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Wherever the art of medicine is loved, there is
also a love of humanity.
- Hippocrates

Sushruta Medical News

A Medical Newsletter of the

American Association of Physicians of Indian Origin



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Editorial

Facing the Fears

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Our ED Team



I am...

Mask, eye shield, cap, gown, gloves. Evaluate patient. Remove gear. Dispose of. Wash hands. Sanitize. Repeat. This has been my norm for the past 2 weeks for at least 20-30 patients a shift at the Emergency Department (ED) at Robert Wood Johnson University Hospital in New Brunswick, NJ.

I have been an Emergency Physician for over 10 years. I have been trained to face HIV, Ebola, Avian Flu, SARS, Swine Flu etc., but nothing compares to this. In all those situations, the risk of exposure was low as very few patients came to the ED with the symptoms. We were trained in personal protective equipment (PPE) and all appropriate clinical protocols and work went on as usual. This time nothing is the usual.

Two weeks ago when the positive cases first started coming to our ED, we were all working our usual 8-12 h shifts and seeing 5-10 patients a shift with chief complaints of cough/fever. Most patients were healthy, young, not tested positive for COVID and sent home.

Now almost every patient we evaluate has respiratory complaints and most of the ones we test, are COVID positive. Patients who are admitted with non-respiratory complaints also turn out to be COVID positive, leading us to believe

that lots of the patients who we are not testing and sending home are COVID positive and they need to practice strict self-quarantine – staying away from others, until no symptoms for 72 h at least.

According to estimates from the Centers for Disease Control and Prevention reported by the New York Times, between 160 million and 214 million people in the US could become infected with COVID-19 and as many as 200,000 to 1.7 million people could die. Estimates for hospitalizations range from 2.4 million to 21 million people.

Given that in the US we have only about 925,000 hospital beds and less than 100,000 ICU beds and patients with severe coronavirus often develop pneumonia and require 7-10 days of hospitalization, it's painfully obvious that our hospitals do not have the capacity.

At RWJUH, the hospital administration, particularly our Chairman, Dr. Eisenstein and our CEO Mr. Gantner are constantly working hard in making a variety of preparations for the influx of patients with coronavirus.

In the past 2 weeks we have created triage tents outside the ED entrances to evaluate patients who are “sick” vs “not-so-sick” with respiratory complaints. Patients who are young, healthy and breathing well (>95% oxygenation), are seen via telemed (video connection via a computer or phone – to protect both patients and healthcare providers) by an ER doc and discharged from the outside tent with self-quarantine instructions. Patients who are elderly or with abnormal vital signs are brought back into the ED and immediately placed in isolation so as to not contaminate the waiting room. Once in the main ED under full PPE precautions the patient is evaluated and treated.

Sick patients who are admitted for possible coronavirus are tested and treated as per RWJUH Infection Prevention protocols. At RWJUH there are special floors dedicated to caring for these patients and special teams of Doctors and Nurse Practitioners trained in wearing PPE responsible for their care.

To further reduce the chances of infections within the hospital, we do not use CPAP machines or nebulizers – which are devices that convert liquid into a breathable mist. Coronavirus particles are very light and can float through the air and linger on surfaces longer than other viruses.

Patients getting treated for strokes, heart attacks, and other non COVID complaints are placed on other dedicated floors within hospital to limit contamination with a separate team of doctors and medical staff to care for them. Daily updates and webex meetings with hospital administrators / staff help us all stay informed and through clarity on protocols we are daily changing practices to adhere to best practices for our patients and ourselves.

In the next 2 weeks, NJ hospitals like NYC will see a surge of patients. We are likely to have shortages of ICU beds, ventilators, masks, surgical gowns and other protective gear. We may see medical personnel wearing bandanas over the face, rigging CPAP machines to function as ventilators, use one ventilator for 2 patients, beds in hallways and longer lines outside our tents. Even with the most optimistic forecast, the numbers of infected people requiring hospital care will vastly exceed our hospital resources.

As an ER doc, I am scared, not for my life, but about how to care the sick under these conditions? I already feel the pressure of a shortage of N95 masks. Two weeks ago I was able to wear a new mask for each patient I was evaluating. Now I wear one single mask for my whole shift. It is not ideal, but it is all we have. While at work I try hard to not touch my face, keep distance from others and practice utmost sanitation at all times. At the end of a shift, I change out of my scrubs before I come home. Once home, I go straight to take a hot shower before interacting with family and place my scrubs for washing. I check my temperature everyday twice to insure I am not getting symptomatic and I do not want to put others at risk.

I am grateful for my job and I feel blessed to be caring for others at this difficult time, but I am nervous that I might get sick and put my loved ones at risk. I am also nervous of the upcoming weeks where I will have to make hard choices about allocating care away from people who are most likely to die to patients who have a greater chance of surviving. I went into this profession to save lives and took the Hippocratic Oath for it. Now, I am being told I will have to practice differently, **I will have to face my fears.**

Call for Contributors

Potential contributors are welcome to submit their works for the following categories. Please enclose a portrait photo with your article along with your qualifications, city and state and email ID.

- **A Piece of My Mind** (an opinion on current day medical and healthcare topics - 400 words)
- **Bench-to-Bedside** (300 words)
- **Bedside-to-Bench** (300 words)
- **Clinical Dilemma** (400 words)
- **Medical Education** (400 words)
- **Pictorial Case Report** (quarter page)
- **Pictorial CME** (quarter page)
- **Medical Quiz** (300 words)
- **YPS & MSRF Lounge** (500 words)
- **AAPI Obesity Awareness Campaigns** (300 words)
- **Veterans Health News** (300 words)

Email contributions to: smn@aapiusa.org

Bedside-to-Bench

Chloroquine in COVID-19: Old Wine in a New Bottle

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Discovered in 1934 by Hans Andersag, chloroquine (resochin) reached the World Health Organization's list of Essential Medicines. Chloroquine has been in clinical practice since 1947, first as a drug against malaria and then for the treatment of rheumatoid arthritis and lupus erythematosus. Its off-label uses include amebic liver abscess and certain dermatological conditions. It has a narrow therapeutic index and so, overdosing can have fatal outcome. Chloroquine interacts with drugs like ampicillin, antacids, cimetidine, cyclosporine and mefloquine. In persons with glucose-6-phosphate dehydrogenase (G6PD) deficiency, an X-linked recessive genetic disorder affecting men, chloroquine can cause acute hemolysis. Hydroxychloroquine, an analog of chloroquine, has longer half-life, more volume of distribution than chloroquine and does not cause acute hemolysis in patients with G6PD deficiency. Chloroquine has more than one mode of action, which appear to be beneficial in the treatment of viral diseases, including COVID-19, making this drug come into limelight recently. One of the oldest known actions of chloroquine is, its lysosomatotropic property, by which it acts as an anti-malarial drug. Chloroquine accumulates in endosomes and lysosomes of the parasite, where it raises the internal pH. Low or acid pH is essential for the function of these organelles, failing which the parasites cannot survive. Although the same lysosomatotropic property of chloroquine has been alluded to its anti-viral activity, there is not enough experimental evidence to prove that this accounts for the anti-coronavirus activity of chloroquine. Chloroquine also appears to act as a zinc ionophore, which allows extracellular zinc to enter the cell and inhibit viral RNA-dependent RNA polymerase. It has been shown that zinc ionophores inhibit the RNA polymerase activity of coronaviruses in vitro. This may give hope in the prevention of COVID-19 disease, especially if supplemented with zinc. However, the therapeutic effect of chloroquine in rheumatoid arthritis and lupus erythematosus is due to its anti-inflammatory and immunomodulatory properties. Chloroquine inhibits cytokine production and release, antigen processing and presentation, cytotoxic T lymphocytes, phospholipase A2 activity, nitric oxide formation in macrophages, matrix metalloproteinases activities, microRNA expression etc. *On the other hand, chloroquine increases Treg activity and upregulates IFN α and IL-2 levels.* As pointed out by Dr. Malireddy S. Reddy in his article in this issue, if lack of immunomodulation may account for the pathophysiology of COVID-19, then perhaps chloroquine or hydroxychloroquine may save the patients. Even then, it appears timing of administration during the course of the disease and the dose of the drug may likely determine the final outcome. It is too early to speculate on therapeutic efficacy of chloroquine in COVID-19. Let us cross our fingers and wait for the outcome of clinical trials initiated recently.



A Piece of My Mind

Is Dysbiosis a Culprit for the Etiology of COVID-19?

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What is dysbiosis? Before I define dysbiosis, let me discuss about the normal human intestinal microbiota and their microbiome. Human intestinal microbiota (the total number of prokaryotic microorganisms of GI tract – approx. 100 trillion), far exceeds the total number of human eukaryotic cells - 10 trillion, by tenfold. Some of the bioactive peptides, bacteriocins and nano particles produced by human microbiota are inhibitory to a wide variety of pathogenic bacteria, and both DNA and RNA virus, perhaps even including SARS - COV-2 of COVID-19.

The human microbiota function as a multifunctional organism whose component cell lineages (consisting of over 1,000 different species belonging to different genera) exhibit diverse metabolic functions, due to their pooled microbiome (the total gene pool of microbiota). This GI tract microbiome far exceeds the total human genome by 100-fold. We can be confident and conclude that such a complex metabolic functionality with production of diverse functional metabolic end products, through several signaling pathways by human microbiota and microbiome, far exceeds the capability and performance of the human genome. The development of human immune system is largely dependent upon the resident microbiota and their microbiome, through their reciprocal relationship with the gut associated lymphatic tissue, which has been established through evolution.

Any adverse, abnormal and persistent disturbance in the normal composition of the GI tract microbiota and thus their microbiome is called dysbiosis. The optimal physiological functioning of the microbiota can be disturbed through unscrupulous use of antibiotics, nutritional factors, environmental changes, and stress etc., through induction of dysbiosis. In my opinion, the COVID-19 disease causing virus is a new variant and it is zoonotic (animal to human and vice versa). It is an RNA virus; whose RNA gets transcribed to DNA (within the human cell) through reverse transcriptase enzyme and then integrates with the human cell DNA to replicate. Thus, this virus can mutate with the highest efficiency. Consequently, it is very hard to treat.

This COVID-19 viral infection, like any other infection, gets attacked primarily by our immune system through involvement and activation of effector T-cells, NK cells and the inflammation provoking interleukins. Here is the problem. The virus excited immune system to kill virus, although can inactivate the SARS -CoV-2, yet it does not know how and when to simmer down after completion of its task, as observed in the case of earlier SARS and MERS infections. Thus, our own activated immune system starts vigorously attacking our own lung tissue to induce severe damage (auto immune syndrome). In my opinion, in COVID-19 infection (at least in extremely susceptible individuals) the immune suppressing T-regulatory cells and immune suppressant interleukins might not have been activated sufficiently to simmer the excess uncontrollable inflammation elicited by the effector T-cells, NK cells and inflammation provoking interleukins, due to improper immunomodulation. However, ironically the T-regulatory cells and immune suppressing interleukins are produced or activated primarily due to the aid of proper well-balanced microbiota of the GI tract, through brilliantly orchestrated immunomodulation.

The COVID-19 disease progression may have different pathophysiology in the geriatric population, since their immune system, specially T-cells and NK cells are naturally weak due to immunosenescence. Thus, in my opinion, proper maintenance of healthy gut microbiota and the microbiome, to curtail dysbiosis, is an essential requisite either to prevent or cure the COVID-19 infection, irrespective of age of the human subject.



**Second Place In AAPI YPS & MSRF Winter Medical Conference
February 16, 2020, Las Vegas, NV**

A Rare Case of Cryptococcosis caused by *Cryptococcus gattii*

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Introduction: Cryptococcal *gattii* cryptococcosis (Cgc) is a rare infection caused by a fungus living in soil and most commonly associated with trees, Cryptococcal *gattii* (CG). Although commonly reported in immunocompromised patients, CG is often also reported in healthy patients in certain parts of the world. Here we present a case of CG bacteremia in an immunocompromised host from New Jersey.

Clinical Case: A 44-year old female with AIDS and medication noncompliance (CD4 count of 19 and viral load of 18,000) two weeks prior to admission (PTA), was sent to the ED for two days of fever (Tmax of 101.8° F), weakness, and headaches. She described headaches as moving, 5/10 in severity, not associated with photophobia, blurred vision, nausea, vomiting, rash or neck stiffness. Associated symptoms include neck pain, and excessive sleepiness. She denied any tobacco smoking, recent travels, or sick contacts. She was born in the US and had lived in the East coast all her life. CT chest done a year PTA reported lung nodules when she was diagnosed with pneumonia and a follow up CT chest without contrast four months PTA done for suspected pneumonia did not show any lung nodules, rather patchy bilateral airspace opacities. Vitals on admission showed that patient was afebrile, but tachycardic with HR of 140 bpm, and BP of 90/68 mm Hg. Physical examination revealed the presence of oral thrush, and a 7 x 5 cm perianal lesion without discharge, but was negative for neck stiffness, focal deficits or meningeal signs. Labs were significant for WBC count of 3.1 K, bandemia of 30 and lactate of 0.8 mmol/L. CT head without contrast showed upper limit of normal size of ventricles. She was admitted for sepsis of unclear source with a normal CXR, a negative UA and Influenza test. She was treated with IVF for hypotension, antibiotics, and PO Fluconazole. CT C/A/P performed to determine the source of fevers reported mild bronchiectasis, resolution of prior air space opacities, and increased precarinal lymphadenopathy. Colorectal surgery deferred any interventions and lower extremity doppler was negative for DVT. One out of two blood cultures showed yeast, which eventually was identified as CG. She underwent LP with CSF opening pressure of 17 mmHg, protein of 137 mg/dL, glucose of 14 mg/dL, total nucleated cell count of 83%, CSF culture growing few CG, a negative BioFire panel, a positive CSF and blood Cryptococcal antigen test positive with 1:256 titre. She was started on liposomal amphotericin B and Flucytosine with plans to repeat LP in 2 weeks and monitoring daily labs. Her symptoms had resolved four days after admission.

Discussion: CG lung infection can present as pneumonia-like illness. It can then spread to the brain causing cryptococcal meningitis, which may be fatal if left untreated. Patients may develop lung, brain, or muscle cryptococcomas (large nodules or mass lesions). Skin manifestations may also include acneiform lesions, ulcers, or subcutaneous tumor-like masses. Cgc have been known for its geographic distribution with majority of the cases being reported in the US Pacific Northwest since 1999.

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<https://www.aapiusa.org/>



**Third Place in AAPI YPS & MSRF Winter Medical Conference
February 16, 2020, Las Vegas, NV**

The Hunt for a Perfect Diagnosis: A Rare Presentation of Ocular Neuromyotonia Arsheya Patel M.D.

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Background: Tolosa-Hunt syndrome is an oculomotor disorder characterized by painful ophthalmoplegia resulting from idiopathic inflammation of the cavernous sinus. The condition is rarely seen in the United States and therefore presents a challenging diagnostic case.

Case Presentation: A 28-year old man with no past medical history presented to the ED for evaluation of sudden onset diplopia, left-sided headache, and decreased sensation of the left orbit. Symptoms lasted approximately three hours, but had improved upon presentation. Initial ocular exam was relevant for difficulty with adduction of the left eye. Ophthalmology was consulted and he was diagnosed with a left cranial nerve (CN) VI neuromyotonia. Neurological exam was otherwise unremarkable. Initial evaluation included a CT of the brain and CTA of the brain and neck which were unremarkable. MRI of the brain and orbit revealed asymmetric enhancement of the left cavernous sinus and left anterior clinoid, without evidence of thrombosis. He underwent a diagnostic lumbar puncture which revealed a normal opening pressure without evidence of infection or malignancy. Inflammatory markers as well as serologies for varicella, HIV, Lyme, tuberculosis, and syphilis were negative. Autoimmune work up, including immunoglobulins, lysozyme, ANA screen, angiotensin converting enzyme (ACE), ANCA, SS-A, SS-B, anti-ribonucleoprotein (RNP), and anti-Smith, was negative. A myasthenia gravis serology panel was unremarkable. A CT of the chest was unremarkable. The patient's symptoms improved with a course of glucocorticoids. He was ultimately diagnosed with a left CN VI neuromyotonia secondary to Tolosa-Hunt Syndrome.

Conclusion: This case highlights the importance of maintaining a broad differential when it comes to assessing patients with neurologic and ocular symptoms. While Tolosa-Hunt syndrome is extremely uncommon, it does have a relapsing-remitting nature and making the diagnosis accurately can assist with long-term management of these patients.

What is this Sushruta Medical News?

The current Executive Committee of the AAPI under the dynamic leadership of Dr. Suresh Reddy initiated the project of *Sushruta Medical News* to usher an academic breeze into the AAPI. This was announced in the AAPI Governing Body meeting in the Long Island, NY on February 8, 2020. We were requested to prepare the groundwork for that, which resulted in this inaugural issue. It is envisioned that this Sushruta Medical News will eventually be nurtured to grow into a peer-reviewed *AAPI Medical Journal* during the leadership of Dr. Sudhakar Jonnalagadda. On behalf of AAPI, we invite all those who are interested in the development of the AAPI Medical Journal to join hands with us by contributing their articles (see Call for the Contributors section), and share your thoughts and suggestions freely with us. We are particularly looking for participation of the members of YPS and MSRF on whom the future of the AAPI rests. Those who actively support the Sushruta Medical News will be inducted into the Editorial Board of the future AAPI Medical Journal, which will be a peer-reviewed professional journal indexed in the PubMed and other databases. Eventually, the Sushruta Medical News will become a section of the AAPI Medical Journal. Thus, the path to the AAPI Medical Journal is transparent, open and objective.

- Editors



Dr. Damania

Winner of the Research Competition at the AAPI Annual Convention in Atlanta, GA 2019

Increased Free Water Usage in Children with Bronchiolitis is Associated with Longer Mechanical Ventilation

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Background: Among children with severe bronchiolitis, use of hypotonic maintenance fluids such as 0.2% NaCl has been associated with prolonged mechanical ventilation (MV), yet it is unknown whether a dose-response relationship exists between intravenous free water (FW) administration and longer duration of MV.

Objectives: To determine the relationship between increased intravenous FW administration to critically ill children with bronchiolitis and mechanical ventilation.

Methods: With IRB approval, we retrospectively reviewed records of 55 children <24 mo with bronchiolitis requiring MV at our academic children's hospital. For the first ~60 h of PICU care (from admission until 6 am on the 3rd morning of PICU care), the volume of FW in administered maintenance fluids, fluid boluses, and continuously-infused medications was calculated using each fluid's tonicity and administered volume. This volume was divided by the subject's calculated expected maintenance fluid volume (using the "4-2-1" rule) to standardize values for time since admission and patient weight, termed "percent of FW" (%FW). Primary outcome was duration of MV. Data are shown as median [IQR].

Results: Median age was 2 [1-5] months with 38% of patients having an identified comorbidity. Duration of MV was associated with %FW by Spearman correlation ($r=0.36$, $p=0.01$) and after adjusting for comorbid status in multivariate linear regression ($\beta=1.3$, $p=0.02$). Duration of MV was longer in the 27 children with a %FW above the median value vs. those with lower %FW (209 [130-275] vs. 140 [76-215] hours, $p=0.02$ by Wilcoxon rank-sum).

Conclusions: In this retrospective study, increased FW administration was associated with longer MV, suggesting clinicians consider limiting FW usage in bronchiolitis. Confirmatory studies and evaluation in other cohorts are needed.

Clinical Trials on the Prevention/Treatment of COVID-19

Hydroxychloroquine Post Exposure Prophylaxis for Coronavirus Disease (COVID-19)

Sponsor: Columbia University

The purpose of this study is to test the hypothesis that post-exposure prophylaxis with hydroxychloroquine will reduce the symptomatic secondary attack rate among household contacts of known or suspected COVID-19 patients.

<https://clinicaltrials.gov/ct2/show/NCT04318444>

Hyperimmune Plasma for Critical Patients with COVID-19 (COV19-PLASMA)

Sponsor: Foundation IRCCS San Matteo Hospital

The outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has become pandemic. To date, no specific treatment has been proven to be effective. Promising results were obtained in China using hyperimmune plasma from patients recovered from the disease. We plan to treat critical Covid-19 patients with hyperimmune plasma.

<https://clinicaltrials.gov/ct2/show/NCT04321421>

Trial of Treatments for COVID-19 in Hospitalized Adults (DisCoVeRy)

Sponsor: Institut National de la Santé Et de la Recherche Médicale, France

This study is a multi-centre, adaptive, randomized, open clinical trial of the safety and efficacy of treatments for COVID-19 in hospitalized adults. <https://clinicaltrials.gov/ct2/show/NCT04315948>

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