of 2-49 years, while the latter can be given to anyone above the age of 6 months (https://www.euro.who.int/en/health-topics/communicable-diseases/influenza/vaccination/types-of-seasonal-influenza-vaccine). An inactivated vaccine does not induce virus-specific T cells in a person and so this drawback of this vaccine may be coming handy now in protecting against COVID-19. Besides the cross-reactivity effect, the anti-flu immune responses can induce bystander immunity[14] that is expected to nonspecifically augment immunity against other viral infections, such as SARS-CoV-2. Furthermore, influenza vaccination itself would generate sustained immunity that overall enhances immunity against SARS-CoV-2. As there is evidence of cross-reactivity between flu and SARS-CoV-2, it may be concluded that flu-induced bystander immunity has more of beneficial effects to COVID-19 than those suggested by measles, mumps and rubella (MMR) and bacillus Calmette-Guérin (BCG) vaccines.[15,16]

Another study conducted in Australia evaluated the immune responses in the blood from a patient with COVID-19 with mild illness.[17] They looked at the cellular and humoral immune responses at different time points during the infection, i.e., before, during and after resolution of the disease. Their longitudinal analysis showed a robust immune response across different cell types associated with clinical recovery. Accordingly, a link is suggested between the quality of the immunity and recovery from COVID-19, at least in part, in patients with mild symptoms. A hypothesis was presented that the immunity against prior influenza infection, at least in part, also developed immunity against SARS-CoV-2. This hypothesis is supported by the previous studies showing cross-reactivity of immunity between flu and coronavirus due to the similarity in their structures.[18,19]

Furthermore, influenza vaccination itself would evoke sustained immunity that would enhance immunity against SARS-CoV-2. As different strains of coronavirus can develop because of mutations and natural selection besides recombination, a directed stable vaccine is very unlikely. Till then, it is recommended that flu vaccine be used, at least in part, as a bystander adjuvant to minimize the severity of COVID-19 disease due to the safety profile of flu vaccine in adults.

Yet, despite the availability of safe flu vaccines, influenza vaccine hesitancy, i.e., low influenza vaccine uptake rates, both in general public and even within specific risk groups remain a significant challenge throughout the globe and contribute to the burden of disease, especially in the elderly.[20-23]

CONCLUSION

At this point in the pandemic, there is inadequate evidence about the effectiveness of antibody-mediated immunity to guarantee the accuracy of an "immunity passport" or "risk-free certificate". People who have received a positive test result may assume that they

are immune to a second infection and, therefore, ignore public health advice. The use of such complacent certificates may heighten the risks of continued transmission.[24] Governments should seriously consider promoting flu vaccination at this time as a bystander adjuvant to minimize the severity of COVID-19 disease.[25] Anticipating the possibility of a deadly potential of a global influenza-COVID-19 co-infection,[26] it has been suggested that the influenza vaccination could be used to indirectly control COVID-19.[25,27]

An almost universal uptake of this influenza vaccination across continents may engender herd immunity and thus protect even those in whom the vaccine may be ineffective to cope better with COVID-19 complications as lockdowns will inevitably be relaxed.[28] To meet the urgent need for a coronavirus vaccine, a new pandemic vaccine development paradigm has been proposed that compresses the development timeline from 10-15 years to 1-2 years.[29] Slowing the spread of the COVID-19 cases will significantly reduce the strain on the healthcare system of the country by limiting the number of people who are severely sick by COVID-19 and need hospital care.[30] To simplify the primary clinicians' work, may the influenza vaccine be targeted for the fall season this year, be it for a larger group of the entire global population as another new wave of COVID-19 is predicted to hit in parallel with the start of the influenza season.

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Over Half a Million People in US may Die of COVID by February, Suggest Estimates

London: Over half a million people in the United States could die due to COVID-19 by the end of February 2021, suggest estimates from a modelling study. However, about 1,30,000 of those lives could be saved if everybody wears masks. A study conducted by researchers at the University of Washington's Institute for Health Metrics and Evaluation suggest that with only few effective treatment options and no vaccines yet available, the country faces a persistent COVID-19 public health challenge through the winter. IHME director Chris Murray, who co-led the research, stated that they are moving toward a very substantial winter surge. The Institute for Health Metrics and Evaluation (IHME) study estimated that large, populous states of California, Texas and Florida will likely face high levels of illness, deaths and demands on healthcare resources… (*NDTV – Reuters*)

Finerenone Reduces Kidney, Heart Risks in CKD and T2D

An investigational antimineralocorticoid agent slowed the progression of chronic kidney disease (CKD) in individuals with type 2 diabetes (T2D), suggested the phase III FIDELIO-DKD trial.

Around 17.8% of the 2,833 patients on finerenone experienced a primary outcome event - kidney failure, a sustained decrease of at least 40% in estimated glomerular filtration rate (eGFR) from baseline, and death from renal causes – compared to 21.1% of the 2,841 on placebo (HR 0.82, 95% CI 0.73-0.93, p = 0.001), reported researchers. Those given the antimineralocorticoid agent had a decreased risk of experiencing a key secondary cardiovascular outcome - death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke or hospitalization for heart failure - compared with placebo group (13% vs. 14.8%, respectively; HR 0.86, 95% CI 0.75-0.99, p = 0.03). The findings were presented at the American Society of Nephrology's virtual Kidney Week… (*Medpage Today*)

Spain Declares National State of Emergency Over COVID-19

Spain has declared a state of emergency and a curfew for the entire country except the Canary Islands to contain a second wave of COVID-19 cases. The state of emergency will continue until early May, Prime Minister Pedro Sanchez said in his speech. He emphasized that the situation being faced was extreme. A government statement said that the state of emergency would initially last for 15 days; however, the government planned to ask the parliament to extend it for a period of 6 months. The Prime Minister added that if conditions allowed, the measures could be lifted earlier than expected. He stated that the state of emergency is the most effective means by which the rate of infection can be decreased… (*NDTV - Agence France-Presse*)

Indian Journal of Clinical Practice, Vol. 31, No. 6, November 2020

The Etiology and Outcome of Patients with Fever Attending Civil Hospital, Ahmedabad, India

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ABSTRACT

Fever is probably the most common symptom for which a person usually seeks medical advice and is one of the major criteria for hospital admission. Knowledge of local prevalence of infections is critical in order to target clinical work up and treatment. Nevertheless, in India, reporting on the etiology of fever, and reliable surveillance data are not available. This was an observational, prospective study conducted at Civil Hospital, Ahmedabad which is a tertiary care center, during period of January 2014 to December 2014. The main objective of this study was to describe the etiology of fever and to study the outcome of such cases at the end of the study. In the present study, out of 108 patients, the major culprits were dengue infection (20%), malaria infection (19%), viral hepatitis (17%), enteric infection (9%), LRTI (7%) and meningitis (5%). Infective etiologies were found in 90% of patients, while 7% had noninfective etiology and in 3% of patients, the etiology remained undiagnosed. So, the findings confirm that the heavy burden of infection was a cause of fever requiring hospitalization and vector-borne disease comprise majority of cases of fever.

Keywords: Fever, infection, etiology

Fever is probably the most common symptom for which a person usually seeks medical advice and is one of the major criteria for hospital admission. The most common reason for it is infection hidden somewhere within body. The World Health Organization (WHO) reports that the main infectious etiologies (that is, pneumonia, diarrhea, human immunodeficiency virus/acquired immune deficiency syndrome [HIV/AIDS], malaria, tuberculosis [TB] and neonatal infections), cause between 0.24 and 1.05 million deaths, per year in low-income countries.[1]

Fever is like the tip of an iceberg. So, surprisingly, a large number of patients have been found to have multi-organ involvement and many other complications, which might cause rapid deterioration in general condition of a patient. In resource-limited settings, fever may be treated empirically or self-treated due to lack of access to diagnostic tests. However, clinical algorithms in order to differentiate malaria, for instance, from other causes of fever are not specific. Knowledge of local prevalence of infections is critical in order to target clinical work up and treatment. Nevertheless, in India reporting on the etiology of fever, and reliable surveillance data are not available, so the main objective of this study was to describe the etiology of fever, and to study outcome of such cases at the end of the study among patients at Civil Hospital, Ahmedabad.

METHODS

Study setting: The present study includes 108 patients of fever admitted in Medical Ward, Civil Hospital, Ahmedabad during the period of January 2014 to December 2014.

Design: This was a prospective observational study among inpatients. Inclusion criteria were all patients with age >12 years irrespective of gender. Exclusion criteria were all patients <12 years of age; critically ill patients; patients who developed fever after hospitalization; patients with other associated symptoms of some local part of body, like eye, ear or skin; postoperative patient and patients with any surgical illness; pregnant and postpartum patients or patients with gynecology-related illness.

Data collection: Data were collected from hospital records, medical staff and by directly asking patients.

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Demographic data, including age and gender, were recorded prospectively, as well as clinical data including fever duration, final diagnoses and deaths. Radiological, biochemical and microbiological tests performed were registered.

RESULTS

During the 1 year study period, 108 febrile patients were enrolled; details are summarized in tables below.

The mean age in this study group was 33.65 years. Males were more affected (64%) than females (36%). Maximum patients were in 21-30 years age group (35%), out of which 74% were males and 34% were females (Table 1).

In the present study, out of 108 patients, following etiologies were recorded: dengue infection (20%), malaria infection (19%), viral hepatitis (17%), enteric infection (9%), lower respiratory tract infection (LRTI, 7%), meningitis (5%), intracranial bleed (3%), febrile neutropenia (2%), diarrhea (2%), malignancy (2%) and 3% of patients remained undiagnosed despite proper workup (Table 2).

Out of other 9 patients (8%), 3 patients had combined malaria and viral hepatitis infection and 1 patient of infective endocarditis, brucella infection, thyroid storm, systemic lupus erythematosus (SLE), upper respiratory tract infection (URTI) and neuroleptic malignant syndrome each were found. In the present study, infective etiologies were found in 90% of patients, while 7% had noninfective etiology and 3% of patients remained undiagnosed. Overall, 13 patients went against medical advice, 2 patients with malignancy were transferred to super specialty hospital and 2 patients had expired during hospital stay. Out of these 2 patients, 1 patient had transient bone marrow edema (TBME) and in 1 patient, diagnosis was not reached despite proper work up.

Table 1. Age-gender Distribution of Study Patients

Age (In years)	No. of males	No. of females	% of total patients (n = 108)
13-15	01	02	3
16-20	09	06	14
21-30	26	12	35
31-40	12	12	22
41-50	09	04	12
>50	12	03	14
Total	**69**	**39**	**100**

DISCUSSION

Due to lack of data on this type of study, we have compared our study with a study by Abrahamsen et al, which was a prospective observational study of 100 patients with fever done at a tertiary care center in Vellore, Tamil Nadu, India, from July 2007 to August 2007. The mean age in our study group was 33.65, whereas in the study by Abrahamsen et al, the mean age was 37.5 years.[2]

In the present study, infective etiologies were found in 90% of patients, while 7% had noninfective etiology and 3% of patients remained undiagnosed. In the study by Abrahamsen et al, 71% had infective etiology, while 15% had noninfective etiology and 13% of patients remained undiagnosed (Table 3). In that study, one patient did not receive a final diagnosis. The etiological difference could be because of geographical variation of some diseases in a particular area and mean duration of fever at the time of presentation, which was 9 days in present study, whereas it was 5.4 weeks in the study by Abrahamsen et al. So in the present study, the most common etiology of fever was due to infective causes; in noninfective causes, intracranial hemorrhage and malignancy were more common. Out of the 2 patients

Table 2. Diagnosis Distribution

Diagnosis	Present study % of patients (n = 108)
Dengue	20 (n = 22)
Malaria	19 (n = 21)
Viral hepatitis	17 (n=18)
Enteric infection	09 (n =10)
LRTI	07 (n = 8)
Meningitis/Encephalitis	05 (n = 6)
Febrile neutropenia	02 (n = 2)
Diarrhea	02 (n = 2)
Chikungunya	02 (n = 2)
ICH	03 (n = 3)
Malignancy	02 (n = 2)
Undiagnosed	03 (n = 3)
Others	08 (n = 9)

LRTI = Lower respiratory tract infection; ICH = Intracranial hemorrhage.

Table 3. Etiological Distribution

Etiology	Present study % of patients (n = 108)	Abrahamsen et al study % of patients[2] (n = 100)
Infective	90	71
Noninfective	07	15
Undiagnosed	03	13

who had expired in present study, 1 patient had TBME and in 1 patient, diagnosis could not be arrived at, despite proper work up. In Abrahamsen et al study, 7% patients expired; out of these, 5 had sepsis, one had spleen abscess and malignancy, and one had lymphomalignant disorder.

Most common etiologies of fever in present study were due to infective causes such as dengue, followed closely by malaria and viral hepatitis. In noninfective causes, intracranial hemorrhage and malignancy were more common. Malaria, dengue and chikungunya are major vector-borne diseases;[3] whereas hepatitis and acute gastroenteritis are the major water-borne diseases.[4] In the present study, out of 108 patients, 48 patients had vector-borne diseases, whereas 30 patients had water-borne diseases. Despite development of various programs for the control of vector-borne diseases, these diseases comprise majority of cases of fever.

The pattern of fever etiology found in this study would not be representative for the causes of fever in the general population. There are three main limitations explaining this. The selection of patients admitted to a tertiary care hospital in India is biased as a result of factors such as severity of disease, gender and accessibility. In this study, only adults were included, while children would be expected to have different fever etiologies due to exposure and immunity. Entomological factors cause seasonal and geographical variations in vector-borne diseases in India.[5] Further studies are needed, both population- and hospital-based, in order to provide more evidence-based information about the etiological prevalence of fever in India.

CONCLUSION

A high number of infective diseases, in the form of dengue, malaria and viral hepatitis infections were found in a cohort of adult patients admitted to a tertiary care hospital with fever. This underlines the importance of vector-borne and water-borne diseases in public health and the need to control the spread of such diseases by proper implication of various health programs and early diagnosis and prompt intervention may help in reducing the mortality and morbidity.

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Face Shields Averted COVID-19, HAIs at Texas Hospital

A program of universal face shields for healthcare personnel (HCP) at a Texas hospital was associated with fewer COVID-19 infections as well as fewer hospital-associated infections (HAI), reported a researcher at the virtual IDWeek.

In the pre-intervention period, conducted from April 17 to July 5, HCP infection rate increased from 0% to 12.9%, but came down to 2.3% during the intervention period from July 6 to July 26, revealed Mayar Al Mohajer, MD, MBA, of Baylor College of Medicine in Houston. In the pre-intervention period, HAI cases increased from 0 to 7, but came down to 0 during the intervention period. Investigators noted that during the study period, 246 of 6,527 employees tested positive for SARS-CoV-2 (3.8%). After the intervention, change in predicted proportion positive in week 13 declined from 22.9% to 2.7%... (*Medpage Today*)

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Indian Journal of Clinical Practice, Vol. 31, No. 6, November 2020

Comparison of the Effect of Natural Protein Diet versus Conventional Intravenous Albumin in Ovarian Hyperstimulation Syndrome

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ABSTRACT

Aim: To compare the effectiveness of natural protein diet and intravenous (IV) albumin in the management of ovarian hyperstimulation syndrome (OHSS). **Material and methods:** One hundred thirty-eight participants at high risk of developing moderate or severe OHSS underwent *in vitro* fertilization (IVF) between October 2016 and September 2018. They were divided into two groups. Group A (n = 73) comprised of oral natural protein diet and Group B (n = 65) received IV albumin following oocyte retrieval. **Results:** The incidence of carry home baby rate in Group A was higher than Group B - 23 (56.09%) vs. 18 (45%), and was not found to be statistically significant (p = 0.96). There was also no significant difference in either groups in clinical pregnancy (41 [56.16%] vs. 40 [61.53%], p = 0.52) and fetal wastage (18 [43%] vs. 22 [55%], p = 0.23). However, Group A had an early syndrome recovery, effective control and management of OHSS than Group B. **Conclusions:** This study concludes that the natural protein diet is highly beneficial and less traumatic for the patient. So far, no medical literature has been published in relation to natural protein diet supplements in management of OHSS. There was also reduction in duration of hospital stay, severity of OHSS and cost-effectiveness among the study population. OHSS complications due to fluid shift, continuous IV fluid infusion with albumin and restriction to bed can be avoided. This is the first-of-its kind study to be conducted in our country till date.

Keywords: Ovarian hyperstimulation syndrome, IV albumin, polycystic ovarian syndrome, natural protein diet

The assisted reproduction technology (ART) is a rapidly advancing field, where clinical practices and laboratory techniques are regularly revised, validated and updated. Controlled ovarian hyperstimulation (COH) is one of the regimens which is actively followed in *in vitro* fertilization (IVF) treatments. The COH can sometimes lead to ovarian hyperstimulation syndrome (OHSS) which is a serious, life-threatening complication. However, the pathophysiology of OHSS still remains obscure.[1-3]

The OHSS is triggered by vasoactive mediators, which are released from hyperstimulated ovaries. The syndrome can also occur due to stimulation with clomiphene and gonadotropins. The occurrence of OHSS is more common in young women (<35 years) with low body mass index (BMI), patients with polycystic ovarian syndrome (PCOS), high serum estrogen concentration, multiple ovarian follicles at the time of human chorionic gonadotropin (hCG) administration and multiple pregnancies.[2-4]

The symptoms of OHSS can vary from mild to severe. Mild OHSS is characterized by mild abdominal discomfort, distension, nausea, vomiting, diarrhea and enlarged ovaries. Moderate OHSS is characterized by similar features as in mild OHSS with additional ultrasonographic evidence of ascites. Severe OHSS is characterized by additional findings of hydrothorax and breathlessness, change in the blood volume, increased blood viscosity due to hemoconcentration, coagulation abnormalities and diminished renal perfusion and function. The OHSS can also lead to free fluid collection in serous cavities, skin edema, antidiuretic hormone production, hypovolemia, oliguria and electrolyte imbalance. In its extreme form,

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OHSS may cause acute kidney injury (AKI), adult respiratory distress syndrome (ARDS), thromboembolic phenomena and ovarian enlargement caused by the multiple follicular development, which can lead to ovarian torsion.[2,4]

Several strategies to manage OHSS have been proposed, which include reduction of hCG dose, cycle cancellation, continuing gonadotrophic analog, steroids, administration of intravenous (IV) albumin, hydroxyethyle starch solution (HES), cabergoline and low-dose aspirin.[2,3,5,6] Prophylactic IV albumin is supposed to interrupt OHSS development by increasing plasma oncotic pressure. IV albumin could be helpful in preventing OHSS in high-risk patients. However, it does not completely eliminate the risk with possible side-effect.[7] Similarly, high-protein diet also reduces the side effects of OHSS such as ascites, pleural effusion by increasing the plasma oncotic pressure. However, there are no studies which have critically investigated to assess this efficacy of high-protein diet on prevention of OHSS. The intervention of high-protein supplements to prevent OHSS has an advantage of low-cost and ease of administration over others, which are much beneficial in resource limited countries, such as India. Our study aims to compare the effectiveness of conventional IV albumin and natural protein diet in the management of OHSS.

MATERIAL AND METHODS

The study was conducted between October 2016 and September 2018 at a single IVF center. One hundred thirty-eight patients who were considered to be at high risk of developing moderate or severe OHSS were included in the study, which was based on the presence of antral follicle count (AFC) of more than 10-15 on both ovaries and oocytes aspirated exceeding >15. A written informed consent was taken from all study patients who were subjected to COH with gonadotropin-releasing hormone (GnRH) agonist and antagonist protocol (Fig. 1 a and b). Each participant underwent comprehensive medical health check-up including medical history, physical examination, ultrasonographic ovarian evaluation, complete blood count, urinalysis, thyroid, liver and kidney function tests.

Ovarian Stimulation Protocols

The study group was subjected to two different stimulation protocols such as long protocol using GnRH agonist, at a dose of 3.6 mg on Day 20 of an oral contraceptive pill (OCP)-induced cycle and a short protocol using a GnRH antagonist as in Figure 1 a and b.

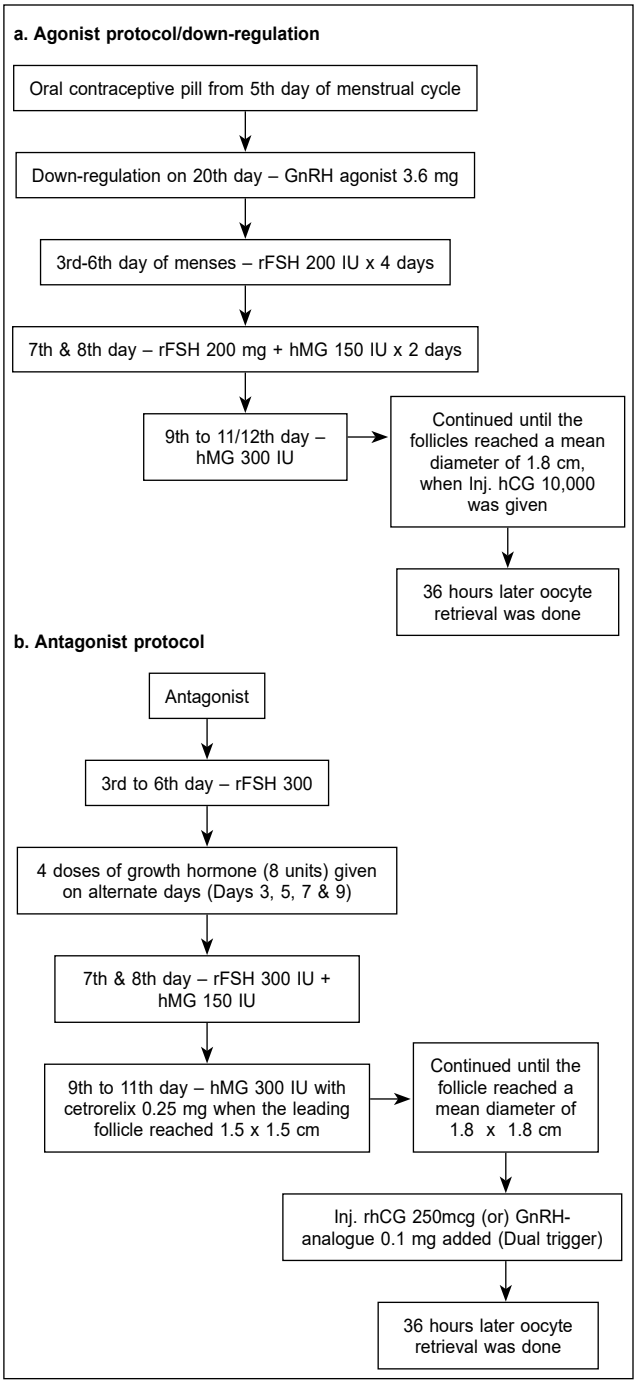

Figure 1. The details of stimulation protocol.

The patients were randomly placed in either group and the evaluation of patients remained the same while the protocols differed.

Agonist protocol

A basic evaluation was conducted by an ultrasound examination on Day 2/3 of the menstrual cycle to rule out functional follicular cysts and assess AFC followed by blood test for hormone levels (follicle-stimulating

hormone [FSH], luteinizing hormone [LH], estradiol [E2] and prolactin). The stimulation injections commenced from 3rd day of menstrual cycle comprising of recombinant FSH (rFSH) 200 IU for 4 days till the 6th day, followed by a combination of rFSH 200 IU and human menopausal gonadotropin (hMG) 150 IU on Day 7 and 8 and from Day 9 to 12, hMG 300 IU was continued till 2-3 leading follicles reached 1.8 × 1.8 cm when surrogate LH surge of hCG 10,000 IU was given. About 35-36 hours later oocyte retrieval is done.

Antagonist protocol

In the antagonist cycle, the stimulation injections commenced from 3rd day of menstrual cycle comprising of rFSH 300 IU for 4 days till the 6th day, followed by a combination of rFSH 300 IU and hMG 150 IU on Day 7 and 8 and from Day 9 to 11, hMG 300 IU was given. In this protocol, 4 doses (8 units) of growth hormone were administered on alternate days such as on Days 3, 5, 7 and 9 of menstrual cycle. Injection cetrorelix 0.25 mg was administered subcutaneously when the dominant follicles reached a mean diameter of 1.5 × 1.5 cm in size and continued till 2-3 leading follicles reached 1.8 × 1.8 cm. A trigger with injection recombinant hCG (rhCG) 250 μg or dual trigger with injection rhCG 250 μg and GnRH-analogue 0.1 mg was given simultaneously.

Transvaginal ultrasound-guided oocyte retrieval was performed 34-36 hours following the trigger. Based on the number of oocytes retrieved and size of the ovary on Day 2/3 following oocyte retrieval, fresh or frozen embryo transfer was planned. Patient was admitted and vital signs were monitored. They were advised to take high natural protein diet. Up to two embryos were transferred on Day 2/3 (48-72 hours) and a single blastocyst transfer on Day 5 (after 120 hours), if available. Freezing of extra-fertilized embryos and blastocysts was offered to all patients. Luteal support was given in the form of oral and vaginal progesterone 400 mg twice a day (800 mg daily).

Study Protocol

A retrospective analysis of two different interventions to prevent OHSS was done. Group A (n = 73) received a diet regimen which comprised of intake of natural protein diet (150 g/day) and Group B (n = 65) received IV albumin up to 1-9 bottles (20 g in 100 mL/bottle) the days following oocyte retrieval along with normal diet (Table 1). IV albumin was administered from 1 to 9 bottles depending upon the severity of OHSS.

Follow-up

During the initial phase, participants from both groups were hospitalized for monitoring and for conservative management. From the first day to recovery, the vital signs were monitored, like weight, input output chart, abdominal girth and daily ultrasonography (USG) to measure the size of the ovary and fluid in the pouch of Douglas. Blood investigations, such as serum electrolytes, hematocrit and coagulation profile were performed every 48 hours depending upon the severity of OHSS. In both groups, the serum albumin level was lower than the normal and the levels persisted to remain less than the normal.

In study Group A, symptoms of OHSS were less when compared to Group B. For patients, where embryo transfers were not done, tablet cabergoline 0.5 mg and injection GnRH-analogue 10 IU was given daily till menses.

Table 1. Demographic Representation of OHSS Patients

Description	Study Group A (n = 73)	Control Group B (n = 65)	P value
Age (years)	29.5 ± 3.75	29.6 ± 3.95	0.67
Infertility duration (years)	6.4 ± 3.30	6.59 ± 3.52	0.59
Endometrial thickness (mm)	1.01 ± 0.12	1.04 ± 0.18	0.257
Oocytes retrieved	19.76 ± 5.11	20.41 ± 7.12	0.0065
Hospital stay (days)	6.82 ± 1.69	8.29 ± 2.44	*0.003
IV Albumin used (1 unit = 100 mL)	0	343 ± 189	--
Albumin (Max-Min)	0	10-2	--
Pouch of Douglas aspiration	0	9	

*Since P-value is < 0.05, duration of hospital stay was reduced in Group A compared to Group B.

Study Group A participants' diet regimen was monitored by the doctors and staff nurses carefully along with their fluid intake during their stay in the hospital. Both groups were hospitalized till they were fit for discharge, the criteria for discharge being the reduction in size of the ovary (5.0 × 5.0 cm) and minimal pouch of Douglas fluid and reduction or maintenance of abdominal girth and weight. Patients were followed-up after discharge every 3rd day to see the ovary size and abdominal girth and vital signs. On each visit, serum estradiol was measured and ovarian size and ascites were evaluated by ultrasound examination. The severity of OHSS was determined according to the criteria of Schenker and Weinstein.[8] Pregnancies were detected by serum β-hCG subunit 2 weeks after embryo transfer and were included in the study records only if fetal heartbeat was present on ultrasound examination.

Study Parameters

Clinical characteristics that were evaluated included patient age, infertility duration and diagnosis. Outcome parameters included number of oocytes retrieved per patient, number of embryos transferred, clinical pregnancies and fetal heart beat as identified on ultrasound and any remnants of OHSS in study group.

RESULTS

One hundred thirty-eight patients were recruited into the study, of which 73 patients in Group A received high dietary protein from natural sources (Table 2) and 65 patients in Group B received IV albumin. Mean patient age, duration and cause of infertility were similar in both groups (Table 1). The two groups were also similar in endometrial thickness, number of oocytes retrieved and number of embryos transferred (Table 1).

In Group B, the average number of albumin used was 343 ± 189 mL. Nine (13.8%) participants of Group B underwent aspiration of excess fluid from third space, of which 2 had pleural effusion, 3 had trans-abdominal aspiration twice and 4 patients had transvaginal aspiration for 3-5 times from pouch of Douglas. However, none of the women in Group A required these procedures. The duration of hospital stay was significantly reduced in Group A compared to Group B (6.82 ± 1.69 vs. 8.29 ± 2.44, p = 0.003). In Group B, 2 participants had deep vein thrombosis and they were managed conservatively.

Moreover, the cost of natural protein diet is significantly lesser than that involved in IV albumin therapy. The cost of natural protein diet for 15 days was ₹ 4,890 (71.40$) with hospital stay of 6-8 days and investigation charges were Rs. 30,000 (438$), giving a total cost of Rs. 34,890 (509.71$). Group B participants were given albumin therapy for ₹ 5,500/day. The total cost of IV albumin, IV fluids with hospital stay and investigations came to around Rs. 90,000 to 1 Lakh (1460$). The cost adds up to three times that of natural protein diet. Table 3 summarizes the incidence rate of OHSS in the two study groups.

The clinical pregnancy rates in Group A and B were 41 (56.16%) and 40 (61.53%), respectively (p = 0.52) and fetal wastage in Group A and Group B were 18 (43%) and 22 (55%), respectively (p = 0.23) (Table 4). There was no significant difference either in clinical pregnancy or

Table 2. Protein Diet Chart

Source of protein	Quantity	Protein content
Egg	5 nos	30.00 g
Almonds	20 nos	05.10 g
Paneer	300 g	42.03 g
Mushroom	200 g	06.18 g
Sprouts	200 g	32.00 g
Protein powder	30 g (2 scoops)	40.00 g
Patient consumed total protein in 24 hours		**155.31g**
Approximately 40-45 g of natural protein was consumed per meal (3 meals/day)		

Table 3. OHSS Incidence Rates

OHSS severity	Group A (n = 73)	Percentage (%)	Group B (n = 65)	Percentage (%)	P value
Mild	59	81	50	77	0.58
Moderate or Severe	14	19	15	23	0.57
Moderate	11	15	10	15	0.96
Severe	3	4	5	8	--

No significant differences between Group A and Group B were observed.

Table 4. Pregnancy Outcome

Description	Group A (n = 73)	Percentage (%)	Group B (n = 65)	Percentage (%)	P value
Fresh transfer	73		65		
Clinical pregnancy rate	41	56.16	40	61.53	0.52
Carry home baby rate	23	56.09	18	45.00	0.96
Fetal wastage rate	18	43.90	22	55.00	0.23

fetal wastage in both the groups. However, the incidence of carry home baby rate in Group A (56.09%) was higher than Group B (45%), but it was not found to be statistically significant (Table 4). Further, there was early recovery observed in patients who took natural protein diet when compared to that of patients who received conventional IV albumin.

DISCUSSION

Ovarian hyperstimulation syndrome is an iatrogenic complication of ART. It is characterized by cystic enlargement of the ovaries and a fluid shift from the intravascular to the third space. Leakage of fluid from follicles, increased capillary permeability leading to third spacing (due to the release of vasoactive substances), or frank rupture of follicles can all cause ascites. Its impact on patient's health can be very deleterious and there have been fatal cases as well. The relationship between hCG and OHSS appears to be driven by the production of the angiogenic molecule vascular endothelial growth factor (VEGF). The incidence of moderate OHSS is reportedly 3-6%, while severe OHSS is estimated to occur in 0.1-3% of all cycles.[9] It is characterized by massive ovarian enlargement, ascites, hydrothorax, hemoconcentration, renal and liver dysfunction, and very rarely venous thrombosis.

The occurrence of OHSS is significantly lower in an antagonist protocol compared to an agonist protocol. These patients need admission to an intensive care unit (ICU) when critical OHSS develops.[7] Several studies show that albumin has both osmotic and transport functions. Its role as a carrier protein enables it to bind and inactivate the vasoactive intermediate released in OHSS patients. Albumin has also got colloid osmotic properties which maintain IV volume and prevent the effects of hypovolemia, ascites and hemoconcentration.[1,4]

Asch et al[10] were the first to administer IV human albumin (50 g) on the day of ovum retrieval in order to prevent OHSS in high-risk patients. According to this study, none of the 36 treated women developed severe OHSS. Of note, 21 of these women did not undergo embryo transfer, thus eliminating the risk of severe OHSS.

A study conducted by Bellver et al,[1] included both patients and oocyte donors; the subjects were divided into control group and IV albumin group. Baseline assessment was performed at oocyte retrieval and 7 days later hyperstimulated assessment was done. There was no significant difference noted between the albumin and control groups. Hence, they conferred that albumin does not improve the evolution of high-risk cases. Al-Inany[4] reviewed the effect of human albumin in the prevention of severe OHSS. IV albumin administration around the time of oocyte retrieval appeared to reduce the risk of severe OHSS in high-risk cases. However, he suggested that further study is necessary to optimize the dosage and timing of administration.

A meta-analysis done by Venetis et al,[5] concluded that prophylactic IV albumin administration following ovarian stimulation for IVF does not appear to reduce the occurrence of severe OHSS in high-risk patients. Soliman[6] compared the effect of cabergoline with IV albumin and combination of both for the prevention of the early onset OHSS. It was evident that administration of cabergoline along with IV albumin is more effective than the administration of albumin alone. Orvieto et al[11] revealed that 16 out of 289 patients treated with conventional IV albumin developed OHSS, in comparison with 26 of 328 patients in the control group. This was not statistically significant. Hence, albumin was ineffective against late severe OHSS. One more case series submitted by Lewit et al,[12] concurred that the administration of IV albumin could have contributed to reducing the level of severity of the syndrome. But, it is far from acting as either a cure or a preventive measure for OHSS.

Contradictory to the above quoted studies, in our study, the Group B patients were administered IV albumin 20 g/100 mL daily for 5-6 days depending on the severity of the OHSS. Three patients in Group A and 5 patients

in Group B developed severe OHSS, but complications like ascites, pleural effusion and thrombosis was seen mostly in Group B.

Cambiaghi et al[13] assessed the effect of oral whey protein for preventing OHSS. Group I patients received conventional treatments for OHSS (IV albumin on the day of oocyte retrieval, rest and orientation for increase water intake) while Group II, besides conventional treatment, received oral whey protein (80 g/day - 20 g four times a day) beginning on the day of oocyte retrieval. The study revealed that there was no difference between the two groups in terms of patient characteristics, but the duration of OHSS was lower in Group II than in Group I. The study concluded that the use of whey protein to prevent OHSS in high-risk patients may serve as a potential alternative, especially to avoid severe forms. Our study also revealed similar findings in the incidence of OHSS between the two groups.

However, since there are no randomized studies yet to authenticate the use of natural protein diet in OHSS patients, further research is needed to elaborate and conclude our results.

CONCLUSION

This study exhibits that the oral intake of natural protein diet acts better in preventing the severe form of OHSS than the administration of IV albumin in high-risk cases. Patients consuming natural protein diet incurred less expenditure, duration of hospital stay, reduced complications of OHSS and emotional stress as compared to patients on parenteral albumin. However, a more randomized study is necessary to validate the role of protein diet in the patients who are suspected to develop OHSS.

Acknowledgment

We thank Ms Suguna R and Ms Srimathi E from HR department for their inputs in editing this article.

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Indian Journal of Clinical Practice, Vol. 31, No. 6, November 2020

Comparison of 3-Port versus 4-Port Laparoscopic Cholecystectomy – A Prospective Comparative Study

SHEKHAR GOGNA*, PRIYA GOYAL†, PRATEEK THAKUR†, SONIA GOYAL‡

ABSTRACT

Laparoscopic cholecystectomy (LC) is the gold standard treatment for gallstones. Since its inception in 1987, it has undergone various changes, with reduced number of ports from standard 4-port LC to 3-port LC being one of them. Three-port LC has been shown to be equal to standard 4-port LC in terms of safety, complications, pain and hospital stay. We conducted a prospective comparative study amongst these two techniques. Three-port LC was found to be superior in terms of less postoperative pain, less need of analgesia, shorter hospital stay and ease of dissection. We concluded that 3-port LC is a better operative technique than 4-port LC.

Keywords: Three-port laparoscopic cholecystectomy, benefits, safety

Standard laparoscopic cholecystectomy (LC) is done by using 4 trocars. Exposing Calot's triangle for satisfactory anatomical details is of paramount importance in safe and proper surgery. The fourth (lateral) trocar is used to grasp the fundus of the gallbladder so as to expose Calot's triangle. The use of the fourth trocar, which is generally used for retraction of the fundus in the American technique, was found unnecessary by some surgeons[1] and LC can be performed safely without using it. With widespread advent of LC, comes the advent of reduction in port size.[2] Most of these studies have demonstrated the advantages of 3-port LC including less postoperative pain, early hospital discharge and less analgesic requirement. We did a prospective comparative clinical study to investigate the safety, and benefit of 3-port LC versus standard 4-port LC in our setup. Benefits associated with 3-port LC were compared in terms of pain on visual analog scale (VAS), requirement of analgesia and hospital discharge.

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MATERIAL AND METHODS

This was a comparative prospective study performed in the Dept. of Surgery, from January 2014 to January 2015. A total of 50 patients, diagnosed to have gallstone disease and confirmed on ultrasound examination, who were willing to participate in the study and gave valid consent, were included in the study. They were allocated into two groups of 3-port LC and 4-port LC with 25 patients in each group.

Exclusion Criteria

Patients with suspected common bile duct stones, history of obstructive jaundice, gallstone pancreatitis, acute cholecystitis.

Preoperative work-up was carried out, which included complete history, clinical examination and standard laboratory investigations for the fitness for surgery, including ultrasonography of abdomen and liver function tests.

In standard 4-port technique, one 10 mm umbilical port for camera was made after creating capnopneumoperitoneum with closed technique, another 10 mm epigastric port 5 cm below the xiphisternum (main working port), one 5 mm port in the right midclavicular line 5 cm below the right costal margin (accessory working port) and another 5 mm port, i.e., the fourth port in the right anterior axillary line

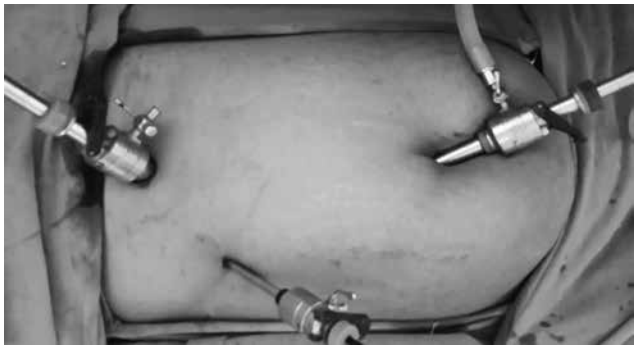

Figure 1. Three-port positions.

at the level of umbilicus were used. In 3-port technique, the 4th port (which was put at right anterior axillary line at the level of umbilicus) was not used (Fig. 1).

The outcomes were measured in terms of operating time, conversion rate, intraoperative complications, pain score, analgesic requirement and hospital stay. Intraoperative complications include gallbladder wall perforation, bile leak, bleeding from liver bed, iatrogenic liver injury and bile duct injury. In all patients, the same analgesics were used. Pain score was measured using VAS every 12 and 24 hourly. A VAS score 1-3 is called as low pain score (mild) and 4-10 as high pain score (severe).

Statistical Tests

The Student's *t*-test was used to evaluate the difference in each parameter. A p value <0.05 was considered statistically significant. Statistical package for Social Science version 19.0 for Windows (SPSS, Chicago, Illinois) was used for statistical analysis.

OBSERVATIONS

On comparing the two groups, we made the following observations (Table 1):

- Operating time: Mean operating time was 38.3 minutes in 3-port group while it was 41.0 minutes in the 4-port group. There was no significant difference in operating time in our study (p = 0.06).
- Conversion rate: Both the groups were equal in terms of conversion rate as it was zero in both of them.
- Intraoperative complications: There were two gallbladder wall perforations in 4-port group and no perforation in 3-port group; this was statistically significant (p = 0.02). There was no bleeding from liver bed on comparing both groups, no iatrogenic liver injury in both the groups and fortunately no bile duct injury was found.

Table 1. The Overall Endpoints of the Study

Findings	3-Port group	4-Port group	P value
Operating time (minutes)	38.3	41.0	0.06 (not significant)
Conversion rate	Nil	Nil	NA
Intraoperative complications			
Perforation of gallbladder only	0	2	0.02 (significant)
Bleeding	0	0	NA
Hepatobiliary injuries	0	0	NA
Pain score	1.8	2.9	0.01 (significant)
Analgesic requirement (number)	3.6	5.2	0.001 (significant)
Hospital stay (days)	1.3	2.4	0.02 (significant)

- Pain score: VAS on the scale of 1-10 was used. Mean score in 3-port group was 1.8, while it was 2.9 in 4-port group. This was statistically significant (p = 0.01). Three-port group had better outcome in terms of 4-port group when compared on the basis of VAS. The more pain experienced in 4-port group was probably due to more tissue trauma while putting the 4th port and putting the visceral peritoneum on more stretch.
- Analgesic requirement: Analgesic requirement was high in 4-port group. Patients in 4-port group required 5.2 injection of IV diclofenac 75 mg/2 mL/patient, while the mean requirement in 3-port group was of 3.6 injections/patient. This was statistically significant (p = 0.001), hence the analgesic requirement was significantly less in 3-port group.
- Hospital stay: Mean hospital stay was 1.3 days in 3-port group as most of the patients were discharged on the next day of surgery and it was 2.4 days in 4-port group.

DISCUSSION

At present, LC is the treatment of choice for gallbladder stones.[3] Less postoperative pain and early recovery are major goals to achieve better patient care and cost-effectiveness. These goals; however, cannot be compromised for patient safety. Since Slim et al reported that 4th port is not necessary in their 710 cases of LC, several studies have shown the technical feasibility,

Figure 2. Cystic duct completely dissected in Calot's triangle.

Figure 3. Cystic duct clipped and ready to be cut; cystic artery seen at the back of scissor.

safety, less pain and early hospital discharge with the 3-port LC.[4,5] In our study, we demonstrated that the advantages of 3-port LC were less intraoperative complications (perforation of gallbladder only), less pain, significantly reduced need for analgesia and shorter hospital stay. Operating time was not significantly different in the two groups in our study.

In our experience, perforations of gallbladder while dissection occurred in 4-port group because of undue and strong traction on fundus of gallbladder by assistant; there is more stretch on the tissues of gallbladder making them prone to perforation. Most of the studies comparing these two techniques conclude that there are either no or equal intraoperative complications, but we could prove that gallbladder perforation and subsequently bile spillage was more in 4-port group. Another surgical aspect that we observed is that the operating surgeon has full control while doing dissection of Calot's triangle and posterior and anterior peritoneal folds were dissected easily. So, skeletonization of cystic duct and artery becomes very easy, because there is no stretch on gallbladder and it is more mobile for dissection (Figs. 2 and 3).

Less pain and significant reduction of analgesia has been a strong push for reduced port surgery. Our study is in accordance with most of the other studies.[2,5-7] Less tissue dissection in abdominal wall, low stretch on visceral peritoneum significantly reduce the postoperative pain and shorten the hospital stay.

Significant reduction in pain and requirement of analgesia translates into shorter hospital stay in 3-port LC group. The reduction in hospital stay has been proved by many of the studies.[5,7] Three-port LC technique is easy to perform as compared to 4-port LC and can be safely performed after good training in LC.

CONCLUSION

We conclude that the 3-port LC technique is feasible, safe and has better outcomes as compared to those of the standard 4-port LC in terms of postoperative pain, need for analgesia and shorter hospital stay. The surgical technique is easy and dissection much easier. It is a better technique over 4-port LC.

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Indian Journal of Clinical Practice, Vol. 31, No. 6, November 2020

Prevalence of Undiagnosed COPD in Western Indian Population

ANAND YANNAWAR*, DAMANJIT DUGGAL, RAM CHOPRA

ABSTRACT

As per World Health Organization (WHO) data, chronic obstructive pulmonary disease (COPD) ranks amongst the top five causes of death in developed as well as in developing countries. Early identification of COPD is critical for preventive care and for instituting therapy. It is widely recognized that many people with COPD are undiagnosed, including some with significant airflow obstruction. A retrospective study was conducted in a Western Indian hospital to find out undiagnosed COPD patients in all admitted and outdoor patients from year 2008 till end of year 2010 for any cause, respiratory or nonrespiratory and also to grade the severity by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines.

Keywords: Chronic obstructive pulmonary disease, spirometry, FEV_1, FVC, GOLD criteria

As per World Health Organization (WHO) data, chronic obstructive pulmonary disease (COPD) ranks amongst the top five causes of death in developed as well as in developing countries. Three million people die every year due to COPD and it ranks as 3rd largest cause of death in world. Half a million people die every year due to COPD in India, which is over 4 times the number of people who die due to COPD in USA and Europe.

Early identification of COPD is critical for preventive care and for instituting therapy. Majority of COPD cases are undiagnosed although magnitude of this problem is very large. Prevalence of COPD in different studies ranges from 2% to 22% in men and 1.2% to 19% in women.

Both smokers and nonsmokers, males and females in rural and urban areas bear the brunt of progressive obstructive airways disease, which, if diagnosed earlier, can be prevented and treated to a larger extent with newer long-acting β_2-adrenergic receptor agonists (LABAs) and long-acting muscarinic receptor antagonists (LAMAs). Indian rural women still use Chullas (kind of wood burning cooking stove) leading to continuous smoke exposure, resulting in airways inflammation and COPD.

AIMS OF STUDY

To find out undiagnosed COPD patients in all admitted and outdoor patients in our hospital from year 2008 till end of year 2010 for any cause, respiratory or nonrespiratory, and also to grade the severity by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines.

MATERIAL AND METHODS

Spirometry data of all indoor patients and outdoor patients from year 2008 till end of year 2010 was retrieved and analyzed for missed out COPD diagnosis by GOLD criteria, i.e., forced expiratory volume in 1 second/forced vital capacity (FEV_1/FVC) ratio <70%. A total of 6,066 patients (3,964 males and 2,102 females) were included in this retrospective study. Previous COPD diagnosed cases were excluded. Demographic, health behavior and quality-of-life data was obtained from spirometry report and indoor records of the patients.

RESULTS

A total of 895 patients (14.75%) were found to meet COPD criteria in our study. Six hundred twenty-nine (70.27%) patients were males and 266 (29.72%) patients were females and all female patients were

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nonsmokers and probably they were exposed to bio fuel/wood burning smoke (Chulla smokers) (Figs. 1 and 2). Table 1 and Figures 3-5 give further analysis of our study.

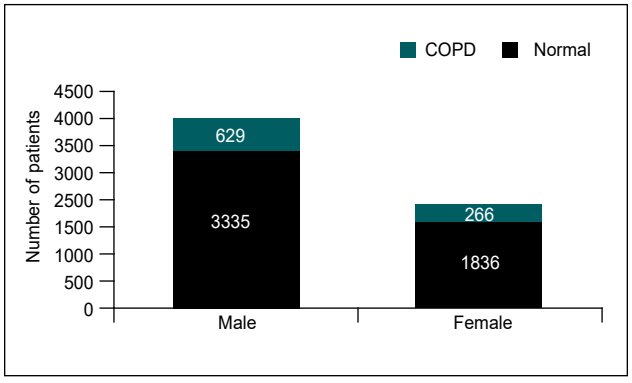

Figure 1. Number of patients diagnosed with COPD.

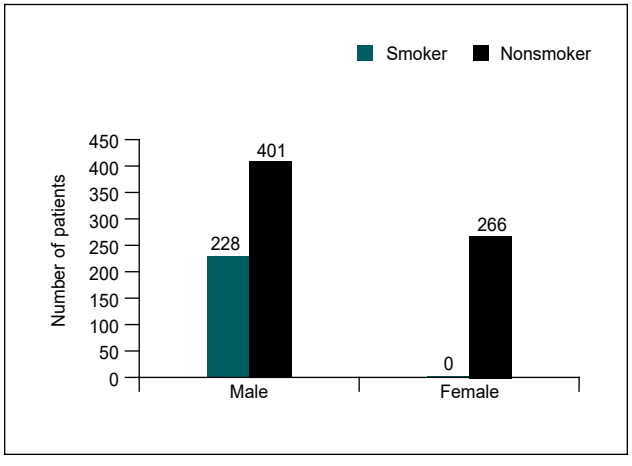

Figure 2. Smokers and nonsmokers who developed COPD.

Table 1. Demographic Profile of COPD Patients

Sex	Smoking status	Severity of obstruction
Male	Smokers 228 (36.24%)	Mild 3 (1.31%)
		Moderate 68 (29.82%)
		Severe 95 (41.66%)
		Very severe 62 (27.19%)
	Nonsmokers 401 (63.75%)	Mild 12 (2.99%)
		Moderate 191 (47.63%)
		Severe 146 (36.40%)
		Very severe 52 (12.96%)
Female	All are nonsmokers 266	Mild 5 (1.87%)
		Moderate 109 (40.97%)
		Severe 112 (42.10%)
		Very severe 40 (15. 03%)

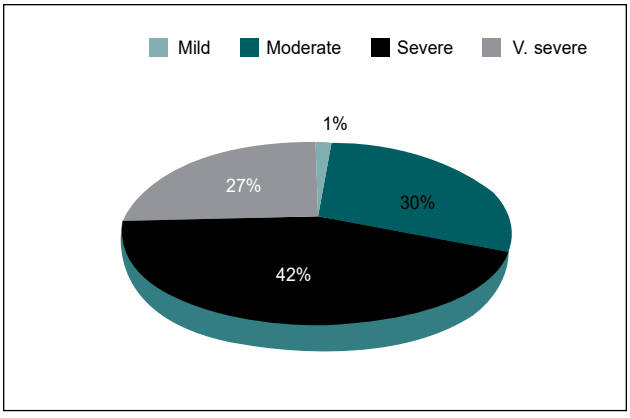

Figure 3. Severity of COPD in smokers.

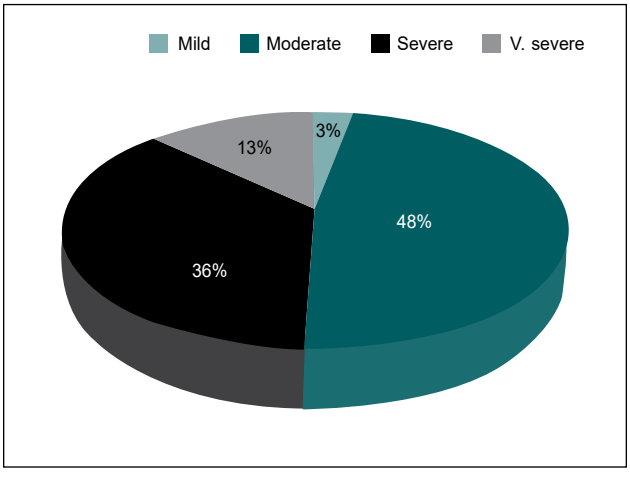

Figure 4. Severity of COPD in male nonsmokers.

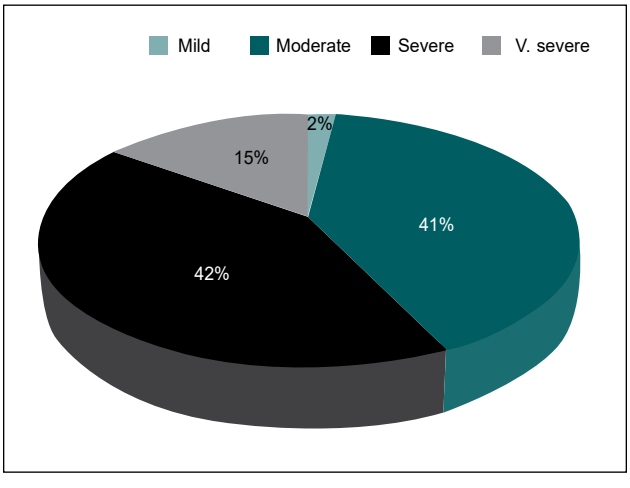

Figure 5. Severity of COPD in females.

DISCUSSION

It is widely recognized that many people with COPD are undiagnosed, including some with significant airflow obstruction. Tobacco smoking is the most important and traditionally famous risk factor for developing

COPD. Indian families use wood and animal dung for cooking food and making water warm for bath and it is the major risk factor for developing COPD in India and developing countries. During her lifetime, every woman who spends 2-3 hours for cooking every day inhales a volume of 25 million liters of highly polluted air, thereby exposing herself to extremely high levels of particulate matter and gaseous air pollutants. Burning one mosquito coil in the night emits as much particulate matter pollution, as that which is equivalent to around 100 cigarettes.

Other causes of COPD are chronic poorly treated persistent asthma, history of tuberculosis, occupational lung diseases and chemical use for killing mosquito and bed bugs. Making a diagnosis of COPD and its differentiation from other diseases presents an important challenge for primary care practitioners and in higher referring centers. Making diagnosis of COPD on the basis of clinical history and examination can underestimate diagnosis.

In our study, incidence of COPD in nonsmoker males was found to be higher (63.75%). Various studies found the prevalence of undiagnosed COPD between 4% and 18.2%. Even though total patients who visited this tertiary care center were 1,22,750, the PET was done in only 6,066 (4.94%) patients. Spirometry is a useful tool to diagnose serious respiratory diseases like COPD. This 14.75% undiagnosed COPD patients of our study seems to be tip of iceberg.

CONCLUSION

- 14.75% COPD patients were undiagnosed even after suffering from long time.
- Significant number of females were undiagnosed (i.e., 29.72%).
- All females were nonsmokers and biomass exposure was the main factor for developing COPD.
- More smokers were suffering from severe COPD as compared to nonsmokers.
- Diagnosing undiagnosed COPD early and treatment are necessary to prevent repeated admission and early deaths.
- Chulla smoking is one of the major culprits for nonsmokers' COPD in developing countries like India.

SUGGESTED READING

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Statins Tied to Lower Mortality Risk from Sepsis

Among individuals admitted to hospitals with sepsis, statin users were found to have a lower mortality, compared to nonstatin users in a recent analysis of a large and diversified cohort of patients in California.

Hazard ratios for mortality at 30 and 90 days were lower by nearly 20% for statin users admitted for sepsis, compared to nonstatin users, revealed the retrospective cohort study. The study included 1,37,019 individuals admitted for sepsis within the Kaiser Permanente Southern California health system from 2008 through 2018. Of these, 36,908 were taking a statin. Differences in mortality were in favor of statin users, compared to nonusers, with HRs of 0.79 (95% CI, 0.77-0.82) at 30 days and 0.79 (95% CI, 0.77-0.81) at 90 days, suggested the report, presented at the annual meeting of the American College of Chest Physicians held virtually… (*Medscape*)

Indian Journal of Clinical Practice, Vol. 31, No. 6, November 2020

Acute Encephalitis Syndrome: A Rare Presentation of Scrub Typhus in Adults

VIRENDRA KR GOYAL*, JITESH AGGARWAL†, MANAN DAVE‡, ROOTIK PATEL‡

ABSTRACT

Scrub typhus or bush typhus or tsutsugamushi disease is a mite-borne acute febrile illness caused by Gram-negative intracellular organism *Orientia tsutsugamushi* (which belongs to the family of Rickettsiaceae). Common presentation of scrub typhus includes fever, headache and inoculation eschar and lymphadenopathy. In severe forms, pneumonia, myocarditis, azotemia, shock, gastrointestinal bleeding and meningoencephalitis are known to occur. Central nervous system (CNS) involvement may be a complication of scrub typhus, which ranges from meningitis to frank meningoencephalitis. Here we are describing a case of acute encephalitis syndrome (AES), following scrub typhus infection in an adult patient. Patient didn't have concurrent infection with any other tropical fever diseases, like malaria, chikungunya, typhoid and dengue fever. Patient was put on injection ceftriaxone, capsule doxycycline, tablet azithromycin, tablet levetiracetam and symptomatic treatment with multivitamin support. By Day 3, patient's sensorium improved and he started to follow verbal commands. Patient was hospitalized in our tertiary care medical college and hospital (AIIMS, Udaipur) for 7 days and recovered completely.

Keywords: Scrub typhus, eschar, thrombocytopenia, acute encephalitis syndrome, Rickettsiaceae

Scrub typhus or bush typhus or tsutsugamushi disease is a mite-borne acute febrile illness caused by Gram-negative intracellular organism, *Orientia tsutsugamushi* (which belongs to the family of Rickettsiaceae). Although the disease has a worldwide distribution, most of the cases are reported from the so-called "tsutsugamushi triangle", which is a wide area bounded by Pakistan, India, Nepal in the West; Siberia, Japan, China and Korea in the North and Indonesia, Philippines, Australia and the Pacific Islands in the South and is mostly related to agriculture and outdoor activities. There is an estimated 1 million new scrub typhus infections each year and over 1 billion people around the world are at risk of this potentially fatal tropical illness.

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It is a common, zoonotic disease in South-East Asia and on account of rapid urbanization of rural and forested areas, it is becoming increasingly common in India. Common presentation of scrub typhus includes fever, headache and inoculation eschar and lymphadenopathy. In severe forms, pneumonia, myocarditis, azotemia, shock, gastrointestinal bleeding and meningoencephalitis may occur. Central nervous system (CNS) involvement may be a complication of scrub typhus which ranges from meningitis to frank meningoencephalitis. The name "typhus" itself, is derived from the Greek word "typhos", which means stupor. Other neurological complications include seizure, cranial nerve deficits, vasculitic cerebral infarct, brain hemorrhages, polyneuropathy, sensorineural hearing loss, meningitis or meningoencephalitis. Here we are describing a case of acute encephalitis syndrome (AES), following scrub typhus infection in an adult patient. The patient did not have concurrent infection with any other tropical fever diseases, like malaria, chikungunya, typhoid and dengue fever.

CASE SUMMARY

A 25-year-old male resident of Southern Rajasthan presented in our hospital with complaints of fever with chills and rigors for 7 days, decreased appetite

and altered sensorium, unable to speak for 2 days and involuntary movements of all four limbs with frothing from the mouth and up rolling of eye balls. On examination, patient was running a high-grade temperature of 101.4°F. Blood pressure 90/80 mmHg in supine position, pulse 120/min, SpO_2 98%. Patient was unconscious, disoriented with time, place and person. Patient was not following any verbal commands. For these complaints, patient was admitted in medical intensive care unit (MICU) in our hospital. On general physical examination of the patient, eschar was found (Fig. 1). Tongue bite was present. CNS examination: Higher mental functions and cranial nerve examination could not be accessed. Pupils were normally reacting to light. There were no signs of increased intracranial pressure (ICP). Neck rigidity and hypertonia were present. Bilateral plantar were extensor. Other systems didn't show any abnormality. There was no organomegaly on per abdomen examination. Fundus examination of the patient suggested no signs of papilledema and increased ICP. Noncontrast computed tomography (NCCT) head was done to rule out hydrocephalus, and it was normal. Magnetic resonance imaging (MRI) brain could not be done due to institutional constraints. Lumbar puncture was done under aseptic precautions and cerebrospinal fluid (CSF) fluid was sent for cytological and biochemical analysis. On gross examination, CSF was drained with normal pressure and was found clear. CSF was found acellular, with proteins 22 mg/dL, sugar 66.8 mg/dL. Corresponding blood sugar was 122 mg/dL. Gram stain and Ziehl-Neelsen staining of CSF fluid was negative. X-ray chest (PA view) of the patient was normal. Complete blood count (CBC) showed mild thrombocytopenia (hemoglobin [Hb]: 13.5, white blood cell [WBC]: 5.63, platelet: 62,000) with mild derangement of liver enzymes with serum glutamic pyruvic transaminase (SGPT): 104.9, serum glutamic oxaloacetic transaminase (SGOT): 78.9. MP QBC, immunoglobulin (IgM/IgG) dengue and NS1 antigen to rule out dengue and IGM typhidot to rule out typhoid fever and enzyme-linked immunosorbent assay (ELISA) test for chikungunya of the patient were negative.

Ultrasonography of abdomen revealed biliary sludge and moderate splenomegaly (Fig. 2). ELISA test to detect IgM antibodies against *O. tsutsugamushi* antigens for scrub typhus was found positive. Patient was put on injection ceftriaxone, capsule doxycycline, tablet azithromycin, tablet levetiracetam and symptomatic treatment with multivitamin supports. By Day 3, patient's sensorium improved and he started to follow verbal commands. He was hospitalized in our tertiary care medical college and hospital for 7 days and recovered completely.

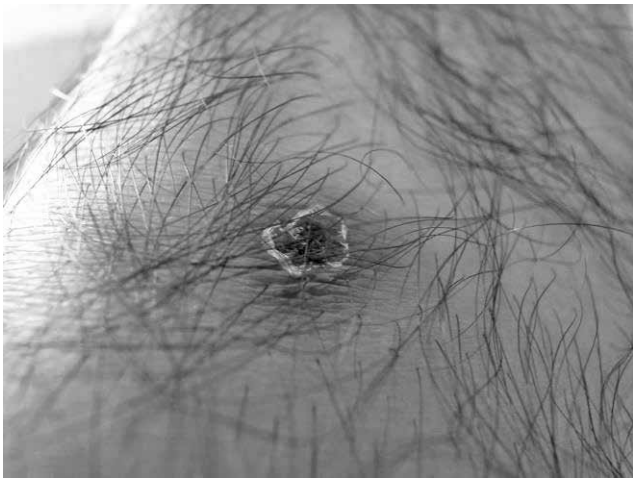

Figure 1. Eschar at left knee.

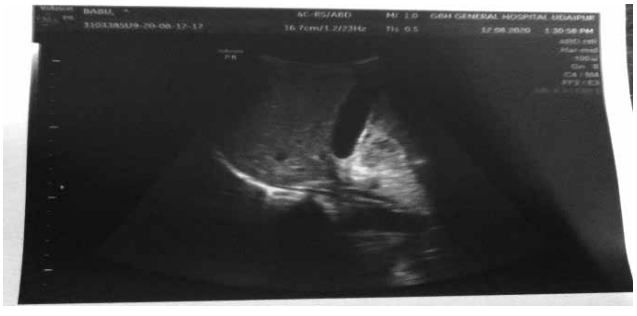

Figure 2. Ultrasonography of the abdomen indicating the presence of biliary sludge in gallbladder.

DISCUSSION

Scrub typhus is a potentially fatal infection, affecting nearly 1 million people each year. The disease first gained significance during the World War II. Several from the US, Ceylon and Burma armies were infected and succumbed to the illness due to lack of proper antibiotic treatment.

Several epidemics of scrub typhus have occurred in India, yet, the literature is still limited. *O. tsutsugamushi* is known to cause this disease and was first identified and studied in Japan in 1930. An obligate intracellular bacterium, it is transmitted to humans by the bite of larval mites (chiggers) of *Leptotrombidium deliense*. The incubation period is 6-21 days with an average of 10 days. The larval mites usually feed on wild rats. There are several serotypes of *O. tsutsugamushi*, and infection with one species provides only transient cross immunity to another. When a forest is cleared, scrubs

tend to grow on those areas. These scrubs later get infested by larval mites. When man comes in contact with these scrubs, he contracts the infection. The basic pathologic changes include focal vasculitis and perivasculitis of small blood vessels in the involved organs. These occur as a result of multiplication of the organism in the endothelial cells lining the small blood vessels.

Acute encephalitis syndrome is characterized by rapid onset of febrile illness associated with convulsions, altered sensorium and focal neurological deficit such as aphasia, hemiparesis, involuntary movements, ataxia or cranial nerve involvement. In a study conducted in India, on acute febrile encephalopathy including 120 patients, the common causes included acute viral encephalitis, pyogenic meningitis, tuberculous meningitis, cerebral malaria and sepsis related encephalopathy. On the contrary, in our case, the etiology was scrub typhus. This unusual presentation of scrub typhus can be easily overlooked (in this COVID era), resulting in delay in initiating life-saving treatment.

CONCLUSION

Acute encephalitis syndrome is not an uncommon neurological presentation following scrub typhus infection in adults. It should be suspected in all patients with fever, altered sensorium and hepatic involvement. Oral azithromycin can be started as soon as possible for better outcomes.

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■■■■

Pfizer Starts COVID-19 Vaccine Trial in Teens

Pfizer is now enrolling teenagers in clinical trials for its COVID-19 vaccine candidate. The participation age has been expanded to include high schoolers and middle schoolers.

Pfizer is the only company that has allowed minors to join the COVID-19 vaccine trials at present. The company previously reduced the age to 16, and this week, Cincinnati Children's Hospital Medical Center vaccinated the first 12-year-old. Amidst this new development, vaccine experts and pediatricians have mixed reactions, reported USA Today. While some are of the opinion that drug manufacturers should wait until the vaccines are approved in adults, others say that it is necessary to start vaccine testing among specific groups, including minors… (*Medscape*)

Indian Journal of Clinical Practice, Vol. 31, No. 6, November 2020

Another Feather to the Tale: Pseudo-vesicular Pityriasis Rosea

SHAURYA ROHATGI*, SAURABH JINDAL*, SHAHNAZ KHAN*

ABSTRACT

Pityriasis rosea (PR) is an acute, self-healing exanthema characterized by oval erythematous-squamous lesions of the trunk and limbs, usually sparing face, scalp, palms and soles. The literature is flooded with reports of increasingly diverse morphology and distribution of lesions associated with this condition. Although vesicular lesion has consistently been reported as one of the atypical presentations of PR, to the best of our knowledge, there is a lack of reports of PR presenting as pseudo-vesicles. We report a case of a 29-year-old female with 2½ months of amenorrhea who presented with asymptomatic, reddish, raised lesions over the trunk and extremities of 2 days duration. She was investigated and diagnosed to have perivascular PR.

Keywords: Pseudo-vesicular, pityriasis rosea, atypical

Pityriasis rosea (PR) continues to elude dermatologists with its controversial etiology and atypical presentations even after two centuries since it was first described. The literature is flooded with reports of increasingly diverse morphology and distribution of lesions associated with this condition.

CASE REPORT

A 29-year-old female with 2½ months of amenorrhea ($G_3P_0L_0A_2$) presented with asymptomatic, reddish, raised lesions over the trunk and extremities of 2 days duration. The lesions first appeared on the right breast and in the following 2 days, similar lesions appeared over the trunk and proximal extremities. Patient also complained of fever prior to the appearance of skin lesions. There was no history suggestive of preceding upper respiratory tract infection, abdominal complaints, arthralgia, myalgia, malaise and headache. She was taking any medication other than routine supplements prescribed for pregnancy. She had history of first trimester abortion in the previous two pregnancies, but never had any skin rash during the corresponding period of loss of pregnancy. Patient was febrile (100^0F), but vitals were stable and general examination showed no positive findings. Cutaneous examination

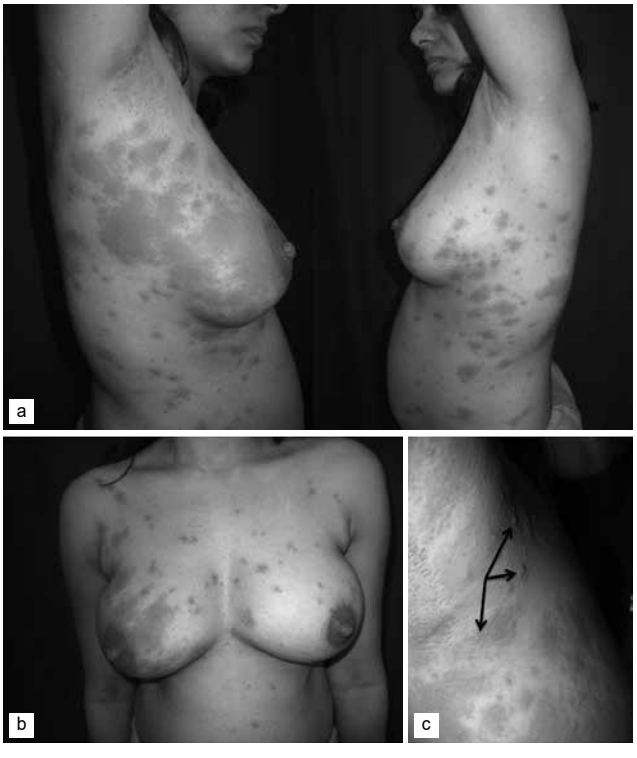

Figure 1. Clinical photographs at presentation. **a)** lateral aspect of trunk showing multiple, bilaterally symmetrical, erythematous papules and plaques; **b and c)** multiple erythematous papules and plaques on the chest and back.

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revealed multiple bilaterally symmetrical, infiltrated, erythematous, nonscaly papules and plaques with pseudo-vesicular surface present on the chest, abdomen, back, pubic area and proximal thighs (Fig. 1 a-c). The lesions had coalesced to form larger plaques but the smaller ones showed some orientation along the lines of skin cleavage, especially over the lateral areas of trunk and back. Mucosa was spared, and scalp, genitals, hair and nails were unremarkable. Systemic examination showed no abnormality. We considered a differential diagnosis of Sweet syndrome and atypical PR. The previous history of first trimester abortions led us to think of an underlying antiphospholipid antibody syndrome (APLAS). Erythrocyte sedimentation rate (ESR) and hemogram were normal except for mild neutrophilia (81%), but without any rise in total leukocyte count. Blood sugar, urine routine, microscopy and liver, renal and thyroid function tests were within normal limits. Human immunodeficiency virus - enzyme-linked immunosorbent assay (HIV-ELISA), hepatitis B surface antigen (HBsAg) and Venereal Disease Research Laboratory (VDRL) tests were negative. Sonography showed a single live fetus with no anomalies. Antinuclear antibodies (ANA) and anti-dsDNA were negative. Likewise, the antibodies against lupus anticoagulant, cardiolipin and β_2-glycoprotein were also negative, thus ruling out APLAS. Skin pathergy test was negative.

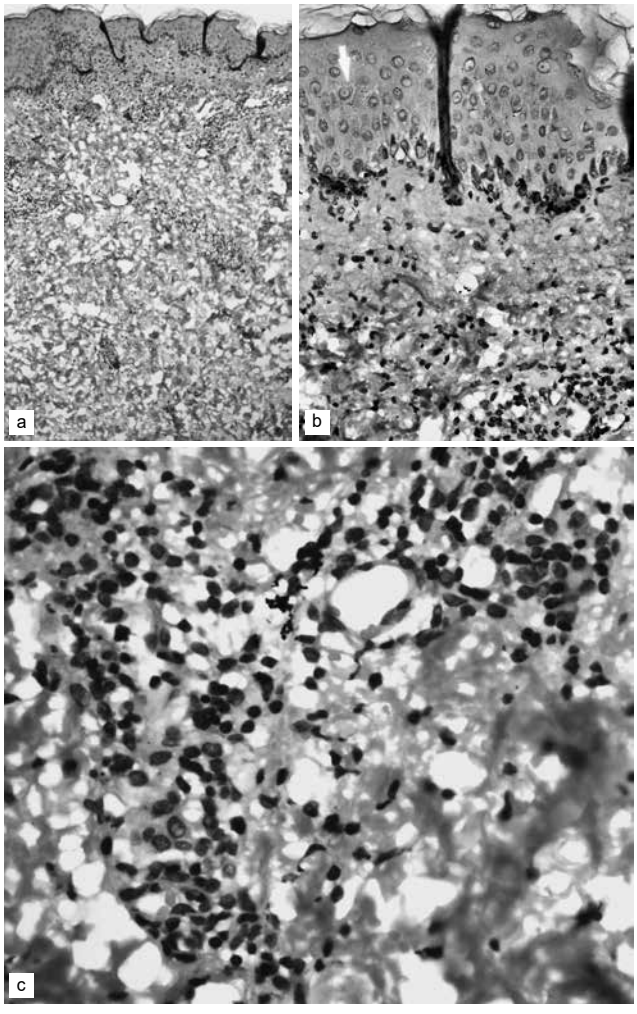

Figure 2. Histopathology: **a)** Epidermis showing minimal acanthosis with dermis showing perivascular and interstitial infiltrate (H&E, x100); **b)** mild spongiosis (*arrow*) seen in stratum spinosum (H&E, x200); **c)** high power view shows RBC extravasation and perivascular infiltrate composed of lymphocytes, neutrophils and occasional eosinophils (H&E, x400).

Histopathology of skin lesions showed very subtle patchy spongiosis in the stratum spinosum and superficial dermal infiltration with lymphocytes, neutrophils and occasional eosinophils (Fig. 2 a-c). The patient was treated symptomatically with antihistamines and topical calamine lotion. Interestingly, the patient showed significant resolution of lesions 1 week following the first visit. The lesions had flattened and all that remained was minimally pigmented macules and patches with few areas showing slight erythema as well (Fig. 3 a-c). This event shifted the final diagnosis in favor of PR.

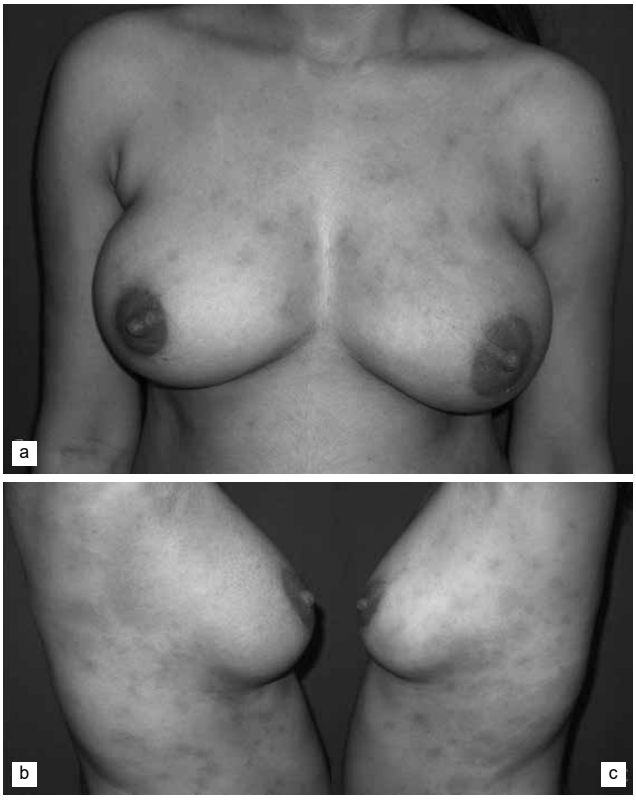

Figure 3. Anterior aspect of trunk showing faintly erythematous patches 1 week following presentation.

DISCUSSION

Pityriasis rosea is an acute, self-healing exanthema characterized by oval erythematous-squamous lesions of the trunk and limbs, usually sparing face, scalp, palms and soles. Variations from this classical description are known to be fairly common, but difficult to quantify. The incidence of the herald patch varies from 40% to 76%, and similar to our patient, its absence does not exclude the diagnosis. Although vesicular lesion has consistently been reported as one of the atypical presentations of PR, to the best of our knowledge, there is a lack of reports of PR presenting as pseudo-vesicles. Purpuric or hemorrhagic, and urticarial variants have also been commonly reported. Other rarer types include large patches (PR gigantea of Darier) and papular PR. Sites such as face, axillae and groins are predominantly involved in PR inversus. Involvement of mucous membranes is not uncommon.

The simplest and most accurate description of the characteristic orientation of secondary eruptions should be "along lines of skin cleavages". On careful examination, we noticed a similar pattern in our patient. Clichés associated with descriptions of the orientation such as "Christmas-tree", "inverted Christmas-tree", "fir tree" and "parallel to the ribs" are imprecise and probably obsolete. The age of our patient and the time of outbreak of the rash correspond to an epidemiological study in the country. Out of 200 cases reported in the study, only one patient presented with PR during pregnancy. Reports of PR in pregnancy in Indian literature are infrequent. However, Corson et al in 1950 reported that PR is more common during pregnancy as compared to the general population (18% vs. 6%), but this finding has not been corroborated by subsequent studies.

Sweet's syndrome patients appear dramatically-ill, whereas our patient had no constitutional signs and symptoms. Although classical Sweet's is known to occur in pregnant females, but absence of features like mucosal lesions, systemic involvement, leukocytosis and confirmatory histopathology diminished the odds even further. Without therapeutic intervention, patients with classical Sweet's may show resolution of lesions, but this usually takes weeks or months. On the other hand, self-resolution is the rule in PR and this may take an average of 45 days. Our patient showed signs of resolution in about 10 days from onset of rash. Cases with similar course, i.e., remission within 2 weeks of appearance of rash have been reported in the past.

A study suggests that PR developing during pregnancy may be followed by premature delivery and even fetal death. The total abortion rate reported was 13%, but it reached a staggering 57-62% if PR developed within 15th week of gestation. The authors recommended a closer follow-up for women who develop PR during the first 15 weeks of gestation, especially with atypical forms. Other than the PR episode, the pregnancy period in our patient was uneventful. Nonetheless, due to the above mentioned risks and given her previous history of abortions, we closely monitored her for occurrence of any adverse event.

Acknowledgments

We thank Dr Rajiv Joshi for his constant support to our department through his impeccable histopathological and clinical skills.

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- Allergic Cough
- Cough with RTI
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COVID-19 and Encephalitis Lethargica

BV MURLIMANJU*, MD MOSHIUR RAHMAN†, LUIS RAFAEL MOSCOTE-SALAZAR‡, SANTOSH WAKODE#, AMIT AGRAWAL¥

In a recent article, Giordano et al[1] share their thoughts "Coronavirus disease 2019 (COVID-19): can we learn from encephalitis lethargica?", and remind us that there are lessons from the past which need attention, i.e., the possibilities of 1918 influenza pandemic, leading to the neurological complications like encephalitis lethargica and Parkinson's disease.[1] Already, there are studies which provide details regarding neurological complications in COVID-19 patients,[2,3] like ischemic stroke, encephalitis and meningitis. Coronaviruses enter the peripheral nerve endings and proceed towards the central nervous system.[4] It is also reported that, there may be direct invasion with the hematogenous spread and spread through the olfactory tract.[3] This is supported by the fact that about 85% of COVID-19 patients have history of anosmia.[5] Altered taste and smell sensation can guide in the diagnosis of COVID-19.[6,7] Coronaviruses can also enter the nervous system by invading the brainstem,[8] through the vagal afferents from the lungs and upper respiratory tract.[2,8]

Published reports suggest that acute myelitis in COVID-19 like Guillain-Barré syndrome may need to be considered as a potential spinal cord involvement.[9] Possible transneural/axoplasmic transfer of coronavirus to the cerebrum, just like the other neurotropic viruses, may be another underestimated mechanism that needs further exploration.[10] Giordano et al[1] gave an insight about the neuroinvasion of COVID-19, which can support the Von Economo's hypothesis and reminiscence about the spreading through the neuron to neuron propagation in diseases like parkinsonism. We agree with the opinion of Giordano et al that we should review the historical and novel evidences. COVID-19 definitely has neuroinvasion, which is supported by anosmia in these patients. We endorse the opinion of Giordano et al, that one should not undervalue the potential long-term complications of COVID-19, like the neuronal degeneration.

It will also be interesting to study the extent to which the coronavirus causes damage to the neurons of functional areas, like cardiorespiratory center in post-mortem samples[4] to find out the association between sudden cardiac death, myocardial infarction and respiratory distress in patients infected with COVID-19. The COVID-19 virus can multiply in the gastrointestinal epithelium and the worst consequence will be the associated alimentary tract symptoms along with the respiratory distress. These patients may require mechanical ventilation.[11] It has been demonstrated that COVID-19 virus can bind with the angiotensin-converting enzyme (ACE)2 receptors.[12] The symptoms of gastrointestinal dysfunction indicate the involvement of enteric nervous system.[13] This concept is further supported by the fact that ACE2 receptors are expressed more in the gastrointestinal tract than the lungs.[14] However, there is a need for further studies to comprehensively understand the role and use of ACE inhibitors on the outcome of patients with COVID-19.[15]

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Soft Drink Consumption and Heart Health

It doesn't take too much soft drink consumption for people to have elevated risk of cardiovascular disease (CVD), revealed a large cohort study in France.

People who consumed the most sugary drinks (a median 185 mL or 6.26 fl oz per day [hardly half a can of ordinary soda]) had increased likelihood of experiencing a CVD event compared with nonconsumers of these drinks (HR 1.20, 95% CI 1.04-1.40), reported researchers in the *Journal of the American College of Cardiology*. Additionally, those who consumed relatively more artificially sweetened beverages (176.7 mL or 5.97 fl oz per day) had higher CVD risk over a median 6.6 years of follow-up compared with nonconsumers (HR 1.32, 95% CI 1.00-1.73)… (*Medpage Today*)

FDA OKs Lotion for Nonprescription Use to Treat Head Lice

The US FDA has approved a lotion to treat head lice for nonprescription or over-the-counter (OTC) use. The approval has been granted through a process called a prescription (Rx)-to-OTC switch.

Initially, the FDA approved ivermectin lotion, 0.5% for the treatment of head lice infestation in patients aged 6 months and above as a prescription drug in February 2012.

This is a single-use lotion with the active ingredient ivermectin 0.5% for the topical treatment of head lice infestations in patients 6 months of age and above. It is for external use only and should only be used on the scalp and dry hair in line with label instructions. The lotion is not approved for any other use… (*FDA*)

Russia Applies for WHO Emergency Use Tag for Sputnik V

Applications have been submitted by the Russian Direct Investment Fund (RDIF) to the World Health Organization for an Emergency Use Listing as well as prequalification of its COVID-19 vaccine, Sputnik V, stated Russia's sovereign wealth fund.

An Emergency Use Listing (EUL) helps make a vaccine available across the globe faster. A WHO prequalification is a global quality tag that ensures that a vaccine is safe and effective. The procedures would allow the vaccine to be included in the list of medical products that meet leading quality, safety and efficacy standards, said RDIF CEO Kirill Dmitriev. This vaccine is based on a platform of human adenoviral vectors… (*Reuters*)

Every citizen of India should have the right to accessible, affordable, quality and safe heart care irrespective of his/her economical background

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"No one should die of heart disease just because he/she cannot afford it"

About Sameer Malik Heart Care Foundation Fund

"Sameer Malik Heart Care Foundation Fund" it is an initiative of the Heart Care Foundation of India created with an objective to cater to the heart care needs of people.

Objectives

- Assist heart patients belonging to economically weaker sections of the society in getting affordable and quality treatment.
- Raise awareness about the fundamental right of individuals to medical treatment irrespective of their religion or economical background.
- Sensitize the central and state government about the need for a National Cardiovascular Disease Control Program.
- Encourage and involve key stakeholders such as other NGOs, private institutions and individual to help reduce the number of deaths due to heart disease in the country.
- To promote heart care research in India.
- To promote and train hands-only CPR.

Activities of the Fund

Financial Assistance

Financial assistance is given to eligible non emergent heart patients. Apart from its own resources, the fund raises money through donations, aid from individuals, organizations, professional bodies, associations and other philanthropic organizations, etc.

After the sanction of grant, the fund members facilitate the patient in getting his/her heart intervention done at state of art heart hospitals in Delhi NCR like Medanta – The Medicity, National Heart Institute, All India Institute of Medical Sciences (AIIMS), RML Hospital, GB Pant Hospital, Jaipur Golden Hospital, etc. The money is transferred directly to the concerned hospital where surgery is to be done.

Drug Subsidy

The HCFI Fund has tied up with Helpline Pharmacy in Delhi to facilitate patients with medicines at highly discounted rates (up to 50%) post surgery.

The HCFI Fund has also tied up for providing up to 50% discount on imaging (CT, MR, CT angiography, etc.)

Who is Eligible?

All heart patients who need pacemakers, valve replacement, bypass surgery, surgery for congenital heart diseases, etc. are eligible to apply for assistance from the Fund. The Application form can be downloaded from the website of the Fund. http://heartcarefoundationfund.heartcarefoundation.org and submitted in the HCFI Fund office.

Important Notes

- The patient must be a citizen of India with valid Voter ID Card/ Aadhaar Card/Driving License.
- The patient must be needy and underprivileged, to be assessed by Fund Committee.
- The HCFI Fund reserves the right to accept/reject any application for financial assistance without assigning any reasons thereof.
- The review of applications may take 4-6 weeks.
- All applications are judged on merit by a Medical Advisory Board who meet every Tuesday and decide on the acceptance/rejection of applications.
- The HCFI Fund is not responsible for failure of treatment/death of patient during or after the treatment has been rendered to the patient at designated hospitals.
- The HCFI Fund reserves the right to advise/direct the beneficiary to the designated hospital for the treatment.
- The financial assistance granted will be given directly to the treating hospital/medical center.
- The HCFI Fund has the right to print/publish/webcast/web post details of the patient including photos, and other details. (Under taking needs to be given to the HCFI Fund to publish the medical details so that more people can be benefitted).
- The HCFI Fund does not provide assistance for any emergent heart interventions.

Check List of Documents to be Submitted with Application Form

- Passport size photo of the patient and the family
- A copy of medical records
- Identity proof with proof of residence
- Income proof (preferably given by SDM)
- BPL Card (If Card holder)
- Details of financial assistance taken/applied from other sources (Prime Minister's Relief Fund, National Illness Assistance Fund Ministry of Health Govt of India, Rotary Relief Fund, Delhi Arogya Kosh, Delhi Arogya Nidhi), etc., if anyone.

Free Diagnostic Facility

The Fund has installed the latest State-of-the-Art 3 D Color Doppler EPIQ 7C Philips at E – 219, Greater Kailash, Part 1, New Delhi.
This machine is used to screen children and adult patients for any heart disease.

Free Education and Employment Facility

HCFI has tied up with a leading educational institution and an export house in Delhi NCR to adopt and to provide free education and employment opportunities to needy heart patients post surgery. Girls and women will be preferred.

Laboratory Subsidy

HCFI has also tied up with leading laboratories in Delhi to give up to 50% discounts on all pathological lab tests.

Help Us to Save Lives

The Foundation seeks support, donations and contributions from individuals, organizations and establishments both private and governmental in its endeavor to reduce the number of deaths due to heart disease in the country. All donations made towards the Heart Care Foundation Fund are exempted from tax under Section 80 G of the IT Act (1961) within India. The Fund is also eligible for overseas donations under FCRA Registration (Reg. No 231650979). The objectives and activities of the trust are charitable within the meaning of 2 (15) of the IT Act 1961.

Donate Now...

About Heart Care Foundation of India

Heart Care Foundation of India was founded in 1986 as a National Charitable Trust with the basic objective of creating awareness about all aspects of health for people from all walks of life incorporating all pathies using low-cost infotainment modules under one roof.

HCFI is the only NGO in the country on whose community-based health awareness events, the Government of India has released two commemorative national stamps (Rs 1 in 1991 on Run For The Heart and Rs 6.50 in 1993 on Heart Care Festival- First Perfect Health Mela). In February 2012, Government of Rajasthan also released one Cancellation stamp for organizing the first mega health camp at Ajmer.

Objectives

- Preventive Health Care Education
- Perfect Health Mela
- Providing Financial Support for Heart Care Interventions
- Reversal of Sudden Cardiac Death Through CPR-10 Training Workshops
- Research in Heart Care

Heart Care Foundation Blood Donation Camps

The Heart Care Foundation organizes regular blood donation camps. The blood collected is used for patients undergoing heart surgeries in various institutions across Delhi.

Committee Members

Chief Patron

Raghu Kataria

Entrepreneur

President

Dr KK Aggarwal

Padma Shri, Dr BC Roy National & DST National Science Communication Awardee

Governing Council Members

Sumi Malik
Vivek Kumar
Karna Chopra
Dr Veena Aggarwal
Veena Jaju
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Nilesh Aggarwal
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Advisors

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Deep Malik
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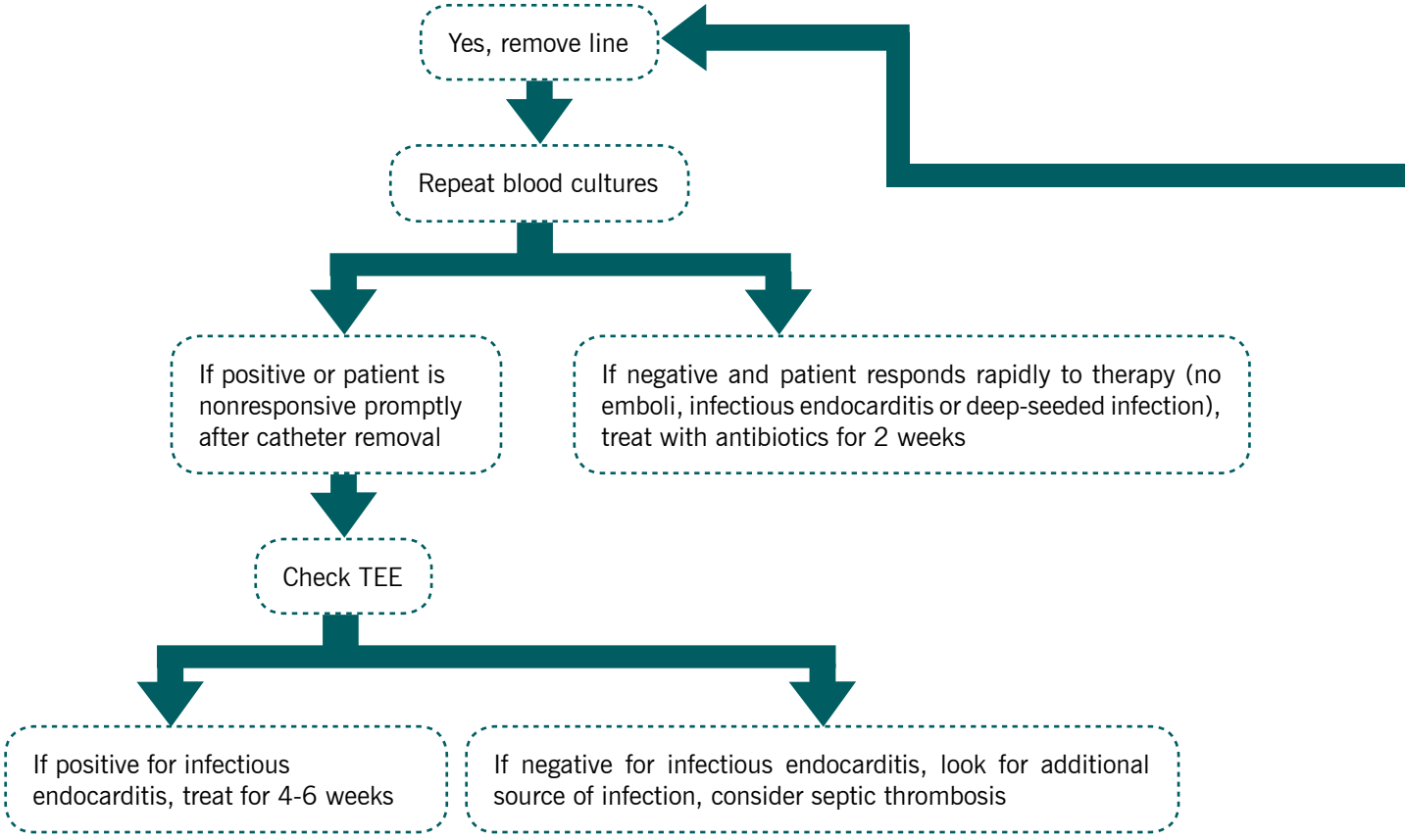
Dr Uday Kakroo
Harish Malik
Aarti Upadhyay
Raj Kumar Daga
Shalin Kataria
Anisha Kataria
Vishnu Sureka
Rishab Soni

This Fund is dedicated to the memory of **Sameer Malik** who was an unfortunate victim of sudden cardiac death at a young age.

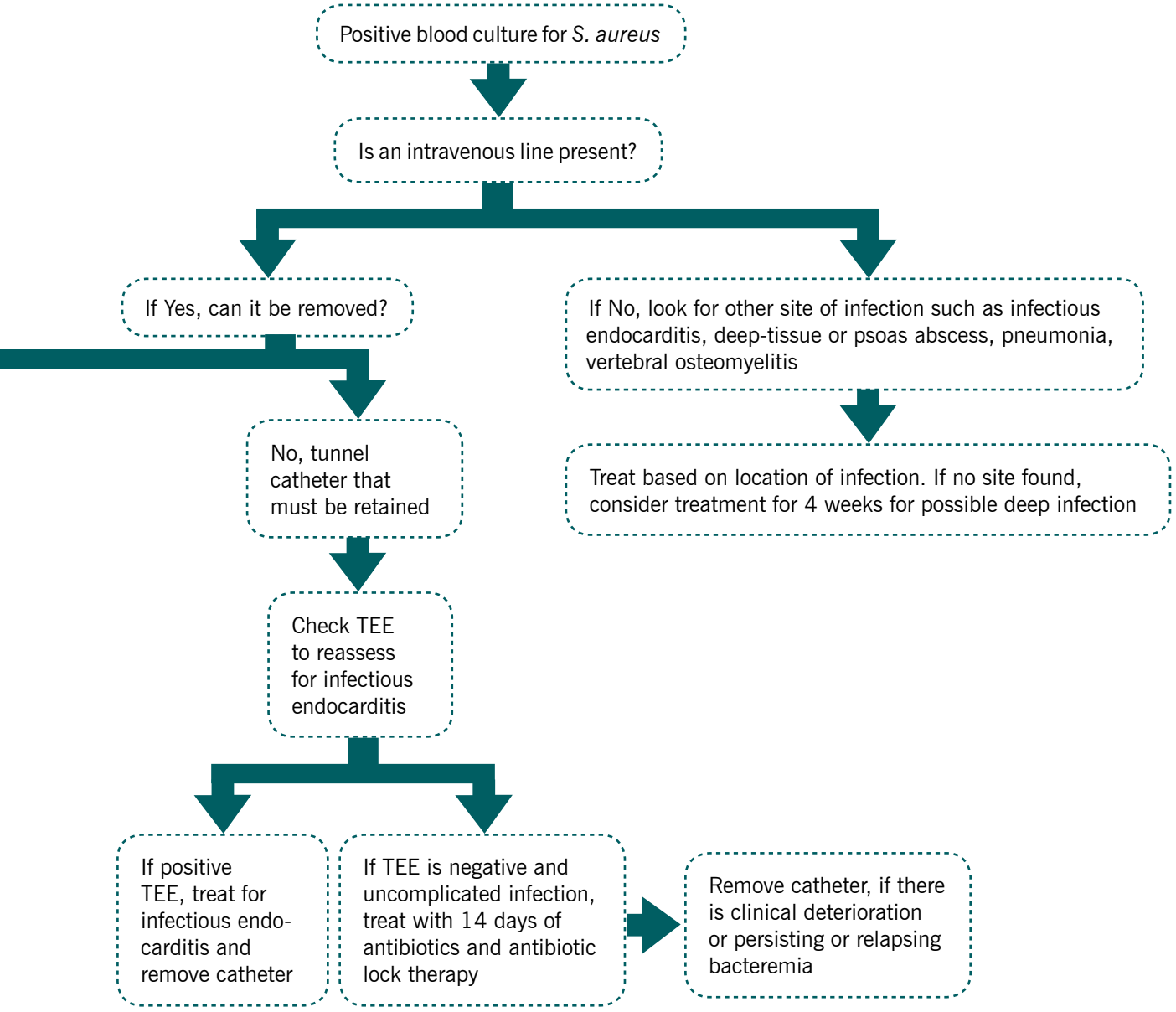
- HCFI has associated with Shree Cement Ltd. for newspaper and outdoor publicity campaign
- HCFI also provides Free ambulance services for adopted heart patients
- HCFI has also tied up with Manav Ashray to provide free/highly subsidized accommodation to heart patients & their families visiting Delhi for treatment.

Management of *Staphylococcus aureus* Bacteremia



TEE: Transesophageal echocardiography.

Adapted from Bamberger DM. Management of *Staphylococcus aureus* infections. Am Fam Physician. 2005;72(12):2474-81.


Positive blood culture for *S. aureus*
Is an intravenous line present?
If Yes, can it be removed?
If No, look for other site of infection such as infectious endocarditis, deep-tissue or psoas abscess, pneumonia, vertebral osteomyelitis
No, tunnel catheter that must be retained
Treat based on location of infection. If no site found, consider treatment for 4 weeks for possible deep infection
Check TEE to reassess for infectious endocarditis
If positive TEE, treat for infectious endo-carditis and remove catheter
If TEE is negative and uncomplicated infection, treat with 14 days of antibiotics and antibiotic lock therapy
Remove catheter, if there is clinical deterioration or persisting or relapsing bacteremia

Indian Journal of Clinical Practice, Vol. 31, No. 6, November 2020

Can you be Punished for Something which is not a Part of the Charge Sheet?

KK AGGARWAL

The judgment of the Calcutta High Court in the matter of **Snigdhendu Ghosh vs. State of West Bengal & Ors on 19 July, 2018** has answered many questions that arise when a medical negligence case is filed against a doctor, as follows:

- Limitation period in filing a complaint.
- Can you be punished for something which is not a part of the charge sheet?
- When can you appeal to GOI as a remedy?
- Can the High Courts interfere before all the remedies are exhausted?
- Can a Council go to the Supreme Court? (This is like the lower court going to the Supreme Court against a High Court order)
- Is error of judgment negligence?
- Does giving three antibiotics in typhoid amount to negligence?
- Is error in judgment an infamous act?
- When to pass a judgment in interim stage?
- Is it necessary for the council to give reasoned judgments?
- What are the principles of natural justice?
- When challenging a council decision, is it not necessary to make the patient a party?
- Can a doctor file compensation from council for wrong decision?
- What did the Supreme Court do in this case?

West Bengal Medical Council vs. Dr Snigdhendu Ghosh on 20 February, 2019/SLP/4132/2019/Arising out of impugned final judgment and order dated 19-07-2018 in MAT No. 28/2018 passed by the High Court at Calcutta. This petition was called on for hearing on 20-02-2019.

Coram: Hon'ble Mr. Justice Arun Mishra, Hon'ble Mr. Justice Navin Sinha

Order: No case is made out to interfere with the impugned order (s) passed by the High Court. The special leave petition is, accordingly, dismissed. However, this order shall not be treated as a precedent. Pending application(s), if any, shall stands disposed of.

HIGH COURT ORDER NO. 1

Calcutta High Court (Appellete Side); Snigdhendu Ghosh vs. State of West Bengal & Ors on 19 July, 2018; in the High Court at Calcutta; Hon'ble Mr. Justice I.P. Mukerji and Hon'ble Justice Amrita Sinha, Ms. Manisha Bhowmick, Mr. Biplab Guha; Judgment On: 19.07.2017; I.P. Mukerji, J.:

I have had the privilege of going through the draft judgment prepared by my sister Amrita Sinha, J. I agree with the conclusions reached by her ladyship. Nevertheless, since this matter is of great importance I would like to deliver a separate concurring judgment.

The appellant is a very qualified and senior medical practitioner. In 1987, he obtained the MBBS degree from the Medical College, Kolkata. Thereafter, in 1992, he got the DCH qualification from Chittaranjan Seva Sadan, Kolkata. In 2009, he obtained MD in Pediatrics and DM in Neurology from PGIMER, Chandigarh. He worked in the Dhanbad Railway Hospital as Pediatrician and thereafter with BR Singh Hospital. Now, he specializes in neurology and works with KG Hospital, in Chittaranjan, district Bardhaman.

It so happened that on or about 24th December, 2010, the regular ward doctors of the hospital were on leave. The appellant was in-charge, although he was a specialist in Neuroscience. On that day, a young girl Purbasha Das of about 19 years of age was admitted to the hospital. Such admission was made on the advice of the outdoor doctor. She was suffering from fever for 2-3 days accompanied by loose motion and nausea. The hospital had no blood testing facility. On clinical examination of the patient, the appellant prescribed a combination of two antibiotics and supporting

Group Editor-in-Chief, IJCP Group

drugs and IV fluid, namely, cefotaxime, ofloxacin, rantac injection, paracetamol and IV fluid. Later, on 25th December, 2010 on receipt of blood test reports, including the report of Widal test he advised the addition of a third antibiotic, chloromycetin, suspecting typhoid. The patient remained under his care till 26th December, 2010.

According to the statement made by the appellant before the State Consumer Disputes Redressal Commission, West Bengal, in the case subsequently started against him, CC Case No. 40 of 2012, "the patient was responding to the treatment and her condition quite stable and improving till 26th December, 2010."

From 27th December, 2010 the appellant relinquished charge of the ward. Dr Dipanjan Basak took charge of the patient.

The patient sharply deteriorated on 29th December, 2010. She developed acute respiratory complication. A chest X-ray was performed. She was then released from KG Hospital by her family and taken to Mission Hospital, Durgapur. She was admitted there on 30th December, 2010 in the very early hours, at 12.40 am. **This hospital made the diagnosis that she was suffering from septicemia with multi-organ failure.** The chest X-ray and CT scan revealed pulmonary edema and acute respiratory distress syndrome (ARDS). She expired that very night at 4.50 am. In the death certificate, the cause of death was stated to be ARDS together with sepsis *plus* multiple organ dysfunction syndromes.

On 12th January, 2011 Mr Himangsu Kumar Das father of Purbasha Das made a complaint to the Officer-in-Charge of Chittaranjan Police Station, Chittaranjan, West Bengal against the appellant, alleging criminal negligence. **On 13th January, 2011, the police drew up an FIR (FIR No. 1 of 2011 dated 13th January, 2011) against him and Dr Dipanjan Basak alleging commission of death by negligence under Section 304A of the Indian Penal Code.**

On 18th March, 2011, the family of the deceased addressed a complaint to the Registrar, West Bengal Medical Council (WBMC) and others, including the Medical Council of India.

Now, further to the complaint of Mr Himangsu Kumar Das the learned Additional Chief Judicial Magistrate, Asansol on 2nd April, 2013 constituted a Medical Board consisting of the ACMOH, Asansol, Dr Nilanjan Chattopadhya and Dr Srikanta Gongopadhya. **This Medical Board opined that the medicines prescribed by the appellant were adequate for enteric fever and pneumonia.**

The family of the deceased did not stop there. **They moved the State Consumer Disputes Redressal Commission. They did not prosecute the matter there and the complaint was dismissed**.

On 6th April, 2011, the Medical Council of India had asked the State Medical Council to enquire into the case and take action within 6 months under Clause 8.4 of the Indian Medical Council (Professional Conduct, Etiquette and Ethics) Regulations, 2002. **On 19th August, 2014, the learned Additional Chief Judicial Magistrate discharged the appellant as *prima facie* no negligence could be attributed to him.**

After an enquiry, on 2nd August, 2016, the appellant was charge-sheeted by the WBMC. It was issued under Section 17 read with Section 25 of the Bengal Medical Act, 1914, The charge-sheet was as follows: "*It appeared that there was some commission of errors in medical management of one patient, young girl, Purbasha Das at KG Hospital, Chittaranjan, which led to her death in multi-organ failure with respiratory complications, even though the case was initially appeared to be a case of enteric fever.* ***Even though she was admitted with the diagnosis of RTI, no blood count or chest X-ray was performed.*** *On 29-12-2010, the patient developed acute respiratory complications and then chest X-ray was performed. She was subsequently referred to Mission Hospital, Durgapur where the diagnosis came out to be septicemia with multi-organ failure. Chest X-ray and CT revealed occurrence of probable pulmonary edema or ARDs.* ***This quick onset indicated that between 27th and 29th December, 2010, there might be some errors in patient surveillance and on this score, you cannot be absolved of your responsibilities and that in relation there to you have been found prima facie guilty of infamous conduct in a professional respect***."

Thereupon, the appellant was charged with "error in patient surveillance" and "infamous conduct under the Bengal Medical Act, 2014."

There seems to be contradiction at the initial stage of the proceedings. The charge-sheet dated 2nd August, 2016 stated that the patient was admitted to KG Hospital "with the diagnosis of RTI" (respiratory tract infections). This is quite contradictory to other records. According to the appellant and not contradicted by any record that the patient was admitted to KG Hospital with 3-4 days history of vomiting, loose motion and fever. **A Widal test performed on the patient stated prior to admission to the hospital stated that there was an indication of Typhoid or enteric fever. At any rate there was no blood testing facility at the hospital.**

In fact, the charge sheet notice did not allege that the administration of triple antibiotics by the appellant caused death or injury to the patient. It simply said that on 29th December, 2010, the patient developed acute respiratory complications. X-ray and CT scan were carried out which revealed the existence of pulmonary edema and ARDS.

This stage quickly set in between 27th and 29th December, 2010. On 25th August, 2016, the appellant gave a detailed reply to the charge-sheet. His main points of defence were:

i) By specialization he is a neurologist. As no regular doctors were available he was put in-charge of the ward where the patient was kept.

ii) The patient was admitted into the hospital with symptoms of vomiting and loose motion. There was a pathological report accompanying her which indicated that she suffered from typhoid. In those circumstances, the appellant administered the combination of three antibiotics. It is an approved practice amongst responsible medical practitioners possessing ordinary skill to use this kind of combination drugs to treat enteric fever or typhoid, according the appellant.

The patient improved while in his charge between 24th December, 2010 till 26th December, 2010. Thereafter, the doctor who was originally in-charge of her, Dr Dipanjan Basak, took over her responsibility on 27th December, 2010 at about 9 am. If at all the condition of the patient deteriorated, it was after the appellant relinquished charge of the patient. The treatment that was given to the patient by the appellant could not have been the cause of her death.

On 21st August, 2017, the appellant received a communication from the Council dated 18th August, 2010 attaching its decision to remove his name from the register of medical practitioners by the required majority of two-third of the members present and voting, for a period of 1 year. The appellant was found guilty of infamous conduct.

The Council made the following observations:

a) The appellant was "not rational" in treating the patient with three antibiotics;

b) He was "deficient in his approach" not advising any blood test;

c) He was "deficient in his approach" not advising any chest X-ray.

On 7th September, 2017, he preferred an appeal from the decision of the WBMC before the Appellate Authority constituted under Section 26(1) of the Bengal Medical Act, 1914.

Simultaneously, a writ was preferred in the Court challenging the decision. On 10th November, 2017, the writ application (WP No. 26252 (W) of 2017) was disposed of by this court directing the Appellate Authority to dispose of the appeal pending before it a within fortnight from the date of communication of the said order. **This order was not complied with, by the appellate authority.**

In those circumstances, the appellant moved the writ application (WP No. 28956 (W) of 2017). Upon having notice of this writ application the appellate authority preponed the hearing of the appeal from 6th December to 5th December, 2017. On 5th December, 2017, the appellant duly appeared before the appellate authority. On 7th December, 2017, the Joint Secretary (Medical Administration) Department of Health and Family Welfare passed an order upholding the decision of the WBMC. It held that between 24th December and 26th December, 2010, the patient was substantially under the care of the appellant. **It held that without blood culture, sensitivity chest X-ray test, etc. three antibiotics could not have been administered simultaneously. On 11th December, 2017, the second writ application was disposed by this court recording that the appeal had been disposed on 7th December, 2017.**

The maintainability point was raised by Mr Bhowmick, learned counsel for the Council. **He said, there was an appeal provision before the Central Government from a decision of the Council removing the name of a medical practitioner from the register. Hence, the appellant ought to have availed of that remedy.**

An appeal from a decision of the Council under Section 17 read with 25 of the said **Act lies to the appellate authority, i.e., the State Government. Under the said Act, there is no further appeal from the decision of the State Government.**

An appeal lies to the Central Government under the Central Medical Act, 1957 read with Rule 27 of the Central Medical Council Rules, 1957 against removal of a doctor's name from the register.

In my opinion, removal of name means permanent removal from the register. It means a situation where the right of a doctor to practice is taken away forever, and irreversibly. The appellant's license to practice was suspended for 1 year. This is temporary. It does not attract Rule 27 of the Medical Council Rules.

Even if there was such a remedy it should not be forgotten that the appellant, complains of various acts of commission and omission of the respondents which allegedly caused breach of the principles of natural justice. In the Whirlpool case (1999) 8 SCC 1 the Supreme Court told us that if a writ complains of breach of the principles of natural justice, a litigant could avoid the alternative remedy and come to the High Court in exercise of its jurisdiction.

Another point raised by Mr Bhowmick was that the issues in this **writ had become *res judicata*.** I do not agree.

An issue becomes *res judicata* if it is adjudicated upon. Only if an issue is adjudicated upon, could the secondary issues be covered by the doctrine of constructive *res judicata.* For example, six reliefs are sought from the court and five are granted, after adjudication. It can be said that the sixth was prayer for and refused. Therefore, an adjudication of some part of the issues raised is a *sine qua non* for operation of the principle of res judicata or constructive *res judicata*. **In this case, there has been no adjudication at all.** In the first writ, the Court referred the appellant to the alternative remedy without adjudication on the merits. In the second writ, the Court merely recorded that the adjudicating authority had made a decision on the complaint made by the appellant. It can by no stretch of imagination be said that the Court had actually adjudicated upon the merits of the matter. **This plea of *res judicata* is in my opinion mischievous and is rejected. For those reasons the maintainability point fails.**

The third point raised by Mr Bhowmick was that this appeal was from an order refusing to pass an interim order interfering with the decision of the Council suspending the registration of the appellant for 1 year. He argued that if this Court proposed to pass any order it would tantamount to disposal of the writ application at the ad interim stage. He prayed for an opportunity to file an affidavit-in-opposition.

I reject the contention. **In this appeal, we propose to dispose of the writ application for the following reasons. The suspension of registration was for a period of 1 year.** More than 11 months of the suspension has been suffered by the appellant. Keeping the writ pending on technical grounds would result in the appellant suffering the whole of the punishment without remedy. The writ would thereby become infructuous.

It is true that the Supreme Court in various decisions has said that the Court at the interim stage should not pass orders that would effectively dispose of the writ application. Reference may be made to Council for Indian School Certificate Examination Vs. Isha Mittal and Anr. reported in (2000) 7SCC 521, State of Uttar Pradesh and Ors. vs. Ramsukhi Devi reported in AIR 2005 SC 284, Secretary, U. P. S. C Vs. S. Krishna Chaitanya reported in 2011 AIR SCW 4682, State of U.P. v. Hirendra Pal Singh reported in (2011) 5 SCC 305 cited by Mr Bhowmick.

This dictum of the Supreme Court is only true when the Court at the interim stage is evaluating the *prima facie* case of the parties. All the documents are not before the Court. They would be available on filing of affidavits. Hence, the Court gives an opportunity to the respondents to file an affidavit dealing with the allegations in the petition. At the same time, on the *prima facie* case an interim order is passed. Since, the entire evidence is not before the Court, the conclusions of the Court are *prima facie*. A final order should never be passed, at that stage. That would make hearing of the writ application, upon completion of affidavits, redundant.

In this case, all the essential documents are appended to the stay petition. The writ also involves substantial questions of law. When it is possible for us to dispose of the entire controversy between the parties on the basis of the papers before us **we do not think that this Court should observe the formality of inviting affidavits and sending the matter to the first Court for adjudication, thereby delaying justice to the point of defeating it.** This point of Mr Bhowmick is also rejected.

Mr Dhar learned senior Advocate, appearing for the petitioner made the following submissions.

He said that the accusation of wrong administration of three antibiotics was not included in the charge-sheet. The appellant had no opportunity of dealing with the charge that he had administered three antibiotics irrationally. Secondly, he submitted that the patient was admitted in the hospital on 24th December, 2010, she was under the care of the appellant till 26th. From 27th onwards, she was admittedly not under the appellant. Her treatment was regulated by the regular doctor at the ward. According to the findings of the Council, the condition of the patient deteriorated when the appellant was not in-charge of the ward.

He argues that the hospital did not have pathological facilities. That is why no blood test could be ordered at the time of the patient's admission. **Evaluating the condition of the patient and the blood test report which the patient's family obtained through an outside**

laboratory, which suggested enteric fever or typhoid, the appellant administered her three antibiotics. The board which was formed by the Additional Chief Judicial Magistrate, Asansol found the treatment adequate to cure typhoid and pneumonia. The appellant according to learned Counsel had adopted a mode of treatment which was approved by a responsible body of medical practitioners, satisfying the Bolam test (discussed later).

The order of the WBMC did not contain sufficient reasons to justify the punishment imposed on the appellant. The appellant had administered the right treatment and that the council has no case against him, Mr Dhar said.

The appellant had been charged under the **Bengal Medical Act, 1914** only. It is now the proper time to examine this Act. It constituted the WBMC. It prescribed a register of registered practitioners to be maintained.

"Section 25: Power to Council to direct removal of names from register, and re-entry of names therein. The Council may direct

(a) that the name of any registered practitioner:

i. who has been sentenced by any Court for any non-bailable offence, such sentence not having been subsequently reversed or quashed, and such person's disqualification on account of such sentence not having been removed by an order which the 68 [State Government] 7070. Word subs. for the word "are" by the Government of India (Adaptation of Indian Laws) Order, 1937. [is] hereby empowered to make, if 7171. Words subs. for the words "they think" by the Government of India (Adaptation of Indian Laws) Order, 1937. [it thinks] fit, in this behalf; or

ii. whom the Council, after due enquiry for *the words "as provided in clause (b) of Section 17" by W.B. Act 16 of 1954. [in the same manner as provided in clause (b) of Section 17] have found guilty, by a majority of two-thirds of the members present and voting at the meeting, of infamous conduct in any professional respect, be removed from the register of registered practitioners 73 [or that the practitioner be warned], and*

(b) that any name so removed be afterwards re-entered in the register.

"It contains a very old and dated expression "in famous conduct". It the council by a majority of two-thirds members of the council present and voting, after due enquiry, finds a registered practitioner guilty of "infamous conduct", his name is to be removed from the register of registered practitioners. Mr Dhar tried to contend that the proceedings were also conducted under the Code of medical Ethics adopted by the WBMC on the basis of the Indian Medical Council (Professional Conduct, Etiquette and ethics) Regulations, 2002. This code of conduct may be supplementary to the Bengal Medical Act, 2014, but the records say that action against the appellant was taken under the said Act only.

An English decision of Bolam Vs. Friern Hospital Management Committee reported in (1957) was affirmed by the Supreme Court in Jacob Mathew Vs. State of Punjab and Anr. reported in (2005) 6SCC 1, cited by Mr Dhar.

If a medical condition involves the use of some special skill or competence then the test of negligent handling of the patient is not to be judged by the standards of an ordinary prudent man but according to the standards of an ordinary man professing and exercising that special skill.

A medical professional is not judged guilty because another professional of greater skill or knowledge would have prescribed a different treatment or conducted a surgical operation in a different way. It is enough that he has acted in accordance with a practice accepted as proper by a responsible body of medical men skilled in that particular art.

Chief Justice R.C. Lahoti pronouncing the judgment of the Supreme Court remarked that a medical professional's skill had to be exercised with a reasonable degree of care and caution. He gains nothing by being negligent. He has everything to lose.

An error of judgment on the part of the professional was not negligence *per se*. A medical professional was entitled to adopt a procedure for the patient involving a higher element of risk but with greater chances of success then a procedure with lesser risk and high chance of failure. If this type of risk taking ended in ill consequences for the patient, the doctor should not be hauled up for negligence. A medical practitioner cannot act in fear. If he has to worry about prosecution for every step he takes, then, he would not be able to render the service which is required of him.

I would like to quote a passage from a judgment of Denning LJ in Roe v. Ministry of Health reported in 1954 2 All ER. 131, referred to in Bolam; "Medical Science has conferred great benefits on mankind but benefits are attended by considerable risks. We cannot take the benefits without taking the risks. Doctors learn by experience which often teaches in a hard way".

In Kusum Sharma and Ors. Vs. Batra Hospital and Medical Research Centre and Ors. reported in (2010) 3 SCC 480, the Supreme Court reiterated the same principles as in the Jacob Mathew Vs. State of Punjab and Anr case. One may refer to a passage from an English decision in Maynard Vs. West Midlands Regional Health Authority reported in (1985) All ER 635 (HL), set out in that judgment: "In the realm of diagnosis and treatment there is ample scope for genuine difference of opinion and one man clearly is not negligent merely because his conclusion differs from that of other professional men The true test for establishing negligence in diagnosis or treatment on the part of a doctor is whether he has been proved to be guilty of such failure as no doctor of ordinary skill would be guilty of if acting with ordinary care." This case was also cited by Mr Dhar.

With regard to the point that the appellant was tried of offences with which he was not even charged, Mr Dhar relied in Union of India and Ors. Vs. Gyan Chand Chattar reported in (2009) 12SCC 78 which said that an **enquiry had to be conducted in compliance with the principles of natural justice. The charges should be specific, definite and detailed. The same principles were reiterated by the Supreme Court in Anant R. Kulkarni Vs. Y. P. Education Society and Ors reported in (2013) 6SCC 515** and in Anil Gilurker Vs. Bilaspur Raipur Kshetriya Gramin Bank and Anr reported in (2011) 14 SCC 379.

I quote a very instructive passage from the judgment of Mr Justice Sabyasachi Mukharji in Sawai Singh Vs. State of Rajasthan reported in (1986) 3SCC 454. Paragraph 16 and 17 are as follows:

"*16. It has been observed by this Court in Suresh Chandra Chakrabarty v. State of West Bengal [1971] 3 S.C.R. 1 that charges involving consequences of termination of service must bespecific, though a departmental enquiry is not like a criminal trial as was noted by this Court in the case of State of Andhra Pradesh v. S. Sree Rama Rao [1964] 3 S.C.R. 25 and as such there is no such rule that an offence is not established unless it is proved beyond doubt. But a departmental enquiry entailing consequences like loss of job which now-a-days means loss of livelihood, there must be fair play in action, in respect of an order involving adverse or penal consequences against an employee, there must be investigations to the charges consistent with the requirement of the situation in accordance with the principles of natural justice in so far as these are applicable in a particular situation.*

17. The application of those principles of natural justice must always be in conformity with the scheme of the Act and the subject matter of the case. It is not possible to lay down any rigid rules as to which principle of natural justice is to be applied. There is no such thing as technical natural justice. The requirements of natural justice depend upon the facts and circumstances of the case, the nature of the enquiry, the rules under which the Tribunal is acting, the subject matter to be dealt with and so on. Concept of fair play in action which is the basis of natural justice must depend upon the particular lis between the parties. (See K.L. Tripathi v. State Bank of India & Ors., [1984] 1 S.C.C. 43) Rules and practices are constantly developing to ensure fairness in the making of decisions which affect people in their daily lives and livelihood. Without such fairness democratic governments cannot exist. Beyond all rules and procedures that is the sine qua non."

The contention of the appellant is absolutely right. **He was not charged with having administered three antibiotics negligently. Yet he was tried for it.** It was not proper for the Council or the appellate authority to hold that administration of three antibiotics without blood test and chest X-ray was not proper conduct on the part of the appellant, when he did not have the chance to explain his line of treatment. This is clear violation of the principles of natural justice.

Moreover, we permitted the appellant to produce and the appellant did produce at the time of hearing of the appeal a British medical advisory. It suggested that the use of three antibiotics concurrently was not uncommon to treat serious and drug resistant bacteria. Furthermore, in the hospital attended by the appellant, there was no facility for blood test. Using his clinical judgment, he prescribed three antibiotics.

It is not controverted that the appellant was not the regular doctor at the ward where the patient was admitted. He was a neurologist. He was asked to take charge temporarily from 24th to 26th December, 2010, in the absence of the regular doctor of the ward. Hence, if the treatment procedure of the medical practitioners from the time of the admission of the patient to the hospital from 24th December, 2010 till her death 30th December, 2010 is to be examined and it is shown that more than one medical practitioner, including the appellant attended to the patient, one has to show whether any action of the appellant, between 24th and 26th December, 2010 contributed to the death of the patient. There is nothing on record to suggest that the administration of any medicine in those three days or the adoption of any other mode of treatment had caused the death of the patient or had contributed substantially or partially to her death. In fact, the records show that the patient got worse only from 27th December, 2010 and that the worsening of her condition was not due to any action on the part of the appellant.

It was contended by Mr Bhowmick that whether the conduct of a registered practitioner complained against was infamous or not was decided by the Council by two-thirds majority present and voting, in accordance with Section 25 of the said Act. The Council might decide that his name was to be removed from the register of registered practitioners or that he be warned. **He said that there was no scope under the said Act to give reasons.**

I am unable to agree.

First of all, the Bengal Medical Act, 1914 is a very ancient Act. The principles of administrative law were just about germinating at that point of time. **It is true that the Act does not say that the Council has to give reasons for its decision.** It only says that the members have to vote with regard to the conduct of the person under enquiry. **But there is a provision for enquiry**. Now this provision of enquiry has to be given an interpretation to make this Act compatible with the principles of administrative law of our age. **The principles of natural justice have to be necessarily read into the ambit and scope of the enquiry.** In my opinion, when the required majority comes to a decision, the reasons in support thereof have to be given. No such reasons are available. The order of the appellant authority suffered from the same vice. The delinquent was being made to suffer serious civil consequences without any reasons.

In my opinion, while applying the Bolam test, one has to not only assess the skill required of a doctor to treat a particular patient and the skill displayed by him in rendering the treatment but one has also to consider the medical facilities and technology available to him at the place of treatment or any other facility, readily available within a reasonable distance, on the requisition of the doctor, to treat the patient. The time available to administer treatment and the time within which the medical facility and technology could be availed of and which were availed of or not availed of by the doctor have to be taken into account. The facilities at the hospital of Chittaranjan were limited. The patient was admitted in the evening of 24th December, 2010. KG Hospital had no blood testing facility. In a small town like Chittaranjan one does not expect to find the most modern facilities for treatment. Therefore, if on the basis of the blood report of the patient of the following day, 25th December, 2010, which indicated Typhoid, the appellant using his clinical judgment had administered two antibiotics, the previous right and the third antibiotic on receipt of the blood report, it could safely be said by a responsible body of medical practitioners having the skill to treat this kind of a tropical infection that the appellant had employed his medical skill reasonably, satisfying the Bolam test.

At the end, I note that the victim patient's family was not represented in Court. On several occasions, we had enquired of learned counsel for the appellant whether the victim had been noticed. He replied that the victim's family had been attempted to be served but could not be found.

Furthermore, I note that Mr Bhowmick did not make any submissions on the merits of the case. He only raised the maintainability points discussed above.

Thus, I hold that the removal of the name of the appellant from the register of practitioners for a period of 1 year or suspension of his right to practice for a period of 1 year was wholly without any basis and hence wrongful and illegal.

I set aside the impugned order of suspension of the appellant's right to practice for a period of 1 year made by the respondent council by its decision dated 18th August, 2017 and affirmed on 7th December, 2017 by the appellate authority, by quashing the same. The appellant will be entitled to resume practice immediately.

I have not gone into the question of any loss and damage suffered by the appellant for being denied the right to practice from 18th August, 2017 till the date of this judgment and order. Such right of the appellant is kept open to be urged in a separate proceeding if he wants to initiate the same.

(I.P. Mukerji, J.)

Amrita Sinha, J.:-

HIGH COURT ORDER NO. 2

This appeal has been filed at the instance of the writ petitioner challenging the order dated 3rd January, 2018 passed by the Learned Single Judge in W.P. No. 31338 (W) of 2017 refusing to pass interim order in the matter. The appellant a medical practitioner filed the aforesaid writ petition being aggrieved by and dissatisfied with the decision of the West Bengal Medical Council (hereinafter referred to as "WBMC" for the sake of brevity) contained in memo bearing no. 3165-C/28-2011 dated 21st August, 2017 and the order dated 7th December, 2017 passed by the Principal Secretary, Health and Family Welfare Department and the Appellate Authority of WBMC.

By the order dated 7th December, 2017, the Appellate Authority dismissed the appeal preferred by the

appellant against imposing penalty for removal of his name from the register of medical practitioners maintained by the WBMC for a period of 1 year from the date of communication of the order under Section 25(a) (ii) of the Bengal Medical Act, 1914.

The facts of the case are as follows:

On 24th December, 2010, a 19-year-old girl was admitted in the female ward of Kasturba Gandhi Hospital, Chittaranjan, Burdwan with symptoms of fever, loose motion and vomiting which according to her father had been continuing for 3-4 days before such admission.

The appellant though attached to the said hospital as Neurologist was in-charge of the female ward of the said hospital on and from 24th December, 2010 to 26th December, 2010 as the regular in-charge Dr Dipanjan Basak was on leave.

The girl was examined by Dr Ajay Kumar at the outpatient department and on his advice the girl was admitted in the hospital. The appellant examined her clinically and administered drugs like cefotaxime, ofloxacin, ondansetron, ranitidine and paracetamol as he was of the opinion that the patient was suffering from typhoid fever. At the time of admission, the father of the girl handed over certain pathological reports which also suggested that the girl was suffering from enteric fever.

According to the appellant, the condition of the girl improved upon administration of the aforesaid medicines and he included another drug namely Chloramphenicol as he came to a fair conclusion that the patient was suffering from typhoid. The condition of the patient was stable till 26th December, 2010.

On 27th December, 2010, the regular in-charge Dr Dipanjan Basak resumed his duties and took over charge of the female ward where the patient was admitted. The appellant did not have any occasion to treat the patient any further.

On and from 28th December, 2010, the condition of the patient deteriorated and on 29th December, 2010, the girl had serious respiratory problem. X-ray was conducted which revealed that one of her lungs was severely damaged and the other was seriously affected by pneumonia. The girl was referred to Mission Hospital, Durgapur. The girl expired on 30th December, 2010.

The father of the victim girl lodged a complaint against the appellant before the WBMC on 12th January, 2011 as well as before the Officer-in-Charge, Chittaranjan Police Station, Burdwan on 13th January, 2011 praying for taking legal action against him and for cancellation of his medical registration.

Pursuant to the complaint lodged by the father of the victim the police registered FIR and initiated a case against the appellant under Section 304A I.P.C. The police investigated the case and submitted the report in final form in the Court of the Learned Additional Chief Judicial Magistrate, Asansol on 20th November, 2013.

The father of the victim being dissatisfied with the final report tendered by the police in the said case filed a Narazi petition before the learned Court which was taken up for consideration and further re-investigation was directed to be conducted by the police. As the question before the learned Court whether the death of the girl was due to rash and negligent act of the doctor required specialized skill the learned Court referred all the medical documents in connection with the treatment of the victim girl to the Chief Medical Officer, Burdwan for his comment who in turn forwarded all the said documents to the Additional Chief Medical Officer of Health, Asansol who constituted a medical board consisting of himself and two other doctors. The board unanimously opined that the medication in the doses mentioned would have in the normal course of the event be sufficient to cure both the enteric fever and pneumonia. They further opined that however in a small percentage of case death may supervene in both enteric fever and pneumonia.

Vide order dated 19th July, 2014, the learned Court after perusal of the case diary came to the conclusion that there was no negligence on the part of the appellant in the treatment conducted by him since her admission in the said hospital. The final report of the police was accepted and the appellant was discharged from the said case.

The victim's father lodged another complaint against the appellant before the State Consumer Disputes Redressal Commission, West Bengal praying for taking legal action against the appellant and for cancellation of his medical registration. However, vide order dated 11th March, 2016, the said complaint case being no. CC/40/2012 was dismissed for non-prosecution. The father of the victim lodged a further complaint against the appellant before the Registrar, WBMC on 18th March, 2011. The WBMC considered the charges and found the appellant guilty of infamous conduct in a professional respect and passed order for removal of his name from the register of registered medical practitioners maintained by the WBMC for a period of 1 year from the date of communication of the order under Section 25(a) (ii) of the Bengal Medical Act, 1914. The appellant had been advised to submit his original medical registration certificate to the WBMC

for the next course of action. The aforesaid order was communicated to the appellant by the Registrar, WBMC vide his letter dated 18th August, 2017.

The appellant challenged the aforesaid order of the WBMC by filing appeal before the Principal Secretary, Health Department on 21st September, 2017. As the said appeal was kept pending for a considerable period of time accordingly the appellant preferred a writ petition before this Hon'ble Court being W.P. 26252 (w) of 2017 and vide order dated 10th November, 2017 this Hon'ble Court passed necessary orders upon the Appellate Authority to consider and decide the appeal in accordance with law within a fortnight from the date of communication of the order.

As the Appellate Authority did not consider and dispose the appeal within the time specified by this Hon'ble Court the appellant filed a second writ petition praying for passing necessary order for disposal of the appeal. The said writ petition being W.P. No. 28956 (W) of 2017 was taken up for consideration and vide order dated 11th December, 2017, the same had been disposed of based on the submission made on behalf of the WBMC that during pendency of the writ petition final order disposing the appeal had been passed by the Appellate Authority on 7th December, 2017.

The order of the Appellate Authority dated 7th December, 2017 communicated to the appellant vide letter dated 11th December, 2017 issued by the Joint Secretary to the Government of West Bengal was the subject matter of challenge in the writ petition being W.P. No. 31338 (W) of 2017. The learned Single Judge vide order dated 3rd January, 2018 had issued direction to file affidavit-in-opposition within 4 weeks and reply thereto within 2 weeks thereafter. The point of maintainability of the writ petition had been kept open. The learned Single Judge felt prudent not to grant any interim order at that stage. Being aggrieved the writ petitioner filed the instant appeal praying for necessary orders.

Submissions on Behalf of the Appellant

The primary charge framed against the petitioner vide letter dated 2nd August, 2016 issued by the Registrar, WBMC was as follows:

"*It appeared that there was some commission or errors in medical management of one patient, young girl Purbasha Das at KG Hospital, Chittaranjan which led to her death in multi-organ failure with respiratory complications even though the case was initially appeared to be a case of enteric fever. Even though she was admitted with the diagnosis of RTI, no blood count or chest X-ray was performed. On 29.12.2010 the patient developed acute respiratory complications and then chest X-ray was performed. She was subsequently referred to Mission Hospital, Durgapur where the diagnosis came out to be septicemia with multi-organ failure. Chest X-ray and CT revealed occurrence of probable pulmonary edema or ARDS. This quick onset indicated that between 27th and 29th December, 2010, there might be some errors in patient surveillance and on this score you cannot be absolved of your responsibilities and that in relation thereto you have been found prima facie guilty of infamous conduct in a professional respect*."

The appellant had been directed to show cause in writing within 21 days why his name should not be removed from the register of registered practitioners pursuant to Section 17/25 of the Bengal Medical Act, 1914. The appellant had been requested to bring the certificate of registration in original and also updated registration certificate and to submit the same before start of hearing failing which his case would be heard and decided *ex parte*.

The appellant submitted his show cause before the Registrar, WBMC on 25th August, 2016. The WBMC took up the case of the appellant for hearing on 12th July, 2017 and after considering the charges found him guilty of infamous conduct in a professional respect and decided that his name be removed from the register of registered medical practitioners for a period of 1 year from the date of communication of this order in this respect under Section 25(a) (ii) of the Bengal Medical Act, 1914.

The WBMC at the time of passing the aforesaid order of removal of the name of the appellant from the register of medical practitioners observed the following:

"(a) Dr Snigdhendu Ghosh was not rational in continuation of treatment of the patient with three antibiotics at the initial stage.

(b) He was deficient in his approach in not advising any blood test to exclude the other prognosis of the case, if any.

(c) He was deficient in his approach in not advising in any chest X-ray of the patient to exclude the other prognosis of the case, if any."

The specific case made out by the appellant is that the charge had been framed after a period of 6 years from the date of the incident. The charge was predetermined and biased. The statements and findings mentioned in the charge were wholly incorrect. The charge specifically

mentioned that 'there was some commission of errors in medical management' of the patient leading to her death. It was further mentioned that 'the quick onset indicated that between 27th and 29th December, 2010, there might be some errors in patient surveillance'.

The appellant strenuously contended that the patient was under his care from 24th December, 2010 to 26th December, 2010. He could not be held responsible for the acute respiratory complications that developed in the patient after the said date. It is also submitted that the patient was admitted in the hospital with the symptoms of fever, loose motion, vomiting for the last 3-4 days prior to her admission in the hospital. There was no indication of any respiratory tract infection as alleged in the memorandum of charge. The Widal test report of the patient was positive and accordingly the necessary antibiotics had been administered to her. Blood test was prescribed to detect (a) Hemogram including malaria parasite, (b) Malaria antigen (MP), (c) Typhoid (Widal test), (d) Liver function (LFT), (e) Hepatic condition (HBsAg) and (f) Sugar/Urea/Creatinine.

It was categorically submitted that chest X-ray had not been advised because the patient did not show any signs of respiratory problem on and from 24th December to 26th December, 2010. It was pointed out that the death certificate issued by the Mission Hospital, Durgapur mentioned the cause of death as 'ARDS, sepsis and multi-organ dysfunction syndrome'.

The learned Advocate appearing for the appellant placed before the Court photocopies of the extracts from the book 'Principles of Respiratory Medicine' written by Farokh Erach Udwadia, Zarir F. Udwadia and Anirudh F. Kohli published by Oxford University Press wherein the clinical features of ARDS has been discussed. **It has been mentioned therein "against a background of one of the etiologies mentioned earlier, the patient with ARDS present with rapidly worsening dyspnea and restlessness.** On examination, such a patient has tachycardia, tachypnea, and increasing hypoxemia despite supplemental oxygen. Auscultation reveals scattered crackers and occasionally a wheeze. The condition may evolve rapidly over a few hours, or may take a few days to reach its maximum intensity. Respiratory distress is obvious, and the accessory muscles of respiration are active. Cyanosis may occur, but is not always evident in spite of severe hypoxemia".

The learned Advocate also placed before this Court photocopy of extracts from the book 'Fishman's Pulmonary Diseases and Disorders' and placed before us a list of drugs which induced lung disease due to nonchemotherapeutic agents and submitted that none of the medicines which had been prescribed by the appellant contained the aforesaid drugs and accordingly the medicines prescribed by the appellant was in no way responsible for the development/aggravation of the acute respiratory distress syndrome which was the cause of the death of the patient.

The learned Advocate further submitted that the medical board which had been formed in terms of the order passed by the learned Additional Chief Judicial Magistrate, Asansol consisting of the Additional Chief Medical Officer of Health, Asansol and two other doctors had unanimously opined that the medication in the doses administered by the appellant would have in the normal course of the event be sufficient to cure both the enteric fever and pneumonia. However, in a small percentage of case death may supervene in both enteric fever and pneumonia. Accordingly, there had been no infamous conduct at all on the part of the appellant.

Section 25 of the Bengal Medical Act, 1914 gives the power to the Council to direct removal of names from the register and re-entry of names therein. Section 25(a)(ii) mentions that the Council may direct that the name of any medical practitioner whom the Council after due enquiry in the same manner as provided in Clause (b) of Section 17 have found guilty, by a majority of two-thirds of the members present and voting at the meeting, of infamous conduct in any professional respect, be removed from the register of registered practitioners or that the practitioner may be warned.

'Infamous conduct' has not been defined in the Act. Clause 37 of the Code of Medical Ethics adopted by the WBMC mentions that disciplinary action may be taken against the registered medical practitioners upon offences and form of professional misconduct, which may be brought before the Council for disciplinary action. Decision on complaint against delinquent physician shall be taken preferably within 6 months.

Clause 38 of the said Code mentions them disciplinary actions that may be taken by the WBMC, namely,

i. Censure,

ii. Warning,

iii. Removal of name of the registered practitioner for a specific period up to 3 years or permanently according to the nature of offence and the decision to be taken by the WBMC.

Clause 39 of the said Code lists the offences for which disciplinary action may be taken by the Council, namely,

a) Adultery or improper conduct or association with the patient,

b) Conviction by Court of Law for offences involving moral turpitude/criminal acts,

c) Misconduct, the following acts of commission or omission on the part of a physician shall constitute professional misconduct rendering him/her liable for disciplinary action;

d) Violation of the Regulation-

i. If he/she commits any violation of these Regulations.

ii. If he/she does not maintain the medical records of his/her indoor patients for a period of 3 years as per Regulations.

(e) Sex determination test.

The appellant contended that since the cause of action arose in the year 2010 and the alleged inquiry was conducted and impugned order passed in 2017, the case was hopelessly barred by limitation and no action far less passing order of penalty could be passed on the basis of the said complaint. He further contended that none of his actions could be treated as infamous conduct in a professional respect and accordingly the penalty of removal of his name from the register of medical practitioners is bad in law and liable to be set aside.

The learned Advocate further submitted that the opening line of the charge-sheet mentioned 'that there was some commission or errors in medical management' and lastly it was mentioned "this quick onset indicated that between 27th and 29th December, 2010, there might be some errors in patient surveillance and on this score you cannot be absolved of your responsibilities" wherefrom it can be understood that there might be some errors in medical management on his part and the same cannot under any stretch of imagination be held to be infamous conduct by him. Moreover, as per the charge-sheet, there might be some error in patient surveillance between 27th and 29th December, 2010, but as the appellant was not in charge of the patient after 26th December, 2010 accordingly he ought not to be held responsible for the same.

It was further submitted that the penalty proposed to be passed against the appellant was mentioned in the charge-sheet itself, which shows that the WBMC had conducted the alleged enquiry with a predetermined and biased mindset. The authorities had made up their mind that irrespective of the outcome of the enquiry the punishment of removal of the name of the appellant was the only order that could be passed in the case. That was exactly the reason why the appellant had been directed to bring with him the original registration certificate at the time of the hearing. The learned Advocate for the appellant has taken a specific plea that the charge framed against the appellant and the reasons for his punishment are different. It has been pleaded that there had been gross violation of the principles of natural justice as the reasons mentioned in the charge sheet were not the reasons for which punishment had been imposed upon the appellant. The issue of administering three antibiotics to the victim was not the charge against the appellant, whereas the order of punishment specifically mentioned that it was not rational for the appellant in continuation of the treatment of the patient with three antibiotics at the initial stage. He further submits that prescription of three antibiotics is not an uncommon phenomena in medical field.

The learned Advocate for the appellant denies that the appellant was in any manner deficient in not advising blood test of the patient which is an absolute perverse finding inasmuch as the appellant had advised as many as six blood tests which were duly conducted and necessary medicines had been administered upon taking into consideration the blood reports of the patient. The prescription to conduct blood test is annexed with the writ petition which is annexed with the application for stay.

It was submitted that principles laid down by the Hon'ble Supreme Court in the various judgments dealing with medical negligence had not been followed by the authorities at the time of deciding the case of the appellant. Judgments relied upon by the appellant:

i. Kusum Sharma and Others vs. Batra Hospital and Medical Research Centre and Others reported in (2010) 3 SCC 480.

ii. Jacob Mathew vs. State of Punjab reported in (2005) 6 SCC 1.

iii. Union of India and Others vs. Gyan Chand Chattar reported in (2009) 12 SCC 78.

iv. Anant R. Kulkarni vs. Y.P. Education Society and Others reported in (2013) 6 SCC 515.

v. Sawai Singh vs. State of Rajasthan reported in (1986) 3 SCC 454.

vi. Anil Gilurker vs. Bilaspur Raipur Kshetriya Gramin Bank and Another reported in (2011) 14 SCC 379.

Submissions on Behalf of WBMC

At the time of hearing the main point raised by the learned Advocate appearing on behalf of WBMC was that the appeal was being heard against refusal to pass interim order and accordingly the main matter ought not to be heard on merits. It had been vehemently contended that there is an alternative remedy available to the appellant under Section 24 of the Indian Medical Council Act, 1956 where the appellant may prefer appeal before the Government against the impugned order of penalty. It had been further contended that this was the third writ petition filed by the appellant on the self-same cause of action and accordingly the writ petition and the appeal arising therefrom is liable to be dismissed on the ground of constructive *res judicata*.

The learned Advocate for the respondent specifically contended that WBMC is not obliged to give reasons for their decision adopted in their meeting held on 12th July, 2017. It has been submitted that the Bengal Medical Act, 1914 is a valid piece of legislation and as per provision of Section 25(a) (ii) the Council by a majority of two-thirds of the members present and voting at the meeting may direct removal of the name of the registered practitioner for infamous conduct in any professional respect.

It has been submitted that since there is a specific provision for preferring appeal as per provision of Section 24 of the Indian Medical Council Act, 1956 accordingly the instant appeal is liable to be rejected on the ground of availability of alternative remedy.

He further submitted that there is no scope for passing any interim order in the instant appeal as the impugned order of penalty had already been given effect to and the name of the appellant had already been struck off from the register of medical practitioners. It has been submitted that the respondents will lose an appellate forum if the appeal is entertained and the scope of the writ petition ought not to be enlarged before the Hon'ble Appeal Court. The learned Advocate further submits that there had not been any occasion on the part of the learned Single Judge to decide the matter on merits and accordingly the appeal Court ought not to hear out the main matter. He submits that the writ petition is at an interim stage and no order ought to be passed, which may decide the main issue and may grant the final relief in favor of the appellant. He prays for remand of the matter before the learned Trial Judge so that he can place the entire facts and defend the case on merits.

Judgments relied upon by WBMC

i. Cicily Kallarackal vs. Vehicle Factory reported in (2012) 8 SCC 524.

ii. Authorized Officer, State Bank of Travancore and Another vs. Mathew K.C. reported in 2018 (1) Supreme 471.

iii. Council for Indian School Certificate Examination vs. Isha Mittal and Another reported in (2000) 7 SCC 521.

iv. Forward Construction Company and Others vs. Provat Mandal (Regd.), Andheri and Others reported in AIR 1986 SC 391.

v. Sheela Devi vs. Jaspal Singh reported in 1999 AIR SCW 2214.

vi. Medical Council of India vs. State of West Bengal reported in 2012 (1) CHN (Cal) 46.

vii. Unreported judgment of this court dated 1st September, 2011 passed in W.P. No. 781 of 2011 (Dr Shyama Prasad Sar vs. The State of West Bengal and Others).

Observations of the Court

In Kusum Sharma and Others (supra) Supreme Court held that medical science has conferred great benefits on mankind, but these benefits are attended by considerable risks. We cannot take the benefits without taking risks. In this case, Court reiterated the observations made in the land mark judgment of Jacob Mathew vs. State of Punjab (supra) that in the law of negligence professionals such as lawyers, doctors, architects and others are included in the category of persons professing some special skill or skilled persons generally. The standard to be applied for judging whether the person charged has been negligent or not, would be that of an ordinary competent person exercising ordinary skill in that profession. It is not necessary for every professional to possess the highest level of expertise in that branch which he practices.

In Jacob Mathew's case the Hon'ble Supreme Court heavily relied on the judgment delivered in the case of Bolam vs. Friern Hospital Management Committee reported in (1957) 2 All. ER 118 wherein it had been observed that a doctor is not negligent if he is acting in accordance with a practice accepted as proper by a reasonable body of medical men skilled in that particular art, merely because there is a body of such opinion that takes a contrary view. Deviation from normal practice is not necessarily evidence of negligence. To establish liability on that basis it must be shown (1) that there is

a usual and normal practice; (2) that the defendant has not adopted it and (3) that the course in fact adopted is one no professional man of ordinary skill would have taken had he been acting with ordinary care. The Hon'ble Supreme Court on scrutiny of the leading cases of medical negligence both in our country and other countries specially the United Kingdom has laid down certain principles while deciding whether the medical professional is guilty of medical negligence or not. Some of them are as follows:

1. Negligence is an essential ingredient of the offence. The negligence to be established by the prosecution must be culpable or gross and not the negligence merely based upon an error of judgment.
2. A medical practitioner would only be liable where his conduct fail below that of the standards of a reasonably competent practitioner in his field.
3. Negligence cannot be attributed to a doctor so long as he performs his duties with reasonable skill and competence. Merely because the doctor chooses one course of action in preference to the other one available, he would not be liable if the course of action chosen by him was acceptable to the medical profession.
4. Just because a professional looking at the gravity of illness has taken higher element of risk to redeem the patient out of his/her suffering which did not yield the desired result may not amount negligence.
5. It is our bounden duty and obligation of the civil society to ensure that the medical professionals are not unnecessarily harassed or humiliated so that they can perform their professional duties without fear and apprehension.
6. The medical professionals are entitled to get protection so long as they perform their duties with reasonable skill and competence and in the interest of the patients.

The Hon'ble Supreme Court in the said judgment of Kusum Sharma (Supra) specifically directed that the aforementioned principles must be kept in view while deciding the cases of medical negligence. It should not be understood to have held that doctors can never be prosecuted for medical negligence. As long as the doctors performed their duties and exercised an ordinary degree of professional skill and competence, they cannot be held guilty of medical negligence. It is imperative that the doctors must be able to perform their professional duties with free mind.

In the case of Union of India and Others vs. Gyan Chand Chattar (supra) relying upon the case of Sawai Singh vs. State of Rajasthan (supra) Supreme Court held that in a domestic enquiry the charge must be clear, definite and specific as would be difficult for any delinquent to meet the vague charges. There must be fair play in action particularly in respect of an order involving adverse or penal consequences. The Court held that an enquiry is to be conducted against any person giving strict adherence to the statutory provisions and principles of natural justice. No enquiry can be sustained on vague charges. The findings should not be based on conjectures and surmises. Every act or omission on the part of the delinquent cannot be a misconduct. The same principle has been reiterated in the case of Anil Gilurker (supra).

The case of Anant R. Kulkarni (supra) cited by the learned Advocate of the appellant is on the similar line of the above case wherein the Court reiterated that a delinquent should not be served with a charge sheet without providing him a clear, specific and definite description of the charge against him. When statement of allegations are not served with the charge sheet, the enquiry stands vitiated, as having been conducted in violation of the principles of natural justice.

The judgment referred to above in the case of Cicily Kallarackal, Authorized Officer, State Bank of Travancore and Another, Council for Indian School Certificate Examination and Sheela Devi is primarily on the ground of not entertaining writ petitions due to availability of alternative remedy. There is no second opinion about it. What is required to be seen is whether the alternative remedy available to the petitioner is efficacious and whether the action of the respondents is vitiated by jurisdictional error or patent violation of the principles of natural justice so as to enable the writ Court to exercise jurisdiction in the matter.

In the instant case, the cause of action arose on 13th January, 2011 when a complaint was lodged by the father of the victim girl who expired on 30th December, 2010. As per Clause 37 (iv) of the Code of Medical Ethics published by the WBMC a decision on complaint against a delinquent physician shall be taken preferably within 6 months. Admittedly in this case the charge memo was issued against the petitioner on 2nd August, 2016, and final order had been passed for removal of the name of the appellant on 21st August, 2017.

Moreover, from the order of punishment it can be seen that the appellant had been punished on the basis of infamous conduct which was not specified in

the memorandum of **charge i.e.; the appellant was punished for an offence not mentioned in the charge memo.** The appellant did not have any opportunity to controvert the allegation mentioned in the order of penalty. The same appears to be gross violation of the principles of natural justice as the Hon'ble Supreme Court has repeatedly observed in various decisions that the **charge levelled against a delinquent must be specific** and there must be fair play in action in respect of an order involving adverse or penal consequences resulting in loss of job or livelihood.

A plain reading of the charge memo issued against the appellant shows that there appeared some commission of errors in medical management in respect of the victim, which led to her death due to multi-organ failure. It was mentioned that no blood count or chest X-ray was performed. It was further mentioned that the quick onset of probable pulmonary edema or ARDS between 27th and 29th December, 2010 indicated there might be some errors in patient surveillance and on that score the appellant cannot be absolved in his responsibilities and had been found *prima facie* guilty of infamous conduct in a professional respect. Admittedly blood tests were advised by the appellant when she was admitted at the hospital. The prescription for conducting blood test and the test reports are annexed with the writ petition. It is further admitted that the appellant treated the patient from 24th December, 2010 to 26th December, 2010. The period when the alleged ARDS developed in the victim the appellant was not in charge of the patient. Accordingly, the question of committing error in patient surveillance between 27th and 29th December, 2010 does not arise at all. **Moreover, neither the charge memo nor the impugned order of WBMC and the appellate authority indicate that the condition of the patient deteriorated and turned fatal due to the medicines administered by the appellant. In the absence of the specific charge to that effect, the appellant could not have been held to be guilty of the alleged misconduct.**

The appellant submitted his show cause to the charges mentioned in the charge memo. The order of penalty speaks otherwise. It states that the appellant was not rational in continuation of the treatment of the patient with three antibiotics at the initial stage. **The order did not suggest that the patient expired due to intake of three antibiotics.** The appellant was not given any opportunity to meet the charge of using three antibiotics for treatment of the patient.

The charge of administering three antibiotics was not mentioned in the charge memo. The appellant did not have any chance or scope to deal with the said charge. The appellant ought to have been given a reasonable opportunity to defend his stand. This in my view is serious violation of natural justice.

It appears from records that on the complaint lodged by the father of the victim before the police station the learned Additional Chief Judicial Magistrate, Asansol referred the medical documents in respect of the victim to the Chief Medical Officer Health, Burdwan who forwarded the papers to the Additional Chief Medical Officer of Health, Asansol. A medical board was constituted consisting of the Additional Chief Medical Officer of Health, Asansol along with two other doctors. The board unanimously opined that the medication in the doses mentioned would have in the normal course of the event the sufficient to cure both the enteric fever and pneumonia. However, in a small percentage of case death may supervene in both enteric fever and pneumonia. The above unanimous **decision of the doctors suggests that the procedure of treatment adopted by the appellant was neither illegal nor new or uncommon in medical jurisprudence**. In fact, it was an accepted practice by the doctors and it was quite normal to treat the patient with the said medicines.

The WBMC may have a divergent opinion about it but the same *ipso facto* does not render the procedure adopted by the appellant wrong or the conduct of the appellant infamous. Moreover, the report of the medical board was not challenged by the complainant and the order of the learned Court dismissing the complaint case had attained finality as far back as on 19-07-2014. Trying the appellant for the same offence all over again and penalizing him for the same is absolutely illegal and not permissible in law. As regards observation of not advising chest X-ray of the patient, the appellant had already dealt with the same in his show cause. He has specifically stated that chest X-ray was not done as there was no symptom of respiratory tract infection (RTI). He further stated that there is no protocol at Kasturba Gandhi Hospital to perform chest X-ray in every case of fever. The report of Widal test conducted for detecting typhoid being positive he was quite certain that it was a case of enteric fever and necessary medicines were administered. The patient responded to the medicines as long as she was under the care and treatment of the appellant.

The judgment of Forward Construction Company and others (supra) referred to by the learned Advocate for the respondents deal with the principles of *res judicata*. It has been strenuously submitted by the learned Advocate for the respondent that the appellant had filed three writ

petitions on the self-same cause of action. This appeal arises out of the third writ petition filed by the appellant. It has been mentioned earlier that the first writ petition was filed praying for expeditious disposal of the appeal filed by the appellant against the impugned order of the WBMC. The second writ had been filed as the appeal preferred by the appellant had not been disposed of within the time as specified by this Hon'ble Court on the first writ petition filed by the appellant. The present writ petition out of which this appeal arises had been filed challenging the order dated 7th December, 2017 passed by the Principal Secretary, Government of West Bengal, Family Welfare Department being the appellate authority of the WBMC. The order impugned in this writ petition was not in existence when the first and the second writ petitions were filed. Accordingly, the question of *res judicata* cannot and does not arise at all.

The judgment of Medical Council of India (supra) referred to by the learned Advocate of the respondent dealt with the vires of certain regulations of the Indian Medical Council (Professional Conduct, Etiquette and Ethics) Regulations, 2002) and the same has no matter of application in the present case.

The judgment of Dr. Shyama Prasad Sar (supra) clearly states that no provision for appeal can create a compulsion to lodge an appeal for a right, essentially a thing conferred, cannot be imposed nor is exhaustion of a statutory remedy of appeal a mandatory requirement for maintaining an application under Article 226 of the Constitution of India. Whether a petition under Article 226 should be entertained when a statutory remedy is not exhausted is to be examined on the facts and circumstances of the case concerned. It has been further held that in cases where it prima facie appears that the impugned order is vitiated by jurisdictional error or patent violation of the principles of national justice discretion can be exercised in favor of entertaining the petition.

In the instant case, it is evident from records available before this Court that there has been flagrant and **patent violation of the principles of natural justice, equity and fair play**.

Relegating the appellant to avail the statutory remedy would not in my opinion be the proper approach in the instant case. The prayer made by the learned Advocate appearing for the respondent for remanding the matter back to the trial court for hearing the same also does not hold good in the facts and circumstance in the instant case. The same will only entail in delay of the matter further. To avoid the same this Court vide order dated 23rd April, 2018 had admitted the appeal and directed that the appeal would be heard out on the papers of the stay petition and all formalities had been dispensed with. The parties have advanced exhaustive arguments for days together and remanding the matter back to the trial Court for deciding the same would result in valuable loss of judicial hours apart from causing immense harassment and mental agony which the appellant is suffering since August 2017 when the order for removal of his name was passed by the WBMC. **No fruitful purpose will be served by remanding the matter to the learned trial Judge.** We have noted that out of the penalty period of 1 year imposed on 18/21 August, 2017 more than 10 months have already elapsed. Less than 2 months are left for the petitioner to serve the entire period of punishment of removal of his name from the register of medical practitioners. He has already suffered enough due to the erroneous decision of the WBMC.

It will not be out of place to mention that there was a direction for filing affidavit in opposition in the writ petition as far back as on 3rd January, 2018. We have been told that no affidavit had been filed in connection with the writ petition in terms of the direction passed by the learned trial Judge. In that view of the matter, this court vide order dated 23rd April, 2018 proposed to hear the appeal finally and dispose of the same on merits on the papers of the stay petition. It is pertinent to mention that the writ petition along with all annexures have been annexed with the application for stay. Going back to the charge memo it is seen that the WBMC charged the appellant for some errors on his part. **The Hon'ble Supreme Court in the case of Kusum Sharma (supra) reiterated the observation made by the Court in the case of Spring Meadows Hospital v. Harjol Ahluwalia, (1998) 4 SCC 39 that an error of judgment is not necessarily negligence.**

In the same case, the Court reiterates the observation made in the case of White House v. Jordan (1981) 1 WLR 246 that an **error of judgment may, or may not be negligent,** it depends on the nature of the error. If it is one that would not have been made by a reasonably competent professional man professing to have the standard and type of skill that the defendant holds himself out as having, and acting with ordinary care, then it is negligence. If, on the other hand, it is an error that such a man, acting with ordinary care, might have made, then it is not negligence.

In Achutrao Haribhau Khodwa v. State of Maharashtra (1996) 2 SCC 634 referred to in Kusum Sharma's case, the Supreme Court noticed that "*44. In the very nature*

of medical profession, skills differ from doctor to doctor and more than one alternative course of treatment is available, all admissible. Negligence cannot be attributed to a doctor so long as he is performing his duties to the best of his ability and with due care and caution. ***Merely because the doctor chooses one course of action in preference to the other one available, he would not be liable if the course of action chosen by him was acceptable to the medical profession.****"*

In Kusum Sharma, the Supreme Court reiterated the observation made in Jacob Mathew case that a doctor faced with an emergency ordinarily tries his best to redeem the patient out of his suffering. He does not gain anything by acting with negligence or by omitting to do an act. The Court goes on to observe that it is a matter of common knowledge that after happening of some unfortunate event, there is a marked tendency to look for a human factor to blame for an untoward event, a tendency which is closely linked with the desire to punish. Things have gone wrong and, therefore, somebody must be found to answer for it. **A professional deserves total protection. It is to be kept in mind that to err is human.** Doctors may make errors of judgment but if they are punished for this then no doctor can practice his profession with a free mind. A doctor cannot perform with a sword hanging over his head. In a third world developing country like India with such huge population, limited resources, lack of proper infrastructural facilities and only a handful of doctor's errors cannot be ruled out in its entirety. It is expected that the doctors would carry out their duty with utmost care and precision. But the doctor cannot be put to blame in each and every case when a mishap happens, and certainly not in this case. It is highly unfortunate that a girl lost her life at such a young age. The parents have lost their only child. May be the same doctor has saved the life of several other children. There are many patients who are desperately in need of medical assistance but due to dearth of medical professionals they have to suffer endlessly. It is the society at large who will suffer if the doctor is not allowed to practice for a certain period of time because the moment the penalty period is over the doctor will restart his practice and make up for his professional loss, but the patient who remained without medical service may not get back the time to recover.

Decision

Applying the aforesaid principles laid down by the Hon'ble Supreme Court in the instant case, **it can be concluded that the act of the appellant certainly cannot be held as 'infamous conduct'**. The punishment of penalty in the absence of any specific charge is patently illegal and gross violation of the principles of natural justice, equity and fair play. **When two divergent and equally efficacious procedures for treatment was possible one by administrating two antibiotics and the other by administering lesser antibiotics adopting one would not amount to any error attracting the penalty of removal of the name of the appellant from the register of medical practitioners.**

The decision of the WBMC contained in memo bearing no. 3165-C/28-2011 dated 21st August, 2017 and the order dated 7th December, 2017 passed by the Principal Secretary, Health and Family Welfare Department and the Appellate Authority of WBMC are set aside. The WBMC is directed to re-enter the name of the appellant in the register of medical practitioners immediately without any delay and **preferably within a period of 48 hours from the date of receipt of a copy of this order.** The appellant is at liberty to resume practice forthwith.

The appeal is allowed. No costs.

(Amrita Sinha, J.)

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Initial GI Symptoms Independently Associated with Poor COVID-19 Outcomes

Initial presence of gastrointestinal (GI) symptoms in patients presenting at the hospital with suspected COVID-19 independently predicted worse outcomes, suggested an electronic records review of over 1,000 patients.

Based on the number of initial GI symptoms (score 1: only one GI symptom, score 2: two or three GI symptoms), investigators noted a stepwise rise in the odds of worsened outcomes compared with no GI symptoms (score 0). The effect persisted after adjustment for demographics, comorbidities, and all other clinical symptoms. Darbaz Adnan, MBChB, of Rush University Medical Center in Chicago noted that more than one in five patients visiting the hospital for COVID-19 symptoms also presented with GI manifestations. Results for 921 patients with available data were presented at the American College of Gastroenterology (ACG) virtual meeting… (*Medpage Today*)

Indian Journal of Clinical Practice, Vol. 31, No. 6, November 2020

India Live 2020: National Course on Percutaneous Cardio - Vascular Interventions

28TH FEBRUARY - 1ST MARCH 2020, TAJ PALACE, NEW DELHI

CORONARY EXOTICA

Dr Ashok Seth, New Delhi

- You may not always get a second chance: Planning is the key to success and the lessons learnt.
- The anomalous right coronary artery (ARCA) arising from the left coronary sinus (LCS) is the second most common anomaly of coronary artery origin encountered by a busy invasive cardiologist.
- US guiding catheter can achieve stable cannulation and support
- A 3D understanding of the guiding catheter sits in the aortic root in relationship to the origin of ARCA is very important to customize these in-lab modifications of guide catheters.

LATEST DAPT GUIDELINES AND CLINICAL TRIALS – IS THE TREND CHANGING?

Dr MS Hiremath, Pune

- The release of the American College of Cardiology/ American Heart Association (ACC/AHA) focused update on the duration of dual antiplatelet therapy (DAPT) is an important event, and its findings will affect six already released ACC/AHA clinical practice guidelines.
- It is recommended to extend use of DAPT in acute coronary syndrome (ACS) patient beyond 1 year following implantation of a second-generation drug-eluting stent (DES)-based on excellent DAPT trial data. The study results suggested that in addition to the reduced rates of stent thrombosis, a reduction in the major adverse cardiovascular and cerebrovascular events and a low rate of myocardial infarction.
- In patients undergoing percutaneous coronary intervention (PCI) for stable coronary artery disease (CAD) who are at high bleeding risk, 1 to 3 months of DAPT may ensure sufficient protection from stent thrombosis reducing the risk of bleeding.
- In patients undergoing PCI for ACS, based on the results of the PEGASUS-TIMI 54 (Prevention of Cardiovascular Events in Patients with Prior Heart Attack Using Ticagrelor Compared to Placebo on a Background of Aspirin-Thrombolysis in Myocardial Infarction 54) trial, ticagrelor may be preferred over clopidogrel or prasugrel.
- In patients undergoing CABG, 12-month DAPT may also be considered in patients with stable CAD to improve vein graft patency.
- In patients with prior myocardial infarction, the 60 mg twice daily dose was subsequently approved by regulatory authorities in both the US and Europe.
- Patients with medically managed ACS were included in the CURE trial for clopidogrel, the TRILOGY ACS trial for prasugrel and the PLATO trial for ticagrelor. Based on these, 12-month DAPT with aspirin and clopidogrel or ticagrelor is given a COR I, LOE A, with ticagrelor recommended over clopidogrel if the bleeding risk is acceptable.
- In patients undergoing noncardiac surgery, the updates recommend the use of a multidisciplinary approach to antithrombotic management in the perioperative period.
- There are lot of clinical trials on DAPT which got presented in last few years which might impact the clinical practice of the intervention cardiologist and the guidelines in near future. These trials have highlighted the interruption and discontinuation of the DAPT drug, Aspirin or P2Y12 inhibitors either at 1 month and 3 months in stable CAD or high bleeding risk (HBR) patients. Some of the landmark trials are STOP DAPT, STOP DAPT 2, ONYX ONE, LEADERS FREE, SMART CHOICE, TWILIGHT, etc.

FFR: WHAT SHOULD BE THE APPROPRIATE USAGE CRITERIA?

Dr Ajit Mullasari, Chennai

Fractional flow reserve (FFR) makes use of a specialized guide wire with micro-pressure sensor to measure blood

pressure within a coronary artery. The use of FFR is established mostly among patients with stable angina, yet revascularization of non-infarct-related coronary arteries at the time of an acute myocardial infarction (AMI) is a much debated topic.

The DANAMi-3–PRIMULTI (The Third Danish Study of Optimal Acute Treatment of Patients with STEMI: Primary PCI in Multivessel Disease) trial reported that FFR-guided staged complete revascularization during the index admission led to significantly reduced future revascularizations at 1 year follow-up than those who received treatment for the infarct-related vessel alone.

As per ACC guidelines on coronary revascularization, FFR is rational for the assessment of angiographic intermediate coronary lesions (50-70% diameter stenosis) and can be useful for guiding revascularization decisions in patients with CAD.

A more recent consensus statement has suggested that to expand the use of FFR in coronary stenosis up to 90%. The use of both FFR and instantaneous wave-free ratio (iFR) for functional lesion assessment in single and multivessel CAD has also been endorsed in the recent appropriate use criteria for coronary revascularization in patients with stable ischemic heart disease report by ACC/AATS/AHA/ASE/ASNC/SCAI/SCCT/STS 2017. The report recommends its use in:

- Invasive measurements like FFR may be very helpful in further defining the need for revascularization and may substitute for stress test finding
- FFR ≤0.80 is abnormal and is consistent with downstream inducible ischemia
- Appropriate use criteria advocate for expanded use of intracoronary physiological testing.

TECHNOLOGIES NOT YET ON CENTER STAGE

Dr Vinay K Bahl, New Delhi

- Intra-arterial septal device creating a hole: Increased left atrial pressure is the fundamental abnormality in patients with heart failure with preserved ejection fraction (HFpEF) and a mechanical approach to reduce left atrial pressure is feasible.
- Coronary sinus reducer for refractory angina alternate path: Balloon-expandable, stainless steel, hourglass-shaped, coronary sinus reducing device creates a focal narrowing and increase in coronary sinus pressure and redistributes blood from nonischemic to subendocardial ischemic myocardium and helps recruit collaterals.
- Robotic angioplasty futuristic: The performance of PCI, using a combination of robotics and telecommunications, by an operator who is in a separate physical location than the patient.
- Bariatric embolization: FDA approved prospective physician-initiated investigational device exemption study where embolization with 300-500 μm embosphere microspheres was done. It resulted in an average weight loss of 8.2% at 1 month and 15.1% at 1 year.
- Some other such technologies include stent retriever embolectomy, next generation bioresorbable vascular scaffolds (BVS), a leadless intracardiac transcatheter pacing system, renal artery denervation, left atrial appendage (LAA) closure, endogenous tissue restoration, 3D printing and transcatheter tricuspid valve repair.

HOW EFFECTIVE IS FRACTIONAL FLOW RESERVE AT GUIDING TREATMENT OF CORONARY ARTERY DISEASE?

Dr Deepak Davidson, Kottayam

The prognosis in patients with CAD is determined by the presence and extent of myocardial ischemia. FFR has enabled cardiologists to accurately determine whether coronary atherosclerotic plaques are responsible for myocardial ischemia and hence need revascularization. It has been said that FFR is still unsurpassed in diagnostic performance when compared to nonhyperemic indices and noninvasive techniques, and continues to be the gold standard for the detection of ischemia-inducing coronary stones.

FFR-guided PCI has been shown to be superior to an angiography-guided PCI and over medical therapy alone. FFR is recommended to be performed routinely in intermediate coronary stenosis between 50% and 70%; its main advantages are: Well-defined cut-off point of 0.80; Not influenced by systemic hemodynamic factors (such as blood pressure, heart rate and contractility); In chronic stable ischemic heart disease, it does not depend on the status of microcirculation; It is influenced by collateral flow, which may sometimes bring a significant blood supply to the distal myocardium, depending on a main narrowed epicardial vessel.

Approximately one-third of patients considered for coronary revascularization have diabetes, which acts as a major determinant of clinical outcomes. A cross-sectional study published in 2020 reported that routine integration of FFR for the management of CAD in patients with diabetes may be associated with a high rate of treatment reclassification. Management

strategies which are guided by FFR, including revascularization deferral, may prove to be useful for patients with diabetes.

BIFURCATION TECHNIQUES: WHEN AND HOW?

Dr Yves Louvard, France

- Potential benefits of side branch (SB) treatment: Avoid peri-procedural occlusion - Non-QMI, Relief of angina, Keep access for future interventions.
- Practical key points – *Pre-intervention assessment:* Diameters, angle, plaque distribution (taking into account limitations of 2D angio imaging), decide which one is the distal SB. Mandatory to include these parameters as well as the global context of the patient in strategy making process.
- Important tips and tricks: 6 French at least-good support; Diameters + angles/evaluation and choice of SB; Jailed wire as landmark, Minimize ballooning on SB; Choose main stent of distal main branch (MB) reference; Proximal optimizing technique (POT) before wire exchange; Recross distal cell; Kissing with NC balloons; High threshold for second stenting.

LEFT MAIN ANGIOPLASTY

Dr Bernard Chevalier, France

- Customize your strategy to a specific lesion with good imaging.
- Master several (at least two) bifurcation techniques.
- Apply a rigorous method following all the steps POT.
- Key points for POT: Place the stent proximally enough (6 or 8 mm); POT before wire exchange; Know your NC balloon (shoulder/marker), Sized to proximal reference (1:1) as calculated by: DMV proxy = 0.67 × (DMV distal + DSB); Distal marker at carena level; Select the view with maximal angle to avoid overlap; Use stent enhancement to check position.
- Share experience with team.

OPTICAL COHERENCE TOMOGRAPHY: CORE CONCEPTS AND CONSENSUS

Dr Rony Mathew, Cochin

- Infrared laser light scans vessel in spiral manner.
- Light penetrates tissue 2-3 mm and is reflected back to optical coherence tomography (OCT) device via catheter.
- Image is generated depending on the length of time taken for light to penetrate the tissue.
- The image depends on tissue property: Reflectivity of light (Backscattering); Absorption of light (Attenuation); Composition (Homogeneous/ Heterogeneous); Borders (Sharp/Diffuse).
- OCT in PCI: Pre-PCI OCT assessment; Post-PCI OCT optimization; Complication and post-procedural assessments. In bifurcations, intravascular OCT has a clear advantage compared to angiography.

HEMODYNAMIC SUPPORT OPTIONS: AN UPDATE

Dr Gurpreet S Sandhu; Rochester, USA

- Shock-use any device to stabilize patient
  - Intra-aortic balloon pump (IABP) and Impella - no change in outcomes: Registry data may favor Impella
  - Extracorporeal membrane oxygen (ECMO) - improves survival, provides oxygenation.
- High-risk PCI - potential for harm: Impella 3.5 - reasonable to use in EF 10-20%, ECMO - use if oxygenation needed.

SCIENCE AND ART OF SVG AND LIMA GRAFT INTERVENTIONS

Dr Marc Silvestri, France

- Saphenous vein grafts (SVG) have modest long-term patency, poor outcome for SVG interventions.
- Don't send young patients too early for coronary artery bypass grafting (CABG) and trust FFR-guided PCI with DES for 3VD and LM cases.
- Require total arterial revascularization from the surgeon.
- Use of DES improves outcome over BMS (TVR).
- Distal EPD should be used in ALL feasible cases:
  - Reduces risk of no reflow
  - Distal embolization
  - Peri-procedural myocardial infarction.
- A CHIP operator will prefer the native vessel in advanced SVG disease-learn to handle chronic total occlusion (CTO) procedures.

ROTATIONAL ATHERECTOMY: WHAT YOU SHOULD KNOW

Dr Samuel Mathew K, Mumbai

- In case of heavily calcified lesions: We need meticulous planning and strategy; Familiarity with

hardware and fair learning curve, Rota actually significantly reduces complications, More often when you do enough of these cases and see calcium if you don't use Rota you will regret not using Rota; Not using Rota often leads to longer and much more difficult procedures and you will spend more money and time and get suboptimal result.

- Finally be quick to adapt: Slow flow and no reflow can be minimized and managed; major complications with good technique in calcified lesions are very rare.

OVERCOMING THE CHALLENGES OF ANOMALOUSLY ARISING ARTERIES: TIPS AND TRICKS

Dr Ashwin B Mehta, Mumbai

- Guide catheters are target-specific.
- Commonly used guide catheters are: AL 1 or 2, undersized JL, LC bypass, for anomalous RCA from LT coronary sinus; AR 1 or 2 for circumflex from LT coronary sinus; 3DR for RCA from noncoronary sinus; Designed and specific shapes based on individual cases.
- Use polymer wire with moderate support (Sion, Whisper).
- Back up support by a: Long sheath, anchoring balloon, buddy wire and guide liner.
- Avoid dissection by gradual balloon dilatation.
- Use most trackable and short stent.

CHOICE OF DIAGNOSTIC AND GUIDING CATHETERS

Dr Upendra Kaul, New Delhi

- Guide catheter selection is an important part of the exercise of doing a successful PCI.
- It is useful to understand, design and specific requirements based upon the vessel anatomy of the target lesion.
- Increasing use of toxic release inventory (TRI) is leading to more advancement of techniques.
- Back up support methods like buddy wire, anchoring techniques and guide catheter extensions are useful to overcome difficult situations.

ROLE OF OCT IN LEFT MAIN INTERVENTION

Dr Keyur Parikh, Ahmedabad

Left main coronary artery (LMCA) stenting is associated with rare but important complications such as stent thrombosis or stent under expansion. These occur commonly after angiography-guided stent implantation.

OCT is an intracoronary imaging modality that is often used for lesion characterization and PCI guidance in non-LMCA disease, especially owing to its higher resolution imaging. It has been seen that OCT enables better identification of incomplete stent apposition and hence be ideal for optimizing stenting in the LMCA.

OCT provides precise information regarding superficial structures down to depths of 2-3 mm within the vessel wall, with axial and lateral resolutions of 10-15 μm and 20-40 μm, respectively. OCT for assessment of LMCA PCI may prove to be superior to intravascular ultrasound (IVUS) in terms of acute assessment of stent strut apposition and long-term follow-up.

OCT is a light-based technology that needs a contrast flush to clear the blood column, which makes imaging of aortic ostial lesions in the left main challenging. Another drawback of the OCT use in LM is imaging is its limited scan diameter (10 mm) considering that the average LMCA diameter is 3.5-4.5 mm.

IVUS IN THE LEFT MAIN: HOW AND WHY IN 2020?

Prof Adrian P Banning, Oxford, UK

Left main PCI in 2020

- Procedural risk fallen from 10-205 to <1% (in all but shock cases).
- Risks of treating left main diseases with PCI or surgery are probably the same.
- Isolated ostial and shaft disease is different to terminal disease.
- Culprit left main PCI should be definitely considered in all emergency cases, many urgent cases.

Why is the left main special to a PCI doctor?

- Large volumes of myocardium are "at risk". Large volumes of plaques required to make a stenosis and the plaque will move!
- Calcification is common and restrictive to stent expansion.
- Loss of 'branches' will have immediate and profound hemodynamic consequences.
- The left main involves a bifurcation. The guiding catheter has an interaction with the lesion. The left main is unforgiving in the long-term. All ostial diseases have a very high restenosis rate, especially if the stent is incompletely expanded.

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Indian Journal of Clinical Practice, Vol. 31, No. 6, November 2020

Medtalks with Dr KK Aggarwal

CMAAO Coronavirus Facts and Myth Buster

Nearly 80% of Asymptomatic Individuals Develop COVID-19 Symptoms

- Around 20% of asymptomatic coronavirus disease 2019 (COVID-19) positive people will remain symptom-free over time, suggested two studies published September 22.
- Hence, most asymptomatic patients should be considered presymptomatic.
- People with asymptomatic infection are infectious.
- Nicola Low, MD, Institute of Social and Preventive Medicine at the University of Bern in Switzerland conducted a living systemic review and meta-analysis to determine the occurrence and transmission of asymptomatic and presymptomatic patients and published their findings in *PLOS Medicine*. Sung-Han Kim, MD, PhD and colleagues conducted a study comparing levels of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in the nose and throat of asymptomatic and symptomatic individuals, and published the results in the journal *Thorax*.
- Low et al searched PubMed, Embase, bioRxiv and MedRxiv for relevant studies in March, April, and June using reverse transcription-polymerase chain reaction (RT-PCR) testing. The data included a statistical modeling study of all 634 passengers from the Diamond Princess cruise ship with RT-PCR positive results. In 79 studies conducted in various settings, 20% of people with SARS-CoV-2 infection remained asymptomatic during follow-up. Restricting to seven studies that screened defined populations with follow-up, around 31% remained asymptomatic over time.
- A subset of five studies included detailed contact tracing. The group calculated that the risk of asymptomatic people transmitting SARS-CoV-2 was lower (summary risk ratio, 0.35, compared with symptomatic people at 0.63).
- Since SARS-CoV-2 can be transmitted a few days prior to an infected person develops symptoms, presymptomatic transmission likely appears to have a major contribution to overall SARS-CoV-2 epidemics.
- Kim et al found that 19% of the 213 patients who did not have severe symptoms of COVID-19 remained asymptomatic through potential exposure, lab confirmation, and hospital admission. The upper respiratory tract viral load was not significantly different between asymptomatic and symptomatic individuals in upper respiratory tract samples in South Korea.
- The mean cycle threshold (Ct) values of SARS-CoV-2 genes, reflecting the viral load, were found to be very similar between asymptomatic individuals and symptomatic patients. This points that asymptomatic individuals have a comparable potential for spreading the virus as symptomatic patients. To prevent the transmission from asymptomatic individuals, the use of face masks by general public, irrespective of the presence of symptoms, is recommended.
- The study included outbreak in Daegu City traced to a single religious group. The 3,000 close contacts that were identified reported symptoms from none to severe, and the asymptomatic individuals were isolated and assessed in dedicated facilities. A subset of 183 patients, including 39 asymptomatic and 144 symptomatic, were subjected to follow-up RT-PCR testing. As most asymptomatic people with COVID-19 continue to live in a community setting, such individuals may potentially contribute to the community spread. As the study population largely comprised of people in their 20s and 30s, the generalizability to other age groups is not known.

(*Excerpts from Medscape*)

IMA-CMAAO Webinar on "Eye Manifestations and COVID-19"

26th September 2020 (4-5 pm)

Participants: Dr KK Aggarwal, President-CMAAO; Dr RV Asokan, Hony Secretary General-IMA; Dr Ramesh K Datta, Hony Finance Secretary-IMA; Dr Jayakrishnan Alapet; Dr VK Goel; Dr RS Hazuria; Dr S Sharma

Faculty: Dr AK Grover, Chairman, Dept. of Ophthalmology, Sir Ganga Ram Hospital, Chairman, Vision Eye Centres, Siri Fort Road and West Patel Nagar, New Delhi

Key points from the discussion

- Left eye conjunctivitis is most common in COVID-19.
- VP Mike Pence, USA, was seen with left eye involvement?
- COVID-19 transmission can occur through the ocular surface or aerosol contact with the conjunctiva. Hence, eye protection is an integral component of the protective measures to be taken by a person taking care of a person with COVID.
- Conjunctivitis may be the first presenting symptom. Conjunctival congestion has also been observed in confirmed cases of infection.
- There are anecdotal reports of vascular occlusion and immune phenomenon occurring in the orbit and other structures of the eye. But these have not yet been documented significantly.
- The risk of transmission in ophthalmology is very real because of the proximity in examination and treatment procedures. The concentration on the surface of the eye may not be so high and the angiotensin-converting enzyme 2 (ACE2) receptors here may not be as dense as in the lungs, so there should not be paranoia. Follow all screening protocols, have a good system of triage and follow hygiene measures to prevent risk of transmission. Eye protection should be used by clinicians to avoid transmission through the surface.
- Studies have shown that the virus is present in tears of patients (moderate-to-severe cases); may also be present in asymptomatic persons.
- A landmark study from India has demonstrated the virus in tears of 24% of patients with lab proven moderate-to-severe COVID-19 by conjunctival swab (RT-PCR). This indicates a high possibility of transmission of the virus through tears in these patients.
- COVID-19 has had a severe impact on day-to-day work.
- COVID-19 and the lockdown that followed have affected patient care. A study from Aravind Eye Hospital, Madurai, done from March 25 to May 3 showed that OPD visits and retinal laser procedures have decreased by 96.5%; sight saving intravitreal injections decreased by 98% and cataract surgeries decreased by 99.7%.
- Very few corneal grafts were being done during this period, resulting in vision loss. Patients with open globe injuries underwent evisceration as they presented late.
- Emergency procedures could not be done due to logistic reasons.
- Community eye care also suffered – no screening camps, no community surgery, eye donations decreased, peripheral vision centers in rural areas were not functioning.
- COVID-19 has greatly affected residency education (theoretical, clinical and surgical); specially designed webinars for PG training have now started.
- COVID-19 has had an impact on day-to-day eye care practices. Most eye care is provided by stand-alone hospitals and most work is elective. The work is now picking up but is still around 50-60%. There was huge impact on turnover; at one point it was close to zero percent. Survival plans had to be worked on. Getting back after lockdown requires lot of modifications.
- A RT-PCR test report (of last 48 hours) is must for all longer procedures; test is also advised for shorter procedures like cataract, but there has been some resistance.

Round Table Expert Zoom Meeting on "Vaccine Update"

10th October, 2020 (11 am-12 pm)

Participants: Dr Jayakrishnan Alapet, Prof Mahesh Verma, Dr Ashok Gupta, Dr Atul Kochhar, Dr Jayalal, Dr Anita Chakravarti, Dr KK Kalra, Dr Anil Kumar, Ms Meenakshi Datta Ghosh, Mrs Upasana Arora, Mr DK Gupta, Ms Ira Gupta, Dr S Sharma

Faculty: Dr KK Aggarwal, President-CMAAO

Key points from the discussion

- There is a critical need for a COVID-19 vaccine as there is a need to end this epidemic; also, vaccine could be important to control future epidemics.
- A vaccine is technically feasible, but there are two concerns: possibility of antibody-dependent enhancement and timelines are faster than before, but still not fast enough.
- The process of vaccine development started as early as 10th January, when the virus sequence was shared.
- COVID-19 is an acute (less than 3 months) manageable immunogenic (trigger) thrombogenic (effect) inflammatory notifiable (infectious) viral disease.
- Any vaccine should be able to prevent the entry of the virus and it should also be able to reduce the

duration of the disease. The vaccine should be able to take away the immunogenic and thrombogenic character of the virus. It should be able to prevent the disease.

- Either the virus as a whole, or its components (membrane, envelope, spike and nucleoprotein), are used in the vaccine.
- The virus enters the cell through receptor binding domain and membrane fusion.
- A large number of trials (193) of vaccine are going on worldwide. These trials are at various stages; 28 vaccines are in phase 1 trial stage, 14 are in phase 2, 11 are in phase 3 trials and 5 have been given limited approval. No vaccine has been approved.
- Types of vaccine: Live virus, inactivated virus, live-attenuated, gene part of the virus, recombinant, spike protein of the virus, monoclonal antibodies, adjuvant.
- A vaccine healthy challenge can be done after giving the vaccine to see if it is effective. Natural exposure in family is happening everyday now.
- Inactivated or killed vaccines are easy to make but do not provide long-lasting immunity; a booster may be required. Examples are hepatitis A vaccine, injectable polio and flu vaccine. The virus is inactivated with formalin or alcohol.
- Three (CoronaVac – Sinovac Biotech, Sinopharm) out of 5 limited approvals are inactivated or attenuated vaccines.
- Covaxin, the Indian vaccine, is based on inactivated virus.
- Live-attenuated vaccines: Examples are MMR, Rotavirus, small pox, chickenpox, yellow fever; produce long-lasting immune response. 1-2 doses may be required. India is working only on BCG recombinant vaccine, not coronavirus. Live-attenuated vaccines cannot be produced in short period of time.
- Vectors: Take another virus and add corona protein or part of corona protein into it. Adenovirus is the most commonly used. Vectors are of three types: Human virus 5 and 26, chimpanzee virus and Gorilla virus. Oxford vaccine ChAdOx1 vaccine is a chimpanzee adenovirus vaccine vector. Vector vaccines are easy to make but there are chances of complications (two cases of transverse myelitis have been reported).
- Two ways to get a vaccine early: vector vaccine or live-attenuated vaccine. Most ongoing work is on these two types of vaccines.
- Some are working on nasal spray; some are working on weakened measles virus or a pill form.
- Vaccines using coronavirus gene fragments are in preclinical stage.
- Viral vector can be replicating (Ebola virus vaccine) or nonreplicating (no currently licensed vaccines are nonreplicating). The Russian Sputnik V vaccine is nonreplicating viral vector vaccine.
- Vaccines can be subunit, recombinant, polysaccharide and conjugate. These give a very strong immune response and can be used in people with weakened immune systems and long-term health problems. Examples - HiB, HPV, hepatitis B, pneumococcal/meningococcal, shingles.
- Boosters are needed to have ongoing protection.
- Spike protein is the most preferred vaccine target.
- Subunits are coronavirus proteins (RBD, peptides, proteins with adjuvant), but no genetic material.
- Genetic vaccines: Moderna mRNA vaccine is in phase 3 trial. Zydus Cadila is working on a DNA-based vaccine. It is undergoing phase 2 trial.
- Universal vaccine: vaccine made with all existing strains of the virus.
- Some people are working on oral vaccine, adjuvant vaccine.
- In Russia and China, healthcare workers and the military have been given the vaccine as phase 3 trial.

COVID-19 Long-term Effects

- **COVID-19 symptoms can sometimes persist for months.**
- Most patients recover completely within a few weeks. However, some of them, even those who had mild disease, continue to experience symptoms after their initial recovery.
- Older people and those with several serious medical conditions have the greatest odds of having lingering COVID-19 symptoms.
- The most common signs include: Fatigue, cough, shortness of breath, headache.
- **Heart.** Imaging tests done months after recovery from COVID-19 have revealed long-term damage to the heart muscle, even among those who experienced mild COVID-19 symptoms. This may heighten the risk of heart failure or other heart complications later on.

- **Lungs.** There can be long-term damage to the alveoli in the lungs. The resulting scar tissue can cause long-term breathing problems and fibrosis.
- **Brain.** Even in young people, this viral disease can cause strokes, seizures and Guillain-Barré syndrome. COVID-19 may also heighten the risk of developing Parkinson's disease and Alzheimer's disease.
- While large clots can cause heart attacks and strokes, much of the heart damage that is caused by COVID-19 is considered to occur as a result of very small clots that block tiny blood vessels (capillaries) in the heart muscle.
- Other organs affected by blood clots include the lungs, legs, liver and kidneys.
- COVID-19 also has the potential to weaken blood vessels, thus contributing to lasting problems with the liver and kidneys.
- Intensive care unit (ICU) experience can make a person more likely to develop post-traumatic stress syndrome, depression and anxiety.
- Many people may develop chronic fatigue syndrome. (*Mayo Clinic)*
- As per World Health Organization (WHO), recovery time appears to be around 2 weeks for mild infections and 3-6 weeks for severe disease.
- In a survey of 350 patients with COVID-19 in the United States, 39% of those who had been hospitalized reported a return to baseline health by 14-21 days following diagnosis.

  (*Tenforde MW, Billig Rose E, et al; CDC COVID-19 Response Team. Characteristics of Adult Outpatients and Inpatients with COVID-19 - 11 Academic Medical Centers, United States, March-May 2020. MMWR Morb Mortal Wkly Rep. 2020;69(26):841.*)
- In a study including 143 patients who were hospitalized for COVID-19, only 13% were reported to be symptom free after a mean of 60 days following disease onset. The most common persistent symptoms included fatigue (53%), dyspnea (43%), joint pain (27%) and chest pain (22%). None of the patients had fever or features concerning for acute illness.

  Persistent severe illness with weeks of fever and pneumonia associated with underlying immunosuppression has also been reported. *(Uptodate)*
- In a survey of 292 patients diagnosed with COVID-19 in the outpatient setting, only 65% reported a return to baseline health by 14-21 days after diagnosis. Those returning to baseline health did so in a median of 7 days following diagnosis. Symptoms most likely to persist beyond 14 to 21 days included cough (43%) and fatigue (35%). Fever and chills persisted in 3% and 4%, only.

  (*Tenforde MW, Kim SS, Lindsell CJ, et al. Symptom duration and risk factors for delayed return to usual health among outpatients with COVID-19 in a multistate health care systems network — United States, March–June 2020. MMWR Morb Mortal Wkly Rep. 2020.*)
- Some recovered patients have persistently or recurrently positive nucleic acid amplification tests. While recurrent infection or reinfection cannot be definitively ruled out, there is evidence to state that these are unlikely. *(Uptodate)*

With input from Dr Monica Vasudev

First Reinfection Death could have been Due to Underlying High IL-6 Levels

Dutch woman dies after contracting COVID-19 twice, the first reported reinfection death.

- An elderly Dutch woman, aged 89, has become the first known person to die from contracting COVID-19 twice.
- The woman in Netherlands suffered from a Waldenström's macroglobulinemia (WM).
- Her immune system was compromised owing to the cell-depleting therapy that was given to her.
- The patient was initially admitted earlier this year with severe cough and fever, and had tested positive for COVID-19.
- She was discharged after 5 days when besides some persisting fatigue, her symptoms subsided completely.
- Two days into chemotherapy treatment, about 59 days after the onset of the first COVID-19 episode, she developed fever, cough and difficulty breathing. She again tested positive for COVID-19. There were no antibodies in her blood system when tested on Days 4 and 6. Her condition worsened on Day 8 and she died 2 weeks later.
- The case is reported by Maastricht University Medical Center in the Netherlands in a paper accepted for publication in the journal *Clinical Infectious Diseases*.
- When the samples from both the cases were investigated, investigators found that the genetic makeup of the two viruses was different.

- Some cases of reinfection have been reported from across the world. The most recent has been the case of a 25-year-old resident of Nevada in the United States. According to researchers in *The Lancet Infectious Diseases*, the man tested positive for COVID-19 in April and again in June, showing symptoms in both cases including sore throat, cough, headache, nausea and diarrhea. He had no underlying health conditions; however, like the Dutch woman, he suffered a more severe episode the second time. Unlike the Dutch woman; however, he developed a measurable antibody response after the second episode.
- A 33-year-old man from Hong Kong was the first person reported to have contracted the infection twice. He got re-infected 4.5 months after the initial infection, showing no symptoms the second time round.

(Source: https://www.kmov.com/news/dutch-woman-dies-after-catching-covid-19-twice-the-first-reported-reinfection-death/article_63e103b4-3ae1-59b7-88f7-f45b44bb050f.html)

Discussion

- The higher levels of angiogenic cytokines in patients with WM point to a role of angiogenesis in WM.
- C-C motif ligand 5 (CCL5) a chemokine, granulocyte colony-stimulating factor and soluble interleukin (IL)-2 receptor are raised in patients with WM; IL-8 and epidermal growth factor levels are lower in comparison with healthy controls.
- CCL5 expression is higher in the BM microenvironment amomg patients with WM, compared to controls.
- CCL5 levels correspond with disease aggressiveness, and there appears to be a functional correlation between CCL5 and IL-6 levels.
- IL-6, a proinflammatory cytokine, is mainly produced by BM stromal cell and plays a role in normal and malignant B-cell biology.
- CCL5 stimulates IL-6 secretion from BM stromal cells by binding to a receptor C-C motif receptor 3 (CCR3) and induction of GLI2, a transcription factor via the PI3K-AKT-B-p65 pathway.
- The enhanced IL-6 production leads to increased IgM production by WM malignant cells via the JAK/STAT pathway.
- The CCL5– IL-6 interaction may be a mechanism by which the WM cells and BM stromal cells stimulate each other; the WM cells produce CCL5, which stimulates the stromal cells to produce IL-6, and IL-6 goes on to stimulate IgM production by the WM cells.
- IgM is a mediator of WM morbidity.
- Other cytokines that are increased in WM include B-lymphocyte stimulator and macrophage inflammatory protein-1 alpha.

(*Clinical Lymphoma, Myeloma & Leukemia, Vol. 13, No. 2, 218-21.)*

Hypothesis

- She might have recovered.
- But, baseline IL-6 could have remained high.
- Reinfection might have precipitated IL-6 storm.

Solidarity Trial Results

After months of testing some repurposed drugs, researchers in the largest study for potential COVID-19 treatments have noted that many of them are not effective against the SARS-CoV-2 virus.

- The WHO's Solidarity trial is the world's largest ongoing randomized control trial of potential COVID-19 therapeutics.
- The agency released an interim report of patient responses to repurposed drugs, including remdesivir, hydroxychloroquine (HCQ), lopinavir/ritonavir and interferon, for the treatment of COVID-19.
- In all, 2,750 volunteers received remdesivir, 954 were given HCQ, 1,411 received lopinavir, 651 were administered interferon plus lopinavir, 1,412 received only interferon and 4,088 received placebo.
- There was little or no effect of these drugs on the outcome of COVID-19 over a period of 28 days.
- Some of these drugs have received emergency–use authorization by governments of many countries. However, these permissions could now change based on the Solidarity trial findings, which includes 11,266 patients hospitalized with COVID-19, across 30 countries.
- The study assessed the impact of these treatments on mortality, ventilator use and length of hospital stay.
- It didn't evaluate other uses of the drugs for COVID-19, like in treating patients in a COVID-19–infected community, or for COVID-19 prevention.
- After finding that HCQ had no positive impact on COVID-19-infected patients, the WHO, FDA,

Oxford University and other countries discontinued their ongoing trials. WHO also discontinued anti-HIV drug combination lopinavir/ritonavir trials in July after reviewing the progress of these drugs during the interim results.

- WHO is now looking at monoclonal antibodies, immunomodulators and some newer antiviral drugs. (*Source: First Post*)

Round Table Expert Zoom Meeting on "Back to Basics in Management of COVID-19"

17th October, 2020 (11 am-12 pm)

Participants: Dr KK Aggarwal, Dr AK Agarwal, Prof Mahesh Verma, Dr Suneela Garg, Dr Jayakrishnan Alapet, Dr KK Kalra, Dr Anita Chakravarti, Dr Anil Kumar, Ms Ira Gupta, Dr S Sharma

Key points from the discussion

- The WHO Solidarity trial has shown that remdesivir, interferon, HCQ and ritonavir + lopinavir are not effective.
- Eli Lilly has halted its trial of its coronavirus antibody drug; J&J paused the trial of its vaccine; although AstraZeneca has resumed the trial of its vaccine in the UK, India, South Africa, Brazil, the US FDA has not given the go-ahead for the trial to restart.
- The WHO will now concentrate on monoclonal antibodies and immunomodulators, which means that treatment will be expensive. So, it's back to basics, which is prevention. Masking (correct, consistent use of proper 3-layered mask) is the only answer.
- The outer layer of the mask should have a splash resistance of more than 120 mmHg.
- The breathability should be less than 49 Pascals per sq. cm.
- The middle layer should be made of melt blown propylene (not spun) and should have filtration efficiency of 80%. There should be no visible holes in this layer.
- The inner layer should be water absorbent.
- The ear loops should be made of good quality elastic and not cause pain when wearing a mask.
- Around 50% of masks do not have nasal clip.
- Since masking is very important, it must be regulated. Medical masks are regulated, but fabric masks are not regulated. They should also be under some regulation for quality.
- Government should ensure that quality masks are procured and made available to everybody at minimum cost.
- Certification of masks is very important. The government has entrusted some agencies. In South India, it is done by SITRA (South India Textile Research Association), DRDO in North, Ahmedabad Textile Industry's Research Association (ATIRA) in the West and West Bengal Textile Research Organization in the East. The coordinating agency is Hindustan Lifecare. There are around 250 labs all over India to test and certify but implementation is poor. Only certified masks should be worn by healthcare workers.
- Bureau of Indian Standards (BIS) has also issued standards for masks.
- Final disposal of masks is also very important.
- Bactericidal or virucidal claims of masks should be evidence-based.
- The important days are Day 3 and Day 5. If rapid doubling of C-reactive protein (CRP) can be detected within this time (prehospitalization), and appropriate anti-inflammatory (steroids) and oral anticoagulants are started, then mortality can be reduced.
- CRP is the marker for cytokine wave.
- While deaths of COVID patients are the focus of study, it was suggested that we also have to look into the survival of COVID patients.

With input from Dr Monica Vasudev

Minutes of Virtual Meeting of CMAAO NMAs on "Drug & Vaccine Failures in COVID-19"

17th October, 2020 (Saturday, 9.30 am-10.30 am)

Participants, Member NMAs: Dr KK Aggarwal, President-CMAAO; Dr Marthanda Pillai, Member World Medical Council; Dr Alvin Yee-Shing Chan, Hong Kong Treasurer, CMAAO; Dr SM Qaisar Sajjad, Secretary General, Pakistan Medical Association; Dr JA Jayalal, President-elect, Indian Medical Association

Invitees: Dr Russell D'Souza, UNESCO Chair in Bioethics, Australia and Dr S Sharma, Editor-IJCP Group

Key points from the discussion

- Three drug trials have been halted in the last 1 week due to unexplained effects.
  - Johnson & Johnson has paused phase III trial of its single dose vaccine JNJ-78436735 (human adenovirus Ad26 combined with spike protein).

- Astra Zeneca and Oxford have resumed trials of their ChAdOx1 vaccine in the UK, India, South Africa, Brazil; however, the US FDA has not given the go-ahead for the trial to restart in the US.
- Eli Lilly has halted the trial of its coronavirus antibody drug LY-CoV555 (ACTIV-3). The comparison drug is remdesivir.

- The WHO Solidarity trial has found that remdesivir, HCQ, interferon and ritonavir + lopinavir had little or no effect on mortality in hospitalized patients with COVID-19.
- Three out of the five approved vaccines are killed vaccines. India is working on a killed vaccine.
- Two of vector vaccine trials (J&J, Oxford) have been halted.
- About 30% of vaccines do not produce antibodies; hence, will a single dose (J&J vaccine) be effective? We do not know.
- This is an inflammatory virus and it is inflammation which kills. Early detection of inflammation/ hypoxia can reduce mortality.
- The inflammatory process is not dependent on the virus; once started, it will continue.
- Antiviral drugs will only reduce communication of the virus to others and will not reduce inflammation. The viral load only indicates infectiousness and not severity of the infection.
- In the current scenario, any three unusual symptoms such as headache, low-grade fever, skin rash, sore throat, dry cough, muscle pain, calf pain without loss of smell and taste is COVID, unless proved otherwise.
- New loss of smell and taste should be presumed to be COVID, unless proved otherwise.
- One must have a high index of suspicion for atypical symptoms.
- In flu, fever is higher than 100.4°F and nasal symptoms are predominant. In COVID, fever is less than 100.4°F and throat symptoms are predominant. If fever is higher than 100.4°F in COVID, this is suggestive of pneumonia.
- CRP is the test for resource-limited countries. Doubling of CRP within 24 hours is indicative of cytokine release. Get CRP done on Day 3 and Day 5. If rapid doubling of CRP can be detected within this time, and appropriate anti-inflammatory (steroids) and oral anticoagulants are started, then mortality can be reduced.
- Masking (consistent and correct use of proper mask) is important.
- The outer layer of the mask should be water resistant and have a splash resistance of more than 120 mmHg. The breathability should be less than 49 Pascals/sq. cm. If splash resistance is high, breathability will reduce.
- The middle layer is important. It should be made of melt blown propylene (not spun) and should have filtration efficiency of 80%. There should be no visible holes in this layer.
- The inner layer should be water absorbent (should not have splash resistance).
- The mask has to fit closely to the face; there should be no gap. Face shield is not a replacement for mask.

IMA-CMAAO Webinar on "Artificial Intelligence in #COVIDTIMES"

17th October, 2020, 4-5pm

Participants: Dr KK Aggarwal, President-CMAAO; Dr RV Asokan, Hony Secretary General-IMA; Dr Ramesh K Datta, Hony Finance Secretary-IMA; Dr Jayakrishnan Alapet; Dr GM Singh; Dr Brijendra Prakash; Dr Ranjan Wadhwa; Dr S Sharma

Faculty: Dr Vidur Mahajan, Associate Director, Mahajan Imaging & Head R&D, Centre for Advanced Research in Imaging, Neurosciences & Genomics, New Delhi

Key points from the discussion

- All of us use artificial intelligence (AI) in our day-to-day life. Some examples are Google maps, Amazon, Netflix search; keyboard tries to figure out what we intend to write and gives word suggestions, etc.
- AI is not a new concept; it existed even in the 1950s, although there was not much of computing power then. But it has recently become popular because of the exponential increase in computing power.
- AI is the ability of the computers to learn without being programmed, i.e., the computer figures it out for itself. Basically this involves using high end computing to find hidden patterns in data.
- There are three types of AI: Artificial "narrow" intelligence, artificial "general" intelligence and artificial "super" intelligence.
- Artificial "narrow" intelligence is the ability of the machine to do one thing very well, e.g., the Deep Blue computer which beat Gary Kasparov in chess. This machine can only play chess. Currently,

machines are artificially "narrowly" intelligent, i.e., intelligent in only one domain.

- Artificial "general" intelligence: learning one thing and then extrapolating that knowledge to another; humans are generally intelligent at varied aspects.
- Artificial "super" intelligence is a much debated topic and describes the point in time when AI becomes stronger than humans.
- AI applications can be broadly categorized into two: what humans can do but AI does better and faster and what humans cannot do.
- Supervised learning - machine figures out patterns in the data itself; most healthcare AI is focused on this, but it is labor intensive and involves feeding labeled data into algorithms so that patterns in the data are recognized.
- Unsupervised learning is what human beings are – we automatically learn from our environment and can transfer knowledge from one aspect to another. It is more computationally expensive and currently its applications in healthcare are limited. Lot of work is being done on can machines learn without being trained.
- Steps in creating an AI algorithm: Find data (heterogenous data related to the problem in question as much as possible), train the model, validate the model and test the model.
- COVID has driven adoption of digital health tools – telemedicine guidelines, eSanjeevani; most records are now getting digitized.
- AI is helping in the war against the entire COVID-19 landscape of prevention, diagnosis and treatment.
- Globally, AI is helping in many public health decisions, e.g., Aarogya Setu App, Delhi Govt. worked with IIT Delhi to find out which areas to lockdown and which to open up using AI, proximity sensors for contact screening.
- Machine learning plus genome sequencing helped Kerala to identify where their cases were coming from.
- AI tools are also an essential part of vaccine development. AI technology is being used to sift through large amount of data and find the most useful literature to make the ideal vaccine (CORD-19 – COVID-19 open research dataset, a free resource of more than 2,80,000 articles about COVID-19 for use by the global research community); molecular biology – AlphaFold (computational predictions of protein structures associated with COVID-19) – using machine learning algorithms to predict how protein structures can interact with each other and potentially vaccine can impact body. AI is being used in vaccine trial – who to give the vaccine to, how many doses, etc.
- Chest X-rays have low sensitivity for COVID diagnosis but is best used in high suspicion situations in resource constrained areas.
- A lot of AI work is going on in India. AI systems built for tuberculosis (TB) are being used for COVID by many people working in this area.
- Two applications of chest X-ray: Diagnosis and triaging and monitor disease progression.
- CT scan has better sensitivity in diagnosing and monitoring; Predible algorithm helps to analyze 15,000 CTs in a month; it is trained on 40,000 COVID images and has 95% volume concordance with calculation of volume involvement by a radiologist.
- In the absence of RT-PCR, AI for COVID played a vital role.
- Many novel attempts at diagnosing COVID using AI are underway, e.g., trying to diagnose from cough samples (AI4COVID-19), detection of COVID-19 from routine blood examinations.
- AI is also at the core of drug development and drug repurposing (*The Lancet, Sept. 18, 2020*).
- Future of medicine is in AI.

IMA-CMAAO Webinar on "COVID-19 and Air Pollution"

24th October, 2020, 4-5 pm

Participants: Dr KK Aggarwal, President-CMAAO; Dr RV Asokan, Hony Secretary General-IMA; Dr Ramesh K Datta, Hony Finance Secretary-IMA; Dr Jayakrishnan Alapet; Dr GM Singh; Dr Brijendra Prakash; Dr S Sharma

Faculty: Dr Tushar Joshi, Former Director, Center for Environmental Research

Key points from the discussion

- Air pollution is not a new phenomenon. Of all the pollutants, particle pollutants are the best studied.
- Air pollution has become the most significant environmental health risk in India.
- We need air for oxygenating our body, which is important for the function of our cells. Brain requires the most oxygen for its optimal functioning.
- We cannot live without air for more than a few minutes, even though we can live without food

for a long time and without water for a few days. Food and water are voluntary, whereas breathing is involuntary and automatic.

- We can survive at oxygen levels lower than 21%. Death is likely at concentrations of 10%. Mental impairment occurs at around 16% and permanent damage to the cardiovascular system can occur at around 12%.
- Particulate matter (PM)2.5-10 are inhalable, not respirable. PM2.5 will not arrest in the nose, it will pass down and go to the end of the lung, i.e., the alveoli.
- It is not easy to define air pollution. All man-made emissions in the air can be called air pollution as they alter the chemical composition of the natural atmosphere.
- Natural events such as forest fires, dust storms, volcanoes also increase pollution.
- There are three types of air pollution: Household (biomass burning in rural areas, crop residues, etc.), indoor (cigarette smoke, incense sticks, dhoop batti, mosquito coils, insecticide sprays, air freshners, etc.) and outdoor or ambient (industry, transportation and burning of trash).
- It is the heart which suffers the most and not lungs.
- The sources of air pollution are: gaseous hydrocarbons, nitrogen oxides, carbon monoxide, particulates and lead.
- Ambient air pollution causes around 4.2 million deaths every year due to stroke, heart disease, lung cancer and chronic respiratory diseases (WHO).
- Around 3.8 million deaths occur every year as a result of household exposure to smoke from biomass burning.
- Low- and middle-income countries bear the maximum burden of air pollution particularly in WHO Western Pacific and South-East Asia regions.
- A study done by IIT Mumbai and the Health Effects Institute (HEI) in 2015 found that particulate matter accounted for around 1.1 million deaths or 10.6% of the total deaths in the country. Residential biomass burning is the single largest contributor to the disease burden in India.
- Residential biomass caused almost 25% of the deaths attributable to PM2.5; coal combustion 15.5% and open burning of agricultural residue 6.1%.
- In the next few decades, air pollution will kill far more people than both malaria and access to clean drinking water. By 2050, about 130 Indians out of every million are likely to die prematurely from exposure.
- Lung cancer trends in the UK show that in the early 20th century, lung cancer was rare. Today, it is associated with the highest death rate in both males and females.
- The impact of air pollution in the womb is transgenerational.
- Children, elderly and individuals with pre-existing diseases are of special concern and need special care. What makes some people have different presentations is still not well-understood yet.
- A recent study, which examined nonaccidental mortality in 72 urban communities across the US, found evidence of association between mortality and organic carbon matter, silicon, elemental carbon and sodium ion. Some constituents of PM2.5 may be more toxic than others.
- Under the National ambient air quality monitoring program, most monitoring stations monitor four air pollutants - SO_2, NO_2, suspended PM10 and fine PM2.5. Meteorological parameters such as wind speed, wind direction, relative humidity and temperature were also integrated with air quality monitoring.
- Coal is the largest source of SO_2. All thermal plants that use coal are closed down; brick kilns cannot use coal and must use the zigzag system to reduce air pollution.
- Diesel smoke has been identified as an independent carcinogen.
- There has been a decline in SO_2 levels; this may have been due to interventions such as reduction of sulfur in diesel, use of cleaner fuels such as CNG, switching from coal to LPG as domestic fuel.
- There has been a slight decrease in NO_2 levels despite increase in vehicles; this may be due to factors like improvement in vehicle technology, use of alternate fuel.
- Ozone is a secondary pollutant and formed from VOCs and NO_2.
- Concentration of benzene in AC car is 6-8 times higher than in non-AC car.
- Most people in urban areas have developed tolerance due to constant exposure, but not rural people. This is not protective as underlying harm will continue to occur.

- A study analyzing outdoor air pollution and emergency room (ER) visits at a hospital in Delhi found that ER visits for asthma, chronic obstructive pulmonary disease (COPD) and acute coronary events increased due to higher than acceptable standards of air pollutants. The study concluded that there is considerable burden of cardiorespiratory diseases in Delhi due to high levels of ambient air pollution.
- Air pollution is also associated with diseases of the central nervous system, including stroke, Alzheimer's disease, Parkinson's disease. Air pollutants can easily move to the CNS and active innate immune responses.
- Saving and protecting the environment is the responsibility of everyone.
- Inverters should be used instead of diesel or petrol run gensets.

Minutes of Virtual Meeting of CMAAO NMAs on "CMAAO Update & COVID-19 and Anti-inflammatory Drugs"

27th October, 2020 (Saturday, 9.30 am-10.30 am)

Participants: Member NMAs: Dr KK Aggarwal, President-CMAAO; Dr Yeh Woei Chong, Singapore Chair-CMAAO; Dr Alvin Yee-Shing Chan, Hong Kong, Treasurer, CMAAO; Dr Ravi Naidu, Malaysia; Dr Marie Uzawa Urabe, Japan; Dr Christine Tinio, Philippines; Dr SM Qaisar Sajjad, Secretary General, Pakistan Medical Association; Dr Md Jamaluddin Chowdhury, Bangladesh; Dr Lochan Karki, Nepal

Invitees: Dr Russell D'Souza, UNESCO Chair in Bioethics, Australia; Dr Suneela Garg; Dr Anita Kant; Dr RP Pareek; Dr Ketan Mehta; Dr Major Prachi Garg; Ms Pooja Banerjee, Editor-IJCP Group; Dr S Sharma, Editor-IJCP Group

Key points from the discussion

- E protein is common to all coronaviruses, but spike protein is different among different coronaviruses.
- When the virus enters the body, various cytokines, tumor necrosis factor (TNF), interferon (IFN)-α take care of the virus. If IFN does not act, the virus is tackled by natural killer cells. If IFN-1 is not formed, then cytokine crisis results.
- Proinflammatory mediators in viral infection: IFN, TFN, ILs, chemokines.
- Inflammatory mediators in viral infection: Prostaglandins (PGs), thromboxanes, leukotrienes.
- If lifestyle is proinflammatory, a virus will make it inflammatory.
- When IFN-1 is not formed, then macrophages produce NLRP3 $\rightarrow$ IL-18 and IL-1β. IL-1β induces production of ferritin, causes tissue damage.
- Th1 cells produce IL-6 $\rightarrow$ fibrinogen and C-reactive protein (CRP); TNF-α and IL-8 produce inflammation, via PLA2 and increased neutrophil migration, respectively.
- Treatment approaches: Either block TNF or interleukin, increase interferon or act at the level of colony-stimulating factors.
- Various treatment strategies: Targeting viral RdRp, modulation of immune defense, supplements and neutraceuticals, vaccines, antivirals, gene therapy, blocking virus entry in the cell, targeting cellular signaling pathways.
- Potentially harmful effects of nonsteroidal anti-inflammatory drugs (NSAIDs) in COVID patients include adverse effects in gastrointestinal tract (GIT), heart and kidneys; exacerbation of asthma; increased incidence of hypercoagulation; increased secretion of some inflammatory cytokines contributing to cytokine storm; reduction of host immune response against the virus and increased formation of neutrophil extracellular traps (NETs).
- Potentially beneficial effects of NSAIDs in COVID patients: Reduce the risk of developing severe COVID-19; reduce entry and replication of virus; inhibit migration and activation of neutrophils and macrophages; inhibit activation of NLRP3 inflammasome and production of inflammatory cytokines and repress inflammatory Th1/Th17 cells.
- Fever in COVID-19 is not only thermal dysregulation, it is cytokine fever.
- Azithromycin (decreases viral entry in cells), HCQ (prevents virus binding to ACE2 receptor), doxycycline (prevents viral entry and replication) and ivermectin (inhibits viral replication) do not act on NLRP3.
- Ivermectin does not act on IL-1β, -6 and -18, TNF-α or NLRP3.
- Paracetamol increases IL-1β, reduces TNF-α; it does not reduce cytokine fever.
- Mefenamic acts on IL-1β, -6 and -18, TNF-α and NLRP3. It is drug of choice for COVID-19 inflammation (including inflammation induced fever).

- Paracetamol reduces fever but not CRP; mefenamic acid reduces both fever and CRP.
- When CRP is persistently high, there are four options: Mefenamic acid, indomethacin, naproxen, nimesulide. Of these, first is mefenamic acid, which can be given for 3 months; nimesulide is approved only for 2 weeks, then come indomethacin and naproxen.
- Diclofenac is anti-inflammatory; it is not a very good antipyretic.
- In post-COVID patients, when an anti-inflammatory is required, we need a drug which reduces fever and CRP and is steroid-sparing.
- In the first phase of the infection, we have to see the presentation, what the virus is doing to the body and in the second phase, what the body does to the virus.
- During the viral replication phase, we should not choose drugs that help the virus to replicate. Mefenamic acid can be used safely right from the first week of infection where there is a tendency to choose steroids to bring down the fever, which can be detrimental. It gives the effect of antiviral, anti-inflammatory and antipyretic.
- COVID-19 illness can be divided into two: Viral (RT-PCR) illness and inflammatory (cytokine - CRP) illness. Once cytokines are released, the virus has no role to play. Responses of Th1, Th2 and Th17 cells decide the future action. If more of the good cytokines are released, the phenomenon is short-lived.
- CRP starts rising within 4-6 hours; it peaks at 36-48 hours and comes down to normal within 17 hours. Therefore, CRP should become normal by Day 4. If it does not return to baseline, this means shifting from viral phase to cytokine wave. By the 10th day, CRP should be less than 10. If more than 10, then the body is under cytokine control → recurrent inflammation → symptoms and cytokine crisis.
- Long COVID is a persistent cytokine disease.
- From 9-90 days, there can be two types of illnesses: CRP normal or CRP more than 2.
- If CRP is less than 2, there is residual damage, which is autonomic dysfunction. If CRP is more than 2, this is persistent cytokine state, where an anti-inflammatory drug is needed (HCQ, mefenamic acid, steroid, colchicine). If there is fever, then mefenamic acid is the drug.
- There are very few patients now in Japan and only limited numbers of hospitals are seeing patients.
- In Australia, the number of patients is coming down. Mefenamic acid has been used as also dexamethasone.
- In Malaysia, all COVID patients are treated at designated government hospitals only.
- There is a strong recommendation now that all tertiary hospitals should have post-COVID clinics. Guidelines should be standardized and adopted by these clinics.
- Ibuprofen and ketoprofen have been shown to upregulate ACE2 receptors, thereby increasing the viremic load. IL-6 reduction with ibuprofen is not as evident as seen with other drugs. Ibuprofen is not contraindicated. The current recommendation is that those patients who are on ibuprofen should continue with it.
- Mefenamic acid can be started from Day 1 itself; it will help bring down the fever and also reduce inflammation. The virus requires serine protease to enter the cells. Serine protease inhibitors are required in such cases. Mefenamic acid is a serine protease inhibitor and this way it can work also as an antiviral.
- Ivermectin has antiviral properties, but it does not reduce inflammation. So, it has to be combined with an anti-inflammatory drug.
- Choose drugs which act at different levels.
- Which drug to choose should be left on the treating doctor; it is the personal experience of the doctor, which decides what works best for the patient.
- While remdesivir may not reduce mortality, it does reduce severity of infection. In severe cases, the viral load definitely comes down. It has been given emergency use authorization in India.
- The presence of CMAAO countries in the forthcoming WMA meeting was raised.
- Post-vaccination deaths have been reported in South Korea, although the government has said that these deaths are unrelated to the flu vaccination. This did create some panic among doctors in Hong Kong that if something happens after vaccination, is it defendable?

■■■■

Indian Journal of Clinical Practice, Vol. 31, No. 6, November 2020

News and Views

Urgent Need for Universal Health Coverage: UN Chief

The coronavirus disease 2019 (COVID-19) pandemic has brought to light the inadequacies in our health systems, stated the UN Chief. UN Secretary-General António Guterres cited weak structures and unequal access to healthcare as the key reasons behind the huge number of coronavirus cases and deaths across the globe.

He added that universal health coverage is essential to end the pandemic, and will also drive progress across all health-related Sustainable Development Goals (SDGs). "COVID-19 has made the need for Universal Health Coverage…more urgent than ever", the UN Chief said. This is among major recommendations in the policy brief that he launched. Other recommendations include intensifying public health measures; coordinating a global response to the pandemic and protecting other health services during the pandemic, which include mental health and sexual and reproductive health programs… (*UN*)

SARS-CoV-2 Matter Detected in Autopsied Brain Tissue

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) - viral RNA, viral protein or both - was found in the brain tissue of over 50% of patients who died with COVID-19, revealed a post-mortem case series in Germany.

The presence of SARS-CoV-2; however, was not linked with the severity of pathological changes in the brain, reported researchers in *Lancet Neurology*.

Brain tissue from 43 people were evaluated in this case series who died in hospitals, nursing homes, or at home with COVID-19 between March 13 and April 24. SARS-CoV-2 RNA or proteins were detected in brain tissues of 53% of the investigated patients, while both were identified in 8 patients. SARS-CoV-2 viral proteins were detected in cranial nerves originating from the lower brainstem and in isolated cells of the brainstem… (*Medpage Today*).

US Signs Agreement with AstraZeneca for Development and Supply of COVID-19 Antibody Treatment

The US government has signed an agreement with AstraZeneca Plc AZN.L for the development and supply of around 1,00,000 doses of COVID-19 antibody treatment, a similar class of drugs that has been used for the treatment of President Donald Trump.

Funding will be provided to AstraZeneca by the US health agency for two Phase 3 clinical trials under operation Warp Speed. The operation aims to expedite treatments and vaccines for COVID-19.

One of the trials will assess the safety and efficacy of the experimental treatment to prevent infection for up to 12 months, in nearly 5,000 participants, while the second one will investigate post-exposure preventative and pre-emptive treatment in around 1,100 participants… (*Reuters*)

Povidone-iodine Gargle: A Prophylactic Measure to Impede COVID-19 Transmission

COVID-19, caused by the SARS-CoV-2 virus, has crossed the 33 million case mark across the world, with the death toll surpassing 1 million (as on September 28, 2020).[1]

Human-to-human transmission occurs through close contact with an infected person. Infection can also occur from surfaces contaminated with droplets or secretions. Respiratory pathogens adhere to the oropharyngeal mucosa and colonize and cause upper respiratory tract infection (URTI).[2]

Given the fact that COVID-19 is transmitted through respiratory droplets, it is reasonable to evaluate if the use of a prophylactic mouth rinse with virucidal activity can impede the spread of infection.

Povidone-iodine (PVP-I) products, as mouthwashes and throat sprays, have been shown to have a prophylactic effect on the transmission of SARS-CoV during previous outbreak. PVP-I products were shown to have strong virucidal activity against SARS-CoV.[3]

SARS-CoV-2 virus is closely related to SARS-CoV, and the viral load in the oropharynx in asymptomatic patients with SARS-CoV-2 infection appears to be as high as that in symptomatic patients.[4]

Reducing the viral load in the oropharynx with adequate oral prophylactic measures seems worth exploring.

A study assessed nasal and oral antiseptic formulations of PVP-I for virucidal activity against SARS-CoV-2. PVP-I nasal and oral rinse formulations from 1% to 5%

concentrations as well as controls were evaluated for virucidal potential. SARS-CoV-2 was exposed to the test compound for 60 seconds. All the tested concentrations of nasal and oral rinse formulations could completely inactivate the SARS-CoV-2 virus. Nasal and oral PVP-I formulations were thus shown to inactive the SARS-CoV-2 virus at different concentrations. Nasal and oral decontamination with PVP-I formulations thus seems to have potential in limiting the transmission of SARS-CoV-2.[5]

PVP-I mouthwash or gargle thus appears to be a promising approach to inactivate the virus, thus checking the spread of COVID-19.

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Some Pre-existing Conditions may Increase Mortality Risk for COVID-19 Patients, Says Study

A study conducted among COVID-19 patients has confirmed that cardiovascular disease (CVD), hypertension, diabetes, congestive heart failure, chronic kidney disease, stroke and cancer can heighten a patient's risk of dying from the viral illness.

Investigators noted that CVD might double the risk of dying from COVID-19. Other pre-existing conditions may heighten the risk of death in a COVID-19 patient by 1½- to 3-fold. Investigators assessed data from over 65,000 patients from 25 studies globally. Certain pre-existing health conditions were found to impact survival rates more than others. In comparison with hospitalized COVID-19 patients without pre-existing conditions, those with diabetes and cancer were 1.5 times more likely to die, those with CVD, hypertension and congestive heart failure were twice as likely to die, and those with chronic kidney disease had three times the likelihood of dying. The findings were published in *PLOS ONE*… (*HT – ANI*)

Novel Coronavirus can Survive on Skin for 9 Hours, Says Study

The SARS-CoV-2 virus may persist on human skin for 9 hours, which is much longer than the flu viruses, suggests a new study.

The influenza A virus (IAV) remained viable on human skin for nearly 2 hours, stated researchers, including those from Kyoto Prefectural University of Medicine in Japan. The study noted that both the viruses were rapidly inactivated on skin with a hand sanitizer. Additionally, it was found that the stability of SARS-CoV-2 on human skin remains unknown. SARS-CoV-2 and IAV were found to be inactivated more rapidly on skin surfaces compared to surfaces like stainless steel, glass and plastic. The survival time was significantly longer, i.e., 9 hours, for SARS-CoV-2, compared to 1.82 hours for IAV. The findings were published in the journal *Clinical Infectious Diseases*… (*HT – PTI*)

Sustained Lipid Reductions Over Statins with LIB003

Novel anti-PCSK9 compound LIB003 considerably decreases low-density lipoprotein (LDL) cholesterol levels over 52 weeks in patients already receiving maximally tolerated statins, suggests an open-label trial extension.

The study included 32 patients from the dose-ranging trial and revealed that over 52 weeks, LIB003 led to sustained reductions in LDL cholesterol levels of 64% on average and in PCSK9 levels of over 80%.

Substantial reductions were also evident in other lipids, including lipoprotein [Lp(a)], and apolipoprotein B. The findings were presented at the European Atherosclerosis Society (EAS) 2020 Virtual Congress. Traci Turner, MD, Metabolic & Atherosclerosis Research Center, Cincinnati, Ohio, stated that LIB003 was well-tolerated and there were no unexpected or significant adverse clinical or laboratory safety signals. Mild injection site reactions (ISRs) and antidrug antibodies (ADAs) were noted in only two patients… (*Medscape*)

Herd Immunity, an Unethical COVID-19 Strategy, Warns WHO Chief

Using the principle of herd immunity to curb the COVID-19 pandemic is unethical and "not an option" that the countries should follow to fight the coronavirus, cautioned the WHO Chief.

WHO Director-General, Tedros Adhanom Ghebreyesus, stated that herd immunity is a concept that is used for vaccination, where the population can be protected from a virus if a threshold of vaccination is attained. This is achieved by protecting people from the virus, not by exposing them to it, he stated.

He added that herd immunity has never been used as a strategy for responding to an outbreak in the history of public health… (*UN*)

Mother's Anxiety and Depression Tied to Asthma in Kids

Children whose mothers had depression and anxiety during pregnancy were found to have a higher risk of asthma in later childhood in a prospective cohort study from the Netherlands.

Mothers who had stress or depression during pregnancy had children with a 46-91% increased risk of asthma later on (range odds ratio [OR] 1.46 [95% confidence interval, CI 1.12-1.90] to 1.91 [95% CI 1.26-2.91]), reported researchers in *Thorax*. Investigators noted that overall psychological distress during pregnancy was linked with lower lung function in the offspring, which included lower forced vital capacity (z-score difference -0.10 per 1-unit increase, 95% CI -0.20 to -0.01). No associations could be seen between paternal psychological distress and risk of asthma in children, thus suggesting mechanisms that occur *in utero*… (*Medpage Today*)

Delayed Cancer Screening could Cause Increase in Deaths

Delays in colorectal cancer screening due to the ongoing COVID-19 pandemic could result in higher rates of advanced-stage cancer and death, reports a new study.

Compared with a delay of less than 3 months, the longer delay seen this year may cause an 11.9% increase in death rates. Researchers developed a model to forecast the effects of delayed cancer screening during 2020. A moderate delay of 7-12 months led to a 3% rise in advanced-stage colon cancer, and a long delay of over 12 months resulted in a 7% increase in advanced cancer. Considering a survival rate of 5 years for stage 3 or stage 4 colorectal cancer, the death rate would increase around 12% if screening is delayed for more than a year, as compared to a delay of less than 3 months.

Investigators presented the research at UEG Week Virtual 2020, an international conference for gastroenterologists, and the study will be published in the *UEG Journal*… (*Medscape*)

In-Hospital Cardiac Arrest Common in COVID-19

Two recent studies have suggested that cardiac arrest is common among critically ill patients with COVID-19, and is tied to poor survival, especially among older patients.

The first report revealed that 60 of 1,309 (4.6%) patients hospitalized with COVID-19 had an in-hospital cardiac arrest. Fifty-four among these had documented cardiopulmonary resuscitation (CPR), and none survived to discharge. The second report stated that 701 out of 5,019 (14.0%) critically ill COVID-19 patients had in-hospital cardiac arrest. Overall, 400 among these received CPR and 48 patients (12%) survived to discharge. Twenty of these patients had moderate-to-severe neurologic dysfunction. The first report is published in *JAMA Internal Medicine* and the second one was published in *BMJ*… (*Medscape*)

Mother-Infant COVID-19 Transmission not Very Common

A study from New York has revealed that there was little evidence for vertical transmission of COVID-19 among a cohort of newborns whose mothers had confirmed or suspected COVID infection.

Among 101 newborns, SARS-CoV-2 viral RNA was not detected in 95.7% of nasopharyngeal polymerase chain reaction tests for an overall transmission incidence of 2% in two newborns, reported investigators in *JAMA Pediatrics*. The two infants who had evidence of vertical transmission had indeterminate tests, thus indicating that they were infected at very low viral copy numbers, and none had symptoms of COVID-19. Around three-quarters of mothers roomed-in with the newborns, six infants had to be separated from severely ill mothers who were in the ICU, and 19 infants were admitted to the neonatal ICU without contact with parents… (*Medpage Today*)

Global TB Progress at Risk, Says WHO

Several countries were making steady progress in fighting tuberculosis (TB) before the COVID-19 pandemic began, with a 9% reduction in incidence from 2015 to 2019 and a 14% decline in deaths over the same period.

However, a new WHO report has revealed that access to TB services remains a challenge, and the global targets for prevention and treatment will likely be missed in the absence of urgent action and investments.

The COVID-19 pandemic has disrupted services, which has caused setbacks. Several countries have

reallocated human, financial and other resources from TB to COVID-19 response. Data collection and reporting systems have suffered. Data obtained from more than 200 countries has shown significant decline in TB case notifications, with 25-30% fall reported in 3 high burden countries, including India, Indonesia, the Philippines, between January and June 2020 compared to the same period in the year 2019. This reduction in case notifications can cause an increase in additional TB deaths… (*WHO*)

FDA Grants Approval to First Treatment for Ebola Virus

The US Food and Drug Administration (FDA) has granted approval to atoltivimab, maftivimab and odesivimab-ebgn, a combination of three monoclonal antibodies, as the first treatment approved by the FDA for *Zaire ebolavirus* (Ebola virus) infection in adult and pediatric patients.

The drug targets the glycoprotein on the surface of Ebola virus. The three antibodies in the drug can bind to the glycoprotein simultaneously and inhibit attachment and entry of the virus. The drug was assessed in 382 adult and pediatric patients with confirmed Ebola virus infection in the PALM trial and as part of an expanded access program conducted in the Democratic Republic of the Congo (DRC) during an Ebola virus outbreak in 2018-2019.

In the PALM trial, 154 patients received the drug (50 mg of each monoclonal antibody) intravenously as a single infusion, while 168 patients were given an investigational control. The primary efficacy endpoint was 28-day mortality. Of the 154 patients who received the antibody combination, 33.8% died after 28 days, compared to 51% of the 153 patients who received a control. In the expanded access program, an additional 228 patients received the study drug… (*FDA*)

People with Blood Type O may have Lower Risk of COVID-19 Infection and Severe Illness

People with blood type O may be less prone to COVID-19 infection and may also have decreased odds of getting severely ill, suggest two studies published recently; however, experts state that more research is needed.

The research provides additional evidence that blood type may have a role to play in a person's susceptibility to infection and their odds of developing severe illness.

In a Danish study, among 7,422 individuals who tested positive for COVID-19, only 38.4% were blood type O. Among a group of 2.2 million people who were not tested, blood type O made up 41.7% of the population. On the contrary, 44.4% of Group A individuals tested positive, while in the wider Danish population, blood type A makes up 42.4% of the population.

In the second study, investigators in Canada noted that among 95 critically ill COVID-19 patients, a higher proportion with blood type A or AB (84%) required mechanical ventilation compared to patients with blood type O or B (61%). Both the studies are published in the journal *Blood Advances*… (*CNN*)

Russia Approves Second Coronavirus Vaccine Before Phase 3 Trials

Russian health authorities have granted approval to a COVID-19 vaccine developed by a former biological weapons research laboratory for public use.

A vaccine developed by the Vector State Virology and Biotechnology Centre in Siberia has been registered, said President Putin, adding that there is a need to increase production of the first and the second vaccine. The vaccine has been registered before completing phase 3 trials, 2 months after the approval of Sputnik V was announced as the world's first COVID-19 vaccine. Deputy PM Tatyana Golikova said that it is safe and the first 60,000 doses will soon be produced. Like Sputnik V, Vector's EpiVacCorona vaccine was tested on a limited number of individuals before being given the provisional registration. Vector general director Rinat Maksyutov stated that there were 100 volunteers in phase 1 and 2 trials and all were feeling fine. No data has been published in a peer-reviewed journal yet… (*ET Healthworld*)

Pediatric IBD Patients at Relatively Low Risk of Severe COVID-19

An analysis of two international databases has suggested that pediatric inflammatory bowel disease (IBD) patients appear to have a relatively low risk of severe COVID-19, even when receiving biologic and other immune-suppressive therapies.

Investigators noted that among 209 IBD patients aged 18 and younger from across 23 countries, the rate of hospitalization was 7%, compared with the 33-66% rates reported by the same group, as well as others, for adult IBD patients with COVID-19. The following factors were found to be associated with hospitalization: Comorbid conditions other than IBD: 50% hospitalized vs. 12% of those without comorbidities ($p < 0.01$); Moderate or severe IBD activity: 64% vs. 15% ($p < 0.01$ overall);

Gastrointestinal symptoms: 71% vs. 19% ($p < 0.01$); Sulfasalazine/mesalamine use: 57% vs. 21% ($p = 0.01$), which continued to be a risk factor after adjusting for disease activity (aOR 4.2, 95% CI 1.3-14.1); and Steroid use: 29% vs. 8% ($p = 0.03$). The findings were published online in *Clinical Gastroenterology and Hepatology*… (*Medpage Today*)

Lack of Handwashing with Soap Puts Millions at Risk for COVID-19 and Other Infections

Handwashing with soap is crucial to fight against infectious diseases, including COVID-19, but millions of people across the world do not have access to a handwashing facility, said UNICEF.

Latest estimates suggest that only 3 out of 5 people across the globe have basic handwashing facilities. Nearly 40% of the world's population, i.e., around 3 billion people, do not have access to a handwashing facility with water and soap at home. Furthermore, 43% of schools do not have a handwashing facility with water and soap, which is estimated to impact around 818 million school-age children.

About three quarters of the people in the least developed nations do not have basic handwashing facilities at home. Additionally, in these least developed countries, 7 out of 10 schools have no place for children to wash their hands with water and soap… (*UNICEF*)

Bariatric Surgery Improves Life Expectancy, Suggest Long-term Data

Bariatric surgery was associated with a reduction in the long-term risk of dying, and longer life expectancy, reported researchers in Sweden.

An additional analysis of the ongoing Swedish Obese Subjects (SOS) study suggested that individuals that underwent bariatric surgery had a 23% lower risk of dying over a median 24-year follow-up compared to those who received usual obesity care (hazard ratio [HR] 0.77, 95% CI 0.68-0.87, $p < 0.001$). The lower mortality risk was primarily driven by a reduction in death due to CVD, the most common being myocardial infarction, heart failure and sudden death, reported the researchers in the *New England Journal of Medicine*. Bariatric surgery was tied to a 30% reduced risk of CVD-related death versus usual obesity care (HR 0.70, 95% CI 0.57-0.85), and a decline in cancer-related mortality in comparison with receiving usual obesity care (HR 0.77, 95% CI 0.61-0.96)… (*Medpage Today*)

New Electronic Survey Manual to Support Countries Fight Micronutrient Deficiencies

A new *Micronutrient survey manual (2020)* and toolkit has been developed by WHO, CDC, UNICEF and Nutrition International to meet the demand of countries that intend to evaluate the micronutrient status of their populations.

This new manual and toolkit is user-friendly and allows program managers, government officials and researchers to access best practices and resources for conducting micronutrient surveys *via* an interactive website. The manual also includes guidance on how to determine the impact of interventions to improve micronutrient status.

The manual highlights the use of indicators recommended by WHO and other internationally recognized agencies for evaluation of vitamin and mineral status, for classification of deficiencies at the individual and population levels, for defining public health problems and for monitoring progress toward the prevention and elimination of micronutrient deficiencies… (*WHO*)

Young and Healthy may have to Wait Until 2022 for Vaccine, Says WHO Scientist

According to experts, the young and healthy may have to wait for immunization. The World Health Organization's chief scientist has suggested that the delay could even last over a year for some.

As per Soumya Swaminathan, a lot of guidance will come out and an average healthy, young person might have to wait until 2022 to get a vaccine. Governments and international organizations will work to ensure that people at the greatest risk get priority and healthcare workers and others on the frontlines may receive the vaccine first, followed by the elderly or sick. The healthy, young people may end up at the back of the line.

Robin Nandy, the Chief of Immunization at UNICEF, stated that vaccines will be available in the initial years in very small quantities to vaccinate the 7 billion people across the globe… (*NDTV – The Washington Post*)

PVP-I Mouthwash against COVID-19: The Potential Role

Antiseptic mouthwashes are known to have a key role in restricting the number of microorganisms in the oral cavity. Mouthwashes are commonly used to rinse the mouth, prior to oral surgery as well. Antiseptic mouthwashes can diminish the number of microorganisms in the oral cavity and the colony-forming units in dental aerosols.[1,2]

The American Dental Association (ADA) recommends the use of pre-procedural mouthwashes prior to oral procedures, which includes the use of povidone mouthrinse.[3] Some recent publications have also shown that rinsing the oral cavity may have a potential role in limiting the risk of transmission of SARS-CoV-2, the virus that causes COVID-19.[4]

PVP-I is a potent antimicrobial solution that has a greater virucidal activity compared to other commonly used antiseptic agents, including chlorhexidine and benzalkonium chloride.[4] Free iodine dissociates from polyvinylpyrrolidone. It then penetrates the microbes, disrupts proteins and oxidizes nucleic acid structures, thus resulting in microbial death.[4,5]

PVP-I mouthwash use for at least 15 seconds has previously been reported to inactivate SARS-CoV, MERS-CoV (Middle East respiratory syndrome coronavirus), influenza virus A and rotavirus.[6] A recent study has reported that PVP-I oral solution can completely inactivate SARS-CoV-2 as well, within 15 seconds of contact.[7]

The findings thus support the use of pre-procedural PVP-I mouthwash. It could prove to be beneficial both for patients and healthcare providers during the ongoing pandemic.

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Women Seem to Fare Worse in Treatment for Spine Disease

Despite there being only few differences in patient and disease characteristics between men and women with nonradiographic axial spondyloarthritis (axSpA), women were found to have significantly lower rates of response to tumor necrosis factor (TNF) inhibitors, suggested Swiss researchers.

While women were slightly older at the time of enrollment in a national cohort, largely because of diagnostic delay, no baseline differences were evident between the sexes in disease activity, physical function, spinal mobility or quality of life. A 40% improvement on the criteria of the Assessment of SpondyloArthritis International Society (ASAS40) after a year of TNF inhibitor therapy was attained by only 17% of the women compared to 38% of men (OR 0.34, 95% CI 0.12-0.93, p = 0.02), reported researchers online in *Arthritis Research & Therapy*… (*Medpage Today*)

India Gained a Decade of Life Expectancy Since 1990, Says Study

India has gained over a decade of life expectancy since 1990; however, there are wide inequalities between states, suggests a new study which looked into more than 286 causes of death and 369 diseases and injuries in over 200 countries and territories worldwide.

The study suggests that life expectancy in India has increased from 59.6 years in 1990 to 70.8 years in 2019, ranging from 77.3 years in Kerala to 66.9 years in Uttar Pradesh. Researchers; however, stated that the rise in healthy life expectancy in the country has not been as dramatic as the growth of life expectancy, as the people are living more years with illness and disability. The study is published in the *Lancet*… (*HT – PTI*)

COVID-19 Heart Autopsies Point More to Clot Damage than Myocarditis

An evaluation of the heart after death from COVID-19 has revealed that cardiac damage was common, but more from clotting in comparison with inflammation, reported researchers.

Autopsies on 40 people who died of COVID-19 demonstrated that 14 of them had cardiac injury as indicated by myocardial necrosis: an acute myocardial

infarction of at least 1 cm^2 in three (7.5%) and smaller focal myocyte necrosis in 11 (27.5%). Microthrombi were frequent, while none of those patients had myocarditis, except sarcoid involvement in one case, reported investigators at the virtual TCT Connect meeting. Epicardial coronary artery thrombosis was evident in two of the myocardial necrosis patients (14.2%) and microthrombi were noted in nine patients (64.3%)… (*Medpage Today*)

Drug Overdose Deaths Increased During Early Days of COVID-19 Pandemic: CDC

According to a report from the CDC, deaths from drug overdoses showed a sharp rise during the first part of this year compared to the previous year. Experts suggest that isolation caused by the COVID-19 pandemic is the cause. The CDC reported that 19,416 people died from drug overdoses from January through March this year, showing an increase of 3,000 over the first 3 months of 2019. The agency added that if the trend continues, the US will record over 75,500 drug overdose deaths this year, compared to 70,980 deaths recorded last year. While the CDC report does not specify that the pandemic is causing the escalation in deaths, health experts do suggest this as the cause… (*Medscape*)

Early Data for ALS Drug Show Promise

Starting treatment earlier with an investigational, proprietary combination of sodium phenylbutyrate and taurursodiol was associated with longer survival in patients with amyotrophic lateral sclerosis (ALS) in an open-label extension of the phase II CENTAUR trial.

ALS patients were randomized 2:1 to sodium phenylbutyrate 3 g and taurursodiol 1 g or to placebo. When the trial ended, participants in both groups could opt for taking the sodium phenylbutyrate-taurursodiol combination for up to 30 months in an open-label extension study. According to the survival analysis of extension study patients, those randomized to sodium phenylbutyrate-taurursodiol at baseline had 6.5-month longer median survival compared to those who started on placebo, reported researchers in *Muscle and Nerve*… (*Medpage Today*)

COVID-19 Vaccine: UNICEF to Stock Over Half a Billion Syringes by Year End

As countries and pharmaceutical companies across the world gear up to distribute COVID-19 vaccines following trials, UNICEF has initiated the groundwork for rapid, safe and efficient delivery of the vaccines by buying and pre-positioning syringes and other equipment.

UNICEF said that as soon as vaccines are licensed for use, the world is going to require as many syringes as doses of vaccine. This year, UNICEF will stock around 520 million syringes in its warehouses, as a part of a larger plan that aims for having a billion syringes ready for use through 2021, to ensure initial supply as well as to ensure that syringes arrive before vaccines are distributed… (*UN*)

CDC Issues Strong Recommendation for Masks on Airplanes, Trains

The US CDC has issued a "strong recommendation" mandating all passengers and employees on airplanes, trains, subways, buses, taxis and ride-share vehicles to wear masks to prevent the spread of COVID-19.

The interim guidance also includes facial coverings at transportation hubs, such as airports and train stations. According to the CDC, wide and routine use of masks on the transportation systems will protect Americans and provide confidence that people can travel more safely even during the pandemic.

The CDC has asked transport operators to ensure that all passengers and employees wear masks for the travel duration and to provide information to those purchasing tickets or otherwise booking transportation on the need to wear masks, and to make masks available where possible… (*Reuters*)

PCOS Linked with Cardiovascular Disease Risk After Menopause

Women with polycystic ovarian syndrome (PCOS) prior to menopause appear to have a higher risk of stroke, heart attack and other cardiovascular events after menopause, suggest findings presented at the virtual American Society for Reproductive Medicine (ASRM) 2020 Scientific Congress.

Investigators completed a secondary analysis of data from the Study of Women's Health Across the Nation (SWAN), a prospective cohort study. Participants were aged 42-52 years at baseline, had a uterus and at least one ovary, and menstruated within the previous 3 months. PCOS was confirmed if the women had both biochemical hyperandrogenism and a history of irregular menses.

Among 1,340 women included in the analysis, 174 (13%) had PCOS and 1,166 did not. After controlling for age at enrollment, race, body mass index (BMI) and smoking status, women with PCOS were found to have 1.6 times higher likelihood of a cardiovascular event after menopause compared with women without

PCOS (OR, 1.6; p = 0.029). Women with PCOS also had significantly higher atherosclerotic CVD risk scores (p = 0.024), though their Framingham 10-year risk score was not significantly different from those without PCOS… (*Medscape*)

COVID-19 Reinfection Possible Once Antibodies Start Depleting, Says ICMR

The Indian Council of Medical Research (ICMR) Director-General (DG), Dr Balram Bhargava, has stated that COVID-19 reinfection is possible if antibodies reduce in the body of a COVID-19 recovered individual in 5 months after the recovery.

The ICMR DG called on people to continue wearing masks and follow COVID appropriate behavior in order to contain the spread of the virus in the country. Dr Bhargava said that antibodies develop in the body following any infection, and in case of coronavirus, the antibodies have been seen to last for at least 5 months. He added that if antibodies decline in the body of a person within 5 months, there is a possibility of reinfection. Therefore, it was crucial to take precautions like wearing a mask, even after someone contracts the disease once… (*NDTV – ANI*)

Green Tea, Coffee Tied to Reduced Mortality Risk in T2DM

Drinking green tea and coffee was shown to be associated with reduced all-cause mortality in Japanese patients with type 2 diabetes, particularly those who drank both, in a study published online in *BMJ Open Diabetes Research & Care*.

A cohort study followed around 5,000 patients for nearly 5 years and noted a dose-response relationship for both beverages. Drinking one cup of green tea daily was tied to a 15% lower mortality risk compared to those who drank no green tea. Consuming 2-3 cups daily was associated with a 27% reduction, while drinking 4 or more cups was linked with a 40% reduction in risk (p = 0.001 for trend). Among those who drank coffee, 1 cup daily was associated with a 12% lower mortality risk, and two or more cups were tied to a 41% reduction compared with those who drank no coffee (p = 0.001 for trend)… (*Medpage Today*)

Apathy a 'Prodrome' of Dementia

A lack of interest in usual activities in older adults could be an early sign of dementia, suggests new research.

A large, prospective study has revealed that individuals with severe apathy at baseline had double the risk of developing dementia over a 9-year period compared to their counterparts who were not apathetic. Investigators assessed 2018 participants (52.3% women; 64.1% White and 35.8% Black; mean age, 74 years) in the Health, Aging and Body Composition (Health ABC) study. None of the participants had dementia at baseline. Of the 255 participants meeting the criteria for clinically depressed mood, 49.5% were in the severe-apathy group, 33.5% were in the moderate-apathy group and 17% were in the low-apathy group. Overall, 381 participants (18.9%) developed probable dementia during the follow-up period. Around 25% of the severe-apathy group developed dementia compared to 19% of the moderate-apathy group and 14% of the low-apathy group. The results were published online in *Neurology*… (*Medscape*)

15% of Deaths Across Mediterranean Attributed to Environmental Factors: UN Report

Nearly 15% of deaths in the Mediterranean could be attributed to preventable environmental factors, revealed a new UN Environment Programme (UNEP) report released. In the year 2016, over 2,28,000 people died prematurely from exposure to air pollution, revealed UNEP's State of the Environment and Development in the Mediterranean (SoED). The report cautioned that increasing inequality, loss of biodiversity, climate change and continuous pressure on natural resources, could result in irreversible damage to the environment in the Mediterranean basin.

Every day the Mediterranean is polluted by approximately 730 tonnes of plastic waste and the overall region is warming around 20% faster than the global average… (*UN*)

Number of South Koreans Dying Following Flu Shot Increases

At least 13 South Koreans have died after they received flu shots in recent days, stated official and local media reports, prompting worries about vaccine safety. Authorities have; however, ruled out a link.

Health authorities have stated that they had no plans of suspending a program to inoculate around 19 million people for free as a preliminary investigation into six deaths reported no direct link to the vaccines. Officials stated that no toxic substances were found in the vaccines, and at least 5 of the 6 people investigated suffered from underlying conditions. The deaths have been reported just a week after the free flu shot program for teenagers and senior citizens was resumed. It had been suspended for 3 weeks after around 5 million

doses, which need to be refrigerated, had been exposed to room temperature while transportation to a medical facility… (*Reuters*)

Daily COVID-19 Cases Below 60K for 3 Consecutive Days in India

New Delhi: India recorded less than 60,000 new COVID-19 cases for the third consecutive day (not including Monday's tally). The daily death toll continued to be over 700 for the second day in a row.

Last week, India recorded a daily average of over 61,000 COVID-19 cases, while in the week preceding that, the figure was more than 70,000 cases. This week, daily new cases have remained below 60,000. On 21st October, 56,096 new cases were reported, which was slightly higher than the 54,486 cases recorded on the previous day. The overall tally in the country has crossed the 77 lakh mark to 77,03,856, according to data obtained by TOI from state governments… (*ET Healthworld – TNN*)

IIT-Kharagpur's "COVIRAP" COVID-19 Test Receives ICMR Certification

New Delhi: The Indian Institute of Technology (IIT)-Kharagpur has developed a low-cost portable COVID-19 testing device that can deliver results within an hour. The test has been certified by the Indian Council of Medical Research (ICMR).

IIT-Kharagpur officials stated that COVIRAP is a cuboid-shaped portable testing device, capable of delivering results in an hour. This makes it an effective tool to enhance coronavirus screening in remote and rural areas. This device would make high-quality and accurate COVID testing affordable for all and the testing would cost around ₹ 500, which can further be reduced through government intervention, stated Union Education Minister Ramesh Pokhriyal "Nishank"… (*NDTV – PTI*)

Could Vertebral Fractures Predict Outcome for Hospitalized COVID-19 Patients?

Among COVID-19 patients, vertebral fractures (VFs) may predict in-hospital mortality, suggests an Italian study.

Charts for 114 hospitalized patients with COVID-19 revealed that nearly 36% had thoracic vertebral fractures detected on lateral chest X-rays performed in the emergency department. Of those with vertebral fractures, nearly half required noninvasive mechanical ventilation in the hospital compared to 27% of the COVID-19 patients without vertebral fractures ($p = 0.02$), reported the study published online in the *Journal of Clinical Endocrinology & Metabolism*. Although not statistically significant, patients with vertebral fractures had a numerically higher mortality rate from COVID-19 compared to those who did not have vertebral fractures (22% vs. 9.6%, $p = 0.07$). Patients with severe vertebral fractures had a significantly higher rate of mortality (60%) compared to those with moderate or mild fractures (7% and 24%, respectively, $p = 0.04$)… (*Medpage Today*)

FDA Approves First COVID-19 Treatment

The US Food and Drug Administration (FDA) has granted approval to the antiviral drug remdesivir to be used in adult and pediatric patients, aged 12 years and above, and weighing at least 40 kg (around 88 pounds) for the treatment of COVID-19 requiring hospitalization.

Remdesivir must only be given in a hospital or in a healthcare setting which can provide acute care comparable to inpatient hospital care. With this, remdesivir has become the first treatment for COVID-19 to receive FDA approval.

However, this approval does not include the entire population that had been authorized to use this drug under an Emergency Use Authorization (EUA) which was issued on May 1, 2020. The approval came after FDA's analysis of data from three randomized, controlled clinical trials including patients hospitalized with mild-to-severe COVID-19… (*FDA*)

WHO and Wikimedia Foundation Expand Access to Reliable Information About COVID-19

The WHO has collaborated with the Wikimedia Foundation to expand public access to the latest and most reliable information about COVID-19.

The organizations have joined hands to make trusted, public health information available under the *Creative Commons Attribution-ShareAlike* license as resurgence of COVID-19 is worrying several countries and social stability at this crucial time depends on the shared understanding of the facts. Through this collaboration, people across the globe will be able to access and share WHO infographics, videos and other public health assets on Wikimedia Commons, a digital library of free images and other multimedia. The WHO content will also be translated across different national and regional languages through Wikipedia's network of global volunteers… (*WHO*)

Sewage can Reveal COVID-19 Outbreaks, Suggests UK Project

Traces of COVID-19 can be detected in sewage, thus giving the health officials an early warning of local outbreaks of the virus, stated the British government.

A project which was initiated in June has proved that fragments of genetic material from the virus can be detected in waste water, and thus suggest if a local community or institution is experiencing a surge in cases. This would help health officials identify large outbreaks, particularly where there are carriers not displaying any symptoms and they would be able to encourage people to get tested or take appropriate precautions. The sewage-testing project has been extended to 90 wastewater sites and presently covers 22% of England… (*Reuters*)

Cancer with COVID-19 Proves Fatal

According to new research presented at the virtual CHEST conference, the annual meeting of the American College of Chest Physicians, patients with cancer and COVID-19 appear to have a higher risk of severe disease and mortality.

Among 89 cancer patients admitted to the intensive care unit (ICU) due to COVID-19, 32 died, for a mortality rate of 36%. Mortality rates were found to be higher among patients with hematologic cancers. Of 51 patients with solid tumors, most commonly non-small cell lung cancer and breast cancer, 14 died, for a mortality rate of 27%. Among 38 patients with hematologic cancers, most commonly leukemia and lymphoma, 18 died, for a mortality rate of 47%. Of 59 patients requiring mechanical ventilation, 32 died, for a 54% mortality rate. Neutropenic patients had a very high mortality rate – 6 out of 9 died… (*Medpage Today*)

Steroids Boost Survival of Preterm Babies in Low-resource Settings: Study

A new clinical trial, published in the *New England Journal of Medicine*, has revealed that dexamethasone can potentially boost survival of premature babies when given to pregnant women at risk of preterm birth in low-resource settings.

The WHO ACTION-I trial thus settles the controversy over the efficacy of antenatal steroids for improving preterm newborn survival in low-income countries. For every 25 pregnant women given dexamethasone, one premature baby's life was saved, thus showing a significant impact. When given to mothers at risk of preterm birth, dexamethasone crosses the placenta and hastens lung development, thus reducing the likelihood of preterm babies to have respiratory problems at birth… (*WHO*)

Bharat Biotech's Covaxin Gets DCGI Approval for Phase 3 Clinical Trial

New Delhi: Bharat Biotech has received approval from the Drugs Controller General of India (DCGI) to conduct phase 3 clinical trials of the indigenous COVID-19 vaccine with certain conditions, stated officials.

A subject expert committee on COVID-19 at the Central Drugs Standard Control Organisation (CDSCO) had recommended giving permission to the company for phase 3 trial of its vaccine named Covaxin, after evaluating the safety and immunogenicity data of the phase 1 and 2 trials. The phase 3 trial will involve nearly 28,500 subjects, aged 18 and above, and will be carried out at 21 sites across 10 states, including Delhi, Mumbai, Patna and Lucknow… (*ET Healthworld – PTI*)

Higher Donor BMI Linked with Improved Lung Transplant Survival

Lung transplant patients who received a lung from obese donors were shown to have a 15-20% reduction in mortality at 1 year in one of the first studies to assess the impact of donor BMI and post-transplant survival.

The retrospective trial included data on patients and donors registered with the United Network for Organ Sharing Standard Transplant and Analysis database. The findings indicate that donor obesity may confer a protective benefit for transplanted lungs.

Investigators noted a survival benefit at 1 year among patients who received a lung transplant from donors in obesity class 1 (HR 0.867, 95% CI 0.772-0.975, $p < 0.01$) and obesity classes II/III (HR 0.804, 95% CI 0.688-0.941, $p < 0.01$), compared to the lungs from normal-weight donors. The trial results were presented at the virtual CHEST conference, the annual meeting of the American College of Chest Physicians… (*Medpage Today*)

■■■■

Indian Journal of Clinical Practice, Vol. 31, No. 6, November 2020

Spiritual Prescription: The Role of Prayer in Healing

KK AGGARWAL

Religious beliefs may have a powerful influence on the health of our patients, and we need to know about them. A large and growing number of studies have shown a direct relationship between religious involvement and positive health outcomes, including mortality, physical illnesses, mental illness, health-related quality of life and coping with illness.

Studies also suggest that addressing the spiritual needs of patients may facilitate recovery from illness. A large number of the nearly 350 studies of physical health and 850 studies of mental health that made use of religious and spiritual variables noted that religious involvement and spirituality have a link with better health outcomes.

Although the relationship between religious involvement and spirituality with health outcomes seems valid, it is difficult to establish causality. The benefits of religious and spiritual involvement are likely conveyed through complex psychosocial, behavioral and biological processes that are incompletely understood. All physicians should take a spiritual history of their patients, which could help discern their spiritual needs during treatment.

According to Dr Harold Keonig of Duke University Medical Center, in majority of cases, the doctor should not attempt to address complex spiritual needs of patients. When the patient is reluctant to talk with clergy and prefers to discuss spiritual matters with a trusted physician, taking a little extra time to listen and be supportive is usually all that is required.

Providing support for religious beliefs and practices that do not conflict with medical care may be appropriate, but when beliefs conflict with medical care, it is important not to criticize the belief, but rather to listen, gather information, enter into the patient's world view and maintain open lines of communication, perhaps enlisting the help of the patient's clergy.

Recently a study published in the journal *Mayo Clinic Proceedings* confirmed the importance of religion and spirituality for many patients undergoing medical treatment. The single-center, randomized, double-blind trial was conducted at the Mayo Clinic in Rochester, Minn. from July 4, 1997 to October 21, 1999 and involved 799 male and female coronary care patients aged 18 years or older. Earlier too, a number of published studies have already assessed the effects of spiritual factors on healthcare outcomes: 75% report a positive effect; 17% report no effect and 7% report a negative effect.

In the study, the patients were randomized into the intercessory prayer group and the control group. Intercessory prayer was administered at least once a week for 26 weeks by five intercessors per patient. After 26 weeks, a medical setback (such as death, cardiac arrest, re-hospitalization, coronary revascularization or an emergency department visit for cardiovascular disease) occurred in 25.6% of the prayer group and 29.3% of the control group. Among high-risk patients, such a setback occurred in 31% of the prayer group and 33% of the control group. Among low-risk patients, the difference between the groups was 17% for the prayer group and 24% for the control group.

Though the results were in favor of prayer yet the study had some limitations, which might have influenced the low positive results. It did not measure the 'power of God', nor was the prayer offered for patients by loved ones, relatives and friends. The researchers said most patients have a spiritual life and regard their spiritual health and physical health as equally important. People may have greater spiritual needs during illness and are looking to have those needs met.

Prayer works on the principle that in the relaxed state, the mind becomes suggestive. The inner healing starts when the intent reaches the inner consciousness or a state of stillness. Prayer is different from meditation. In prayer, one is talking to the GOD and in meditation, GOD is talking to you. Meditation is much stronger than prayer as it bypasses the mind and deals with the spirit or the consciousness. In prayer, the mind is in an active working phase. Meditation is the phase of restful alertness.

It all works at the level of autonomic nervous system. The parasympathetic state of mind is the healing state. Both prayer and the meditation take one from sympathetic to the parasympathetic state.

Group Editor-in-Chief, IJCP Group

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The Old Man and the Rose

During the mid-1950s when I was a kid, my dad worked in a furniture shop at Spadina and Queen in Downtown Toronto. Sometimes, I got to go to the shop with him and I made a bit of pocket change running to the restaurant and getting coffee for everybody. I would pass the rest of the day away just hanging around the store, not doing much of anything and not paying much attention to all the hustle and bustle of people and things that were all around me.

One day, as my dad and I were driving to the shop, I looked out the passenger window of the car and I saw an old man standing at the street corner. For some reason, our eyes met and held for about 20 seconds as we went by the corner. There was nothing fearful about this man but it was a significant encounter for me. Up to that point in my life, I had given no thought to anyone I saw on the street, in stores or anywhere else. My life was my family and my friends on the block and that was it. I had no interest in anyone beyond that circle.

But, I was intrigued by that old man. For the first time, I had an empathy and an interest in what that person was all about. What kind of life had he lived? Where had he been in his time? How had he come to this corner just at the moment I was going by?

Over the years, I had long forgotten about this old man, but he came to mind for me recently and I remembered those 20 seconds or so that I looked into the eyes of a stranger and wondered what he was all about.

It seems we are all so busy these days. There are so many details, so many calls to make and so many things to look after that we barely have time for sincere and genuine interest in others.

We are inundated by warnings from great thinkers in our society encouraging us to 'stop and smell the roses'. But I'm afraid it has taken me decades to really appreciate the wisdom of these words.

If I ever have the opportunity to speak to a young person today, I do my best to convey this message. But unfortunately, young people are too busy to heed good advice. Much like I was so many years ago. Youth indeed is so often wasted on the young.

If I had the chance, I would tell young people to stop what they are doing and look around. I would tell them to try as hard as they could to fully understand what is right in their line of sight, what is in the range of their hearing at the moment, what is in their immediate reach and grasp.

I would like so much to tell people, especially young people, that if you are thoughtless and indifferent to others on your road in life, then you are missing life itself. Do not be intrusive or tactless, for heaven's sake, but take a moment and ask someone, how did you come here or how did you get into this business?

No matter what that person tells you, their answer will make you richer. You can grow emotionally, you can excel as a person and you can be wealthy by every measure if you just appreciate the gifts that people and life all around you are ready to give right at this moment just by their simple presence.

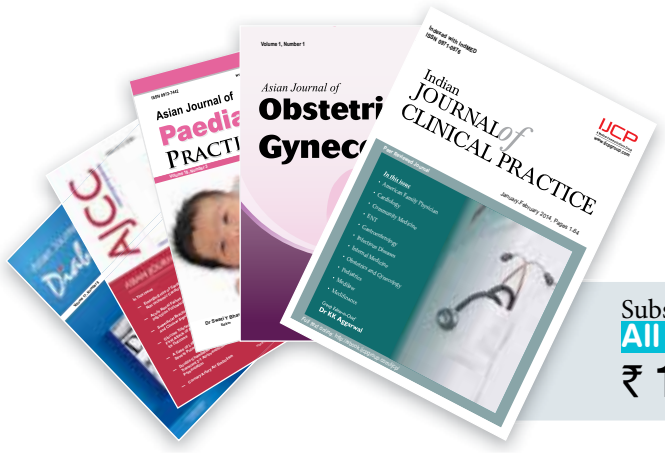
We should appreciate that great symphonies were written from only seven simple notes that God gave the entire universe. We should know that great works of art are measured by the emotions they evoke, not just how they look next to the plant stand.

We should never forget that heartache cannot be cured, but can be eased by someone willing to give genuine sympathy. The true greatness of joy can only be known when it is shared with others.

Recently, I attended a trade show at the convention centre in downtown Toronto. During the lunch break, I went to a book sale along the trendy Queen West area. I was thinking about returning to the show or carrying on my walk when I realized I was standing at the corner of Spadina and Queen. At that moment a car went by and I caught the eye of a young boy looking at me from the passenger window. We looked at each other for about 20 seconds before the car disappeared around the corner. I wondered if that boy was thinking about what sort of person I was.

And I realized that I was now an old man. Like the man I saw so many years ago. I wondered if 50 years had just simply flashed by or whether that boy and I had just simply changed places in the span of 20 seconds.

Before I returned to the trade show, I stopped at a florist. I bought a rose and put it in the lapel of my jacket. For some reason, I felt it was the most important thing I would do for the rest of the day.



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Lighter Side of Medicine

HUMOR

TRAFFIC COURT

A New York man was forced to take a day off from work to appear for a minor traffic summon. He grew increasingly restless as he waited hour after endless hour for his case to be heard. When his name was called late in the afternoon, he stood before the judge, only to hear that court would be adjourned for the next day and he would have to return the next day. "What for?" he snapped at the judge.

His honor, equally irked by a tedious day and sharp query roared, "Twenty dollars contempt of court. That's why!" Then, noticing the man checking his wallet, the judge relented. "That's all right. You don't have to pay now." The young man replied, "I'm just seeing if I have enough for two more words."

WHOEVER TELLS THE BIGGEST LIE

Two boys were arguing when the teacher entered the room. The teacher says, "Why are you arguing?"

One boy answers, "We found a 10 dollar bill and decided to give it to whoever tells the biggest lie."

"You should be ashamed of yourselves," said the teacher, "When I was your age, I didn't even know what a lie was."

The boys gave the 10 dollars to the teacher.

MY GRADES

A high school student came home one night rather depressed.

"What's the matter, Son?" asked his mother.

"Aw, gee," said the boy, "It's my grades. They're all wet."

"What do you mean 'all wet?'"

"You know," he replied, "…below C–level."

MASTERPIECE

One day a girl came home crying to her mom. The mom asked what was wrong.

The girl responded, "I'm not a creation, God made men first! I'm nothing!"

Then the mom said, "Oh baby that's not true, God may have made men first, but there's always a rough draft before the masterpiece."

SMART KID

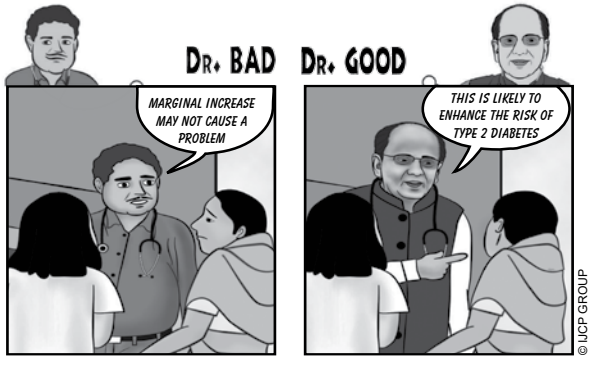
So little Johnnie comes home with his report card for 5th grade, and shows it to his mother. His mom reads the report card and gets more and more upset as she sees his grades. "Johnnie, you have 5 "F's" and a "D" in Math! Wait until your Father sees this!"

So Johnnie's dad comes home from his job at the lab, looks the report card over thoughtfully. Johnnie's Mom says, "Well, aren't you going to say SOMETHING to him??"

Johnnie's dad pulls him aside, and says, "Son, I think you are putting too much time and effort on your Math."

Dr. Good and Dr. Bad

SITUATION: A 41-year-old obese female was asked to get her lipid profile tested, the findings of which showed high levels of TC, TG and TC/HDL-C ratio.



LESSON: The researchers have shown that the risk of diabetes increases with high serum levels of TC, TG, TC/HDL-C and TG/HDL-C ratios. The risk also correlates with interactions between high TC and TG levels and TC/HDL-C and TG/HDL-C ratios and age and BMI.

Diabetes Res Clin Pract. 2017;135:150-7.

IJCP SUTRA: *"Use mobile phones when you are mobile and use stationary phone (landline) when you are not mobile, i.e., when you are at home or in office."*

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MedIND (http://medind.nic.in/)

University Grants Commission (20737/15554).

ISSN number 0971-0876

RNI number 50798/1990.

The Medical Council of India (UGC, ICI)

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The journal **ISSN number** is 0971-0876 and the **RNI number** is 50798/1990.

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- The statistical universe i.e., the population from which the sample for the study is selected.
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- These should be concise and include only the tables and figures necessary to enhance the understanding of the text.

Discussion

– This should consist of a review of the literature and relate the major findings of the article to other publications on the subject. The particular relevance of the results to healthcare in India should be stressed, e.g., practicality and cost.

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These should conform to the Vancouver style. References should be numbered in the order in which they appear in the texts and these numbers should be inserted above the lines on each occasion the author is cited (Sinha[12] confirmed other reports[13,14]...). References cited only in tables or in legends to figures should be numbered in the text of the particular table or illustration. Include among the references papers accepted but not yet published; designate the journal and add 'in press' (in parentheses). Information from manuscripts submitted but not yet accepted should be cited in the text as 'unpublished observations' (in parentheses). At the end of the article the full list of references should include the names of all authors if there are fewer than seven or if there are more, the first six followed by et al., the full title of the journal article or book chapters; the title of journals abbreviated according to the style of the Index Medicus and the first and final page numbers of the article or chapter. The authors should check that the references are accurate. If they are not this may result in the rejection of an otherwise adequate contribution.
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Paintal AS. Impulses in vagal afferent fibres from specific pulmonary deflation receptors. The response of those receptors to phenylguanide, potato S-hydroxytryptamine and their role in respiratory and cardiovascular reflexes. Q. J. Expt. Physiol. 1955;40:89-111.

Books

Stansfield AG. Lymph Node Biopsy Interpretation Churchill Livingstone, New York 1985.

Articles in Books

Strong MS. Recurrent respiratory papillomatosis. In: Scott Brown's Otolaryngology. Paediatric Otolaryngology Evans JNG (Ed.), Butterworths, London 1987;6:466-470.

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– Special features should be indicated by arrows or letters which contrast with the background.

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– Do not use clips/staples on photographs and artwork.

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Indian Journal of Clinical Practice
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New Delhi - 110 048. Tel: 40587513
E-mail: editorial@ijcp.com Website: www.ijcpgroup.com

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R.N.I. No. 50798/1990
Date of Publication 13th of Same Month
Date of Posting 13-14 Same Month

POSTAL REGISTRATION NO. DL (S)-01/3200/2018-2020
Posted in N.D. PSO New Delhi