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Indian JOURNAL of CLINICAL PRACTICE
A Multispecialty Journal
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Delhi	Mumbai	Bangalore	Chennai	Hyderabad
Dr Veena Aggarwal 9811036687 E - 219, Greater Kailash, Part - I, New Delhi - 110 048 Cont.: 011-40587513 editorial@ijcp.com drveenaijcp@gmail.com **Subscription** Dinesh: 9891272006 subscribe@ijcp.com	Mr Nilesh Aggarwal 9818421222 Unit No: 210, 2nd Floor, Shreepal Complex Suren Road, Near Cine Magic Cinema Andheri (East) Mumbai - 400 093 nilesh.ijcp@gmail.com	H Chandrashekar **GM Sales & Marketing** 9845232974 11, 2nd Cross, Nanjappa Garden Doddaiah Layout Babusapalya Kalyananagar Post Bangalore - 560 043 chandra@ijcp.com	Chitra Mohan **GM Sales & Marketing** 9841213823 40A, Ganapathypuram Main Road Radhanagar, Chromepet Chennai - 600 044 Cont.: 22650144 chitra@ijcp.com	Venugopal **GM Sales & Marketing** 9849083558 H. No. 16-2-751/A/70 First Floor Karan Bagh Gaddiannaram Dil Sukh Nagar Hyderabad - 500 059 venu@ijcp.com

GM: General Manager

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

COVID-19: All Questions Answered

WHAT IS COVID-19?

Coronavirus disease or COVID-19 ('CO' stands for 'corona,' 'VI' for 'virus' and 'D' for disease) is a disease caused by a new coronavirus. Since it was a previously unknown virus, it was called the "2019 novel coronavirus (nCoV)" and the disease was earlier known as nCoV. It was given the name COVID-19 on 11th February.

The name has been given in line with World Health Organization (WHO) guidelines previously developed with the World Organization for Animal Health (OIE) and the Food and Agriculture Organization (FAO). It is the WHO policy to not link the name to a person, animal, place or country. The WHO also refers to the virus as "the virus responsible for COVID-19" or "the COVID-19 virus" when communicating with the public.

WHAT DO YOU MEAN BY THE WORD CORONA?

The word 'corona' means crown or the halo around the sun. Heart is considered a crown. Therefore, the arteries that supply oxygen to the heart are also called coronary arteries. Under an electron microscope, the virus appears round with spikes poking out from its periphery; hence, the name coronavirus.

WHAT IS THE COMPOSITION OF THIS VIRUS?

It is a single-strand, positive-sense RNA genome that ranges from 26 to 32 kilobases in length; a beta coronavirus from Corona family.

WHAT ARE OTHER DREADED CORONAVIRUSES?

COVID-19 is one of the three deadly human respiratory coronaviruses. The other two are severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV).

COVID-19 virus is 75-80% identical to the SARS-CoV.

WHERE DID IT ORIGINATE?

It was first reported from Wuhan, China, on December 31, 2019 as pneumonia of unknown cause. The first case was informed to the world by Dr Li Wenliang who died on 6th February.

WILL THIS VIRUS SURVIVE HEAT?

The virus is likely to be killed by sunlight, temperature, and humidity. SARS was reported to have stopped around May-June, 2003 owing to more sunlight and more humidity.

IS COVID-19 A PANDEMIC?

As per WHO and the Centers for Disease Control and Prevention (CDC), pandemic declaration is likely. WHO says outbreak is "getting bigger", can spread worldwide and is "literally knocking at the doors".

On January 30, 2020, the International Health Regulations Emergency Committee of the World Health Organization declared the outbreak a "public health emergency of international concern (PHEIC)" within a month after the first reported cases, as a result of the signs of human-to-human transmission outside China.

On 21st February, the CDC said, *"This new virus represents a tremendous public health threat"*.

On 22nd February, WHO said that it is concerned about the number of cases with no clear epidemiological link, such as travel history to China or contact with a confirmed case. Cases have been detected in Singapore,

South Korea, Taiwan, Vietnam, Hong Kong and Japan where the source of the infection is not known.

On 28th February, WHO raised the global risk for coronavirus to the highest level of alert "*We have now increased our assessment of the risk of spread and the risk of impact of COVID-19 to very high at global level*" (WHO).

CDC published an Interim Guidance for Healthcare Facilities, "Preparing for Community Transmission of COVID-19 in the United States" on 29th February.

WHAT IS A PANDEMIC?

- The WHO defines a pandemic as "the worldwide spread of a new disease", "across several countries or continents, affecting a large number of people".
- According to the CDC, "pandemic refers to an epidemic that has spread over several countries or continents, usually affecting a large number of people".
- "Viral outbreak markedly different from recently circulating strains and humans have little or no immunity to it," according to the UK's Health and Safety Executive.

WHAT IS CORANXIETY?

Anxiety about falling ill and dying; avoiding or not approaching healthcare facilities due to fear of becoming infected during care; fear of losing livelihood; fear of not being able to work during isolation; fear of being dismissed from work if found positive; fear of being socially excluded; fear of getting put into quarantine; fear of being separated from loved ones and caregivers due to quarantine; refusal to take care of unaccompanied or separated minors; refusal to take care of people with disabilities or elderly because of their high-risk nature; feeling of helplessness; feeling of boredom; feeling of depression due to being isolated; stigmatization of being positive infection; possible anger and aggression against government; unnecessary approaching the courts, possible mistrust on information provided by government; relapses of mental illness in already mentally-ill patients; overstress on people to cover work of infected colleagues, quarantined for 14 days and insufficient or incomplete information leading to myths and fake news.

WHAT WILL HAPPEN IF THIS ANXIETY IS NOT TACKLED?

If this anxiety is not tackled, healthy people will buy masks, get the tests done, get hospitalized and exhaust resources meant for persons who are actually at high risk.

WHAT IS THE REASON FOR ANXIETY IN YOUNGER POPULATION, WHEN DEATHS ARE FEWER IN PEOPLE BELOW 50 YEARS OF AGE?

The younger population has more fear of getting quarantined for 14 days or fear of losing their beloved elderly ones with comorbid conditions.

DOES COVID-19 AFFECT DOCTORS AND OTHER HEALTHCARE WORKERS ALSO?

As on 14th February, 1,716 medical workers have contracted the virus and 6 have died in China; 1,502 belong to Hubei province, with 1,102 from Wuhan. The number amounts to 3.8% of China's overall confirmed infections as of February 11 with 0.3% deaths. On 18th February, the Director of Wuhan Hospital died. Over 3,000 workers have been involved so far. Two workers who were sent to Wuhan in January end to help build new hospital got infected.

WHAT IS THE SERIOUSNESS PROFILE OF COVID-19?

COVID-19 causes mild illness in 82%, severe illness in 15%, critical illness in 3% and death in 2.3% cases. About 6% patients admitted in ICU require mechanical ventilation, or died (*NEJM*).

WHAT IS THE MORTALITY RATE IN PATIENTS WITH NO COMORBID CONDITION?

Patients who reported no comorbid conditions had a case fatality rate of 1.4%.

HOW MUCH TIME DOES IT TAKE TO RECOVER FROM CORONAVIRUS DISEASE?

People with mild illness recover in about 2 weeks; those who are sicker may take 3-6 weeks to recover.

IN WHICH CASES IS IT RISKIER?

It caused death in 15% of admitted serious cases. About 71% deaths have occurred in patients with comorbidity (72,314 Chinese cases, largest patient-based study, *JAMA*).

WHAT IS THE CASE FATALITY RATE OF COVID-19?

Globally, the mortality rate for COVID-19 is 3.4% as estimated by the WHO on 3rd March, which is higher than previous estimates of about 2%.

- 3.8% nationwide

- 5.8% in Wuhan
- 0.7% in other areas
- NEJM report: Among 1,099 cases from China, a lower rate of 1.4% was noted. The death rate may be even lower, if there are many mild or symptom-free cases that have not been detected. The actual death rate could be like that of a severe seasonal flu, below 1%.
- Case fatality is 10% in Iran; probably they are underreporting mild cases.

WHAT IS THE CASE FATALITY RATE OF COVID-19 BY AGE?

Age	Death rate (Confirmed cases)	Death rate (All cases)
80+ years old	21.9%	14.8%
70-79 years old		8.0%
60-69 years old		3.6%
50-59 years old		1.3%
40-49 years old		0.4%
30-39 years old		0.2%
20-29 years old		0.2%
10-19 years old		0.2%
0-9 years old		No fatalities

This table represents the risk of dying if infected with COVID-19 for a person in a given age group.

(Source:https://www.worldometers.info/coronavirus/coronavirus-age-sex-demographics/)

WHAT IS THE CASE FATALITY RATE BY COMORBIDITY?

Percentage does not represent the share of deaths by pre-existing condition. It represents, for a patient with a pre-existing condition, the risk of dying if infected by COVID-19.

Pre-existing condition	Death rate (Confirmed cases)	Death rate (All cases)
Cardiovascular disease	13.2%	10.5%
Diabetes	9.2%	7.3%
Chronic respiratory disease	8.0%	6.3%
Hypertension	8.4%	6.0%
Cancer	7.6%	5.6%
No pre-existing conditions		0.9%

(Source: https://www.worldometers.info/coronavirus/coronavirus-age-sex-demographics/)

WHAT IS THE CASE FATALITY RATE OF OTHER VIRUSES?

- MERS: 34% (2012, killed 858 people out of the 2,494 infected)
- SARS: 10% (November 2002 - July 2003, originated from Beijing, spread to 41 countries, with 8,096 people infected and 774 deaths).
- Ebola: 50%
- Smallpox: 30-40%
- Measles: 10-15% developing countries
- Polio: 2-5% children and 15-30% adults
- Diphtheria: 5-10%
- Whooping cough: 4% infants <1 year, 1% children <4 years
- Swine flu: <0.1-4%
- Seasonal flu: 0.01%
- Number of flu deaths every year: 2,90,000 to 6,50,000 (795 to 1,781 deaths per day)

DOES IT AFFECT ALL SEXES?

Nearly 56% patients are males. Although men and women have been found to be infected in roughly equal numbers, the death rate among men has been noted to be 2.8%, compared with 1.7% among women.

DOES IT AFFECT ALL AGES?

- 87% aged 30-79 years
- 10% aged <20 years
- 3% aged >80 years

WHAT IS THE INCUBATION PERIOD OF COVID-19?

The incubation period (time between exposure and onset of symptoms) varies from 1 to 14 days, most commonly around 5 days. An incubation period of 24 days has also been observed. WHO said that it could point to a second exposure rather than a long incubation period. Hubei province local government on February 22 reported a case with an incubation period of 27 days.

WHAT ARE THE DIFFERENT NUMBERS FOR THE DISEASE?

- Mean time to symptoms: 5 days.
- Mean time to pneumonia: 9 days.
- Mean time to death: 14 days.
- Mean time to CT changes: 4 days.

- Reproductive number (R_0 or R not): Number of persons infected by one infected person - In COVID-19 it is 3-4; R_0 of flu: 1.2; R_0 of SARS: 2.
- Epidemic doubling time: 7.5 days.
- Epidemic doubling time in South Korea: 1 day, probably due to super-spreader.
- Epidemic tripling time in South Korea: 3 days, again due to a super-spreader.

WHAT IS THE POSITIVITY RATE IN CONTACTS WHO ARE TESTED?

The positivity rate for COVID-19 is as follows: UK 0.2%, Italy 5.0%, France 2.2%, Austria 0.6%, South Korea 4.3% and USA 3.1%.

WHICH COUNTRIES ONE SHOULD NOT TRAVEL TO?

The Ministry of Health & Family Welfare has advised Indian citizens to refrain from travel to China, Iran, Republic of Korea, Italy and Japan and advised to avoid nonessential travel to other COVID-19 affected countries.

Travel Alerts

- Level 1 in all countries (exercise normal standard hygiene precautions).
- Level 2 in all affected countries (exercise a high-degree of caution).
- Level 3 in all countries with secondary cases (reconsider need to travel).
- Level 4 in affected parts of China and South Korea, Iran, Italy (avoid travel).

IS IT A ZOONOTIC DISEASE?

It is zoonotic and 55% cases with onset before January 1, 2020 were linked to Huanan Seafood Wholesale Market vs. only 8.6% of subsequent cases. The Chinese government put a ban on wild life trade until the epidemic is over. The virus is now spreading from person-to-person.

The new corona virus is a close relative of other bat coronaviruses. SARS-CoV was transmitted to humans from civet cats and MERS-CoV was transmitted by dromedary camels. Possible animal sources of COVID-19 have not yet been confirmed. In the case of the new coronavirus, the central hosts were probably bats; however, snakes and pangolins have been thought to be the intermediate hosts.

There is no evidence yet that companion animals can spread the disease.

WHAT ARE THE DIFFERENT TYPES OF TRANSMISSION?

There are three main types of transmission:

- Droplets, large >5 μ organisms - flu, coronavirus (COVID-19).
- Air-borne <5 μ organisms - TB, chickenpox, measles.
- Contact on the surface: COVID-19, SARS, Flu (It may be possible to contract COVID-19 by touching a surface or object that has the virus on it and then touching your own mouth, nose or possibly eyes).

WHICH IS MORE IMPORTANT: DROPLET PRECAUTIONS OR CONTACT PRECAUTIONS?

Both are important. However, contact precautions become more important in the event of community spread. During SARS outbreak, in Hong Kong, the contact precautions worked more than the droplet precautions.

CAN THE VIRUS BE TRANSMITTED FROM MOTHER TO THE BABY DURING PREGNANCY?

There is currently no evidence for intrauterine infection caused by vertical transmission in women who develop COVID-19 pneumonia in late pregnancy (*The Lancet*. February 12, 2020).

WHICH PART OF THE RESPIRATORY TRACT DOES THE VIRUS AFFECT?

COVID-19 virus affects both the upper and the lower respiratory tract.

- Upper respiratory tract infection (URTI) causes fever with sore throat and mild cough.
- Lower respiratory tract infection (LRTI) causes fever with cough, and breathlessness.

WHY ARE LRTIs MORE INFECTIOUS?

SARS is high inducer. When it infects the lower part of the lung, a very severe reaction occurs against it which leads to inflammation and scarring. In SARS, after the first 10-15 days, it was not the virus but the reaction of the body that was killing patients. Is this new virus like the MERS or SARS or is this some other type of virus – a milder coronavirus like the NL63 or the 229? It may be the mild inducer (Dr John Nicholls, University of Hong Kong).

WHAT IS THE CLINICAL PRESENTATION OF COVID-19?

- Clinically all patients have fever (subjective or evident). *No fever, no coronavirus.*

- 75% have cough
- 50% have weakness
- 50% have breathlessness
- Low total white count
- Deranged liver enzymes.

The illness starts with fever, followed by a dry cough. A week later, it can lead to shortness of breath, with about 20% of patients requiring hospital treatment.

COVID-19 infection rarely seems to cause a runny nose, sneezing or sore throat (observed in only about 5% of patients). Sore throat, sneezing and stuffy nose are most often signs of a cold.

HOW MANY NEED ADMISSION AND ICU CARE?

About 20% need ICU care and 15% of them are fatal. Cases categorized as critical have the highest fatality rate—at 49.0%.

WHAT IS THE TREATMENT?

Treatment is mainly symptomatic; though chloroquine, antiviral and anti-HIV drugs have shown some efficacy.

WHAT DO YOU MEAN BY PHEIC?

COVID-19 was declared a PHEIC on 30th January 2020, which means it is mandatory to report each human and animal case to WHO.

IS IT THE FIRST TIME THAT A PHEIC HAS BEEN DECLARED?

No, there have been five prior PHEICs:

- Swine flu: April 26, 2009 – August 10, 2010
- Resurgence of wild polio: May 2014
- Ebola: August 2014 (First PHEIC declared in a resource-poor setting)
- Zika: February 1, 2016 to November 18, 2016
- Kivu Ebola: 2018-20.

WHAT IS PUBLIC HEALTH EMERGENCY OF A STATE?

- Kerala declared it when it had three cases and later lifted it on 12th February.
- San Francisco declared it even without a case on 26th February.
- Washington declared a state emergency on 1st March.
- New York state declared a state of emergency on 7th March.

DID CHINA DELAY IN REPORTING OF CASES?

While there were 300 cases and 5 deaths with SARS before the Chinese government reported it to the WHO, there were merely 27 cases and no deaths with COVID-19 before it was reported to the agency.

Chinese authorities imposed lockdown measures on 10 cities in an effort to contain the outbreak of coronavirus and built a specialized hospital (Huoshenshan Hospital) in just 10 days as part of its efforts to fight coronavirus. A second facility with 1,500 beds is also being opened. During SARS in 2003, a facility in Beijing for patients was constructed in a week.

WHAT ARE LAB-CONFIRMED CASES?

Cases with positive throat swab test are lab-confirmed cases.

WHAT ARE CT-POSITIVE CASES?

CT-positive cases mean CT showing pneumonia like changes.

HOW IS THE TOTAL NUMBER OF CASES COUNTED?

The total number of cases includes lab-confirmed and CT-diagnosed cases. This was the criteria used from 12th to 19th February in China.

Before and after that, only lab-confirmed cases are counted.

The sudden jump in deaths and new cases on 12th February was due to inclusion of CT-diagnosed cases.

WHAT WILL BE THE ESTIMATED DEATHS IF CT-DIAGNOSED CASES WERE ALSO INCLUDED?

Around 5% deaths will be added to total deaths.

WHAT ARE THE POSSIBLE MODES OF SPREAD? MYTHS AND FACTS

- **Person-to-person:** The virus can spread from one person to another, most likely through droplets of saliva or mucus carried in the air for a distance of up to 6 feet when an infected person coughs or sneezes, or through viral particles that can be transferred on shaking hands or sharing a drink with someone who has the virus.
- **Casual exposure:** No; human-to-human contact requires prolonged contact (possibly 10 minutes or

more) within 3-6 feet. But with contact transmission, this may not be applicable.

- **Currency notes:** The central banking authorities of China are disinfecting, stashing and even destroying cash in a bid to stop the spread of the coronavirus. People's Bank of China says that the cash collected by banks must be disinfected before being released to customers.
- **Fabric, carpet and other soft surfaces:** Currently, there's no evidence.
- **Hard surfaces:** Virus could be present on frequently-touched surfaces, such as doorknobs, although early information suggests viral particles would be likely to survive for just a few hours (WHO).
- **Biometric attendance:** Biometric attendance has been suspended in Delhi, UP, Kerala and Bihar.
- **Kissing:** Kissing scenes have been banned in movies in China. France has advised to cut back on "la bise", the custom of giving greetings with kisses, or air kisses, on the cheeks.
- **Breath analyzer for alcohol:** Kerala exempted air crew from breath analyzer tests.
- **Public gatherings:** Affected countries have banned death ceremonies and people gathering.
- **Uncovered eyes:** The transmission is through mucus membrane contamination. One case got infected while using gown, but eyes not covered.
- **Eating meat, fish or chicken:** It's not a food-borne illness but a respiratory illness. It cannot occur by eating any food or meat. However, it is always advised not to touch raw meat, eat raw meat or eat partially cooked meat to prevent meat-related food-borne illnesses. Eating fish and chicken is safe.
- **Eating snakes or drinking bat soups:** No, eating wild animals cannot cause it. Handling their secretions can cause it.
- **Handling wild animals or their meat:** Yes, if their secretions are handled.
- **Semen:** We do not know; in patients infected with Ebola, the virus may persist for months in the testes or eyes even after recovery, and can infect others and keep the epidemic going.
- **Sex, like Ebola and Zika:** We have no evidence yet.
- **Goods from affected areas:** People receiving packages from China or other affected areas are not at risk of contracting the COVID-19 as the virus does not survive for long on objects, such as letters or packages.
- **Pipes:** Ventilation system connects one room to the other. There has been concern that the coronavirus can spread through pipes.
- **Stress:** Stress and anxiety suppress the immune system, thus rendering people more vulnerable to contracting the virus.
- **Patients without symptoms:** Both SARS-CoV and MERS-CoV affect the intrapulmonary epithelial cells more than the upper airway cells. Transmission thus occurs principally from patients with known illness and not from patients with mild, nonspecific signs. However, *NEJM* has reported a case of COVID-19 infection acquired outside of Asia in which transmission appears to have occurred during the incubation period in the index patient, but the same has been challenged now.
- **Corona beer:** It has nothing to do with coronavirus. It's a brand of beer.

WHAT IS NO CONTACT POLICY?

Greeting people by namaste, bowing or elbow touch. Corona Namaste is a no contact policy in public. Let's not shake hands; IMA and CMAAO promote the concept of Corona Namaste.

WHY DID THE CASES NOT OCCUR IN OTHER COUNTRIES IN THE INITIAL PHASE?

Initial serious illness in other countries was less as patients with breathlessness were unlikely to board and patients with mild illness or asymptomatic illness are less likely to transmit infections. For transmission, you require cough secretions or nasal discharge.

SHOULD WE BE AFRAID?

It's time for facts, not fear; for rationality, not rumors and for solidarity, not stigma.

WHAT IS THE HELPLINE NUMBER?

- The Helpline Number for coronavirus: +91-11-23978046
- The Helpline Email ID for coronavirus: ncov2019@gmail.com

WHAT IS A BIPHASIC INFECTION?

Coronavirus follows a biphasic infection wherein the virus persists and causes a different set of symptoms than those noted in the initial bout. The recovered person

can also develop other symptoms, including insomnia and neurological problems, said Angela Rasmussen, a Virologist at Columbia University. (*NY Times*)

WHAT DO THE TERMS "SPREADER" AND "SUPER-SPREADER" MEAN?

Spreader: An infected person with normal infectivity.

Super-spreader: An infected person with high infectivity can infect hundreds of cases in no time. What causes a person to become a super-spreader is not known; HIV person becomes a super-spreader if he or she is coinfected with sexually transmitted infection (STI).

The examples are the first case in Wuhan, a female in the South Korea Daegu fringe Christian group Shincheonji Church where she infected more than 51. In the church, people shout out amen after every sentence the pastor says, pretty much every few seconds, at the top of their lungs. This sends respiratory droplets flying everywhere.

WHAT CAN BE THE CAUSE OF A CLUSTER OF CASES OR A HOT SPOT WITHOUT A SUPER-SPREADER?

People catching the virus from infected surfaces. We don't know how long the germs stay on surfaces, but similar viruses can live for a week.

WHAT ARE THE VARIOUS CLUSTERS OF CORONA VIRUSES?

- The largest cluster was Wuhan itself where over 5 crore people were locked down ending up with over 2,000 deaths.
- The second largest lockdown was in Japanese Diamond Princess ship where over 3,000 patients were locked up and 23% of them developed COVID-19 virus infection.
- The third example – the cult church in South Korea – where one lady infected with the virus spread it to other people attending the church and she also infected multiple people in a hospital where she was treated and one person later died.
- Shandong province in China reported of 207 cases of the new coronavirus in Rencheng prison as of February 20. A jail in the Zhejiang province reported 34 infections. All of them were inmates. A jail will behave like a ship and end up with 21% getting infected.

CAN THE COURT TAKE COGNIZANCE IN CORONAVIRUS EPIDEMIC?

- Despite CDC protest, 14 Americans infected with coronavirus on the Diamond Princess cruise ship shared a plane back to the US with healthy passengers, separated by plastic sheeting. (*New York Post*)
- A court temporarily prevented the US government from sending nearly 50 people infected with a new virus from China to a Southern California city for quarantine after local officials argued that the plan lacked details about protection of the community from the outbreak. (*Washington Post*)
- Hong Kong police has caught a part-time security guard at a shopping mall for allegedly writing on social media that multiple staff members had caught a fever and gone on sick leave. The messages caused panic and helped create paranoia. (*The Print*) The government blamed rumor-mongers for fuelling a run on goods at supermarkets.
- Singapore has announced severe penalties for non-compliance of the quarantine order, including fines or jail time.
- Prosecutors may investigate the founder and top leaders of Shincheonji Church of Jesus. Its members account for >60% of confirmed cases in the country. They may be probed on murder and other charges for failing to provide an accurate list of church members and by interfering with the government's efforts to fight the outbreak.
- **IPC: Section 270 in the Indian Penal Code:** *"Malignant act likely to spread infection of disease dangerous to life.—Whoever malignantly does any act which is, and which he knows or has reason to believe to be, likely to spread the infection of any disease dangerous to life, shall be punished with imprisonment of either description for a term which may extend to two years, or with fine, or with both."*

DID IT ORIGINATE FROM THE WUHAN BIOTERROR LAB?

This is unlikely; nobody will produce a bioweapon to be used on themselves or without simultaneously making an anti-weapon or antidote. It's a myth that the virus was part of China's "covert biological weapons program" and may have leaked from the Wuhan Institute of Virology and was linked to the suspension of a researcher at Canada's National Microbiology Lab.

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IS IT TRUE THAT CHINA KILLED 20,000 COVID-19 PATIENTS?

This is fake news linked to a diversion to a sex site.

IN INITIAL DAYS, DOES IT HAVE HIGH VIRAL LOAD?

Detection of COVID-19 RNA in specimens from the upper respiratory tract with low CT values on Day 4 and Day 7 of illness suggests high viral loads and potential for transmissibility (*NEJM*).

WAS DIAMOND PRINCESS CRUISE SHIP QUARANTINE A SUCCESSFUL MODEL?

The on-ship quarantine appears to have failed as 23% of the ship passengers got infected; 705 cases got the virus (they tested positive for the virus); there were 6 deaths and 36 patients were still serious as on 1st March. This would mean 6 + 36 × 15 = 1-12 cases will die.

Contacts and suspected cases are placed under a 14-day quarantine period. If placed together, if anyone is diagnosed with the infection during that period, the quarantine will add another 14 days.

The longer several thousand people are placed together, waves of infection are propagated.

A better way to quarantine is to divide the people into smaller groups and quarantine them separately. Why quarantine children <15 years of age when the virus is not risky for them and why not separate elderly people with comorbid conditions at high risk of death and quarantine them separately in one to one or small groups.

HOW LONG WAS THE QUARANTINE ON THE SHIP?

Fourteen days for the passengers and another 14 days for the crew who took care of the people during the first 14 days.

WHAT ARE DIFFERENT WAYS TO CONTROL THE INFECTION IN THE COMMUNITY?

- **Lockdown in China**: Unprecedented quarantines across Hubei, locking in about 56 million people, to stop it from spreading; Results 2% deaths.
- **Locking of a village in Vietnam**: More than 10,000 people in villages near Vietnam's capital placed under quarantine on 13th February after 6 cases of the new coronavirus were identified there. These cases did not become a hotspot probably; there was no super-spreader in those cases. Only 16 cases so far.
- **Kerala model of containment in India**: Hospital one-to-one quarantine of infected patients and individual home quarantine of contacts. They could contain the virus in the state.

WAS IT CORRECT FOR INDIA TO HAVE CULTURAL EVENINGS BY QUARANTINED PEOPLE BROUGHT FROM CHINA?

It was risky to allow people to celebrate and have cultural programs during quarantine. As was seen in India, people danced together with surgical masks during quarantine period.

IS THERE A ROLE OF QUARANTINE IN THE SUNLIGHT?

Quarantine patients like TB sanatoriums with both sun-balconies and a rooftop terrace where the patients would lie all day either in beds or on specially designed chairs.

WHAT IS THE PROTOCOL AT THE TRIAGE SECTION OF EMERGENCY ROOM?

Surgical 3-layered mask for patients; Isolation of two beds with at least 3 feet distance; cough etiquette; hand hygiene for all.

WHAT ARE DIFFERENT PRECAUTIONS?

- **Droplet precautions:** Surgical 3-layered mask for patients, their contacts and healthcare workers, in an adequately ventilated isolation room; healthcare workers caring with secretions should use eye protection, face shields/goggles. Limit patient movement, restrict attendants and observe hand hygiene.
- **Contact precautions:** Use gown, mask, goggles, gloves when entering room; remove before leaving the room; dedicated equipment/disinfection after every use; care for environment - door knobs, handles, articles, laundry; avoid patient transport and practice hand hygiene.
- **Airborne precautions when handling virus in the lab and while performing aerosol-generating procedures:** Room should be with negative pressure with minimum of 12 air changes per hour or at least 160 L/sec/patient in facilities with natural ventilation. There should be restricted movement of other people and gloves, long-sleeved gowns, eye protection and fit-tested particulate respirators (N95 or equivalent, or higher level of protection) should be used by all.

WHAT ARE THE PRECAUTIONS FOR THE GENERAL PUBLIC?

- Strict self-quarantine if sick with flu-like illness: 2 weeks.
- Wash hands often and for at least 20 seconds with soap and water or use an alcohol-based hand sanitizer.
- Avoid touching eyes, nose, and mouth with unwashed hands.
- Avoid close contact: (3-6 feet) with people who are sick with cough or breathlessness.
- Cover your cough or sneeze with a tissue, then throw the tissue in the trash.
- Clean and disinfect frequently touched objects and surfaces.

WHICH MASKS SHOULD BE USED BY HEALTHCARE PROVIDERS AND PATIENTS?

- For patients and close contacts: Surgical 3-layered masks.
- For healthcare providers when handling respiratory secretions: N95 masks.

WHAT ARE THE LAB TESTS?

There are two ways to detect a virus: through the genetic material DNA or RNA or to detect the protein of the virus. The rapid tests look at the protein. It takes 8-12 weeks to make commercial antibodies. Currently, PCR is being used which gives a turnaround in 1-2 hours.

WHAT ARE FALSE-POSITIVE AND FALSE-NEGATIVE RESULTS?

- Polymerase chain reaction (PCR) tests may detect the remains of the measles virus months after people who had the disease stop shedding the virus.
- Negative test can come if the test is not done properly, or the samples are stored at a temperature at which the virus deteriorates. A throat swab may miss the virus that is present elsewhere in the body.
- A test is positive if the virus is present on the swab in sufficient quantities at the time of swabbing the person. A negative test is not a confirmation that there is no more virus in that person.

CAN YOU GIVE AN ANALOGY OF A NEGATIVE TEST?

A jam jar with mold on top; clearing the surface might suggest that the jam is now mold-free, but the jar may still contain mold that continues to grow.

WHAT SAMPLE SPECIMENS SHOULD BE COLLECTED?

Samples should be collected from both the upper respiratory tract (URT; nasopharyngeal and oropharyngeal) and lower respiratory tract (LRT; expectorated sputum, endotracheal aspirate or bronchoalveolar lavage). Use viral swabs (sterile dacron or rayon, not cotton) and viral transport media.

CAN IT BE DONE BY PRIVATE LABS?

Not yet in India. In the US, in January, all testing had to be done in CDC laboratories. However, on February 4, the US FDA issued an emergency-use authorization for the CDC's COVID-19 Real-Time RT-PCR Diagnostic Panel, allowing its use at any CDC-qualified laboratory in the US.

WHAT PRECAUTIONS TO TAKE IN THE LAB?

Biosafety level (BSL) 2 (3 for viral culture labs).

WHY DID THE PHARMA COMPANIES NOT MAKE SARS VACCINE?

- With SARS, in 6 months the virus was gone, and never came back. Companies may not spend millions to develop a vaccine for something, which may never come back.
- The UN agencies should have initiated the development of vaccine against coronavirus, SARS or MERS strain. If that was available, it might have reduced the case fatality of COVID-19.

CAN IT CAUSE SECONDARY INFECTION?

Secondary infection, such as *Escherichia coli*, is most likely the cause of death of the patients in Hong Kong and the Philippines.

IS THERE ANY PROVEN TREATMENT?

No, there is no proven treatment.

WHICH ANTIVIRALS HAVE BEEN TRIED?

A combination of lopinavir and ritonavir showed promise in lab in SARS. Combination of lopinavir, ritonavir and recombinant interferon beta-1b was tried in MERS.

HAVE WE BEEN ABLE TO RECREATE LAB-GROWN VERSION OF THE VIRUS?

Scientists in Australia have reportedly recreated a lab-grown version of COVID-19.

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IS CHLOROQUINE EFFECTIVE?

Chloroquine had potent antiviral activity against the SARS-CoV; it has been shown to have similar activity against HCoV-229E in cultured cells and against HCoV-OC43 both in cultured cells and in a mouse model.

IS THERE ANY ROLE OF ANTI-HIV DRUGS?

- In Thailand, oseltamivir along with lopinavir and ritonavir, both HIV drugs, have been used successfully.
- The Drug Controller General of India (DCGI) has approved the "restricted use" of a combination of drugs (lopinavir and ritonavir) used widely for controlling HIV infection in public health emergency for treating those affected by novel coronavirus.
- Arbidol, an antiviral drug used in Russia and China for treating influenza, could be combined with darunavir, the anti-HIV drug, for treating patients with the coronavirus.

WHAT IS THE ROLE OF EXPERIMENTAL DRUG "REMDESEVIR" FROM GILEAD SCIENCES INC.?

Trials have started on 6th February, in China and late February in USA.

WHAT OTHER TREATMENTS HAVE BEEN TRIED?

- Povidone-Iodine (PVP-I) mouthwashes and gargles significantly reduce viral load in the oral cavity and the oropharynx. PVP-I has high potency for viricidal activity against hepatitis A and influenza, MERS and SARS.
- In SARS, people were put on long-term steroids ending with immunosuppression and late complications and death. The current protocol is short-term treatment.
- Pneumococcal vaccine and *Haemophilus influenzae* type b (Hib) vaccine do not provide protection against COVID-19.
- Regularly rinsing the nose with saline does not protect people from infection with COVID-19 or respiratory infections although it hastens recovery from the common cold.
- There is no evidence that using mouthwash will protect you from infection with COVID-19 although some brands of mouthwash can eliminate certain microbes for a few minutes in the saliva in your mouth. Keeping your throat moist, avoiding spicy food and loading up on vitamin C cannot kill the virus.
- There is no evidence that eating garlic protects people from COVID-19.
- Sesame oil does not kill the new coronavirus. Chemical disinfectants that can kill the COVID-19 on surfaces are bleach/chlorine-based disinfectants, either solvents, 75% ethanol, peracetic acid and chloroform.
- Antibiotics do not work against viruses.

WHO IS MORE VULNERABLE?

People with pre-existing medical conditions (such as asthma, diabetes, heart disease) appear to be more susceptible to become severely ill with the virus.

WHAT ARE VARIOUS FAKE NEWS IN CIRCULATION ABOUT THE NEW CORONAVIRUS DISEASE?

COVID-19 linked to Donald Trump, US intelligence agencies or pharmaceutical companies. Avoiding cold or preserved food and drinks, such as ice cream and milkshakes, for at least 90 days can help. Experts have been aware of the virus for years: The virus is not new, its two deadly forma have already caused SERS and MERS in the world. These types of viruses will keep on coming.

WHAT IS THE ROLE OF CMAAO AND OTHER MEDICAL ASSOCIATIONS?

Get prepared for containment measures, including active surveillance, early detection, isolation and case management, contact tracing and prevention of spread of the virus and to share full data with WHO. All countries should emphasize on reducing human infection, prevention of secondary transmission and international spread. Intensify IEC activities.

CMAAO IMA FOMA MAMC Recommendations

- Price control of PPE
- Accreditation of private labs for testing
- Private insurance should cover the infection
- IEC and CME activities to be intensified
- Allow paid leaves for airborne and droplet infections
- Allow teleconsultations in flu-like diseases
- CSR funds for vaccine research
- Surgical three-layered masks at public places
- Start National program on respiratory secretions borne illnesses
- Incorporate respiratory infection control under Swachh Bharat Abhiyan in India

HOW TO SUSPECT A CORONAVIRUS CASE?

CDC has already revised its criteria to guide evaluation of PUI (person under investigation) for COVID-19:

- Fever or signs/symptoms of lower respiratory illness (cough or shortness of breath) AND Any person, including healthcare workers who has had close contact with a laboratory-confirmed COVID-19 patient within 14 days of symptom onset
- Fever and signs/symptoms of a lower respiratory illness (cough or shortness of breath) requiring hospitalization AND history of travel from affected areas (China, Iran, Italy, Japan, South Korea) within 14 days of symptom onset
- Fever with severe acute lower respiratory illness (pneumonia, ARDS) requiring hospitalization and no alternative explanatory diagnosis (e.g., influenza) AND no source of exposure has been identified.

WHAT IS A PROBABLE CASE?

A suspect case with inconclusive testing for COVID-19 or testing was positive on a pan-coronavirus assay.

WHAT IS A CONFIRMED CASE?

A confirmed is a person with laboratory confirmation of COVID-19 infection, regardless of clinical signs and symptoms.

WHAT IS UNCOMPLICATED ILLNESS?

Patients with uncomplicated upper respiratory tract viral infection may have non-specific symptoms such as fever, cough, sore throat, nasal congestion, malaise, headache and muscle pain.

The elderly and immunosuppressed may have atypical symptoms. These patients have no signs of dehydration, sepsis or shortness of breath.

WHAT DO YOU MEAN BY CLOSE CONTACT?

Close contacts are people providing direct care to patients, working with infected healthcare workers, visiting infected patients or staying in the same close environment, working together in close proximity or sharing the same classroom environment with an infected patient, traveling together with infected patient, living in the same household as an infected patient. The epidemiological link may have occurred within a 14-day period prior to or after the onset of illness. But once the community spread occurs, the definition will no longer be correct.

WHAT IS THE DEFINITION OF DIFFERENT CASES?

- Primary case: Who got infected first in Wuhan in China.
- Secondary case: When the primary cases infected the second person and tertiary when the secondary cases transmitted infection to another person.

Primary case: The first case in Wuhan in late December.

Index case: The first case in any country or province.

WHAT IS COMMUNITY SPREAD?

Community spread means when the infection spreads without any contactable contact. Once that happens, closing borders will not contain the virus. All cases with flu-like illness will be presumed to be COVID-19 and only those with breathlessness will be tested.

WHAT ARE MITIGATION GUIDELINES?

- Universal nonpharmaceutical interventions including personal practices, covering coughs and washing hands, and community and environmental measures such as surface cleaning.
- Universal community measures including social distancing, or limiting contact in face-to-face settings, closing schools, telework or tele schools for children, and recommending to modify, postpone, or cancel mass gatherings.
- In healthcare system triaging patients, conducting patient visits via telemedicine, and delaying elective surgeries.
- Commercial labs need to pitch in for testing.
- Better to be overprepared than underprepared.
- The testing criteria may change to testing only symptomatic cases and admitting cases only with breathlessness. (*Probably Iran is doing this*)

WHICH ARE THE HIGH RISK PLACES?

China, Macau, Hong Kong, Taiwan, South Korea, Singapore, Italy, Iran and Japan.

WILL IRAN BE THE NEXT CHINA?

- With 54 deaths in Iran, looks like that Iran government is hiding the true extent of the outbreak. If the virus kills about 2% of known victims, then the number of cases should be 2100. In fact the death rates outside china are 1% and in that case the number will be much higher in Iran.

- Cases in Iraq, Afghanistan, Bahrain, Kuwait, Oman, Lebanon, United Arab Emirates and Canada have been linked to Iran. Millions of religious pilgrims, migrant workers and others cross the borders of Iran. This is one of the biggest causes for worry in what threatens to become a global epidemic.

WILL AFGHANS BE THE NEXT SOURCE OF CARRYING INFECTION IN INDIA?

- Religious pilgrims, migrant workers, businessmen, soldiers, etc., move constantly across Iran's borders, often crossing into countries with few border controls, weak and ineffective governments and fragile health systems.
- Many Afghanis are coming to India on a daily basis on health visa and many of them come via Iran. It is likely many of them would carry the virus to India.

WHAT IS THE ROLE OF 14 DAYS QUARANTINE?

Quarantines and travel restrictions currently in place in many counties, intend to break the chain of transmission. Public health authorities may recommend other approaches for people who may have been exposed to the virus, including isolation at home and symptom monitoring (usually for 14 days), depending on level of risk for exposure. (*Harvard Medical School*)

SHOULD I WEAR A FACE MASK TO PROTECT AGAINST CORONAVIRUS?

Currently, face masks are not recommended for the general public. Some health facilities require people to wear a mask if they have traveled from the city of Wuhan, China or surrounding Hubei province, or other affected countries or have been in contact with people who did or with people who have confirmed coronavirus.

For those with respiratory symptoms like coughing or sneezing, wearing a mask helps protect others. This may help contain droplets with any type of virus, including the flu, and protect close contacts (anyone within 3-6 feet of the infected person).

SHOULD SOMEONE WHO IS IMMUNOCOMPROMISED WEAR A MASK?

Only if you are attending a public gathering. However, if your healthcare provider advises you to wear a mask in public areas as you have a vulnerable immune system, follow his advice.

SHOULD I ACCEPT PACKAGES FROM CHINA?

There is no reason to suspect that packages from China carry COVID-19. This is a respiratory virus like the flu. We don't stop receiving packages from China during their flu season. The same applies here.

CAN I BE INFECTED WITH THE CORONAVIRUS BY EATING FOOD PREPARED BY OTHERS?

COVID-19 and other coronaviruses have been detected in the stool of certain patients, so the possibility of occasional transmission from infected food handlers cannot be completely ruled out. The virus would likely be killed by cooking the food.

SHOULD I TRAVEL ON A PLANE IF I HAVE FEVER?

Of course, if anyone has a fever and respiratory symptoms, that person should not fly if possible, but anyone who has a fever and respiratory symptoms and flies anyway should wear a mask on an airplane.

WHAT SHOULD PEOPLE DO IF THEY THINK THEY HAVE CORONAVIRUS, OR THEIR CHILD DOES? GO TO AN URGENT CARE CLINIC? GO TO THE ER?

Call your doctors instead of rushing to emergency room (ER).

CAN PEOPLE WHO RECOVER FROM THE CORONAVIRUS STILL BE CARRIERS AND THEREFORE SPREAD IT?

There is no current evidence.

ARE WE MISSING INFECTIONS IN INDIA?

We do not know. In Iran, the country missed hundreds of cases till two persons died. In fact, the first case was the one who died.

CAN PEOPLE WHO RECOVER FROM A BOUT WITH THE NEW CORONAVIRUS BECOME INFECTED AGAIN?

- The Japanese government has reported of a woman in Osaka who had tested positive for the coronavirus for a second time, weeks after recovering from the infection and being discharged from a hospital. With similar reports from China, the case in Japan has raised some questions. Reinfections are common among people who have recovered from coronaviruses that cause the common cold.
- Reinfection in a short time is not likely. Even the mildest of infections should confer at least short-

term immunity against the virus in the recovering patient. It is possible that the "reinfected" patients still had low levels of the virus at the time of discharge from the hospital, and testing failed to detect it.

- Even if there are occasional cases of reinfection, they do not seem to be occurring in numbers large enough to be a priority.

HOW LONG DO THE ANTIBODIES LAST?

Research with MERS has shown that the strength of the immune response depends on the severity of the infection. However, even in those with severe disease, which should yield the strongest immune responses, the immunity seemed to disappear within a year.

WHY SARS NEVER ENTERED INDIA EXCEPT FOR A FEW CASES IN NEIGHBORING COUNTRIES?

Either cases were not detected or by the time it reached India there was already summer.

ARE ANTIBODIES PROTECTIVE?

On February 13, a Chinese senior health official called on people who had recovered from the new coronavirus to donate blood plasma, as it could contain proteins that could be used to treat sick patients, according to *The New York Times*.

WHEN SHOULD I SUSPECT CORONAVIRUS CASES IN INDIA?

Suspect coronavirus infection in H1N1-negative flu-like illness.

WHAT IS ENVIRONMENTAL DISINFECTION?

According to the CDC, routine cleaning and disinfection procedures are appropriate for COVID-19 virus. Products approved by the Environmental Protection Agency (EPA) for emerging viral pathogens should be used.

- SARS and MERS have been found to persist on surfaces, including metal, glass or plastic, for as long as 9 days if it had not been disinfected, reported a research published in *The Journal of Hospital Infection*.
- Human coronaviruses can be inactivated by surface disinfection procedures with 62-71% ethanol, 0.5% hydrogen peroxide or 0.1% sodium hypochlorite or with bleach within one minute.
- For SARS, the persistence on surfaces ranged from less than 5 minutes to nine days.
- According to the CDC, the flu virus can persist on some surfaces for as long as 48 hours and infect someone if the surface has not been cleaned and disinfected.

IN WHICH CONDITIONS SEASONAL FLU IS MORE DANGEROUS?

The flu is more dangerous to young children. Children infected with the new coronavirus tend to have mild or no symptoms. It is also dangerous for pregnant women. Whether the COVID-19 poses a serious threat to pregnant women is not clearly known.

HOW MANY PEOPLE DIE OF SEASONAL FLU?

As of February 22, in the current season, there have been reports of around 32 million cases of flu in the United States, 310,000 hospitalizations and 18,000 deaths, according to the CDC.

CAN THE WARM ATMOSPHERE KILL THE VIRUS?

Coronavirus may retreat as the weather warms, just like influenza. But this is a new virus, and there is no information about how the weather might affect it.

Even if the virus decreases in the spring, it might rebound in the fall, as the weather cools. This pattern is often seen in severe flu seasons.

CAN DENGUE COEXIST WITH COVID-19?

In Thailand, a 35-year-old man who was diagnosed with dengue and COVID-19 died. In combination with the emerging infectious disease, it created complications, leading to multiorgan failure.

WHAT IS THE PREPAREDNESS IN INDIA?

The two designated nodal hospitals in Delhi are RML and Safdarjung. Both have an OPD of thousands of people. Ideally, such OPDs should be held at places where there is no mix up with other types of patients.

DO WE HAVE A CHINA LIKE MAKE-SHIFT HOSPITAL LIKE FACILITY IN INDIA?

Not so far.

HOW IS THE INDIA GOVERNMENT COORDINATING WITH THE IMA?

I am not aware of any such meeting.

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HOW MANY INDIANS GOT CORONAVIRUS IN THE DIAMOND PRINCESS SHIP?

Sixteen Indian citizens on board the Diamond Princess ship tested positive for the new coronavirus.

WHAT IS THE ROLE OF ARMY IN CONTAINMENT OF ANY EPIDEMIC?

In March 2016, there was the biggest military mobilization in Brazil's history: 2,20,000 army, navy and air force personnel jumped into action, with 3,15,000 public officials. The enemy was *Aedes aegypti* mosquito which is believed to be responsible for the spread of the Zika virus.

WHAT CAN HAPPEN IF THE DISEASE SPREADS IN A CITY?

- Like Diamond princess ship, quarantine will lead to 23% getting infected.
- Like the 1200 people who attended church, 14% of them have exhibited cough and other symptoms.
- China locked down 5 crore people with self-quarantine policy, 80,000 got infected (0.0016% of the community) and 2760 deaths (0.0000552% of the population) were reported.
- 6,47,406 people close contact with infected patients (1:8 patients).

WHAT IS THE EXPECTED NUMBER OF CASES IN DELHI IN A WUHAN-LIKE SITUATION?

- Total expected positive in 1.67 crore population = 26,720
- Likely contacts: 2,13,760
- Expected serious cases = 20% = 4,008
- Likely deaths: 926
- At risk 60+ population in Delhi = 11,64,147

WHAT WILL BE THE PREPAREDNESS NEEDED THEN IN DELHI?

Four thousand coronavirus beds (15% of patients); self-quarantine of 17-20,000 patients; no admission for patients without breathlessness; paid teleconsultation of mild cases; ICU beds with ventilator care 3% (801 beds); Listing of hospitals with ECHMO machines; PPE 5 per patient (20,000 per day); Surgical masks usage: 2,13,760 per day; Hand sanitizers: at least 2 lac per day; Healthcare providers dedicated with coronavirus handling training: 20,000; 250 persons trained in handling dead bodies of infected cases; 500-1,000 dedicated mental health counselors to tackle coronavirus anxiety; 20 coronavirus spokesmen to speak the same language; Price cap of masks, other related diagnostics and PPEs; censoring of myths and fake news on social media and earmarked and segregated areas for coronavirus triage: suspect but not serious; suspect and serious; confirmed but not serious and confirmed and serious.

WHAT IS THE ROLE OF CMAAO IN COVID-19?

CMAAO has been covering the disease daily since it first came to notice and has issued timely alerts about COVID-19.

- 26th December 2019: Viruses like SARS detected and Chinese scientists alerted the world about it.
- 3rd January 2020: Transition from human-to-human raised concern.
- Despite this, on January 5, the Wuhan administration mentioned that the illness doesn't seem to unfold from people to people. China lastly formally confirmed on January 20 that the coronavirus was spreading from human-to-human.
- 7th January: WHO to monitor China's mysterious pneumonia of unknown virus outbreak
- 8th January: CMAAO warns Asian citizens traveling to China over mystery pneumonia outbreak.
- 10th January: It's a new strain of coronavirus in the China pneumonia.
- 13th January: China Virus Outbreak Linked to Seafood Market.
- 15th January: 1st Case of China Pneumonia Virus Found in Thailand outside China.
- 21st January: New China coronavirus can spread between humans.
- 22nd January: New China virus now in US, Thailand, Japan, South Korea and Taiwan: Will India or other Asian countries be spared?
- 23rd January: Coronavirus: Will it be declared as International Public Health Emergency by WHO
- 24th January: Coronavirus 1st death outside Wuhan Epicentre is reported. WHO Decision: Coronavirus is spreading, but the organization says it is not a global emergency.
- 25th January: Indian Govt. should pay for the treatment of India trapped in China with coronavirus.

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Sustenance in Chronic Kidney Disease: Beyond the Calorie Count

HEM SHANKER SHARMA*, ABHISHEK KUMAR TIWARI†

ABSTRACT

Diet and nutrition play key roles in the management of metabolic disorders like hypertension, obesity, hyperlipidemia and diabetes. All these conditions are linked with the pathogenesis of chronic kidney disease (CKD). Patients with CKD frequently exhibit a progressive loss of muscle and fat mass that may not be related to reduced intake alone. This article provides a comprehensive overview of protein-energy wasting (PEW) in CKD, including its etiology and the obesity paradox and the nutritional guiding principles.

Keywords: Chronic kidney disease, protein-energy wasting, nutrition, deficiencies, supplementation

DWINDLING GFR BLOCKING THE EXIT OF NITROGENOUS WASTE

Diet and nutrition have an extremely pivotal role to play in the management of metabolic disorders like hypertension, obesity, hyperlipidemia and diabetes, all of which are bonded stalwartly with the pathogenesis of chronic kidney disease (CKD).

As the glomerular filtration rate (GFR) experiences a downhill movement, the nitrogenous metabolites tend to be retained, resulting in a decreased ability to regulate the levels of electrolytes and water. Alongside this, certain vitamin deficiencies can occur due to dietary changes. Adding up, protein-energy depletion is frequently observed and predicts a pitiable outcome.

THE UNMET NEEDS OF NUTRITION: PROTEIN-ENERGY WASTING

Patients with CKD, particularly more advanced stages, frequently exhibit a progressive loss of muscle and fat mass that may not be related to reduced intake alone. Because malnutrition refers to an intake that is inappropriate for the needs of the individual, it can be misleading to use this blanket term when reduced intake is not necessarily the sole cause of wasting. Protein-energy wasting (PEW) is defined as a state of nutritional and metabolic derangements in patients with CKD that may negatively affect nutritional status and lean body mass, leading to frailty.

PERCEPTION OF PROTEIN-ENERGY WASTING

Protein-energy wasting was proposed in 2007 by the International Society of Renal Nutrition and Metabolism as a notion defining the multifactorial nature of metabolic processes and nutritional consequences of uremia in CKD. PEW involves a hypermetabolic state that promotes protein catabolism, attributed to both metabolic consequences of CKD—including inflammation, oxidative stress, uremia, metabolic acidosis, diminished efficacy of anabolic hormones and a multi-morbid condition—and the catabolic nature of hemodialysis (HD), which can lead to protein losses and muscle and fat wasting (Fig. 1).

Therefore, the reduction in energy and protein intake associated with PEW is often secondary to other factors, rather than a primary consequence of inadequate access to adequate energy and protein to meet nutritional needs, as in primary malnutrition. In clinical practice, the reduction in nutritional intake and causes may be difficult to separate because they are synergistic and may exacerbate each other.

*Associate Professor
†PG Student
Dept. of Internal Medicine, Jawahar Lal Nehru Medical College and Hospital, Bhagalpur, Bihar
Address for correspondence
Dr Hem Shanker Sharma
Associate Professor
Dept. of Internal Medicine
Jawahar Lal Nehru Medical College and Hospital, Mayaganj, Bhagalpur, Bihar 812001

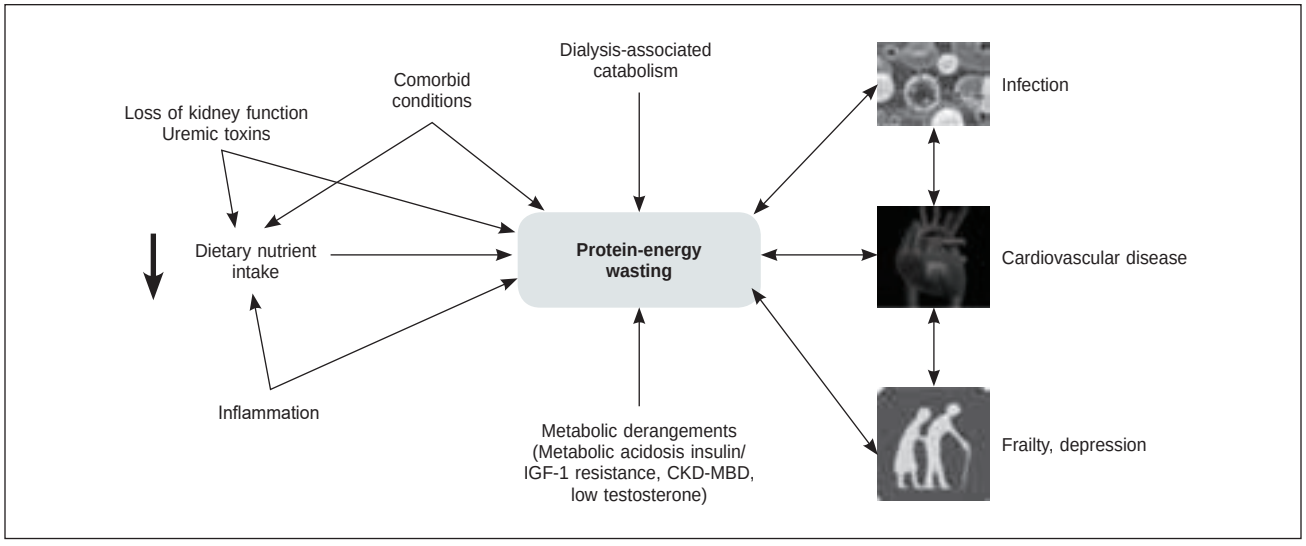

Figure 1. The conceptual model for protein-energy wasting in CKD.

CKD-MBD = Chronic kidney disease-mineral bone disorder; IGF-1 = Insulin-like growth factor 1.

PERPETRATOR OF PROTEIN-ENERGY WASTING IN CHRONIC KIDNEY DISEASE

Understanding the features that have a say in the etiology of PEW is critical to put in the picture, the suitable assessment and treatment strategies (Table 1). Furthermore, adequate nutritional intake will not alter some of the contributing factors, such as hypermetabolism secondary to inflammation, the reduction in anabolic response, the catabolic nature of HD, insulin resistance or frailty associated with reduced physical activity. A multifaceted therapeutic approach for this complex syndrome is therefore necessary.

The prevalence of PEW in dialysis patients ranges from 10% to 70%, depending on the choice of nutritional marker and the population studied. There is also diminished nutritional status before initiation of dialysis, which strongly predicts mortality on dialysis. Several factors contribute to the high incidence of PEW.

There is a spontaneous reduction in nutrient intake that parallels the decrease in GFR and is largely driven by CKD-associated anorexia. This anorexia is caused by impaired taste acuity and diminished olfactory function, medications, autonomic gastroparesis, psychological and socioeconomic factors and inadequate dialysis. Frailty, poverty, advanced age and multiple acute or chronic comorbidities also may contribute to suboptimal intake. Protein and amino acid losses occur during dialysis treatment. Metabolic acidosis and periods of acute or chronic illnesses may induce protein catabolism. This is mediated in large part through the ubiquitin-proteasome pathway of protein degradation.

Table 1. Causes of Protein-energy Wasting in CKD

Decreased protein and energy intake
• Anorexia, problem in organs involved in nutrient intake
• Dietary restrictions
• Depression, frailty, dependency
Hypermetabolism
• Increased energy expenditure
• Metabolic acidosis
• Inflammation
• Hormonal disorders
▪ Insulin resistance of CKD
▪ Increased glucocorticoid activity
Decreased anabolism
• Resistance to GH/IGF-1
• Testosterone deficiency
• Low thyroid hormone levels
Comorbidities and lifestyle
• Comorbidities (DM, CHF, depression, CAD, PVD)
• Poor physical activity
• Unhealthy dietary pattern
Dialysis
• Nutrient losses into dialysate
• Dialysis-related inflammation and hypermetabolism

CKD = Chronic kidney disease; GH = Growth hormone; IGF-1 = Insulin-like growth factor 1; DM = Diabetes mellitus; CHF = Congestive heart failure; CAD = Coronary artery disease; PVD = Peripheral vascular disease.

Chronic inflammation may contribute to both an increase in nutritional needs and anorexia. Alterations

in intestinal microbiota and increased permeability of the intestinal barrier may play a pivotal role in the pathogenesis of inflammation. Endocrine disorders, such as insulin resistance (associated with increased muscle breakdown), vitamin D deficiency and increased parathyroid hormone concentrations have long been considered contributors to PEW.

THE OBESITY PARADOX IN CKD: REVERSE EPIDEMIOLOGY

Although there is a high prevalence of PEW in patients with CKD associated with poorer outcomes, paradoxically a higher body mass index (BMI) is associated with better survival. This is termed *reverse epidemiology*.

APPRAISAL OF NUTRITIONAL STATUS

The measurement of nutritional status does not lend itself to one simple test, and a panel of measures is required.

Intake Composition

Diet history, recall and food diaries are the mainstays for estimation of dietary intake. In addition, a gradual decrease in blood urea nitrogen and reduced phosphate and potassium levels may indicate a decrease in protein intake in dialysis-dependent patients, and low serum cholesterol level may indicate a poor calorie intake. The emission of urea is easily calculated and is often used to estimate adequacy of dialysis. The protein equivalent of total nitrogen appearance (PNA) can be estimated on HD from interdialytic changes in urea nitrogen concentration in serum and the urea nitrogen content of urine and dialysate.

Index of Body Mass

The BMI (BMI = weight [kg]/height [m^2]) is the most commonly used parameter for nutritional assessment. BMI cannot distinguish muscle from fat mass and is affected by hydration status.

Composition of the Body

An assortment of techniques can make a distinction between body compartments on the basis of physical characteristics, which can provide information about nutritional state (body lean tissue and fat content) and hydration. Skinfold thickness can be used to assess body fat, and muscle mass can be assessed by measurement of mid-upper arm muscle circumference. Although these anthropometric parameters are inexpensive and relatively easy to measure, they are limited by inconsistency, both on the part of patient and examiner. Sequential measures of bioelectrical impedance are used as an appendage to the day-to-day clinical appraisal of hydration status and body composition management of patients on dialysis.

The Primeval Protein

Fluid status, impaired hepatic function, age and acute inflammatory conditions can affect albumin levels. However, despite its relatively longer half-life (20 days), albumin remains an important measure of nutritional status and health of the patient. Clinically, it may be possible to observe the growth of white nails when there has been a transient period of hypoalbuminemia. Serum transferrin is linked to body iron stores and may be altered with changes in iron status.

NUTRITIONAL GUIDING PRINCIPLES

Guideline campaigners advocate that it is important that dietary restrictions are not gratuitously made obligatory for each and every individual, rather the advice be tailored to the individual and altered as circumstances dictate (Table 2).

DYSREGULATED LIPID COMPOSITION

Although disturbances in lipid metabolism are commonly seen in CKD, there is a paucity of data on the effect of diet therapy in this group. A diet low in fat (particularly saturated fat) with an increased intake of soluble fiber may be helpful in reducing cholesterol levels, although the role of cholesterol lowering in CKD patients is controversial. Losing weight and consuming a diet lower in sugar may improve hypertriglyceridemia, but a balance needs to be struck between healthy eating concepts and nutritional adequacy.

VITAMINS, MINERALS AND TRACE ELEMENTS

Vitamins, minerals and trace elements deficiencies are not uncommon in patients with CKD and it relates to dietary restriction, dialysate losses and the necessity of integral renal function for normal metabolism of certain vitamins. However, the dietary requirements for patients with CKD are not lucid. Protein and potassium restrictions can lead to inadequate intakes of pyridoxine, vitamin B12, folic acid, vitamin C, iron and zinc. The use of recombinant human erythropoietin may increase the requisite for iron and folic acid. In the absence of firm guidance, it is prudent to have a low threshold for commencing water-soluble vitamin

Table 2. Nutritional Recommendations for CKD

Daily intake	Predialysis CKD	Hemodialysis	Peritoneal dialysis
Protein (g/kg ideal BW) (refer to KDOQI for estimation of adjusted edema-free BW)	0.6-1.0 Level depends on the nephrologist's viewpoint. 1.0 for nephrotic syndrome.	Min ≥1.1 Recommendations are in conjunction with an adequate energy intake. Requirements may be higher during illness because of multiple comorbidities or during acute periods of infection, including peritonitis.	Min 1.0-1.2
Energy (kcal/kg BW)	35 (<60 y) 30-35 (>60 y)	35 (<60 y) 30-35 (>60 y) 30-40 kcal/kg ideal BW	35 including dialysate calories (<60 y) 30-35 including dialysate calories (>60 y)
Sodium (mmol)	<100 (more if salt wasting)	<100	<100
Potassium	Reduce if hyperkalemic	Reduce if hyperkalemic	Reduce if hyperkalemic; potassium restriction is generally not required. May need to enhance potassium intake if hypokalemic.
	If hyperkalemic, advice will be to decrease certain foods (e.g., some fruits and vegetables) and giving information about cooking methods.		
Phosphorous	Reduce because of phosphate retention. Monitor levels. Advice will be to reduce certain foods (e.g., dairy, offal, some shellfish) and processed foods with high content of added phosphates, and giving information about the timing of binders with high-phosphorus meals and snacks.		

preparations. High-dose vitamin C supplements should be avoided in CKD because of the increased risk for secondary tissue oxalate deposition. A review on fat-soluble vitamins in advanced CKD concluded that there is universal agreement that supplementation with vitamin A is generally not recommended (unless a patient is receiving total parenteral nutrition) because deficiencies are rare, dialysis losses are minimal and buildup leading to toxicity can occur.

Vitamin E has been suggested to have antioxidant properties and beneficial effects for patients with CKD. Evidences suggest that most dialysis-dependent patients have subclinical vitamin K deficiency, and there is no known toxicity but, its benefits are waiting to get approval from the clinical trials. Novel, orally administered potassium-exchanging compounds are being investigated as possible treatment options for the management of hyperkalemia. Sodium zirconium cyclosilicate and patiromer act by enhancing potassium removal, predominantly through the gastrointestinal (GI) tract.

BENEVOLENT SUPPLEMENTATION

If food fortification advice is insufficient, supplements, in the form of high-protein, high-calorie drinks, powders and puddings, should be considered. Enteral tube feeding is also an option if nutrient intake cannot be increased sufficiently by use of oral supplements. Renal-specific tube feeds and supplements are available that have lower fluid and electrolyte contents. A systematic review suggested that enteric multinutrient support increases serum albumin concentration and improves total dietary intake in patients receiving maintenance dialysis.

The GI route is the preferred choice for nutritional supplementation. However, intradialytic parenteral nutrition (IDPN) has been used to provide intensive parenteral nutrient therapy with use of concentrated hypertonic solutions infused into the venous blood line three times weekly during HD treatments for patients who cannot tolerate oral or enteral administration of nutrients. IDPN typically provides 800-1200 kcal three times weekly, in the form of glucose and fat emulsion and 30-60 g of protein and so will only supplement rather than provide full nutritional needs.

Intraperitoneal amino acids (IPAAs) can be used in peritoneal dialysis. A 1.1% amino acid solution is substituted for glucose in peritoneal dialysis (PD) fluid, and about 80% of the amino acids are absorbed in a 4-hour period. The long-term effects of IPAAs on nutritional status and clinical outcomes are not known, and the solution is often used primarily to reduce glucose exposure. Expert opinion on the use of these approaches is inconsistent. The Kidney Disease Outcomes Quality Initiative (KDOQI) has suggested that IPAAs (for PD) or IDPN (for HD) should be considered for patients

who have evidence of protein or energy malnutrition and inadequate protein or energy intake and who are unable to tolerate adequate oral supplements or tube feeding.

HUNGER SYRUPS

Megestrol acetate, a progesterone derivative, moderately improves appetite in HD patients, as shown in small studies. However, megestrol acetate has adverse effects and larger trials are required before recommendations can be made for CKD patients. More studies are also required for ghrelin, anorexigenic hormone and melanocortin-receptor antagonists.

GUT-WELL-MICROBIOME

There is accumulating evidence that the GI tract may be a major source of chronic inflammation in CKD. It is hypothesized that altered diets (low potassium, phosphorus and fiber) may affect the gut microbiome, resulting in overgrowth of bacteria that produce uremic toxins and a leaky epithelial barrier that allows toxins to get into the circulation. It has been suggested that prebiotic and probiotic formulations may lower serum levels of uremic toxins. However, more trials investigating gut-targeted therapeutics are needed before they could be recommended for use in clinical practice.

pH BALANCE

Although some trials have shown no detrimental effect of mild metabolic acidosis, many others have reported that normalization of serum bicarbonate concentration is beneficial for protein nutritional status and bone metabolism. Current guidelines recommend the correction of acidosis in dialysis-dependent patients.

CONCLUSION

Protein-energy wasting is a relatively common metabolic complication inherent to CKD. A worsening of quality of life and an increase in the risk for comorbidities, hospitalizations and death accompany the onset and progression of PEW. The cause of PEW is multifactorial, involving undernutrition (insufficient or inadequate nutrient intake) and excess protein catabolism that altogether favors the progressive and continuous loss of energy and fat fuels. This multifactorial nature makes diagnosis difficult; it must be based on the combined interpretation of complementary nutritional screening and assessment tools.

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Typhoid Fever – An Overview

Good Hygiene is the Key to Prevent Typhoid Fever

RAGHAVENDRA RAO MV*, DILIP MATHAI†, MOHAMMED KHALEEL‡, KHIZER HUSSAIN JUNAIDY#, JITHENDRA KUMAR NAIK$

ABSTRACT

All animals are susceptible to infection with *Salmonella*, a genus of Gram-negative, non-spore forming, usually motile, facultative anaerobic bacilli belonging to the family *Enterobacteriaceae. Salmonella* are differentiated into over 2,200 serologically distinct types (serotypes) based on differences in somatic, flagellar and capsular antigens. *Salmonella* Typhi causes the most severe form of enteric fever/typhoid fever. Unlike the other serotypes of *Salmonella*, humans are the only known host for this pathogen. The infection is commonly spread through fecal contaminated food and water. Typhoid fever has a slow, insidious onset and if untreated, lasts for weeks. The primary symptom is slowly rising fever often accompanied by abdominal pain. It ends either by a gradual resolution or in death due to complications (rupture of intestine or spleen). All infections occur almost always via oral route, usually with water or food contaminated by sewage or via hands of carrier.

Keywords: Vi polysaccharide vaccine, adenylate cyclase, randomized controlled trials, chloramphenicol, streptomycin, sulfonamide, tetracycline

Salmonella is a human and animal pathogen that causes considerable disease burden worldwide. The genus contains two species, *Salmonella bongori* and *Salmonella enterica.* In the United States, an estimated 11% of the foodborne illnesses are caused by *Salmonella.* The two most common disease manifestations of human *Salmonella* infections are gastroenteritis and typhoid fever. *Salmonella* Typhi and *Salmonella* Paratyphi A can cause typhoid fever, a more severe systemic disease. Salmonellosis outbreaks have been linked to the consumption of fruits, leafy green vegetables, sprouts, eggs, milk products and meat. Enteric fever is a systemic infection caused by *Salmonella* Typhi and Paratyphi A, B and C and is a significant cause of morbidity and mortality. Interactions between *Salmonella* spp. and the native microbial communities are hypothesized to contribute to the ability of this human pathogen to colonize. The typhoid fever surveillance in Africa program (TSAP) revealed a significant burden of *Salmonella* disease in sub-Saharan Africa. Low moisture foods (LMF), including spices and seasonings, dried protein products, such as dried eggs or dried milk and seeds, have been increasingly implicated as the source of foodborne Salmonellosis outbreaks.

Although most microbial hazards cannot grow in LMFs due to the low water activity (a_w), many pathogens can survive and remain viable for months to years in these foods, posing potential risks to consumers.

Several national and international outbreaks of foodborne illnesses, as well as product recalls, have occurred in recent years due to *Salmonella* spp. contamination of LMF products such as spices, nuts (including peanut butter), cereal products (e.g., breakfast cereals), tahini paste and chocolate, among many others.

Recent high-profile outbreaks of foodborne illness and product recalls due to microbial contamination of LMF, particularly from *Salmonella* spp., have increased global attention and response to the microbial safety of LMF.

S. enterica subspecies serovar Typhi *(S.* Typhi) is a major cause of invasive bacterial infection, particularly in children in low- and middle-income countries. Vaccines available for prevention of typhoid fever include

*Scientist-Emeritus and Director of Central Research Laboratory
†Professor of Medicine and Dean
Apollo Institute of Medical Sciences and Research, Hyderabad, Telangana
‡Professor of Microbiology, Clinical and Diagnostic Microbiologist
Dept. of Microbiology, Deccan College of Medical Sciences, Hyderabad, Telangana
#Resident, Dept. of Pharmacology, Gandhi Medical College, Secunderabad, Telangana
$Professor of Toxicology, Dept. of Zoology, Osmania University, Hyderabad, Telangana
Address for correspondence
Dr MV Raghavendra Rao
Scientist-Emeritus and Director of Central Research Laboratory
Apollo Institute of Medical Sciences and Research, Hyderabad, Telangana
E-mail: reachdrmvrrao@gmail.com; Dr.rao_m@apolloimsr.edu.in

Vi capsular polysaccharide vaccine (Vi-CPS) and live attenuated oral vaccine Ty21a.

Vaccination against *S.* Typhi using the Vi-CPS, a T-cell independent antigen, can protect from the development of typhoid fever. This implies that antibodies to Vi alone can protect in the absence of a T-cell-mediated immune response; however, protective Vi antibodies have not been well-characterized.

Enteric fever is principally caused by *S. enterica* serovar Typhi *(S.* Typhi*). S.* Typhi is the leading pathogen isolated from blood cultures in South Asia.

The fatality rate of enteric fever is low (<1%) but it is higher when antimicrobial therapy is delayed or unavailable.

Alternative molecular serotyping methods have been described previously, including pulsed-field gel electrophoresis, sequence-based polymerase chain reaction (PCR) (rep-PCR) and combined PCR- and sequencing-based approach that directly targets O- and H-antigen-encoding genes.

Paratyphoid fever, however, often shows milder symptoms than that of *S.* Typhi infection.

Typhoid *Salmonellae* are human-restricted, and nontyphoidal *Salmonella* (NTS) are broad host-range serovars infecting both humans and animals.

Symptoms of typhoid include fever, headache, weight loss, lethargy, stupor, malaise, leukopenia, thrombocytopenia, gastrointestinal bleeding and neurological complications.

Healthy carriers shed *S.* Typhi in their stool, which passes on the bacterium through the contamination of food and water sources.

CHRONOLOGICAL RECORD OF SIGNIFICANT EVENTS

Salmonellae are Gram-negative motile bacilli. The genus *Salmonella* belongs to the family *Enterobacteriaceae*. Daniel E Salmon first isolated *Salmonella*. In 1880, Karl Joseph Eberth described a bacillus that he suspected was the cause of typhoid.

In 1884, pathologist Georg Theodor August Gaffky (1850-1918) confirmed Eberth's findings.

British bacteriologist Almroth Edward Wright first developed an effective typhoid vaccine at the Army Medical School in Netley, Hampshire. It was introduced in 1896 and was used successfully by the British during the Boer War in South Africa.

Karl Joseph Eberth, doctor and student of Rudolf Virchow, in 1879 discovered the bacillus in the abdominal lymph nodes and the spleen. He went on to publish his observations in 1880 and 1881. His discovery was then verified and confirmed by German and English bacteriologists, including Robert Koch.

The genus "*Salmonella*" was named after Daniel Elmer Salmon, an American veterinary pathologist, who was the administrator of the USDA research program, and thus the organism was named after him, despite the fact that several scientists had contributed to the quest.

In 1909, Frederick F Russell, a US Army physician, adopted Wright's typhoid vaccine for use with the army, and 2 years later, his vaccination program became the first in which an entire army was immunized. It eliminated typhoid as a significant cause of morbidity and mortality in the US military.

As a cook of Sloane Maternity in Manhattan, Mary Mallon contaminated, over a period of 3 months, at least 25 people, doctors, nurses and staff. Two of them died. She had managed to be hired as "Mary Brown". Since then, she was stigmatized as "Typhoid Mary" and became the butt of jokes, cartoons and eventually "Typhoid Mary" appeared in medical dictionaries, as a disease carrier.

Both salmonellosis and the microorganism genus *Salmonella* derive their names from a modern Latin coining after Daniel E Salmon.

CLINICAL PRESENTATION

Without treatment, some patients develop sustained fever, bradycardia, hepatosplenomegaly, abdominal symptoms and occasionally, pneumonia. In white-skinned patients, pink spots, which fade on pressure, appear on the skin of the trunk in up to 20% of cases. In the third week, untreated cases may develop gastrointestinal and cerebral complications, which may prove fatal in up to 10-20% of cases. The highest case fatality rates are reported in children under 4 years. Around 2-5% of those who contract typhoid fever become chronic carriers, as bacteria persist in the biliary tract after symptoms have resolved.

THE MECHANISM INVOLVED IN TYPHOID FEVER/ ENTERIC FEVER

Enteric fever is endemic in many developing countries due to poor sanitation and substandard water supply.

Enteric fever is caused due to infection by the genus *Salmonella,* which comprises of *S.* Typhi, *S.* Paratyphi A, *S.* Paratyphi B, *S.* Paratyphi C. All these organisms can cause a bacteremic illness known as enteric fever.

In the initial stages of infection, the pathogen invades small and larger bowel walls, creating an inflammatory response. It is an intracellular pathogen.

The infection is spread to the body via the regional lymph nodes and bloodstream. Initial symptoms of infection are headache, fever, general malaise and abdominal tenderness. Once the organism has spread throughout the body, it reaches the gallbladder and payer's patches in the colon, initiating the diarrheal illness.

The organism can frequently be recovered from blood and stool cultures. Appropriate antibiotic use results in clinical improvement; however, stool cultures often remain positive, which can serve as a source of infection for other individuals. Some patients can develop chronic colonization of their gallbladder, biliary tree, leading to persistent shedding of the organism with potential transmission to others.

S. Typhi is a human host-restricted pathogen that is responsible for typhoid fever in approximately 10.9 million people annually. The typhoid toxin is postulated to have a central role in disease pathogenesis, the establishment of chronic infection and human host restriction.

Mucosal invasion and inflammation are clearly important, at least accounting for the bloody mucoid type of stools, which occur commonly but do not explain the copious watery stool in early stages. Observations in experimental animals of enteropathy with water and electrolyte transport defects suggest the existence of secretary mechanisms.

Production of prostaglandins and other mediators by the inflammatory tissues and toxin production by the organisms have been suggested. *Salmonella* produces an enterotoxin and a cytotoxin. The enterotoxin activates adenylate cyclase and has some physicochemical characteristics in common with cholera toxin but limited antigenic homology.

Typhoid fever is caused by the bacterium *S. enterica* subsp. *enterica* serovar Typhi. It is mainly due to the inadequate access to safe water and sanitation, which is a major problem in developing countries. The global burden of typhoid fever was estimated to be 12 million cases and 1,30,000 deaths in the year 2010. It exceeded 100 cases per 1,00,000 people/year in South East Asian countries, and has especially high burden rates in India. A recent systematic review and meta-analysis estimated the prevalence of laboratory confirmed typhoid and paratyphoid cases in India to be 9.7 and 0.9%, respectively.

NEW APPROACHES IN THE DETECTION OF *SALMONELLA*

Randomized controlled trials (RCTs) have found that people with *Salmonella* infection treated with norfloxacin versus placebo had significantly prolonged excretion of *Salmonella* species. In addition, six of nine Campylobacter isolates obtained after treatment showed some degree of resistance to norfloxacin.

Continued evolution of antimicrobial resistance among enteric pathogens has meant that agents previously found to be effective in clinical trials, such as trimethoprim-sulfamethoxazole or ampicillin, no longer show *in vivo* activity.

Molecular techniques for the detection of *Salmonella* species such as PCR, offer considerable advantages in terms of specificity, speed, and standardization over the conventional methodologies. However, it is difficult to perform PCR directly on fecal samples due to presence of inhibitory substances and large quantities of bacterial DNA extraction from feces can be improved by pre-treating the sample with polyvinylpyrrolidone (PVP).

It has been found that culture and PCR methods used for detection of *Salmonella* from clinical fecal samples were of similar sensitivity. However, culture results are available in 2-3 days, whereas those obtained by real-time PCR assays can be available within 3 hours, which can be advantageous for rapid intervention and appropriate treatment.

RECENT ADVANCES IN DIAGNOSTIC TECHNOLOGY

In enteric fever and septicemia, blood culture results are often positive in the first week of the disease.

In enteric fever, the stools yield positive results from the second or third week on. In enterocolitis, the stools yield positive results during the first week. Bone marrow cultures may be useful. Urine culture reports may be positive after the second week. A positive culture of duodenal drainage establishes the presence of *Salmonellae* in the biliary tract in carriers. EMB, MacConkey or deoxycholate medium permits rapid detection of lactose nonfermenters (not only *Salmonellae* and *Shigellae* but also *Proteus, Pseudomonas,* etc.) Bismuth sulfate medium permits rapid detection of *Salmonellae,* which form black colonies because of H2S production. Many *Salmonellae* produce H2S.

The specimen is plated on *Salmonella-Shigella* (SS) agar, hektoen enteric (HE) agar, Xylose-lysine decarboxylase (XLD) agar or deoxycholate-citrate agar, which favors the growth of *Salmonellae* and *Shigellae* over other

Enterobacteriaceae. The stool specimen is also put into selenite F or tetrathionate broth. Both of these inhibit replication of normal intestinal bacteria and permit multiplication of *Salmonellae*. After incubation for 1-2 days, this is plated on differential selective media. Suspect colonies are identified by biochemical reaction patterns and slide agglutination tests.

Hektoen enteric agar was introduced in 1968 by Sylvia King and William I Metzger. They formulated HE agar medium while working at the Hektoen Institute in Chicago, to increase the recovery of *Salmonella* and *Shigella* from clinical specimens. It is a selective as well as differential medium. HE agar is currently used as both a direct and indirect plating medium for fecal specimens to enhance the recovery of species of *Salmonella* and *Shigella* from heavy numbers of mixed normal fecal flora.

The gold standard diagnosis of enteric fever is the isolation of the organism from the blood, bone marrow, stool or urine. A number of serological assays has been overutilized in this part of the world but need to be discouraged for the diagnosis of such acute infection.

The Widal test has been in use for the past 100 years but at times, it can be misleading. Its potential to yield false-positive and false-negative results limits its use. This assay can be misleading in endemic countries and no interpretive titer should be recommended. Urinary antigen detection assays have also not been able to improve the diagnostic yield. Some rapid agglutination tests for *S.* Typhi alone are in use, but their utility cannot be evaluated due to a lack of data.

BIOTECHNOLOGY OF MOLECULAR DIAGNOSIS OF ENTERIC FEVER

Detection methods rely on traditional bacterial culture procedures that employ the use of serial enrichments with increasing selectivity culminating in the isolation of *Salmonella* on selective-differential agar plates.

Even with newer automated technologies that permit simultaneous testing of multiple analytes, at least 24 hours are needed for confirmation of *Salmonella.*

DNA fingerprinting techniques, such as pulsed-field gel electrophoresis (PFGE), ribotyping and intergenic sequence (IGS) ribotyping, have all been used to subtype *Salmonella* isolates.

For ribotyping, genomic DNA is digested, separated on an agarose gel and then hybridized to rRNA operons to visualize the banding pattern.

After comparison to a database of fingerprints species, serovar and occasionally strain identifications can be made.

The DNA fragments are separated on an agarose gel subjected to a pulsed electric field. DNA is visualized by ethidium bromide staining and fingerprints are analyzed using specific software.

PCR as a diagnostic modality for typhoid fever was first evaluated in 1993 when Song et al successfully amplified the flagellin gene of *S.* Typhi in all cases of culture proven typhoid fever and from none of the healthy controls. Studies have reported excellent sensitivity and specificity when compared to positive and healthy controls. The turnaround time for diagnosis has been less than 24 hours.

OPENING THE DEBATE ON THE MANAGEMENT OF TYPHOID FEVER/ENTERIC FEVER

Because of the efficacy and low relapse and carrier rates, associated with their use, the four quinolone drugs are now the drugs of choice in the treatment of adult typhoid fever.

However, because of cheapness, chloramphenicol will continue to be used in areas where the local strains are sensitive. Azithromycin may be in the future a useful alternative, especially in children.

Early Recognition and Management of Enteric Fever/Typhoid Fever

Salmonellae were the foremost of the food poisoning organisms for almost the whole of the 20th century. A dirty and unhygienic toilet is a source of many infectious diseases such as typhoid, cholera, hepatitis A and other diarrheal diseases, including parasitic infestations.

Hence, toilet hygiene is essential for good health. Timely and appropriate management of typhoid fever can reduce both morbidity and mortality. During the past two decades, *Salmonella enteritidis* has emerged as a leading cause of human infections in many countries, with hen eggs being a principal source of the pathogen. This has been attributed to this serovar's unusual ability to colonize ovarian tissue of hens and be present within the contents of intact shell eggs. Broiler chicken is the main type of chicken consumed as poultry in many countries. Large percentages are colonized by *Salmonellae* during grow-out and the skin and meat of carcasses are frequently contaminated by the pathogen during slaughter and processing. Considering the major role eggs and poultry have as vehicles of human cases of salmonellosis, an assessment of different factors affecting

the prevalence, growth and transmission of *Salmonella* in eggs and on broiler chicken carcasses and the related risk of human illness would be useful to risk managers in identifying the intervention strategies that would have the greatest impact on reducing human infections.

RESEARCHERS STRUGGLE TO DEVELOP A NEW TREATMENT FOR ENTERIC FEVER/TYPHOID FEVER

Patients with persistent vomiting, inability to take oral food, severe diarrhea and abdominal distention usually require parenteral antibiotic therapy, preferably in a hospital. Antibiotic therapy must be guided by *in vitro* sensitivity testing.

Chloramphenicol (500 mg 4 times daily), ampicillin (750 mg 4 times daily) and co-trimoxazole (2 tablets or IV equivalent twice daily) are losing their effectiveness due to resistance in many areas of the world, especially India and South East Asia. Fluoroquinolones are the drugs of choice (e.g., Ciprofloxacin 500 mg twice daily), if nalidixic acid screening predicts susceptibility, but resistance is common, especially in the Indian subcontinent and also in the UK.

Extended-spectrum cephalosporins are useful alternatives but have slightly increased treatment failure rate. Azithromycin 500 mg once daily is an alternative when fluoroquinolone resistance is present. *Salmonella*-resistant to chloramphenicol can respond to norfloxacin, ciprofloxacin therapy. For gastroenteritis in uncompromised hosts, antibiotic therapy is often not needed and may prolong the convalescent carrier state. For enteric fever, appropriate antibiotics include beta-lactams and fluoroquinolones.

With the limitations of the two existing *Salmonella* vaccines, particularly their lack of effectiveness in young children, along with their lack of widespread uptake in endemic countries, the *Salmonella* community and global health policymakers are keenly awaiting the arrival of new vaccines against *Salmonella.* Vaccine is indicated for those persons who travel or live in areas where typhoid fever is endemic. Multidrug resistance transmitted genetically by plasmids among the strains of *S.* Typhi had been reported for the first time in 1972 from Mexico. The transmissible plasmids carry R determinants to chloramphenicol, streptomycin and sulfonamide and tetracycline. Multiple drug resistance has become a problem in India and South East Asia. Chloramphenicol-resistant typhoid fever had appeared first in epidemic form in Kerala (Calicut), India in 1972. The drug-resistant strains of *S.* Typhi that had been reported from India were originally confined to include phase D1-N, but later to types C5, A and O.

Prevention

Handwashing with soap and water is the simplest and also the most economical way to remove dirt and prevent the transmission of harmful microorganisms and control the spread of infection. But, it is important to choose the right type (quality) of soap. The quality (or grading) of soap is determined by the total fatty matter (TFM), defined as the total amount of fatty matter (fatty acids - oleic, stearic and palmitic), which can be separated from a sample after splitting with mineral acid (hydrochloric acid).

Hand hygiene is inexpensive and forms an integral part of infection control practices in healthcare. Our hands are home to two types of bacterial flora - the resident flora and the transient flora.

The resident flora is found in the deeper layers of skin. Proper sewage disposal, correct handling of food and good personal hygiene are important for prevention. Between 1995 and 2008, Bangladesh made significant progress in providing improved sanitation services throughout the country.

Vaccination is recommended for people who travel from developed countries to endemic areas including Asia, Africa and Latin America.

AN OPINION ARRIVED AT THROUGH A PROCESS OF REASONING

Outbreaks make the news, but most cases occur in individuals or as sporadic events.

Current surveillance systems remain insensitive to diffuse and sporadic cases and resources for laboratory investigations are limited. Food-borne illnesses are an important public health challenge. The new discoveries are probably a result of - 1) Recent acquisition of key virulence factors and 2) Detection of newly developed laboratory methodologies.

There is a need for education programs that inculcate the importance of good agriculture practices, as well as safe post-harvest handling and preparation of food.

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US$675 Million Required for New Coronavirus Global Preparedness and Response Plan

In order to fight further spread of the new coronavirus outbreak in China and across the globe, and protect states with weaker health systems, the international community has launched a US$675 million preparedness and response plan covering the months of February to April 2020.

"My biggest worry is that there are countries today who do not have the systems in place to detect people who have contracted the virus, even if it were to emerge," said Dr Tedros Adhanom Ghebreyesus, WHO Director-General. "Urgent support is needed to bolster weak health systems to detect, diagnose and care for people with the virus, to prevent further human to human transmission and protect health workers." (*WHO*)

Global Measles Vaccination Campaign to Protect up to 45 Million Children

Gavi, the Vaccine Alliance, is set to help vaccinate up to 45 million children in 7 developing countries over the next 6 months in a series of major vaccination campaigns to curb a recent rise in global measles cases.

The campaigns will be conducted by governments with funding from Gavi and support from Vaccine Alliance and Measles & Rubella Initiative (M&RI) partners, including the WHO and UNICEF. The focus will be on children under 5 years old, with Bangladesh also aiming to reach children under 9 years of age… (*UNICEF*)

Lower Glucose Treatment Threshold OK for Newborn Brain

Lower glucose targets for otherwise healthy newborns at risk for hypoglycemia did not result in worse cognition in a randomized noninferiority trial. Compared to the traditional treatment threshold of 47 mg/dL, giving treatment to newborns only when the glucose level fell below 36 mg/dL led to similar average cognitive scores at 18 months (102.9 for lower threshold vs. 102.2, mean difference 0.7, 97.5% CI -1.5 to 2.9), reported researchers in the *New England Journal of Medicine*.

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Unscheduled Emergency Department Revisits in a Tertiary Care Hospital – A Quality Improvement Study

MOHAMMED NAZIM KT*, NITHYANAND M†, DODIY HERMAN‡, SOURABH M PRAKASH*, SHAHANA SHERIN#, BENITA FLORENCE¥

ABSTRACT

Patients who revisit the emergency department (ED) within 72 hours constitute an integral key performance indicator of quality emergency care. The number of patient footfalls to the ED in a tertiary care hospital in a rural area of a district in India from December 1, 2018 to May 31, 2019 was 7,808 and the average re-attendances recorded during that period was 0.32%. With increase in the number of healthcare setups, rising standards of the healthcare industry and increase in the expectations of the population visiting hospitals, ED re-attendance within 72 hours has been considered as an important key performance indicator of emergency patient care. The early ED revisit rate at this tertiary care hospital for 6 months was found to be only 0.32% (at an average of 4 cases per month). This is less when compared to many other international hospitals where it ranges from 1.5% to 2.5%. Since readmissions cause unnecessary overcrowding in ED, it would be best if each hospital evaluated their rate of readmission and its causes, and then tried to address the problems found. This can be effective in better management of ED, reduction of treatment costs, increasing patient satisfaction and prevention of ED overcrowding.

Keywords: Emergency department visit, revisit, emergency care

Patients presenting to the emergency department (ED) have been gradually increasing all over the world over the last few years.[1,2] Unscheduled return visit to the ED within 72 hours is a proposed quality indicator by the Royal College of Emergency Medicine. These visits include critically ill patients and those with acute illnesses. However, over the last few years, there has been an increasing trend of stable patients registering themselves in the ED to be seen immediately and demanding early disposal based on first-cum-first serve basis, irrespective of their illness or the triage category. This adds on to the stress faced by frontline healthcare personnel.

With increase in the number of healthcare setups, rising standards of the healthcare industry and increase in the expectations of the population visiting hospitals, ED re-attendance within 72 hours has been considered as an important key performance indicator of emergency patient care. The revisits can be due to various reasons such as nature of the disease, medical errors, deficiencies in initial management, missed diagnosis, noncompliance with medications prescribed, etc.[3]

ED revisits may include patients belonging to high-risk population, those with suboptimal discharge summaries and those approaching due to overcrowding, resulting in decreased efficiency of the working staff.

One of the major concerns for hospital managers and clinicians as a step towards quality improvement is reduction in the number of re-attendances in the ED. An unscheduled repeat visit by a patient within a short period (within 72 hours) after discharge from the ED is known as an early revisit. Over the past decades, a

*MRCP Trainee
†Clinical Coordinator
Dept. of Emergency Medicine
DM Wayanad Institute of Medical Sciences, Wayanad, Kerala, India
‡Consultant
Dept. of Emergency Medicine, Shrewsbury and Telford Hospital, UK
#Resident
Dept. of Emergency Medicine
DM Wayanad Institute of Medical Sciences, Wayanad, Kerala, India
¥Specialty Doctor
Dept. of Emergency Medicine, Shrewsbury and Telford Hospital, UK
Address for correspondence
Dr Benita Florence
Specialty Doctor
Dept. of Emergency Medicine, Shrewsbury and Telford Hospital, UK
E-mail: benitaflorence@yahoo.com

lot of research work has been carried out related to ED re-attendances.

One of the purposes of this study is to help clinicians analyze some clinical factors that might have been missed in routine emergency care and to rectify and avoid the same mistake again.

Considering all the above factors a retrospective audit was conducted in the ED of DM Wayanad Institute of Medical Sciences, Wayanad, Kerala, India, for a period of 6 months, i.e., December 1, 2018 to May 31, 2019.

The main objectives of this study were to identify the following:

- The rates of ED revisits in the duration mentioned above in this tertiary care hospital.
- The reasons for patients revisiting ED in less than 72 hours of discharge from ED.
- The demographic profile of these patients.
- Corrective measures that need to be taken to avoid these revisits.

METHODOLOGY

A register was maintained in the ED where patients who revisit within 72 hours are documented along with the reason for revisit, time and other basic demographic details. The revisit cases from December 1, 2018 to May 30, 2019 were noted and analyzed.

A total of 25 patients had revisited during this period. Cases in which the patients were initially advised for admission but were not willing or took discharge against medical advice (DAMA) or were leaving against medical advice (LAMA), were excluded from the study. The diagnoses of the revisiting patients were assessed.

RESULTS

The number of patients who had visited the ED during this period was 7,808. Twenty-five patients revisited in less than 72 hours and this was an acceptable 0.32%. Out of these 25 patients, there was a change in diagnosis in 11 patients. The demography showed 16 males and 9 females. Pediatric (<15 years) cases were 6 in number, 13 patients were in the age group of 16-45 years and 6 of them were more than 45 years of age.

- Of the 25 cases, 9 were discharged (36%) and 15 cases were admitted (60%) and 1 patient was discharged against medical advice (4%).
- Maximum numbers of revisits were in the month of March (8 cases) and minimum in April (1 case) (Fig. 1).

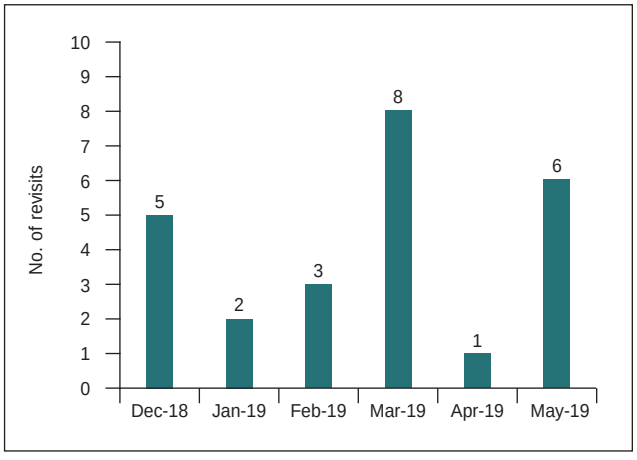

Figure 1. Graph showing number of revisits on a monthly basis over a period of 6 months (December 2018 to May 2019).

- Males were more in number than females (16:9).
- There was a significant variation in the diagnoses of the 11 out of 25 ED revisit cases compared to their initial visits (i.e., 44% of the revisit cases had a different diagnosis within 72 hours of their discharge from ED).
- It was noted that 9 patients had visited on weekends or public holidays.
- Twelve out of the 25 patients had their first visit during off regular working hours, especially the early morning hours.

DISCUSSION

The early ED revisit rate is regarded as a quality of care indicator and a tool for improving the quality of care provided to ED patients. ED staff who care for patients making an early revisit are responsible for managing patients' problems with discretion. Patients who make early ED revisits have increased mortality risk and are at high risk of medical and legal problems arising from medical errors or patient dissatisfaction.

A study comparing the results of readmission rates in various hospitals worldwide concluded that the causes can vary not only among different countries but also among different hospitals of the same country.[4]

Unplanned ED revisits are associated with medical errors in prognosis, treatment, follow-up care and information. With free availability of over-the-counter drugs causing masking of clinical features, frequent change of clinicians and unavailability of treatment documents makes it difficult to differentiate between the natural course of a disease, partially treated infections, anxiety of the patient, medical errors or missed diagnosis.

It has been recognized that senior emergency physicians are more aware of the fact that "medicine is an uncertain science", as compared with the junior emergency physicians.[5] This could be the reason for the revisits on weekends, public holidays or off regular duty hours.

The parameters that assessed the quality of medical care provided by an ED were described under the following headings: mortality rate, revisit rate, patient waiting time, and the number of patients who left the ED without being seen by a doctor.[6]

Though ED revisits are quality indicators in the Western Countries, less data is available for comparison from India.

The early ED revisit rate at this tertiary care hospital for 6 months was found to be only 0.32% (at an average of 4 cases per month). This is less when compared to many other international hospitals where it ranges from 1.5% to 2.5%.

One of the reasons for this could be the prolonged waiting period for consulting specialists; so patients tend to revisit ED much more in the western countries than in India.

CONCLUSION

Our ED early revisit rates could be improved to bring it further below the observed levels. Most of the revisits were attributed to the disease factor itself. Some of the causes were avoidable and hence necessary actions should be evaluated and implemented in future.

Further prospective studies are needed to evaluate the most common and the most serious causes of revisits to see if and how improvements can be made.

Since readmissions cause unnecessary overcrowding in ED, it would be best if each hospital evaluated their rate of readmission and its causes, and then tried to address the problems found. This can help in better management of ED, reduction of treatment costs, increasing patient satisfaction and prevention of ED overcrowding.

An action plan and recommendation to reduce the ED revisit time further, to involve ED consultants in encountering difficult cases or as an when required, to evaluate patients appropriately and involve multiple departments promptly when the requirements are felt needs to be brought into practice.

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Vegetarian Diet Tied to Lower Stroke Risk

A vegetarian diet rich in nuts, vegetables and soy has been found to be associated with a lower risk of both ischemic and hemorrhagic stroke, in a new research published online in *Neurology*.

In two large cohorts of over 13,000 individuals, a vegetarian diet was shown to be linked with a 60-74% decreased risk of ischemic stroke and 65% lower risk of hemorrhagic stroke.

Targeted Treatment for Pancreatic Cancer Beneficial

Patients with pancreatic cancer linked with specific mutations lived a year longer on receiving a therapy targeting the mutation protein, suggested a retrospective review of more than 1,000 cases. Treatment targeting actionable mutations yielded a median overall survival (OS) of 2.58 years as compared with 1.51 years for patients who had actionable mutations but were not given targeted therapy. Patients who received targeted therapies also lived more than a year longer in comparison with patients who did not have cancers with actionable mutations, reported researchers in *Lancet Oncology*.

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Effectiveness of Contraceptive Counseling: Prime Practices to Ensure Quality Communication and Enable Effective Contraceptive Use

SUNITA CHANDRA*, SUHANI CHANDRA†, ADITI JAIN‡

ABSTRACT

Background: Effectiveness is the leading characteristic for most women when choosing a contraceptive method, but they often are not well-informed about the effectiveness of the methods. Because of the serious consequences of misinformed choice, counseling should proactively discuss the most effective methods—long-acting reversible contraceptives and permanent methods—using the WHO tiered-effectiveness model. **Methods:** One hundred twenty-six postpartum women in the age group of 16-35 years, requesting contraception, were enrolled in the study at Rajendra Nagar Hospital & IVF Centre, Lucknow from February 2018 to December 2019. Meticulous contraception counseling was administered using a definitive protocol with comprehensive education material on the available contraceptive methods. Questions were explored about the information on the women's pre- and post-counseling choice of contraceptive method, her perceptions and the reasons behind her post-counseling decision were filled by the participating women. **Results:** Maximum women enrolled for the study were in the age group of 22-29 years. In pre-counseling evaluation, 40% postpartum women selected a contraceptive method, 20% a nonhormonal method and 12% a hormonal method. After meticulous contraception counseling, 95% of women chose a contraceptive method. There were significant differences between the women's choices of contraceptive methods in the pre- and post-counseling sessions. **Conclusion:** This study showed that progesterone-only pills (POPs) are the most frequently preferred contraceptive methods among postpartum women followed by inj-DMPA and then IUD. Using standardized protocol, proper and meticulous counseling resulted in a significant increase in selection of contraceptive methods by postpartum women.

Keywords: Postpartum women, contraception counseling, intrauterine device, progesterone-only pills

Family planning in a country like ours is largely dependent on the efforts sponsored by the government. Between 1965 and 2009, contraceptive usage was reported to increase threefold (from 13% of married women in 1970 to 48% in 2009) and the fertility rate was reported to have nearly halved (from 5.7 in 1966 to 2.4 in 2012). The national fertility rate still remains high, raising concerns for long-term population growth. Every year, India adds more people to world population numbers than any other country.[1-5] Family planning should be a priority in order to restrict the projected population of 2 billion by the end of the twenty-first century.

In 2015, the total fertility rate of India was 2.3 births per woman.[6] There were an estimated 15.6 million abortions, with an abortion rate of 47.0 abortions per 1,000 women aged 15-49 years. The rate of unintended pregnancies was 70.1 per 1,000 women aged 15-49 years.[7] Overall, the abortions in India made up for one-third of pregnancies and out of all pregnancies, almost half were not planned.[7] On the Demographic Transition Model, India is currently in the third stage owing to a decline in birth rates and death rates.[8] By 2026, it is projected to enter in stage 4 once the total fertility rate reaches 2.1.

MATERIAL AND METHODS

Subjects

One hundred twenty-six postpartum women in the age group of 16-35 years, requesting contraception, were enrolled in the study at Rajendra Nagar Hospital

*Chairperson and Director
†Consultant
Rajendra Nagar Hospital & IVF Centre, Lucknow, Uttar Pradesh
‡Consultant, Jain Hospital, New Delhi
Address for correspondence
Dr Sunita Chandra
74, Second Street, Rajendra Nagar, Lucknow - 226 004, Uttar Pradesh
E-mail: drschandra50@gmail.com

and IVF Centre, Lucknow from February 2018 to December 2019, within 8 weeks of delivery. All the study participants were counseled for hormonal and nonhormonal methods of contraception. The sample size with 80% power was calculated based on the assumption that the survey will detect at least a 25% increase in the proportion of women choosing a method (the more reliable contraceptive methods: progesterone-only pill [POP], injectable contraceptive, intrauterine system [IUS], intrauterine device [IUD]/condoms/lactation amenorrhea) after counseling compared to that before counseling. Underlying assumption was that 25% of women switch from less-reliable contraceptive methods (e.g., withdrawal, fertility-based awareness techniques, improper lactation amenorrhea method) or contraception choice to more-reliable contraceptive methods (e.g., POP, injectable contraceptive, IUD, IUS, condoms/proper lactation amenorrhea) after counseling. The type 1 error probability associated with this test of this null hypothesis was 0.05. The uncorrected Chi-squared statistic was used to evaluate this null hypothesis.

Inclusion criteria

- Postpartum women within 8 weeks of delivery.
- Women who agreed to sign an informed consent form.

Exclusion criteria

- Postpartum women choosing permanent method of contraception (sterilization).
- Postpartum women more than 8 weeks post delivery.

Procedure

The study was reviewed and approved by the ethical committee of Rajendra Nagar Hospital and IVF Centre, Lucknow. Couples were informed about this study. During these meetings, all couples received written information.

Counseling

Counseling was provided using a standardized protocol with balanced and comprehensive education material on the available contraceptive methods. Counseling card for nonhormonal methods was developed specifically for the study. In addition, a questionnaire was prepared to record information on the women's pre- and post-counseling contraceptive choice, and the reasons behind her post-counseling decision. The demographic variables (age, highest educational level, employment status, breastfeeding and number of children) were also included in the questionnaire.

Figure 1 depicts the number of patients enrolled, administered questionnaires and counseled.

Statistical Methods

The contraceptive methods opted for by women in the pre- and post-counseling program was represented as a shift table and was analyzed using McNemar's Chi-square test. Pre- and post-counseling, proportions of women opting for any one of the contraceptive methods were recorded and compared.

RESULTS

One hundred thirty-five women were screened for the eligibility criteria of the study. Of these, 9 were excluded. Major reasons for exclusions were not meeting the study eligibility criteria and not filling the study questionnaire completely. This resulted in a total of 126 eligible women who were included in the final analysis and counseled using hormonal and non-hormonal contraceptive cards. Table 1 summarizes the characteristics of the study participants.

Maximum women enrolled in this study were in the age group of 22-29 years. In pre-counseling, 40% postpartum women selected a contraceptive method. After meticulous contraception counseling, 95% of women chose a contraceptive method. There were significant differences between the women's choices of contraceptive methods in the pre- and post-counseling sessions.

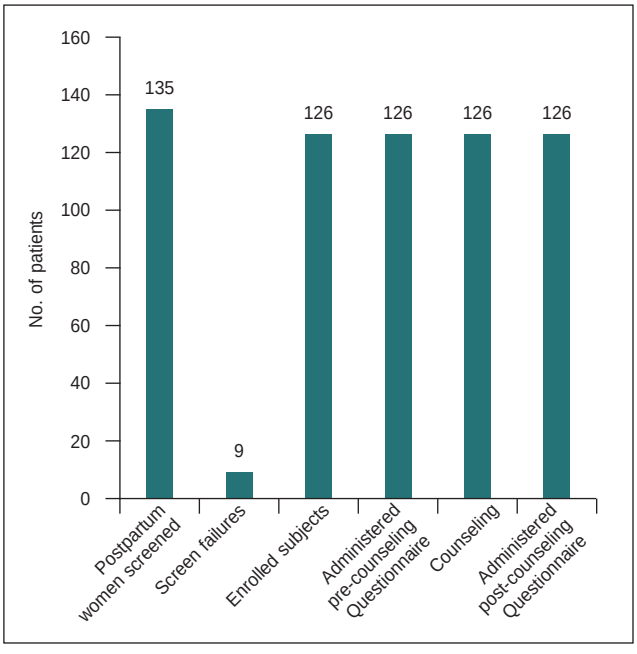

Figure 1. Number of patients enrolled, administered questionnaires and counseled.

Table 1. Characteristics of Participating Women in the Study (n = 126)

Characteristics	Number	%
Education		
Uneducated	10	8
Less than Xth pass	7	6
Xth pass	5	4
XIIth pass	15	12
Graduate	34	27
Postgraduate	55	44
Employment	89	71
Unemployed	12	10
Unplanned pregnancy	30	24
No. of children	3	2
Nil	69	55
One	45	36
Two	25	20
Three and more	28	22
Breastfeeding	27	21
Exclusive breastfeeding	78	62
No breastfeeding	12	10

POPs were found to be the most frequently preferred contraceptive method among postpartum women followed by inj-DMPA and then IUD.

DISCUSSION

The number of unintended pregnancies in India is quite high and these are associated with inadequate birth spacing. The postpartum period is a vital time period to initiate contraception. Closely spaced pregnancies pose several health risks both to mothers and newborns. An analysis of data from the Demographic and Health Survey (DHS) for various years shows that babies born within a period of less than 2 years after the next oldest sibling have a more than twofold increased risk of death in the first year compared with babies born after an interval of 3 years.[9] Women who have short interpregnancy intervals of less than 6 months were at higher risk of maternal death (odds ratio [OR] = 2.54), third trimester bleeding (OR = 1.73), premature rupture of membranes (OR = 1.72) and anemia (OR = 1.30).[10] Adequate spacing - 24 months from delivery to the next pregnancy - could save the lives of mothers and newborns. Family planning can potentially prevent nearly one-third of all maternal deaths as it allows women to delay motherhood, adequately space births, avoid unintended pregnancies and unsafe abortions, and enables them not to conceive when they have reached their desired family size.[11] Surveys conducted on a national level have shown that the adoption of contraceptive methods for spacing has remained low in India, despite the fact that nearly 50% women desire a gap of at least 3 years between two births. National Family Health Survey (NFHS-3) data has shown that among the married women 15-34 years of age, only 20% were using any contraceptive method for spacing. Postpartum contraception is thus important for the reduction of short interval pregnancies, which has a significant contribution to neonatal morbidity and healthcare costs. The variety of contraceptive methods available for postpartum women include hormonal contraception (POP, inj-DMPA), IUD, lactational amenorrhea, barrier contraception, natural family planning and sterilization.

The present study was designed to explore the impact of a balanced and comprehensive structured counseling session on increasing contraceptive acceptability among postpartum women. Several studies have reported the need and utilization of contraceptives in India. However, there is a lack of studies evaluating the impact of contraceptive counseling on the selection of contraceptive methods among postpartum women. A study conducted by Goel et al[12] shows that women who received advice on family planning were had increased odds of adopting postpartum contraception (unadjusted OR = 1.63 $p < 0.001$) as compared to those who were not advised at all. The hormonal contraceptive methods have been shown to be the preferred contraceptive method selected by postpartum women in India. This complies with the results for India in the world contraceptive use pattern survey.

Contraceptive choices have been found to be affected by counseling sessions, noted by the change in proportion of women opting for a particular method before versus after counseling.

In the present study, structured contraception counseling of an average duration of 30 minutes about various available hormonal and nonhormonal contraceptive methods helped most women to choose a contraceptive method. The effect of counseling on the selection of combined hormonal contraceptive methods in 11 countries has been reported by Yeshaya et al.[13]

The low usage of contraceptives observed in the present study may be linked to the low education status of the postpartum women. This could be associated with the poor accessibility and information among these women regarding the available contraceptive methods. Counseling provided knowledge to these postpartum women regarding the advantages and disadvantages of different contraceptive methods thus assisting them in making well-informed contraceptive choices as per their specifications and requirements. The results of the present study stress upon the significance of communication interventions in educating postpartum women.

CONCLUSION

Meticulous contraceptive counseling has huge potential to enable women, who do not want pregnancy, to choose a method of birth control that can be used consistently over time, thus reducing the incidence of unintended pregnancy. This study showed that POPs are the most frequently preferred contraceptive method among postpartum women followed by inj-DMPA and then IUD.

In order to obtain the benefits of family planning, both at the individual and community levels, all methods of family planning should be extensively available. Provision of the family planning methods must include comprehensive counseling.

Acknowledgments

The authors would like to thank all the women for their participation in this study. We would also like to thank the personnel of the Rajendra Nagar Hospital and IVF Centre.

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■■■■

Better Oral Hygiene Associated with Lower Diabetes Risk

A large retrospective study published online in *Diabetologia* has suggested that frequency of tooth-brushing was associated with risk of new-onset diabetes. Among 188,013 individuals followed for a median of 10 years, individuals who brushed three or more times a day were 8% less likely to develop diabetes (hazard ratio [HR] 0.92, 95% CI 0.89-0.95, $p < 0.001$), compared to those who brushed less frequently. Having periodontal disease escalated diabetes risk by 9%, and having many missing teeth - 15 or more - increased the risk by 21%.

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Detection of Pulmonary Nocardiosis Mimicking Tuberculosis: Role of Sputum Microscopy

SHASHI CHOPRA*, SHAVETA DHIMAN†, GOMTY MAHAJAN‡, SILKY MAHAJAN#

ABSTRACT

Background: Nocardiosis is an opportunistic infection and most commonly presents as pulmonary disease. Unless investigations like Gram's stain and modified acid-fast stain are specially done, pulmonary infection may be mistaken for tuberculosis. They are useful for early diagnosis of Nocardia infection. The present study was conducted for the early detection of pulmonary nocardiosis mimicking tuberculosis by sputum microscopy with Gram staining, modified Ziehl-Neelsen (ZN) staining. **Material and methods:** The current study was conducted on 2,466 sputum samples over a period of 4 years from July 2011 to June 2015 for ZN staining for evaluation of pulmonary tuberculosis. Those sputum samples which were negative with 20% H_2SO_4 and showed weakly stained acid-fast bacilli (AFB) were confirmed for Nocardia by modified ZN staining with 1% H_2SO_4, Gram's staining and culture. **Result:** Out of 2,466 sputum samples, 433 (17.55%) were found positive for AFB by microscopic examination. Ten (2.30%) out of 433 cases were positive for Nocardia. Amongst the Nocardia positive samples, 7 (70%) were of male and 3 (30%) were of female. **Conclusion:** Gram's staining and modified acid-fast stain are useful for early diagnosis and appropriate treatment of pulmonary nocardiosis.

Keywords: Pulmonary nocardiosis, sputum microscopy, modified Ziehl-Neelsen staining

Nocardiosis is a rare disorder caused by Gram-positive, weakly acid-fast, filamentous aerobic actinomycetes, which tends to affect the lung, brain and skin. The genus Nocardia belongs specifically to the family Mycobacteriaceae and contains tuberculostearic acid but differ from the mycobacteria by possession of shorter-chained (40- to 60-carbon) mycolic acids.[1]

Pulmonary nocardiosis is the most common clinical presentation and has several features similar to tuberculosis. It is a major cause of morbidity and mortality in immunocompromised patients.[2] Lack of suspicion, nonspecific clinicoradiological presentation, diagnostic intricacies and lack of systematic reporting are the probable reasons that have hindered the true estimation of its incidence, worldwide.[3] In tuberculosis endemic countries like India, nocardiosis should always be excluded among patients not responding to antitubercular treatment. Early recognition and appropriate individualized treatment is the key to a successful outcome.[2] New methodologies were developed for the identification of Nocardia, but evaluation of appropriate specimens by smear and culture remains the principal method of diagnosis.[4,5] Unless investigations like Gram's stain and modified acid-fast stain are specially done, pulmonary infection may be mistaken for tuberculosis and are useful for early diagnosis of Nocardia infection.[6] Hence, the present study was conducted for the early detection of pulmonary nocardiosis mimicking tuberculosis by sputum microscopy with Gram staining, modified Ziehl-Neelsen (ZN) staining.

AIM

Early detection of pulmonary nocardiosis mimicking *Mycobacterium tuberculosis* by sputum microscopy.

MATERIAL AND METHODS

The current study was conducted on 2,466 sputum samples which were received in the Microbiology Department of a tertiary care hospital in North India,

*Professor
†Tutor
‡Associate Professor
Dept. of Microbiology
#Tutor
Dept. of Pathology
Punjab Institute of Medical Sciences, Jalandhar, Punjab
Address for correspondence
Dr Shashi Chopra
EJ 227-228, Chahar Bagh, Jalandhar City - 144 001, Punjab
E-mail: dr.shashichopra@yahoo.com

over a period of 4 years from July 2011 to June 2015 for acid-fast bacilli (AFB) by ZN staining for evaluation of pulmonary tuberculosis.

All the samples were processed in laboratory without delay in order to avoid contaminants to grow. Homogenization of sputum samples were done by Petroff's method.[7] Next, concentrated specimens were used for smear preparation and culture. Few slides on ZN staining showed weakly stained AFB with some filamentary structure. Nocardia spp. are acid-fast and can survive the decontamination of clinical specimens with sodium hydroxide method.[8]

These patient's sputum samples were repeated with another two fresh sputum samples to exclude Nocardia by doing Gram's staining and modified ZN staining[9] using 1% H_2SO_4. On microscopic examination, Gram-stained smear showed thin, delicate, weakly to strongly Gram-positive, irregularly stained or beaded branching filament and Modified ZN staining revealed filamentous acid-fast organism suggestive of Nocardia.

Further 250 µL of each concentrated sputum specimen suspected to be Nocardia was inoculated onto Sabouraud's dextrose agar (SDA) media and blood agar. All cultures were incubated at 37°C with 5% CO_2 and humidity. Cultures were examined daily for the growth of Nocardia species for up to 3 weeks. On SDA, colonies were white to brown in appearance and on blood agar, filamentous colonies having chalky-white or cotton-ball appearance were seen.[4] Colonies were examined with Gram staining and modified ZN staining methods to confirm the growth of Nocardia (Fig. 1).

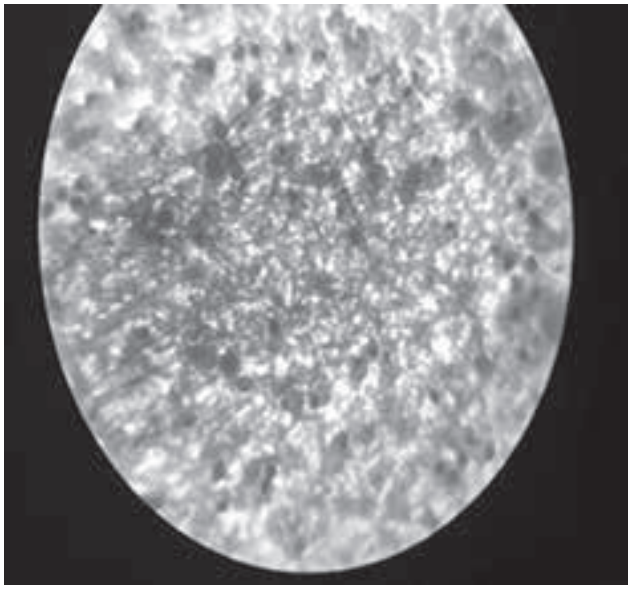

Figure 1. Microscopic picture of Nocardia (Gram's staining).

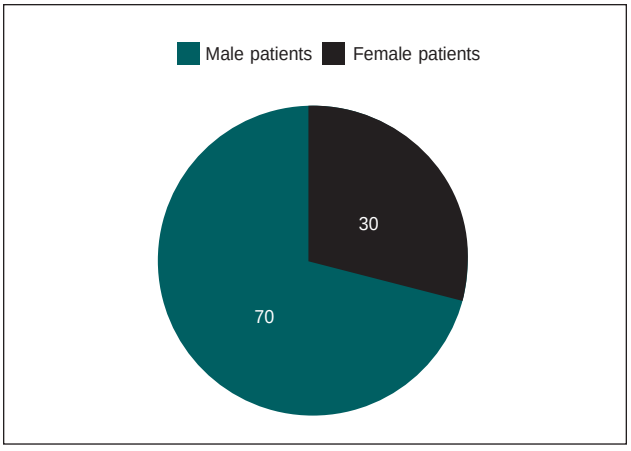

Figure 2. The percentage of Nocardia positivity in patients.

RESULTS

Two thousand four hundred sixty-six samples from patients of all ages and both sexes were studied during a period of 4 years (July 2011 to June 2015). Out of the total, 73.52% were males and 26.48% were females. Of the total cases, 433 (17.55%) were found positive for AFB by microscopic examination. Ten (2.30%) out of 433 cases were positive for Nocardia, which were confirmed by Gram's staining, modified ZN staining and culture. Out of these 10 cases, 70% were males and 30% were female cases (Fig. 2).

DISCUSSION

Pulmonary nocardiosis is the most common clinical presentation of nocardial infection because inhalation is the primary route of bacterial exposure.[10] It can be fatal if untreated. Untreated pulmonary nocardiosis is similar to tuberculosis and *Nocardia asteroides* is the most frequent cause of pulmonary infection in humans (85%).[11] In the present study, we included 2,466 sputum samples, out of which 73.52% were from males and 26.48% were from female patients, whereas a similar study done by other workers included 44.8% sputum samples of male and 55.2% sputum samples of females.[12] Lungs are the most common site of involvement for tuberculosis and Nocardia.[13] In our study, 17.55% sputum samples were found positive for AFB, whereas other workers reported 7.6% positivity by microscopy examination.[14] Pulmonary nocardiosis is the most common clinical presentation of infection and can occur in persons of all ages, even neonates.[10]

In our study, out of 433 AFB positive sputum samples, 10 (2.30%) were positive for Nocardia, whereas other workers reported it to be 3.57%,[15] which was confirmed

by Gram's staining, modified ZN staining (1% H_2SO_4) and by culture. Nocardia incidence in pulmonary disease has been reported to be 1.4%, 2.7% and 4% by different workers in different areas.[16-18] McNeil and Brown highlighted the importance of direct microscopic examination because, despite the new methodologies developed, there is no test replacing it.[4] Amongst the Nocardia positive samples, 70% samples were of male patients and 30% were of female patients almost similar results were reported by other workers also (75% and 25%, respectively).[19]

The exact reason for gender difference is not known, though hormonal effect may be attributed to virulence or growth of Nocardia species.[15] In India, the prevalence of Nocardia as reported in 1973 was 4.6% among patients who were suspected to have tuberculosis.[20] The clinical diagnosis of nocardiosis is difficult. Signs, symptoms and radiologic studies may suggest the diagnosis but are not pathognomonic. Serologic diagnosis is unreliable, and serologic tests are not available commercially,[5] so isolation and identification of the organism from the clinical specimens form the backbone for diagnosis of pulmonary nocardiosis.

CONCLUSION

This study highlights the importance of nocardiosis in differential diagnosis of pulmonary disease patients. The initial diagnosis of pulmonary nocardiosis requires fast and accurate methodology for early recognition and appropriate individualized treatment due to the clinical aspects and bacteriologic similarity to the genus Mycobacterium. The direct microscopic examination of sputum specially, with Gram's stain and modified acid-fast stain with 1% sulfuric acid highlighted the importance in early diagnosis despite of the development of new methodologies. Hence, a microbiologist should process the respiratory tract specimens not only for Mycobacteria but should also be alert to the fact that organisms such as Nocardia may cause pulmonary infection.

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Indian Journal of Clinical Practice, Vol. 30, No. 10, March 2020

A Peripheral Marker for a Central Cause – Hyponatremia

E SUMANRAJ*, A NANJIL KUMARAN†, R UMARANI‡, P MUTHIAH‡

ABSTRACT

Hyponatremia is among the commonest electrolyte abnormalities, with an incidence ranging from 10% to 30%. The condition is associated with increased morbidity and mortality. Although endocrine disorders, including adrenal insufficiency and hypothyroidism, are uncommon causes of hyponatremia, yet testing for pituitary-adrenal-gonadal hormone profiles should be part of the hyponatremia workup. Presented here is the report of an uncommon cause of hyponatremia.

Keywords: Hyponatremia, hypothyroidism, adrenal insufficiency, SIADH

Hyponatremia is the most common electrolyte disorder, with an incidence ranging from 10% to 30%. Acute (<48 hours) and chronic hyponatremia are both associated with increased morbidity and mortality. Endocrine disorders, including adrenal insufficiency and hypothyroidism, are uncommon causes of hyponatremia. The appropriate diagnosis of the causative factor is of paramount importance for the proper management and avoidance of treatment pitfalls. Herein, we report an uncommon cause of hyponatremia.

CASE REPORT

A 50-year-old male presented to the outpatient department with complaints of giddiness and easy fatigability of 1 month duration, which was not associated with nausea or vomiting and associated with loss of weight and loss of appetite for the past 3 months. There was no preceding history of fever, headache, abdominal pain, loose stools or vomiting. The patient also did not have any visual disturbances, polyuria, polydipsia, polyphagia, yellowish discoloration of urine or syncopal attacks. Patient consumes alcohol and denied intake of drugs, including steroids and diuretics, in the past.

General physical examination was unremarkable. His height was 161 cm and weight was 58 kg. His vitals were normal except repeated low blood pressure readings of around 100/60 mmHg without any postural change, which responded to fluid challenge. Pulse rate was 78/min which was regular in rhythm. There were no hyper- or hypopigmented patches. Cardiovascular and respiratory systems examinations were normal. Neurological examination revealed no abnormalities, with no localizing cerebellar findings. Ophthalmological examination revealed no visual field defects and normal fundus.

The initial laboratory results were as follows: random blood sugar - 56 mg/dL, hemoglobin - 14.3 g/dL, white cell count - 4.8 × 10^9/L, platelet - 178 × 10^9/L, serum creatinine - 0.9 mg/dL, serum sodium - 116 mmol/L, serum potassium - 4.3 mmol/L and normal liver function tests. Urine osmolality was 223 mOsm/kg and serum triglyceride levels were within normal limits. Electrocardiogram (ECG) and chest X-ray were normal. In the absence of cardiac, renal, liver failure and with no preceding history of vomiting and diarrhea, diagnosis of euvolemic hyponatremia was made. As there were features of fatigability with low blood pressure values and documented hypoglycemia and the absence of pigmentation, secondary adrenal insufficiency was suspected. Pituitary hormone profile was then carried out and the results were as follows: free tetraiodothyronine (fT_4) - 0.52 ng/dL (N = 0.8-2.0), thyroid-stimulating

*Postgraduate
†Lecturer
‡Professor
Dept. of General Medicine and Radiodiagnosis
Rajah Muthiah Medical College, Chidambaram (RMMCH), Tamil Nadu
Address for correspondence
Dr E Sumanraj
Postgraduate
Dept. of General Medicine, RMMCH, Chidambaram, Tamil Nadu

hormone (TSH) - 4.17 μIU/mL (N = 0.35-5.5), luteinizing hormone (LH) - 2.15 mIU/mL (N = 1.7-8.6), follicle-stimulating hormone (FSH) - 3.57 mIU/mL (N = 1.5-12.4) and prolactin - 39.17 ng/mL (N = 4.79-23.3). His morning (6 am) serum cortisol level was 0.17 μg/dL (N = 6.02-18.4). The absence of clinical features of primary adrenal failure together with low cortisol levels, presence of euvolemic hyponatremia and ultrasonically normal adrenals, pointed the finger towards a central cause for hyponatremia. Magnetic resonance imaging (MRI) brain revealed T2 hyperintense mass lesion (20 × 17 mm) in sella with suprasellar extension displacing optic chiasma superiorly, raising the possibility of a pituitary macroadenoma (Fig. 1).

On contrast administration, there was patchy enhancement of lesion, suggestive of pituitary macroadenoma (Fig. 2).

The diagnosis of a nonfunctioning pituitary macroadenoma with secondary hypoadrenalism was made. However, his prolactin level was slightly high, probably due to hormone release from local pressure effect on pituitary stalk. Patient was started on hormone replacement with prednisolone and was referred to neurosurgery department for surgical resection of pituitary adenoma. Adrenocorticotropic hormone (ACTH) stimulation and other hormonal assays were not done as neuroimaging studies were diagnostic.

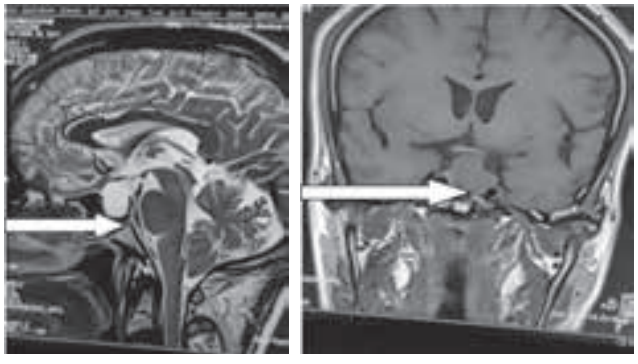

Figure 1. MRI brain revealed T2 hyperintense mass lesion (20 × 17 mm) in sella with suprasellar extension displacing optic chiasma superiorly.

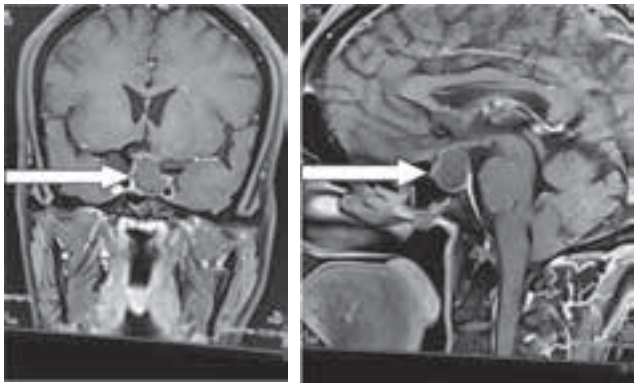

Figure 2. Patchy enhancement of lesion, suggestive of pituitary macroadenoma, on contrast administration.

DISCUSSION

Hyponatremia (serum sodium <135 mmol/L) is generally attributed either to water retention or to loss of effective solutes in excess of water. Hyponatremia can be hypovolemic hyponatremia (diarrhea, vomiting, diuretics, cerebral salt wasting syndrome, mineralocorticoid deficiency), euvolemic hyponatremia (syndrome of inappropriate antidiuretic hormone secretion [SIADH], hypothyroidism, ACTH deficiency) and hypervolemic hyponatremia (congestive cardiac failure [CCF], hepatic cirrhosis, renal failure). Even though endocrine disorders are uncommon causes of hyponatremia, testing for adrenal insufficiency and hypothyroidism should be part of hyponatremia work-up, as the disorder responds promptly to hormone replacement.

Endocrine causes of hyponatremia are as follows:

Adrenal insufficiency

- Primary
  - Addison's disease
  - Autoimmune adrenalitis
  - Infections (tuberculosis, acquired immunodeficiency syndrome [AIDS])
  - Metastatic carcinoma
- Secondary
  - Pituitary or hypothalamic tumors
  - Infections (tuberculosis, histoplasmosis)
  - Craniopharyngioma
  - Empty sella syndrome
  - Lymphocytic hypophysitis

Primary adrenal insufficiency (Addison's disease) is characterized by both aldosterone and cortisol deficiency which contributes to hyponatremia by causing sodium wasting and hypovolemia resulting in hypovolemic hyponatremia, in contrast to euvolemic hyponatremia in secondary adrenal insufficiency. Cortisol is a physiological inhibitor of antidiuretic hormone (ADH) secretion. Hyponatremia in patients with adrenal insufficiency should be ascribed to inappropriate secretion of ADH. The hypersecretion

of ADH by cortisol deficiency may be in part due to the reduction of systolic blood pressure and cardiac output.

Pituitary adenomas are considered the third most frequent intracranial neoplastic lesion (15%), after meningioma and gliomas. The nonfunctioning pituitary adenomas are considered the second most common pituitary adenoma, exceeded only by prolactinoma. Usually, these tumors are manifested by the effect of mass compression, such as headache, blurred vision and seizures. Histopathologically, most nonfunctioning pituitary adenomas have positive immunohisto-chemistry staining for FSH/LH. Hypopituitarism, especially due to space-occupying lesions, is usually accompanied by more than one pituitary hormone deficiency. Hypopituitarism with secondary adrenal insufficiency is another overlooked cause of hyponatremia, often presenting with a 'SIADH-like picture' (euvolemic hyponatremia, low serum uric acid and urea levels, high urine sodium and osmolality).

Hypothyroidism

Hypothyroidism can result from a defect anywhere in the hypothalamic-pituitary-thyroid axis. In the vast majority of cases, it is caused by thyroid disease (primary hypothyroidism). Much less often, it is caused by decreased secretion of thyrotropin (TSH) from anterior pituitary gland or by decreased secretion of thyrotropin-releasing hormone (TRH) from the hypothalamus (secondary or tertiary hypothyroidism).

Hyponatremia has been reported in patients with moderate-to-severe hypothyroidism. For every 10 mIU/L rise in TSH, serum sodium has been shown to be decreased by 0.14 mmol/L. Mechanism by which hypothyroidism induces hyponatremia involve the inability to maximally suppress ADH. This is due in part to a reduced cardiac output, which can lead to the release of ADH via the carotid sinus baroreceptors. On the other hand, the glomerular filtration rate has been reported to be decreased in hypothyroidism, which leads to diminished water delivery to the diluting segments and subsequently diminished free water excretion. The net effect of impaired water excretion is retention of ingested water and dilutional hyponatremia.

Diagnostic Clues of Hyponatremia due to Endocrine Causes

The diagnosis of acute adrenocortical insufficiency (adrenal crisis) is relatively straightforward in a patient presenting with weakness, abdominal pain, confusion, nausea, vomiting, diarrhea, fever and hypotension combined with hyponatremia, hyperkalemia and raised blood urea. The co-existence of hypoglycemia, hypercalcemia, hypotension is also helpful, if present.

Addison's disease can be recognized by the presence of hyperpigmentation, salt craving, hypotension and hyperkalemia. Hyperkalemia may be absent in approximately 30-50% of patients with Addison's disease. Secondary adrenal insufficiency due to pituitary adenoma can be diagnosed by the presence of mass effect like headache, nausea, vomiting and visual disturbances.

The SIADH is the most common cause of hyponatremia. It is suggested that hypopituitarism should be thought of in all patients with an SIADH-like clinical picture without an obvious cause and even in patients who appear to be mildly dehydrated. The diagnosis of SIADH is suspected in patients with hyponatremia and hypo-osmolality, increased urine osmolality, inappropriate natriuresis, normovolemia, normal renal, pituitary, adrenal and thyroid function and normal acid-base and potassium balance. The diagnosis of SIADH is also supported by the presence of hypouricemia, as well as by low serum urea and phosphate levels.

The differential diagnosis of hyponatremia with a high urine sodium osmolality includes diuretic use, primary and secondary adrenal insufficiency, cerebral salt-wasting, salt-wasting neuropathy and SIADH. Uric acid serves as a valuable index to assess the extracellular fluid volume expansion (SIADH, hypocortisolism), as uric acid reabsorption in the renal proximal tube is inhibited, producing a low serum concentration and a high fractional excretion.

A tendency towards metabolic alkalosis suggests SIADH or diuretic use, whereas metabolic acidosis suggests primary adrenal insufficiency. It has been proposed that secondary adrenal insufficiency might be differentiated from SIADH by the presence of low plasma bicarbonate level and low carbon dioxide levels. Hypokalemia may accompany hyponatremia in diuretic use, whereas hyperkalemia is more typical for primary adrenal insufficiency.

CONCLUSION

Endocrine disorders, including adrenal insufficiency and hypothyroidism, are uncommon causes of hyponatremia. Testing for pituitary-adrenal-gonadal hormone profiles should be part of the hyponatremia workup, as this disorder responds promptly to hormone replacement, while the consequences can be grave when the diagnosis is missed.

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FDA Oks New Therapy for Patients with Previously Treated Multiple Myeloma

The US FDA has given approval for isatuximab-irfc, combined with pomalidomide and dexamethasone, for the treatment of adults with multiple myeloma who have received at least two previous therapies including lenalidomide and a proteasome inhibitor.

Isatuximab-irfc is a CD38-directed cytolytic antibody that assists certain cells in the immune system attack multiple myeloma cancer cells. The drug is administered through intravenous (IV) infusion… (*FDA*)

Variation in Nightly Bedtime, Sleep Duration Tied to CVD Risk

People who frequently change the amount of sleep and the time they go to bed each night have double the odds of developing cardiovascular disease, independent of traditional CVD risk factors, suggests new research published in the *Journal of the American College of Cardiology*. Investigators used data of 1,992 Multi-Ethnic Study of Atherosclerosis (MESA) participants, aged 45 to 84 years, who were free of CVD and were followed for a median of 4.9 years. About 39.5% had sleep duration standard deviation (SD) >90 minutes and 25.6% had sleep-onset timing SD >90 minutes. In comparison with people who had <1 hour of variation in sleep duration, the risk for incident CVD was 9% higher for those whose sleep duration varied 61 to 90 minutes, even after controlling for several cardiovascular and sleep-related risk factors including BMI, systolic blood pressure, smoking status, total cholesterol, average sleep duration, insomnia symptoms, and sleep apnea.

Indian Journal of Clinical Practice, Vol. 30, No. 10, March 2020

Pleomorphic Adenoma of the Submandibular Gland: A Rare Occurrence

SUBRAMANIAM VINAYAK EASWERAN*, RAGHVENDRA UDUPA†, MAMTA HEGDE‡

ABSTRACT

Pleomorphic adenoma is the most frequent benign tumor of the salivary gland. It is a slow-growing tumor and is characterized by varying amount of myxochondroid stroma, produced by the myoepithelial cells. About 90% of benign neoplasm of major salivary glands is associated with the parotid gland. The occurrence of submandibular gland pleomorphic adenoma is uncommon. Pleomorphic adenoma have low proliferative rate and have a good prognosis. Presented here is the case of a 35-year-old lady with a swelling below the right angle of the mandible.

Keywords: Pleomorphic adenoma, salivary gland neoplasm, sub-mandibular gland

Salivary gland tumors are rare and account for nearly 3% of head and neck tumors. About 90% of benign neoplasm of major salivary glands is associated with the parotid gland. Pleomorphic adenoma is the most common benign tumor of the salivary gland.[1] Pleomorphic adenoma is characterized by varying amount of myxochondroid stroma that is produced by the myoepithelial cells. Microscopic findings of necrosis, nuclear atypia, hyalinization, invasion of adjacent tissue and heightened abnormal mitotic activity are linked with an aggressive behavior or malignant transformation of pleomorphic adenoma. At times, histopathological confusion could occur due to extensive squamous differentiation, usually seen on fine-needle aspiration cytology (FNAC). Thus, at times, it could be misdiagnosed. Capsule infiltration, though not associated with malignant transformation, might play a role in pleomorphic adenoma recurrence.[2] Pleomorphic adenoma have low proliferative rate and have a good prognosis.[3]

CASE REPORT

A 35-year-old lady presented to the outpatient department (OPD) with a swelling below the right angle of the mandible (Fig. 1 a and b).

The swelling was present since 2-3 years which was slowly growing in size. The swelling was nontender and mobile and measured 5 × 6 cm. There was no rise in temperature.

Patient was then planned for surgery after getting the basic preoperative investigations done which were: Hemoglobin (Hb) - 12.4 g/dL, total leukocyte count (TC) - 9,800 cells/mm^3, differential count (DC) - $N_{55}L_{38}E_6M_1$, erythrocyte sedimentation rate (ESR) - 18 mm/hr, bleeding time (BT) - 2 minutes 15 seconds, clotting time (CT) - 3 minutes 35 seconds, blood group - B-ve, ICTC - negative, random blood sugar (RBS) - 104.5 mg/dL, urine - within normal limit. The surgery was done under general anesthesia (Fig. 2).

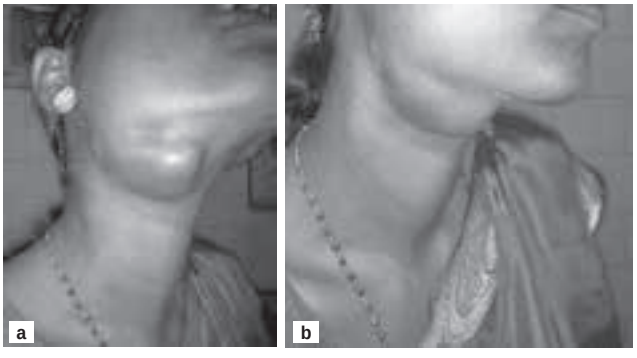

Figure 1 a and b. Swelling below the right angle of the mandible.

*ENT Specialist
Dept. of ENT
†Anesthesiologist
Dept. of Anesthesiology
Pandit General Hospital, Sirsi, Uttar Kannada, Karnataka
‡Pathologist
Dept. of Pathology
Marikamba Hospital, Sirsi, Uttar Kannada, Karnataka
Address for correspondence
Dr Subramaniam Vinayak Easweran
ENT Specialist
Dept. of ENT
Pandit General Hospital, Sirsi, Uttar Kannada - 581 401, Karnataka
E-mail: vinoo121071@gmail.com

The gland was excised *in toto* (Fig. 3), hemostasis was checked for and achieved. The patient tolerated the procedure well.

The excised gland was sent for histopathological examination (Fig. 4). The microscopic picture coincided with the diagnosis of pleomorphic adenoma (Fig. 5). The microscopic picture showed proliferation of both epithelial and stromal elements.

The epithelial proliferation is in the form of acini, tubercles, trabeculae. The stromal component is of chondromyxoid; at places stroma were seen having cartilaginous tissue.

Patient was put on broad-spectrum antibiotic postoperatively for a week and discharged on the 5th postoperative day. On the 10th postoperative day, the patient was called for follow-up and subcuticular suture removal; wound was healthy (Fig. 6).

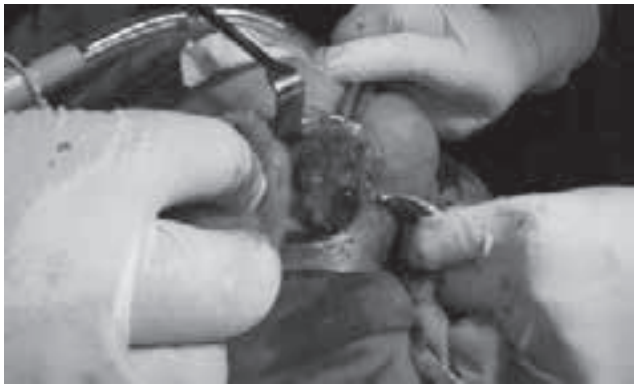

Figure 2. Intraoperative image.

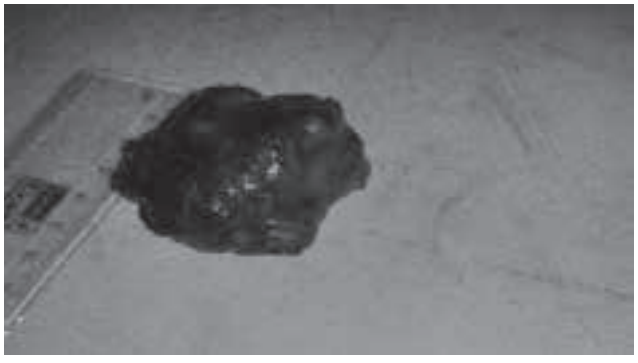

Figure 3. Excised gland.

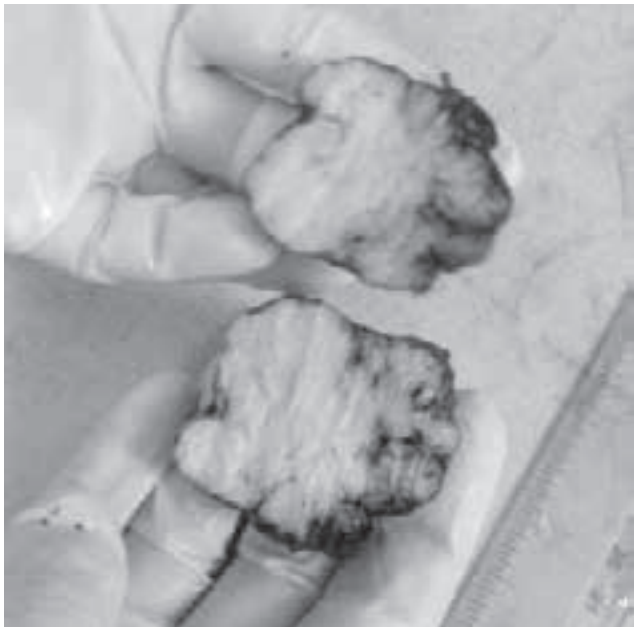

Figure 4. Cut section of the gland.

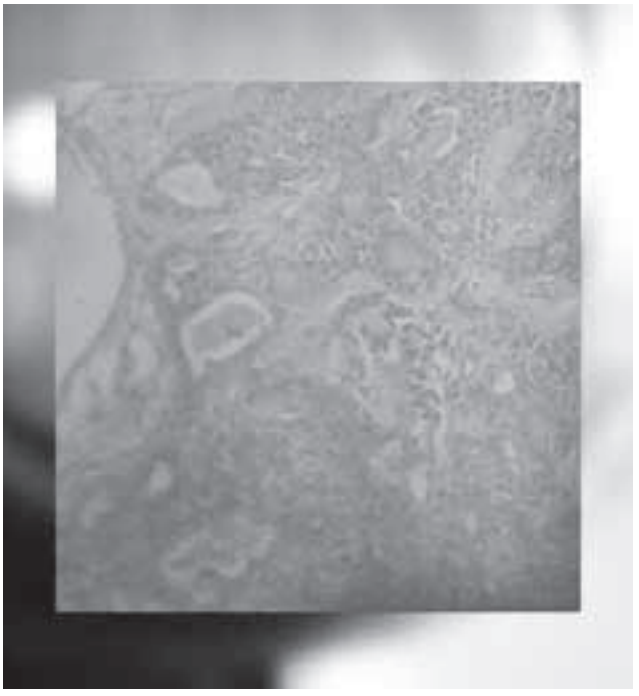

Figure 5. Microscopic picture pointed to diagnosis of pleomorphic adenoma.

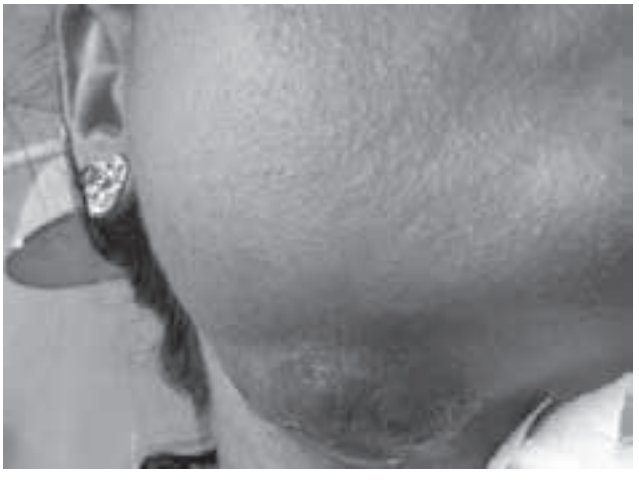

Figure 6. Healthy wound on 10th day postoperatively.

DISCUSSION

Cases of submandibular gland pleomorphic adenoma are uncommon, though parotid gland cases are often encountered.[1] Pleomorphic adenoma is the commonest benign tumor of the salivary glands[4] and accounts for 90% of all salivary gland tumors.[1]

The submandibular gland represents the second most common site of pleomorphic adenoma after the parotid gland.[1]

Pleomorphic adenoma, an epithelial tumor of complex morphology, has epithelial and myoepithelial elements intermingled with mucoid, myxoid or chondroid tissue arranged in varied patterns and embedded in a mucopolysaccharide stroma.[1]

The differential diagnosis includes basal cell adenoma, adenocarcinoma, mucoepidermoid carcinoma and lymphoma.

Investigations like magnetic resonance imaging (MRI) and computed tomography (CT) are gold standard, while adjunctive procedures such as ultrasound-guided needle aspiration and FNAC may not assist with confirmation of diagnosis.

A direct submandibular incision is generally recommended, which gives easy access. The excision should be always *in toto*. Incomplete removal would result in recurrence. At times, the benign pleomorphic adenoma could transform into a malignant one (carcinoma ex-pleomorphic adenoma), with 25% of untreated pleomorphic adenomas estimated to undergo malignant transformation;[5] hence, early definitive treatment is needed.

CONCLUSION

Pleomorphic adenoma is the most common benign neoplasm of the salivary gland and more commonly seen in parotid gland. It is uncommonly seen in submandibular gland. Surgical excision *in toto* is the treatment of choice. If left untreated, it could cause recurrence and long-standing pleomorphic adenoma could become malignant.

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Brief Cognitive Therapy Promising for Chronic Pain

A brief cognitive behavioral therapy (CBT) program showed promising results in treating chronic pain among Veteran Affairs (VA) patients, revealed a clinical demonstration project.

By mid-treatment, patients with chronic pain had significant improvements in pain interference and pain self-efficacy, reported researchers at the American Academy of Pain Medicine annual meeting. The program included six 30-minute, one-on-one sessions aiming at decreasing functional limitations among patients with chronic musculoskeletal pain. After the third session, a composite measure of pain intensity and functional limitations showed statistically significant improvements, with pain-related self-efficacy outcomes showing a similar pattern.

ACR Guideline on Reproductive Health in Rheumatic Diseases

The American College of Rheumatology (ACR) has issued guidelines for the management of reproductive health in patients with rheumatic and musculoskeletal diseases (RMD). The guidelines address concerns such as contraception, medication use during pregnancy and assisted reproductive technology. Special considerations have also been addressed for women with systemic lupus erythematosus (SLE) or those positive for antiphospholipid (aPL) antibodies. The guidelines were published online in *Arthritis & Rheumatology* and *Arthritis Care & Research*.

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A Case of Marchiafava-Bignami Syndrome

MANISH N MEHTA*, PRANAV I PATEL†, HEMANG K ACHARYA‡, AC TANNA#, JEMIMA BHASKAR¥

ABSTRACT

Drinking alcohol is a serious social and health problem in our country and throughout the world. It causes varied diseases in different organs of the body, which many do not care to know about. Marchiafava-Bignami disease is one such rare but serious disorder. We are presenting this case to show the serious disorders associated with alcoholism.

Keywords: Corpus callosum, alcohol, mutism, alcohol dehydrogenase, neurological deficit

Marchiafava-Bignami syndrome is one of the central nervous system (CNS) complications of chronic alcohol intake. There is degeneration of the corpus callosum similar to a disconnection syndrome. It is possibly due to B complex deficiencies related to chronic alcohol intake. The prognosis is guarded as most patients present with coma.

CASE REPORT

A 50-year-old male, chronic alcoholic, laborer was admitted to Guru Gobind Singh Hospital, Jamnagar, Gujarat. He presented with fever, vomiting, altered mental status, disorientation to time-place-person and first episode of generalized tonic-clonic convulsions.

On examination, he presented with mutism, altered sensorium, no ophthalmoplegia, no nystagmus, inability to move all limbs, bilateral extensor plantars with semi-dilated reactive pupils bilaterally. Neck stiffness was not present. No focal neurological signs were present. Fundus examination showed no signs of papilledema. A clinical diagnosis of meningoencephalitis or hepatic encephalopathy was made. Meanwhile, contrast-enhanced computed tomography (CECT) brain was done to look for secondary causes of convulsions. Magnetic resonance imaging (MRI) cuts were taken in addition to CT which showed "Ill-defined non-enhancing hypodense area in middle part of corpus callosum, possibly degeneration due to Marchiafava-Bignami syndrome" (Fig. 1 a and b). Hence, diagnosis of Marchiafava-Bignami syndrome was made. Patient received injections (cefotaxime, metronidazole, mannitol, thiamine, vitamin B_{12}, hydrocortisone, sodium valproate, IV glucose, amino acids, soybean oil and lecithin) and supportive treatment. On Day 3, he regained consciousness. On Day 4, he became oriented to surroundings. Later he was able to walk with support.

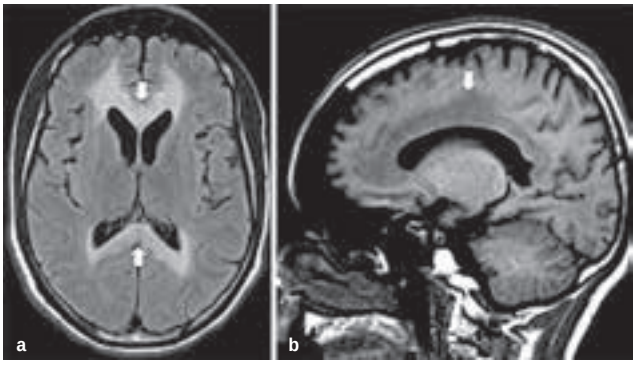

Figure 1. High signal intensity noted in axial FLAIR image with involvement of anterior and posterior portion of corpus callosum and periventricular white matter (**a**). Sagittal T1-weighted image with low signal intensity seen in entire length of corpus callosum shown with arrow (**b**).

DISCUSSION

Marchiafava-Bignami disease is a rare and toxic encephalopathy seen mostly in alcoholics due to progressive demyelination and necrosis of corpus callosum, which may extend to adjacent regions and even up to subcortex. It was first described by Italian

*Professor and HOD
†Second Year Resident
‡Professor and HOU
#Assistant Professor
¥Medical Officer
Dept. of Medicine
MP Shah Medical College and Guru Govind Singh Hospital, Jamnagar, Gujarat
Address for correspondence
Dr Jemima Bhaskar
404, King's Palace, Opposite BSNL Telephone Exchange
Mehulnagar, Jamnagar, Gujarat - 361 006
E-mail: jemimabhaskar@yahoo.com

pathologists, Marchiafava and Bignami, in alcoholic patients who died after having seizures and coma. Most accepted cause for the pathogenesis of this disorder is deficiency of multiple vitamins of vitamin B complex. It can be divided into two subgroups as type A having altered consciousness, stupor, coma and upper motor neuronal signs with involvement of entire corpus callosum and type B having mild impairment of consciousness with small callosum lesion. Type B has good prognosis. Altered mental status, impaired walking and loss of consciousness is seen in more than 50% of patients with this disease.

Other symptoms are dysarthria, impaired memory, signs of disconnection, pyramidal signs, seizures, primitive reflexes, rigidity, hemi-/tetraparesis, incontinence, nystagmus, etc. Mutism, sensory symptoms and gaze palsy are seen in only 10% of patients, but when present, can be useful in differentiating this syndrome from other disorders. Hence, they are more specific for this disease. Diagnosis of this disease is made by history, presentation, examination and radio-imaging modalities such as CT scan and more preferably MRI brain, which shows hypodense lesion due to degeneration in corpus callosum. No specific treatment is available but treatment with parenteral thiamine within 15 days of presentation for 15 days along with other vitamins, proteins and high dose steroids has shown better prognosis as compared to controls in previous studies. Antiparkinsonian drug amantadine showed improvement as per one study. Rest and supportive treatment should be given. Prognosis of this disease varies as some patients improve and some deteriorate to even death in spite of treatment.

Certain risk factors predispose to alcohol toxicity:

- Pattern of drinking - more duration means more toxicity; continuous drinking is more dangerous than intermittent; drinking more than 80 g/day is dangerous.
- Women achieve higher blood levels of alcohol than men.
- Certain genes namely HLA-B8 and ADH gene 2 are considered to increase alcohol toxicity.
- On the other hand, presence of food in the stomach, especially proteins, decreases alcohol toxicity.

Other than Marchiafava-Bignami syndrome, alcohol can cause other CNS effects - acute intoxication (from euphoria to coma), withdrawal syndrome, alcoholic dementia, cerebrovascular accidents, alcoholic cerebellar degeneration, central pontine myelinolysis, peripheral neuropathy, Saturday night palsy, etc. Other than effects on the brain, alcohol has toxic effects on liver, blood cells, fetus, gastrointestinal tract, cardiovascular system, genitourinary system, skeletal system, endocrine system, respiratory system, etc. Addiction, social and psychological problems are also threats associated with alcohol intake. In addition, alcohol interacts with a lot of commonly used medications. Alcohol toxicity varies from gastric ulcers, which is easily treatable, to even malignancies which have serious prognosis.

In our case, the patient presented in a coma-like state. On examination, it was not a deep coma but patient had altered sensorium with mutism. Hence, there was no verbal output. Mutism is one of the rare presentations in this disorder. There was significant improvement with parenteral vitamin replacement although the prognosis is not good in most cases.

CONCLUSION

This case has been presented to highlight the various serious CNS complications in chronic alcoholics. Because it is uncommon, it is rarely diagnosed clinically. This disease should be kept in the mind in chronic alcoholics presenting with coma. Thankfully, our patient recovered in spite of the guarded prognosis of the disease.

"Think before you drink, because if you drink, you may not be able to think again." (Alcoholism can cause brain degeneration)

"As there is no intervention, start with prevention."

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Huge Denture Causing Acute Obstruction in Esophagus and Stridor

SHAMENDRA KUMAR MEENA

ABSTRACT

We report a rare case of an unusually long foreign body (denture) impacted in the mid esophagus of a 62-year-old man. He was illiterate and drank wine regularly. He came with some attendants with history of taking wine with lunch, followed by acute obstruction since lunch at 12:30 pm and reached Kota by 9:30 pm. Till then, he was nil by mouth (NBM). Following investigations, a diagnosis of foreign body esophagus was made and with the help of rigid esophagoscopy under general anesthesia, the foreign body was removed. Next morning, he could swallow food and water without any difficulty, and he was discharged.

Keywords: Foreign body, esophagus, denture

A large number of ingested foreign bodies, especially smooth or <12 mm in diameter, tend to pass safely through the gastrointestinal tract. However, severe problems, such as perforation, may occur following ingestion of sharp objects, bone fragments, pins or long foreign bodies (>6.5 cm).[1,2] The postcricoid region is a common site of impaction of foreign bodies (in nearly 84% of the subjects). Impaction of a bolus of food in the distal esophagus in adults is often associated with a pre-existing stricture, diverticulum or tumor.[2] Adults with non-food foreign bodies have a high incidence of psychiatric and social derangements. Most foreign bodies pass through the pylorus; however, some objects may remain in the stomach for a long period. Once they have crossed the pyloric canal, most objects, even sharp edged foreign bodies such as pieces of glass or nails, pass without harm. But, terminal ileum is again a site with predisposition for impaction. Sometimes, the ingested foreign bodies may remain fixed in the cecum, ascending colon or sigmoid colon.[2] Noncontrast computed tomography (CT) scan is done for diagnosing suspected upper esophageal foreign bodies that may not be visible on plain radiography,[3] and in order to rule out perforation.[4]

Assistant Professor
Govt. Medical College, Kota, Rajasthan
Address for correspondence
Dr Shamendra Kumar Meena
KR-21, Civil Line, Nayapura, Kota, Rajasthan - 324 001
E-mail: shamendra.meena82@gmail.com

CASE REPORT

A 62-year-old gentleman presented to the emergency services at night with complaints of difficulty in swallowing, pain on swallowing, drooling of saliva and pain in the chest following the accidental ingestion of denture while drinking wine and eating lunch. He reported that suddenly he swallowed a piece of denture, measuring approximately 4-5 cm, that caused acute obstruction and distress. He was also having problem in respiration. He came to me at 9:30 pm at night from Bundi. He could not retrieve it and landed in emergency department.

He was illiterate, without any chronic disease, and at presentation, there were symptoms of respiratory distress or hoarseness. The general physical examination was unremarkable except that he was looking anxious (Fig. 1). Examination of the ear, nose and throat was all within normal limits and on indirect laryngoscopy, there was pooling of saliva in both pyriform sinuses. An X-ray of the neck and chest region, anteroposterior and lateral view, was unremarkable (Fig. 2).

Subsequently, a CT scan of the neck and chest region revealed a long radio-opaque foreign body in the whole length of the esophagus and also impinging into the stomach. So, a diagnosis of foreign body esophagus was made and the patient was subjected to rigid esophagoscopy under general anesthesia. Using an adult esophagoscope, upper end of the foreign body was encountered just beyond the cricopharynx and

Figure 1. Patient with respiratory distress and looking anxious.

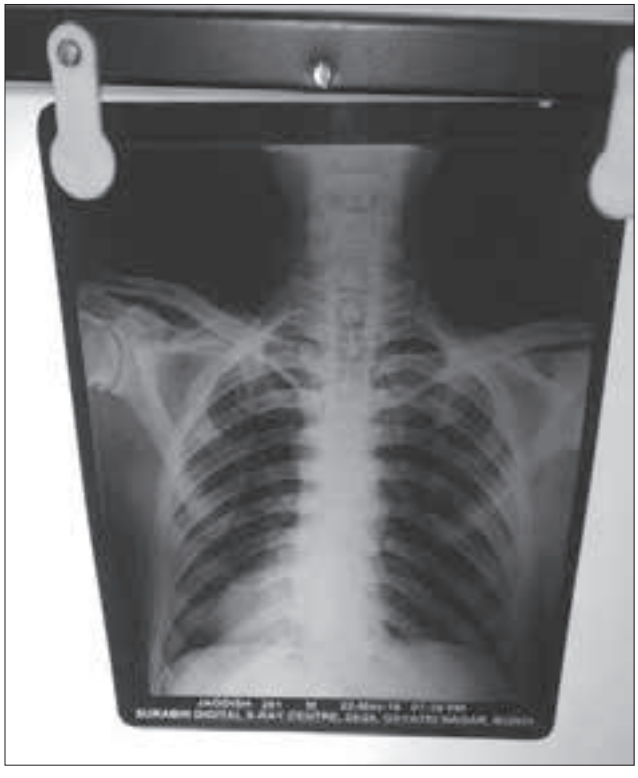

Figure 2. X-ray evaluation was unremarkable.

it was grasped securely with a grasping forceps and the foreign body was removed with the Jackson's rigid esophagoscope (Fig. 3).

A check esophagoscopy was done and revealed no injury to the esophageal mucosa. The postoperative period was uneventful and the patient was allowed food orally after 12 hours.

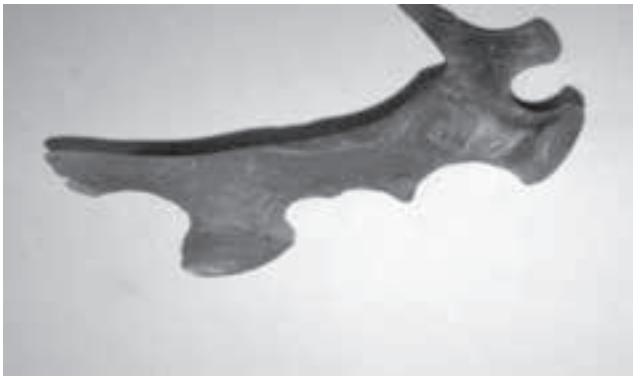

Figure 3. Foreign body removed.

DISCUSSION

A foreign body impacted in the esophagus calls for immediate attention and treatment. Dysphagia (92%) and tenderness in neck (60%) have been found to be the most common clinical features. A vast majority of patients come to the hospital within 24 hours of foreign body impaction. X-ray of the neck (lateral view) appears to be the most valuable investigation tool. Presence of air in the esophagus is a significant finding.[5] Most foreign bodies are radio-opaque and can be recognized on a plain radiograph. Their progress can be checked periodically in the bowel. Bone fragments look like linear or slightly curved densities with sharp margins. Small fish bones or pieces of plastic and wood; however, can appear only faintly radio-opaque calling for a CT scan for their detection.[2] Foreign bodies in hypopharynx and cervical esophagus such as chicken and fish bones often require radiologic evaluation. Noncontrast CT scan may show these small calcified esophageal foreign bodies when X-ray and barium swallow fail.[6]

Indirect signs that can be seen on plain radiography include soft tissue swelling and/or air due to edema or hematoma. In case of suspected perforations, esophagography should first be performed with hydrosoluble contrast medium to exclude perforation and can then be followed by a barium examination. The contrast medium may impregnate the surface of the foreign body and making it noticeable. Dilatation of the esophagus proximal to the obstruction with air fluid level and absence of air in the fundus of the stomach are signs of impaction in the distal esophagus, as evidenced on a radiograph.[2]

The postcricoid region was found to be the site of impaction of foreign bodies in 84% of the subjects in a study. Esophagoscopy was successful in 97% of the patients and failed in 3%. Coins appear to be the most common foreign bodies (60%), followed by meat-related

foreign bodies (22.5%) and dentures (5%). Complications were noted in 18% patients and were more common in adults (37.1%) in comparison with children (8.8%). Pneumomediastinum was the most serious of all complications. Maximum complications occur with dentures (80%) and bone chips (42%).[5] Foreign body in the esophagus is therefore a serious condition and warrants early removal by rigid esophagoscopy as it is a safe and effective procedure.

Other treatment interventions involve removal with a laryngoscope in case of foreign bodies impacted in the pharynx, or with a hypopharyngoscope for hypopharyngeal foreign bodies. Less easily, foreign bodies can be removed using a flexible esophagoscope. The common complications encountered with a rigid esophagoscope include injury to the lips, teeth, tongue, palate and esophageal perforation commonly at the level of cricopharyngeal sphincter.[2] Complications can; however, be limited if treatment is initiated within 24 hours of foreign body impaction.[7]

Sharp end of the foreign body has to be taken in the lumen of the endoscope to avoid complications. Partial dentures with sharp hooks, metallic springs and screws are the most difficult and dangerous objects to remove from the esophagus.[8] One can cause laceration and perforation during removal of such objects.

CONCLUSION

Early diagnosis and immediate removal of a foreign body are key to avoid any complications. Although 80-90% of the foreign bodies pass smoothly through the gastrointestinal tract, the nature of foreign body has to be determined. In case of a disc battery, it should be removed surgically if it remains in any one position for more than 24 hours. Sharp and large foreign bodies such as a screw have to be removed to prevent any further complications.

It is advisable to have a team approach while dealing with sharp and impacted foreign bodies.

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Wearable Sensor Detects Worsening Heart Failure

A wearable multisensor patch has been shown to detect signals of patients' heart failure (HF) exacerbations days before hospital readmission in the LINK-HF study.

Continuous 24-hour monitoring analyzed by a machine learning algorithm identified precursors of hospitalization for HF exacerbation with 76-88% sensitivity and 85% specificity, reported researchers in *Circulation: Heart Failure*.

FDA Approves Dulaglutide for Primary and Secondary CV Risk Reduction

The US FDA has additionally approved dulaglutide for reducing the risk of major adverse cardiovascular events (MACE) in adults with type 2 diabetes with and without established cardiovascular disease (CVD) or several CV risk factors.

Dulaglutide is the first and only type 2 diabetes medicine that has been approved to reduce the risk of CV events for both primary and secondary prevention populations… (*Medscape*)

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

HEART CARE FOUNDATION OF INDIA
A Not-For-Profit Organisation

Sameer Malik Heart Care Foundation Fund

An Initiative of Heart Care Foundation of India

E-219, Greater Kailash, Part I, New Delhi - 110048 E-mail: heartcarefoundationfund@gmail.com Helpline Number: +91 - 9958771177

"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

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Deep Malik
Geeta Anand
Dr Uday Kakroo
Harish Malik
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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.

Indian Journal of Clinical Practice, Vol. 30, No. 10, March 2020

Malignant Peripheral Nerve Sheath Tumor Arising in a Neurofibroma

MONICA KUMBHAT M*, LEENA DENNIS JOSEPH†, ARCHANA B*, ARULAPPAN‡

ABSTRACT

Malignant peripheral nerve sheath tumor (MPNST) is a rare variety of soft tissue sarcoma of ectomesenchymal origin. These tumors present diagnostic difficulties in differentiating from other high-grade spindle sarcomas. This is a case of a 45-year-old lady who presented with pain and swelling in the groin for past 4 months, which on excision and histopathology revealed an MPNST in a neurofibroma.

Keywords: Malignant peripheral nerve sheath tumor, soft tissue sarcoma, ectomesenchymal, neurofibroma

Malignant peripheral nerve sheath tumor (MPNST) is a malignant neurogenic tumor that occurs with high frequency (8-13%) in association with neurofibromatosis type 1 (NF-1), arising either *de novo* or in transition from neurofibroma.[1] It either develops from peripheral nerves, pre-existing benign neurofibromas or schwann cells. NF-1 patients are more frequently diagnosed with MPNST in the third or fourth decades of life, whereas the sporadic form of MPNST is most frequently diagnosed in the sixth or seventh decades of life.

CASE REPORT

A 45-year-old female developed pricking type of pain in the right groin extending to right knee for a duration of 4 months. There was also a history of fever on and off for 1 month. She gave a history of neurofibromatosis for 35 years. On local examination, a large neurofibroma was seen in the right inguinal region. Neurofibromas were also seen in the knee and arms (Figs. 1 and 2). On ultrasound, there was a well-defined heterogeneous mass involving predominantly deep subcutaneous and muscular planes of proximal right thigh measuring 9.7 × 5.7 × 5.8 cm. Fine needle aspiration cytology (FNAC) of the same lesion showed fibrocytes, mature adipocytes, a few spindle-shaped cells with sharp ends suggestive of wavy nerve fibers. She had history of excision of the swelling in the same region 2 years ago, which was histologically proved to be a neurofibroma.

In the same region, the patient presented with the present swelling. On excision of the mass, histologically it showed an undifferentiated pleomorphic sarcoma (Fig. 3), which was confirmed on immunohistochemistry

Figure 1. Single, small neurofibroma seen on lateral aspect of the left knee.

*Postgraduate Student
†Professor
Dept. of Pathology
‡Professor
Dept. of General Surgery
Sri Ramachandra Medical College, Chennai, Tamil Nadu
Address for correspondence
Dr Leena Dennis Joseph
Professor
Dept. of Pathology
Sri Ramachandra University, Porur, Chennai - 600 116, Tamil Nadu
E-mail: leenadj@gmail.com

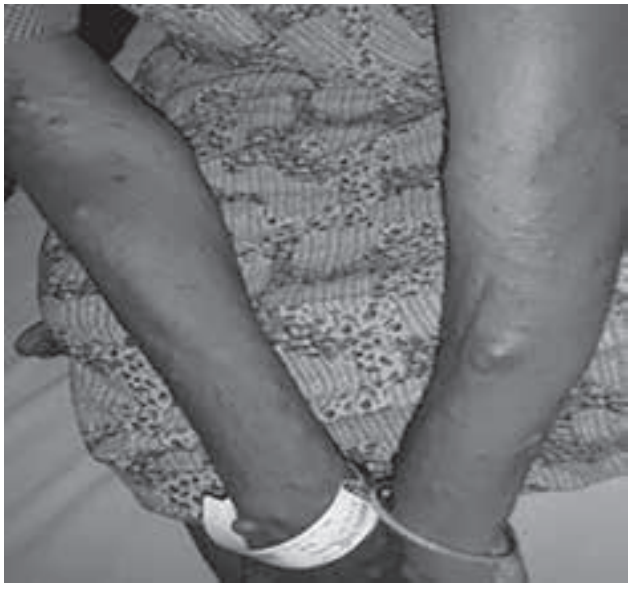

Figure 2. Both arms showing multiple neurofibromas of varying sizes.

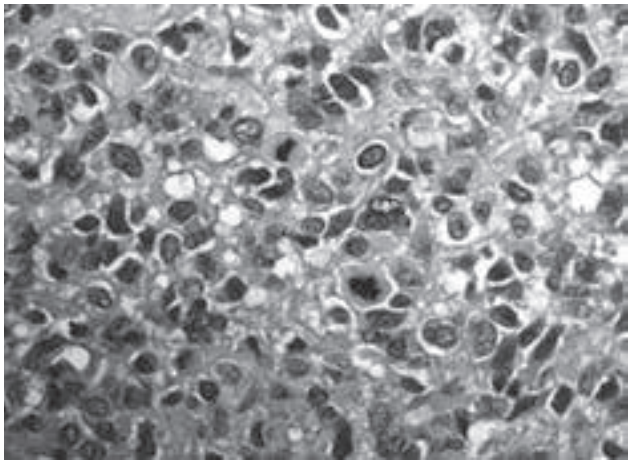

Figure 3. Pleomorphic tumor cells with mitotic figures (H&E x400).

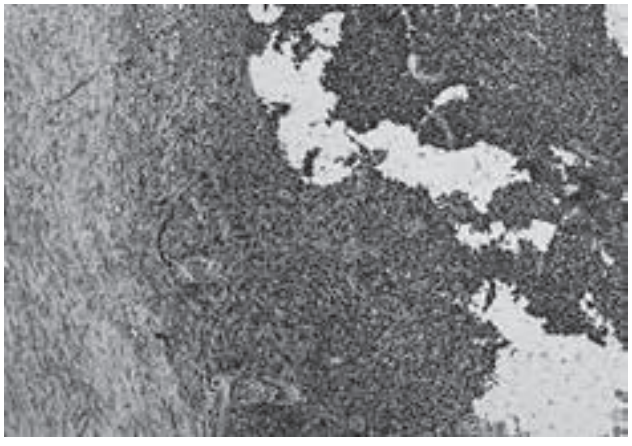

Figure 4. S-100 positivity in the tumor cells (IHC x100).

to be positive for vimentin and S-100 (Fig. 4) suggesting a neural origin. The tumor cells were markedly pleomorphic with increased mitosis, many of them being atypical. Thus, a diagnosis of MPNST in a neurofibroma was given. Patient was referred to a radiation oncologist for further management.

DISCUSSION

MPNST is a rare malignant tumor with poor prognosis accounting for 3-10% of all soft tissue sarcomas. It is the second most common variety of soft tissue sarcomas seen. A combination of gross and microscopic findings along with immunohistochemical studies is commonly used to diagnose a case of MPNST.

These tumors occur in equal frequency in males and females and some series have shown a female preponderance. The majority of these tumors are seen involving the extremities; although tumor were also seen in unusual sites, such as the pelvis, retroperitoneum and infratemporal fossa. Imaging is routinely performed to assess the extent of the disease and plan surgical resection. However, it does not reliably determine the malignant transformation from neurofibroma to MPNST. Magnetic resonance imaging (MRI) is the investigation of choice because it can reveal the nerve of origin. Grossly, the tumor size ranges from 4 to 24 cm in greatest dimension.[2]

Histologically, following criteria are used for the diagnosis of MPNST: a) Gross fusiform tumors in relation to nerves; b) microscopic feature of spindle cell with fascicular pattern and varying degrees of mitosis, necrosis and tumor calcification; c) presence of associated benign neurofibroma or schwannanian cells and d) positive immunohistochemical staining for S-100 protein, neuron-specific enolase and others like actin, cytokeratin, smooth muscle actin and vimentin to differentiate from other spindle cell sarcomas. The tumors are classified as low-grade and high-grade on the basis of their cellular differentiation, mitotic count, tumor necrosis and expression of MIB-1 proliferation marker.[3]

However, it is not always possible to demonstrate the origin from a nerve, especially when it arises from a small peripheral branch. This point was exemplified in a series by Nambisan et al,[4] in which nerves could not be identified in 61% of cases of MPNST and in another series, in which nerve origin could be identified only in 45-56% cases. Still, there are several other distinct features, such as proliferation of tumor in the subendothelial zones of vessels with neoplastic cells

herniating into vessel lumen and proliferation of small vessels in the walls of the large vessels, which are very characteristic features of MPNST. Syndromes that are associated with MPNST are NF-1 and NF-2.

Histologically, strict morphologic criteria must be applied to distinguish the spectrums of MPNSTs from cellular schwannoma, atypical and malignant meningioma and from a variety of rarely occurring intracranial sarcomas, such as high-grade pleomorphic sarcoma "malignant fibrous histiocytoma" fibrosarcoma, synovial sarcoma and leiomyosarcoma. On the benign side of the spectrum, cellular schwannoma is another tumor to be distinguished from MPNST. This tumor is particularly prone to be mistaken for malignancy, given the presence of hypercellularity, mitotic activity, and occasional locally aggressive growth. Strong S-100 protein as well as collagen IV/laminin immunoreactivity is the rule in this tumor. With respect to separating MPNST from benign nerve sheath tumors, p53 may be useful, strong immunostaining being seen in the majority of MPNSTs.[5] Ten percent of MPNSTs exhibit focal divergent differentiation, either mesenchymal (rhabdomyosarcoma, chondrosarcoma, osteosarcoma, angiosarcoma) or epithelial (mucin-producing, neuroendocrine or squamous type).

CONCLUSION

MPNSTs are aggressive, high-grade, therapy-resistant and associated with poor prognosis. A combination of clinical, pathological and immunohistochemistry helps in diagnosing these tumors. Proliferation marker (MIB-1) can be a good adjunct to grade and tailor the treatment in MPNST. Sex and cellular differentiation are the new adverse prognostic factors for survival of the patients. Postoperative radiotherapy has a definitive role in both disease free and overall survival. Though multimodality therapy, including surgical resection and adjuvant radiotherapy, is available, the prognosis remains dismal. Modern clinical studies and the development of effective targeted chemotherapy are needed to gain control of the disease.

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Positive Effects of Meditation Seen on Brain Imaging

Reductions in perceived stress and anxiety after transcendental meditation (TM) have been associated with functional changes in key regions of the brain, reported the first study investigating the effects of the practice on the brain with the help of resting-state functional magnetic resonance imaging (fMRI).

Meditators had lower levels of anxiety and stress following TM practice for 3 months, and the changes in perceived psychological well-being were tied to modifications in brain functional connectivity, reported researchers in the journal *Brain and Cognition*.

Smoking and Drinking Linked to Recreational Drug Use by Young People

The use of alcohol and tobacco by young people and children is associated with the use of illicit drugs, stated a UN-backed narcotics control body.

The International Narcotics Control Board (INCB) annual report mentioned studies that suggested that in young people 16-19 years of age, early use of alcohol, tobacco and cannabis leads to higher odds of the use of opiates and cocaine in adulthood… (*UN*)

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Indian Journal of Clinical Practice, Vol. 30, No. 10, March 2020

Piggyback Aspergillosis: Pulmonary Hydatid Cyst with Aspergillus Co-infection

SANJEET KUMAR SINGH*, KALPANA CHANDRA†, UMAKANT PRASAD‡, MONA LISA#, ANITA KUMARI¥

ABSTRACT

Aspergilloma is a saprophytic infection that colonizes pre-existing cavities in the lung. These cavities are caused by tuberculosis, bronchiectasis, lung cancer and other pulmonary diseases. Development of aspergilloma in the residual cavities after pulmonary hydatid cyst surgery is rarely described in terms of co-existence of the two conditions. Here we report co-infection of pulmonary hydatid cyst and aspergilloma in a 43-year-old male who had history of minor thalassemia and suffered from chest pain, dyspnea, non-productive cough for at least 5 months and hemoptysis for 20 days.

Keywords: Aspergillosis, hydatid cyst, pulmonary hydatid cyst

Aspergilloma infection consists of a mass of fungal hyphae, inflammatory cells, fibrin, mucus and tissue debris and can colonize lung cavities due to underlying diseases such as tuberculosis, sarcoidosis, bronchiectasis, cavitary lung cancer, neoplasms and bronchial cysts.[1,2] Active invasion and proliferation of fungi in the laminated ectocyst or sometimes the pericyst of the hydatid is very unusual.

CASE REPORT

A 43-year-old male presented to the Pulmonary Medicine OPD with nonspecific complaints of mild weakness, cough, dyspnea, hemoptysis and chest pain for last 5 months. There was no history of fever or night sweats. He had visited local doctors. He got no relief even after a course of antibiotics. On radiological examination, X-ray chest showed a large cavitary lesion involving left lung. Sputum examination for acid-fast bacilli did not reveal any bacilli and GeneXpert evaluation for tuberculosis too was negative. Computed tomography (CT) chest showed a large cavitary lesion (5 × 6 × 6 cm) involving left lower lobe of lung (Fig. 1). A diagnosis of hydatid cyst was suggested on radiology.

The patient underwent surgical excision of the cyst after a course of antihelminthic treatment. Grossly, a grey-white already punctured cyst was received. When cut open, there was a foci of dirty black soft tissue and few daughter cysts (Fig. 2).

On histopathological examination, the section revealed lamellated hyaline acellular ectocyst of hydatid cyst (Fig. 3). There were collections of acute angle branching septate hyphae along with inflammatory cells, fibrin, mucus and tissue debris, conforming to morphology of Aspergillus (Fig. 4). Thus, a final diagnosis of Piggyback aspergillosis on pulmonary hydatid cyst was made. Itraconazole 100 mg/day was given for 3 months. The patient

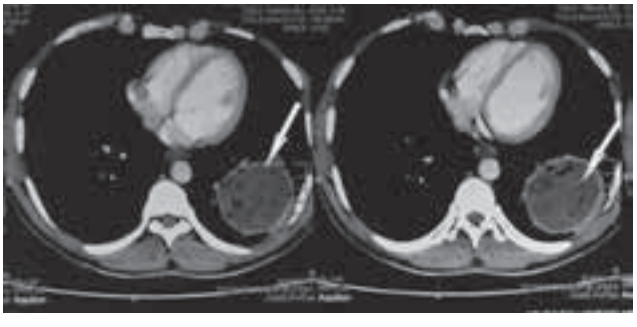

Figure 1. CT chest showing a large cavitary lesion (*white arrow*) in left lower lobe of lung.

*Associate Professor
†Assistant Professor
Dept. of Pathology
‡Assistant Professor, Dept. of Radiology
#Senior Resident, Dept. of Pathology
¥Senior Resident, Dept. of Physiology
Indira Gandhi Institute of Medical Sciences (IGIMS), Patna, Bihar
Address for correspondence
Dr Sanjeet Kumar Singh
Associate Professor
Dept. of Pathology
IGIMS, Patna, Bihar - 800 014
E-mail: drsanjeetsingh@gmail.com

Figure 2. Grey-white already punctured cyst with foci of dirty black soft tissue (*gray arrows*) and few daughter cysts (*black arrows*).

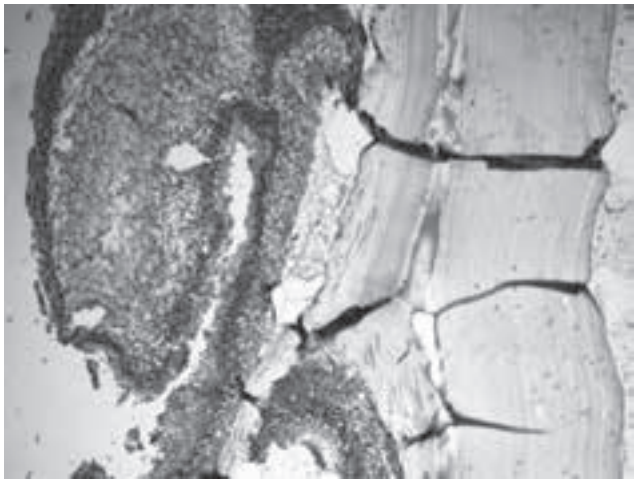

Figure 3. Lamellated hyaline acellular ectocyst of hydatid cyst with ball of Aspergillus attached (scanner view).

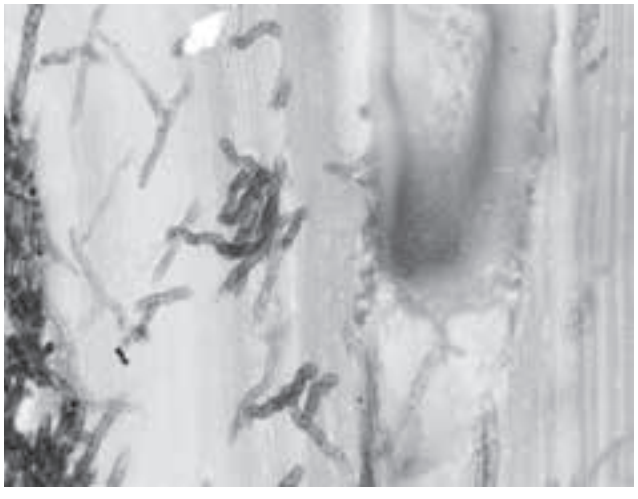

Figure 4. Acute angle branching septate hyphae along with fibrin, mucus and tissue debris (100x).

remained asymptomatic with normal radiological control after more than 9 months.

DISCUSSION

Pulmonary aspergilloma is a saprophytic infection which occurs as a colonizer of pre-existing pulmonary cavity lesions of any etiology such as sequelae tuberculosis, sarcoidosis, bronchiectasis, cavitatory neoplasia and lung abscess, producing a fungus ball or a mycetoma.[1-3]

Radiological diagnosis is made upon visualizing a well-defined heterogeneous density within a pre-formed cyst cavity, separated from the cyst wall by an air crescent. Aspergillosis and echinococcosis share the same symptoms and crescent signs on chest CT, making it difficult to distinguish.[4] CT usually reveals globules of gas within the hyphal ball, which may be loose or attached to the cavity wall by granulation tissue.[5]

Hydatid cysts containing fungi resembling Aspergillus are extremely rare. At present, such cases have been uncommonly reported. From 100 archival cases of hydatid disease, Koçer et al found two cases of simultaneous Aspergillus infection, and such infections were seen only in the lung.[6] The reason for such association still remains unclear.

The surgical treatment of lung hydatid cyst aims to avoid lung parenchyma resection. This surgery is based on the removal of the cyst membrane (cystectomy or pericystectomy), the closure of bronchial fistulas and eventually obliteration of the residual cavity with sutures (the capitonnage).[7]

Finally, aggressive surgical treatment with lung resection and antifungal therapy for pulmonary aspergilloma in residual hydatid cavities are safe and effective treatment options, and can achieve favorable outcomes.

CONCLUSION

As this co-infection is an incidental finding, a high-degree of suspicion is needed to predict the superimposed mycosis. Early diagnosis and treatment is important to prevent potential complications stemming from infection by these two pathogens.

Acknowledgment

I take this opportunity to extend my gratitude and sincere thanks to all those who helped me to complete this study.

I am highly thankful to Dept. of Surgery, Pathology, Microbiology and Radiology for providing me adequate facility which helped me to carry out this study.

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Dreaded Complication of Free Flap Failure Managed Intelligently

ASHOK SHARMA*, SANJIV K GOYAL*, SANDEEP SINGH MAAVI†, VIJAY JAGAD‡, AMITABH KUMAR UPADHYAY#

ABSTRACT

Salvage surgery in head and neck carcinoma is often followed by dreaded postoperative complication. Reconstruction with free flap is usually the ideal treatment option. Here, we present the case of a 46-year-old man with necrosis of free flap in post-radiotherapy carcinoma buccal mucosa. The flap was thus taken down and was replaced by a large pectoralis major myocutaneous flap to cover the intra-oral defect and part of the facial defect. The area in front of ear was left bare, to be reconstructed after stabilization of the patient. Later, the patient was taken up for surgery and posterior auricular flap was used to cover the defect anterior to the ear. Astute knowledge of local flap with preserved blood supply is thus needed in post-radiotherapy cases with failure of free flap.

Keywords: Head and neck carcinoma, free flap, salvage surgery

Salvage surgery in head and neck carcinoma is often met with dreaded postoperative complication. Reconstruction with free flap becomes the ideal intervention as it gets new blood supply to the area and hence theoretically improves the chances of viability of flap. In case of necrosis of free flap, very little options are left for the cover of the defect. Here, we are presenting the case of necrosis of free flap in post radiotherapy carcinoma buccal mucosa. After multiple surgeries, patient received adequate cover of the defect with local flaps but with poor functionality.

CASE REPORT

A 46-year-old man presented to us with history of ulcer in left buccal mucosa and severe trismus for past 3 months. In past, patient had undergone surgery and radiation for carcinoma left buccal mucosa 1½ year back.

On examination, patient had severe trismus Grade IV and the lesion was seen starting from left anterior commissure; due to severe trismus, posterior extent of the lesion was not assessable. Magnetic resonance imaging (MRI) scan of the face and neck revealed irregular thickened lesion involving whole of left buccal mucosa extending from upper alveolus to the lower gingivobuccal sulcus. Biopsy from the buccal mucosal lesion revealed squamous cell carcinoma. In accordance with the extent of lesion and the post radiotherapy status of the neck skin, we planned for wide excision and cover with free flap.

Patient underwent wide excision with left hemimandibulectomy, left upper alveolectomy and cover with anterolateral free flap. Post-op on second day, the free flap became dusky and revision surgery was planned (Fig. 1). The flap was taken down and was replaced by a large pectoralis major myocutaneous (PMMC) flap to cover the intra-oral defect and part of the facial defect. The PMMC flap did not cover the defect completely and the area in front of left ear was left open (Fig. 2). Patient was managed conservatively and later

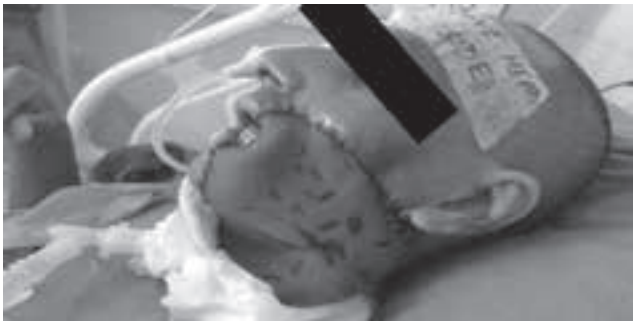

Figure 1. Free flap getting dusky at post-op Day 2.

*Consultant General Surgeon
†Junior Consultant
‡Consultant Oncosurgeon
#Consultant Medical Oncologist
Grecian Super Speciality Hospital, Mohali, Punjab
Address for correspondence
Dr Vijay Jagad
House No. 661, Sector 69, SAS Nagar, Mohali, Punjab - 160 062
E-mail: vijayoncowinmail.com@gmail.com

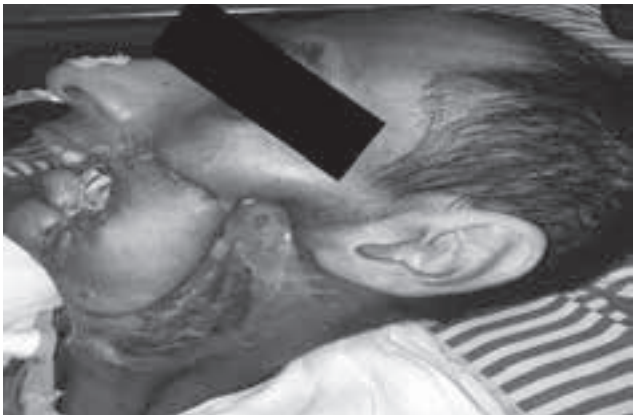

Figure 2. PMMC flap covering part of the defect after taking down the free flap, preauricular area still left uncovered.

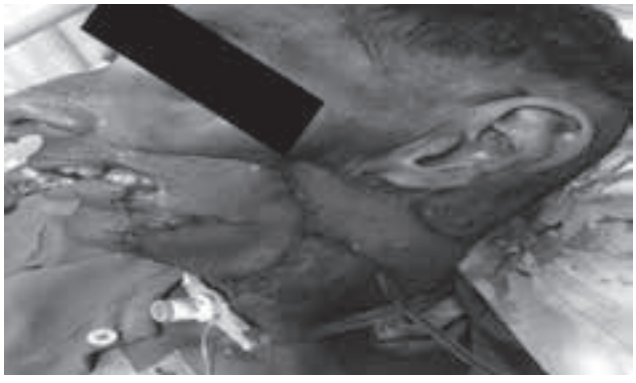

Figure 3. Complete cover of the defect after using posterior auricular flap.

after complete recovery, posterior auricular flap was used to cover the defect anterior to left ear (Fig. 3).

DISCUSSION

Post radiotherapy recurrent tumors in head and neck regions are taxing for surgeons to deal with. These cases are met with maximum postoperative complication due to reduced vitality of the tissue. The tissue, after radiotherapy, undergoes fibrosis with severe contractures and reduced blood supply. Reconstruction of the defect after full thickness excision is another challenge. The option of local rotation flap is not viable due to extensive radiotherapy effect and associated contracture. Plastic surgeon needs to bring viable tissue from nonirradiated area to the site of defect and anastomose to it. This can be best done by myofasciocutaneous free flap. Still postoperative complication rate of infection, fistula formation, flap necrosis remains high in these cases.

An ideal free flap which suits best for the defect and has least complication is not derived yet. One has to choose according to the site and size of the defect for optimal functional and cosmetic rectification. This patient of ours had lesion involving left buccal mucosa right from anterior commissure to the retromolar trigone and also the left lower gingivobuccal sulcus. The left cheek was puckered post radiotherapy, but frank invasion of tumor into the skin was not there. In view of extensive buccal mucosal involvement and thick nonpliable cheek skin, we planned for complete full thickness excision and reconstruction with free flap. Anterolateral thigh flap was used for reconstruction of inner buccal mucosal lining and for the outer skin coverage.

On post op Day 2, flap became dusky and on stroking the flap no prompt bleeding was noted. Plan was made to take down the flap and for local flap cover. Patient's left side face and neck was irradiated and hence there were minimal options for local flap. PMMC flap was used to cover the defect, intra-oral lining was covered completely but the face was partly covered. The area in front of ear was left bare for reconstruction after stabilization of the patient. After 2 weeks, he was taken up for surgery and posterior auricular flap was used. Patient was discharged after complete take up of the flap. Astute knowledge of local flap with preserved blood supply must be there in post radiotherapy cases with failure of free flap.

CONCLUSION

Free flaps are the best to cover the defect after salvage surgery in head and neck carcinoma. Free flap failure leads to bad functional as well as cosmetic aspect of head neck region. A redo surgery with cover from local flaps is difficult and that compromises the final outcome of the patient.

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Vitamin D Deficiency – A Reversible Cause of Proximal Myopathy

SUBHASH MEEL*, SAMEER AGGARWAL†, DEEPAK JAIN‡, HK AGGARWAL#, RAHUL CHAUDA*, PROMIL JAIN¥

ABSTRACT

A 22-year-old married Hindu female, vegetarian, with lower socioeconomic status, presented with an insidious onset progressive bilateral lower limb symmetrical proximal muscle weakness without sensory and bladder and bowel involvement, from last 2 years. Bone scan reports were suggestive of mineral and bone disease. Vitamin D deficient osteomalacia was diagnosed based on elevated serum alkaline phosphatase levels, raised intact parathyroid hormone levels, decreased 25-hydroxyvitamin [25(OH)D] levels. Patient's symptoms improved after oral active vitamin D and calcium administration. The present case highlights the importance of considering vitamin D deficiency in patients presenting with musculoskeletal symptoms and a routine evaluation for vitamin D deficiency should be considered in all patients.

Keywords: Vitamin D deficiency, proximal myopathy, hypocalcemia, osteomalacia

Although the prevalence of vitamin D deficiency is common worldwide, it is often under-estimated. It is estimated that vitamin D deficiency or insufficiency affects around 1 billion population worldwide.[1] According to the previously published study reports, the prevalence of varying degrees of vitamin D deficiency with low dietary calcium intake in Indian population is extensive (50-90%).[2] However, the exact incidence of myopathy in individuals with hypovitaminosis D is unknown. Proximal myopathy has been reported to be present in 60-75% of patients with vitamin D deficiency.[1]

The weakness usually occurs in proximal muscles and it is often minimal and subclinical. Osteomalacia, by definition, means that osteoblasts have laid down a collagen matrix, but there is a defect in its ability to be mineralized. In children, a defect in the mineralization of the osteoid in the long bones and the failure or delay in the mineralization of endochondral new bone formation at the growth plate leads to the classic skeletal deformities of rickets. However, in adults, the mineralization defect takes on a different character due to the failure of mineralization of newly formed osteoid at sites of bone turnover of periosteal or endosteal apposition. Here, we present a case of severe muscle weakness with osteomalacia due to vitamin D deficiency, which rendered the patient wheel chair bound.

CASE REPORT

A 22-year-old female visited our outpatient clinic with weakness of bilateral lower limbs, which was gradually progressive from last 2 years. The patient, who was wheel chair bound from past 3 months, complained of bilateral lower limb pain, backache, severe fatigue and inability to walk without support and to get up from squatting position and slight difficulty in combing of hair and lifting of weight from last 3 months. There was no history of any trauma/steroid intake/periodic paralysis/chronic diarrhea/carpopedal spasm/hematuria/neck swelling/palpitations/tremors/jaundice/height loss/fragility fracture/antiepileptic intake/antitubercular intake. Patient had history of recent blood transfusions and was currently on oral iron and multivitamins supplements.

On examination, patient was conscious, well-oriented, had pallor with slight dark complexion. Her vitals

*Resident
†Professor
‡Associate Professor
#Senior Professor and Head
Dept. of Medicine
¥Associate Professor
Dept. of Pathology
Pt. BD Sharma University of Health Sciences, Rohtak, Haryana
Address for correspondence
Dr Deepak Jain
Associate Professor
Dept. of Medicine
Pt. BD Sharma University of Health Sciences, Rohtak - 124 001, Haryana
E-mail: jaindeepakdr@gmail.com

were: blood pressure (BP) - 120/80 mmHg, pulse - 84 bpm, respiratory rate (RR) - 16/min, body mass index (BMI) - 19.4 kg/m^2. She had regular bowels, bladder habits and sleep cycle. Her cardiovascular, respiratory and abdominal examinations were normal.

Central nervous system (CNS) examination revealed symmetrical proximal muscle weakness in bilateral lower limb with power of 3/5 at hip joint and in upper limb with power of 4/5 at shoulder joint and brisk deep tendon reflexes (DTR), and there was no sensory involvement. Skeletal examination revealed tenderness over lower back, hip and shin. Rest of the examination was normal.

Lab investigations revealed hemoglobin (Hb) - 10.4 g/dL, total leukocyte count (TLC) - 4,500, differential leukocyte count (DLC) - $P_{68}L_{28}M_2E_2$, platelet count - 4.2 lac. Kidney and liver function tests were normal. Patient had low serum calcium - 8.0 mg/dL, low serum phosphate - 1.8 mg/dL, raised serum alkaline phosphatase (ALP) - 874 IU/L and serum albumin - 3.8 g/dL. Serum intact parathyroid hormone (PTH) level was 93.06 pg/mL (normal: 10-65 pg/mL) and serum 25-hydroxyvitamin D [25(OH)D] level was 18.68 nmol/L (normal: 75-100); immunoglobulin A anti-tissue transglutaminase antibodies (IgA-tTG) level was normal. The urine was negative for urinary albumin and glucose and pH was 6.0; 24-hour urinary calcium was 49.3 mg/day (100-300 mg/day). Antinuclear antibodies (ANA), thyroid function test and total creatine phosphokinase (CPK) level were normal. The bone mineral density (BMD) T-score and Z-score, as measured by dual-energy X-ray absorptiometry, was -2.7 and -2.5 at the lumbar spine and -2.8 and -2.0 at the femoral neck, respectively, indicating a low BMD for her chronological age.

Radiographic images revealed a pseudo-fracture in the right radial shaft and lower end of left femur (Fig. 1), bilateral superior pubic rami (Fig. 2), and first, second and fifth metatarsal bones along with diffuse osteopenia in B/L tarsals, metatarsals and phalanges (Fig. 3). Bone scan (technetium 99m-methyl diphosphonate [^{99m}Tc-MDP]) showed abnormal increased uptake by skull bone, scapula and upper limb bones, multiple ribs and vertebrae, pelvic bone, lower end of left femur and multiple metatarsal bones (Fig. 4). Electrophysiological study was suggestive of myopathy.

On the basis of examination and investigations, patient was diagnosed as a case of vitamin D deficiency with secondary hyperparathyroidism. The patient was treated with once weekly doses of cholecalciferol 60,000 IU along with calcium carbonate 500 mg twice daily.

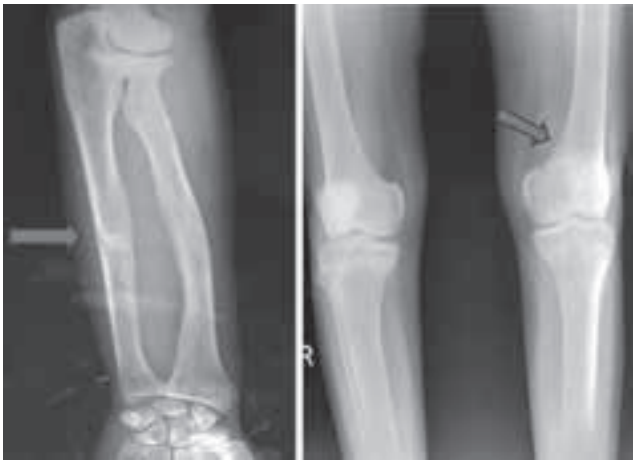

Figure 1. X-ray right forearm and lower end of left femur shows looser zone.

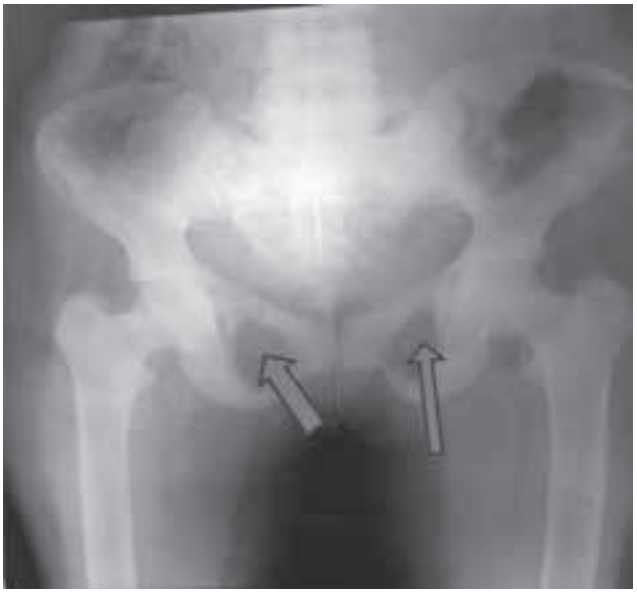

Figure 2. X-ray pelvis shows pseudo-fracture.

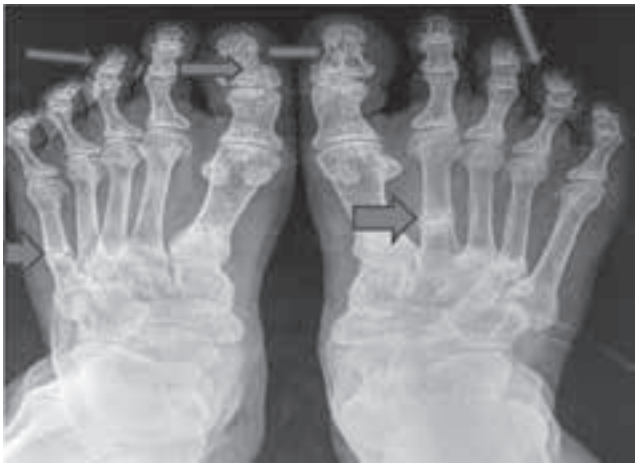

Figure 3. X-ray shows looser zone (*thick arrows*) and diffuse bone resorption (*thin arrows*).

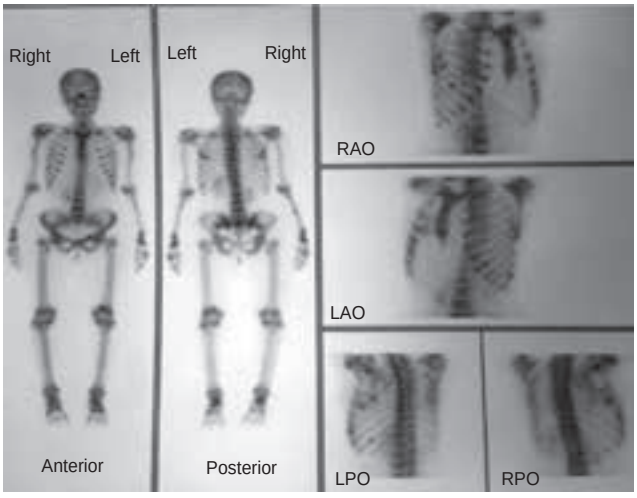

Figure 4. Bone scan.

Follow-up conducted at 4 weeks showed a gradual improvement in her symptoms. She was able to get up from chair and move without support and got significant relief in pain and fatigue. Levels of serum calcium and phosphorus were normalized but serum alkaline phosphatase (ALP) levels were still high (814 IU/L). At 3-month follow-up, pain, muscle weakness and gait disturbance had been completely alleviated and she resumed her routine daily activities. Biochemical parameters showed normal serum calcium, phosphorus as well as serum PTH and ALP. Patient is now on regular follow-up.

DISCUSSION

It has been estimated that over 1 billion people worldwide have vitamin D deficiency.[3] Vitamin D deficiency leads to decreased intestinal absorption of calcium and phosphorus, causing hypocalcemia and hypophosphatemia. Consequently, PTH secretion increases to overcome hypocalcemia which ultimately causes bone demineralization and osteomalacia in adults. In adults, osteomalacia usually does not present with any overt skeletal signs. However, patients with osteomalacia complain of throbbing, aching bone discomfort. Bone discomfort is worse when sitting or lying in bed. This is usually associated with proximal muscle weakness and aching in muscles.[4-6] Pressing on the skeleton resulting in discomfort is consistent with a trigger point that can lead to the misdiagnosis of fibromyalgia. In many cases, these patients are suffering from periosteal bone discomfort consistent with osteomalacia.

Several studies have shown an association between vitamin D deficiency and proximal myopathy. In most of the patients, muscle weakness, which is usually minimal, is revealed mostly on detailed history and physical examination. In infants, myopathy is evident from muscle weakness and hypotonia.[7] Adults may present with predominant proximal muscle weakness with difficulty in getting up from squatting position or climbing stairs. Other clinical characteristics of the disease include uniform generalized muscle wasting with preservation of sensation and DTR, and waddling gait.[8] Bone pain may also be present.

The case presented here had disabling muscle weakness and was not able to walk independently. Her serum calcium level was low-normal with low serum phosphorus with secondary hyperparathyroidism and elevated serum ALP. Normal serum levels of calcium and phosphorus in healthy individuals are achieved predominantly through interaction between the two hormones: PTH and calcitriol. In patients with vitamin D deficiency, secondary hyperparathyroidism causes release of calcium stored in bone and reabsorption of calcium by kidneys to maintain normal serum calcium till bony calcium is available. Hence, mild-to-moderate vitamin D deficiency is usually accompanied by normal blood levels of calcium, high-normal or elevated levels of PTH, elevated levels of ALP, a low 24-hour urine calcium excretion rate. Overt hypocalcemia and/or hypophosphatemia may appear only in patients with severe and long-standing vitamin D deficiency.[9]

While the exact cause of the muscle weakness and bone discomfort is not fully understood, it is believed that because the major cause of osteomalacia is vitamin D deficiency and because skeletal muscle has a vitamin D receptor (VDR), the lack of 1,25-dihydroxyvitamin D [1,25(OH)2D] interacting with the skeletal muscle VDR increases muscle weakness.[10]

Metabolic myopathies may be often accompanied by secondary hypovitaminosis D. Biopsies can help in differentiating hypovitaminosis D myopathy (HDM) from other myopathies, but this is rarely performed in current clinical practice due to its invasiveness and better availability of noninvasive biochemical and radiological markers.

The mechanism of HDM remains controversial, and it is still not clear whether vitamin D deficiency itself or in association with secondary hyperparathyroidism is the primary cause of muscle tissue and functional abnormalities. PTH production, induced by low vitamin D levels, may confer direct effects on skeletal muscles.

It is important to evaluate vitamin D deficiency as a cause of myopathy in suspected cases. Severe vitamin D

deficiency is easily treatable. Generally, advocated strategy is to prescribe a loading dose (50,000 IU of oral vitamin D once a week for 2-3 months or three times weekly for 1 month). A previous analysis of multiple loading algorithms indicated that a minimum total dose of 6,00,000 IU best predicted an end-of-treatment 25(OH)D concentration >30 ng/mL. For mild-to-moderate deficiency (11-25 ng/mL), a shorter term treatment or lower dose may be effective. In cases with recurrent deficiency, maintenance daily dose of 800-2,000 IU or more will be required. Treatment using high-dose vitamin D for 6 months or more may be essential for full normalization of HDM.

The present case highlights the significance of considering treatable causes first in patients presenting with musculoskeletal symptoms. A routine test for hypovitaminosis D should be considered in patients with musculoskeletal symptoms such as bone pain, myalgia and generalized weakness; as there is an increased chance for misdiagnosing hypovitaminosis D-associated symptoms as fibromyalgia, chronic fatigue, age-related weakness or depression.

CONCLUSION

It is always worthwhile to look for common and treatable factors causing metabolic bone disease. HDM is a common cause for proximal muscle weakness and osteomalacia. Raised ALP and PTH levels should always be worked up to diagnose vitamin D deficiency, which is easily treatable. Myopathy linked to vitamin D deficiency is completely reversible.

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Brain Activation in Unresponsive Patients with Acute Brain Injury: Words of Caution

AMIT AGRAWAL*, LUIS RAFAEL MOSCOTE-SALAZAR†, RAVISH KENI‡

Functional and structural integrity of severely injured brain remains a challenge for clinicians and neuroscientists.[1] New studies[2] are further expanding our understanding on noninvasive methods to evaluate the structural integrity of brain functions.[1,3] Apparently, it has been presumed that the patients have normal hearing; however, auditory response has been shown to be reduced after brain injury in many clinical studies.[4,5] There is a need to identify the presence or absence of pre-existing hearing impairment to find out its impact on brain activation. It needs to be further clarified whether evoked potential can help us to confirm the integrity of hearing. It is also important to note that apparently global insult due to systemic factors (cardiac arrest) causes more damage than more focal insult (TBI > SAH). There is a further need to understand the severity of injury, e.g., imaging evidence of global versus focal injuries, dominant versus non-dominant side lesions. Studies have shown promising results as majority of the patients at follow-up though dependent were alive. How to interpret and apply these findings on individualized basis is the next challenge.

*Dept. of Neurosurgery, Narayana Medical College and Hospital, Nellore, Andhra Pradesh, India
†Neurosurgeon-Critical Care, Center for Biomedical Research (CIB) Director of Research Line Cartagena Neurotrauma Research Group Faculty of Medicine - University of Cartagena, Cartagena de Indias, Bolivar
‡Dept. of Neurology, Narayana Medical College and Hospital, Nellore, Andhra Pradesh, India
Address for correspondence
Dr Amit Agrawal
Professor of Neurosurgery
Dept. of Neurosurgery, Narayana Medical College and Hospital, Chinthareddypalem, Nellore - 524 003, Andhra Pradesh, India
E-mail: dramitagrawal@gmail.com

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FDA Approves First Orally Disintegrating CGRP for Migraine Relief

The US FDA has given approval to rimegepant, the first calcitonin gene-related peptide (CGRP) receptor antagonist, available in a fast-acting orally disintegrating formulation for the acute treatment of migraine in adults.

In a trial, a single 75 mg dose of rimegepant has been found to yield rapid migraine pain relief with patients returning to normal activities within 1 hour. Sustained benefit was shown to last up to 2 days in many patients. About 86% of the patients treated with a single dose did not need a migraine rescue medication within 24 hours… (*Medscape*)

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Basics of Banking System

SAURABH AGGARWAL

Bank: A bank is a financial institution that accepts deposits from the public and creates credit.

Regulatory body: Reserve Bank of India (RBI).

Types of banks: Public sector banks also known as Nationalized Banks, Private sector bank, Foreign Banks, Regional Rural Banks, Small Finance Banks, Cooperative Banks, Payments Banks. SBI is the largest public sector bank by volume.

Types of accounts: Saving Account, Current Account, NRI Account (NRO, NRE, FCNR Account).

Saving bank account: A basic type of bank account that allows you to deposit money, keep it safe, and withdraw funds, all while earning interest. Interest earning is in the range of 3.5%. Some private banks are even offering higher interest up to 6-7%.

Current bank account: Also known as financial account, it is a type of deposit account maintained by professionals, companies, firms, etc., who carry out significantly higher number of transactions with banks on a regular basis. Such account doesn't not earn any interest rate.

NRI account: Non-Resident Indian (NRI) or a Person of Indian Origin (PIO) can choose to open NR accounts with any bank or financial institution which is authorized by the RBI. These are rupee dominated and can be opened in the form of savings, current, recurring deposits or fixed deposits. These accounts can be jointly opened with any Resident Indian on Former or Survivor basis.

NR Accounts are of 2 types:

- Non-Resident External (NRE) – No tax levied on the interest earned from these accounts, i.e., they are tax exempt. Money is easily repatriable, i.e., transferable. These are primarily opened for transfer of foreign earnings in India.
- Non-Resident Ordinary (NRO) – TDS is applicable on the interest earned from these accounts. Money is only repatriable based on regulatory approval. These are primarily opened for depositing earnings earned within India.
- **Foreign Currency Non-Resident (FCNR) Account:** It can be opened in different currencies such as US Dollars, Canadian Dollars, Australian Dollars, Sterling Pounds, Euro, Japanese Yen, etc. Money is easily repatriable. Interest earned is tax-free. Usually interest earned is very low as compared to regular NR deposit.

Type of deposits: Fixed deposit account, Recurring deposit account, Tax saver fixed deposit -

- A fixed deposit also called as FD is a financial instrument provided by banks or NBFCs which provides investors pre-defined usually higher rate of interest than a regular savings account, until the given maturity date.
- Recurring Deposit provides a person with an opportunity to build up saving through regular monthly deposits of fixed sum over a period of time and helps individuals to invest fixed contribution systematically.
- Tax saver fixed deposit (FD) is a type of fixed deposit, by investing in which, you can get tax deduction under Section 80C of the Indian Income Tax Act, 1961. Any investor can claim a deduction of a maximum of Rs. 1.5 lakh by investing in tax saver fixed deposits. There is a lock-in period of 5 years.

Modes of operations: It specifies how a bank account will be operated and by whom -

- Singly - When account is in a single name.
- Either or survivor - Either of the two can operate.
- Anyone or survivor - if there are more than two account holders, anyone can operate the account singly.
- Former or survivor - Till such time the former, i.e., the first name holder is alive, only he can operate the account.
- Jointly - Account will be operated by both or all account holders jointly.

Bank Insurance: In case of an unlikely bank failure, deposit up to ₹1 lakh is insured and paid back to the depositor by Deposit Insurance and Credit Guarantee Corporation, a wholly owned subsidiary of the RBI. Recently the limit has been increased to 5 lakhs/ depositor, effective from 4th February.

Ex-Banker and Director of HCFI

Indian Journal of Clinical Practice, Vol. 30, No. 10, March 2020

HCFI Activities: January-February 2020

KK AGGARWAL

Homoeopathy Cardiology Seminar and CPR 10 Training Workshop

Date: January 5, 2020

Place: Hotel Imperial Palace, Faridabad

Heart Care Foundation of India organized CPR Training Workshop for Homoeopathic Doctor's Association, Faridabad. A Lecture on Homoeopathy and Cardiology was given by Dr KK Aggarwal. Sixty homoeopathic doctors attended CPR 10 Training and lecture.

CPR 10 Training Workshop

Date: January 7, 2020

Place: HCFI Mera Clinik, Kotla Mubarakpur, New Delhi

Heart Care Foundation of India organized CPR 10 Training Camp for students of economically weaker section from American India Foundation at HCFI Mera Clinik, Kotla Mubarakpur, New Delhi. Twenty-five students attended the training. Certificates were given to all.

President, HCFI

Free Health Checkup Camp

Date: January 14, 2020

Place: HCFI Mera Clinik, Kotla Mubarakpur, New Delhi

Heart Care Foundation of India organized free health checkup camp in memory of Late Sh. Q R Aggarwal and Dr (Col) KL Chopra. Thirty-eight people attended the camp.

Seminar on Health Impact of Air Pollution

Date: January 14, 2020

Place: Hotel Crown Plaza, Okhla

The Seminar was organized by ECHO India and was attended by Dr KK Aggarwal and Dr Anil Kumar.

Conference on Positive Journalism

Date: January 24, 2020

Place: C-599, Acharya Sushil Muni Ashram, Defence Colony, New Delhi

Heart Care Foundation of India and RJS-TJAPSKBSK organized a conference on positive journalism. Ninety-four people attended the program.

Workshop on Health Awareness

Date: January 28, 2020

Place: Constitution Club of India, New Delhi

Heart Care Foundation of India, in collaboration with Shyama Prasad Mukherji College, organized a workshop on Health Awareness for teachers. Padma Shri Prof. Dinesh Singh, Chancellor K R Mangalam University was invited as Chief Guest. Topics included First AID, Choking and Cardiac Arrest, Science behind rituals, Handling Environment pollution. Seventy teachers from 22 colleges attended the workshop.

CPR 10 Training Workshop

Date: January 29, 2020

Place: Karkardooma Court, New Delhi

Heart Care Foundation of India organized a CPR 10 training workshop for judges at Karkardooma Court. Eighty judges attended the program.

World Leprosy Day

Date: January 30, 2020

Place: A-344, KP Thakkar Block, Asiad Village, Khel Gaon, New Delhi

Heart Care Foundation of India organized a health talk on World Leprosy Day. Dr KK Aggarwal, President, HCFI gave a lecture on "Leprosy is curable and no more ground for divorce". Twelve people attended the program.

CPR 10 Training Workshop

Date: February 4, 2020

Place: Amazon Seller Service Pvt. Ltd., D6,Udyog Nagar, Rohtak Road, Peeragarhi, Delhi

Heart Care Foundation of India organized CPR Training Workshop at Amazon Seller Service Pvt. Ltd, Peeragarhi, Delhi. Eighteen people attended CPR 10 training.

Sameer Malik Fund Dil Ka Darbar

Date: February 16, 2020

Place: C-599, Acharya Sushil Muni Ashram, Defence Colony, New Delhi

Heart Care Foundation of India, in association with Vishwa Ahimsa Sangh and IMA, New Delhi Branch, organized Sameer Malik Fund Dil Ka Darbar. Dr Vanita Arora was invited as Chief Guest. Our guest of honor Dr OP Yadava, Dr Mini Mehta, Dr AK Merchant, Dr Chanchal Pal interacted with SM Fund beneficiaries. Success stories of various heart patients were discussed. Free Health Checkup and consultation was provided. Three hundred people participated.

CPR 10 Training Workshop and Health Checkup Camp

Date: February 21, 2020

Place: Delhi Pharmaceutical Sciences and Research University, Mehrauli-Badarpur Road, Sector 3, Pushp Vihar, New Delhi

Heart Care Foundation of India organized CPR 10 Training workshop and Health Checkup camp at DPSR University, New Delhi for the teachers, students and delegates of International Conference on Cardiovascular Sciences. Four hundred fifty people attended CPR 10 training and Health Checkup Camp.

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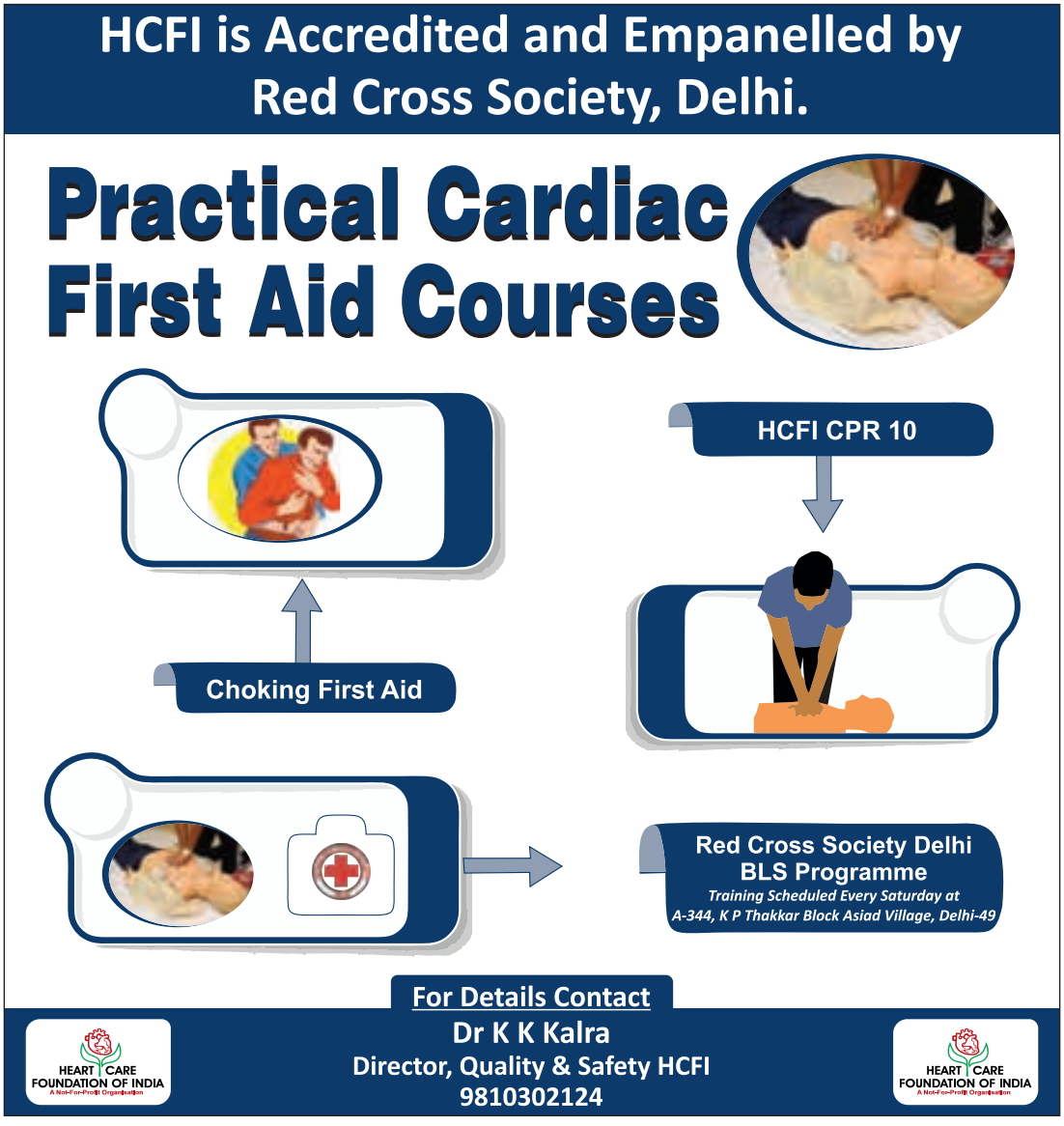
Lecture on Heart Attack

Date: February 22, 2020

Place: A-344, KP Thakkar Block, Asiad Village, New Delhi

Heart Care Foundation of India organized a lecture on Heart Attack. Fifteen people attended.



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Report of Environmental Health Division of HCFI (January-February 2020)

KK AGGARWAL

The Environmental Health Division of Heart Care Foundation of India (HCFI) has taken up a series of environmental activities for protection and improvement of environment including monitoring and control of air, water, noise and land pollution. Strategy for such activities includes environment education/training/awareness programs/workshops as well as action oriented activities with various stakeholders like schools, colleges, community, etc.

The activities include:

- Development of low-cost solutions for air pollution monitoring and control.
- Solution for noise monitoring and control in different use zones.
- Awareness workshops with Schools and Colleges on various environmental and pollution control issues.
- Awareness and action w.r.t. Sustainable Development Goals (SDG) and Climate Change issues.

On these lines, an awareness workshop on Health & Environment Awareness was conducted on 28 January, 2020 at Constitution Club of India wherein 22 colleges of Delhi University participated. There were lectures, demonstration and discussion on air and noise pollution issues.

Environmental Health Division of HCFI has taken up a project on Healthy Environment School Index with funding support from Envirotech Instruments Pvt. Ltd. The aim of this project is to establish/develop a healthy Environment School Index for schools. This pilot project is being done in 10 selected schools by using various environmental indicators like air quality in terms of AQI, noise levels, status of sanitation, cleanliness, waste management, plantation, etc.

Environmental Health Division has also focused on plantation activities. In this regard, a park opposite the head quarter of HCFI at Asiad Village has been adopted wherein medicinal plants, kitchen plants and anti-pollution plants are being planted. This park is being developed as model park for awareness on values/uses of plants for masses. Plant saplings are also distributed to participants in various programs of HCFI.

Further, Environmental Health Division of HCFI has also envisaged to collaborate with various Government Departments/Agencies and Institutions to take up research and development projects and activities in the area of environment and pollution control.

President, HCFI

■■■■

Carrying Diabetes Tools 'in the Pocket' Improves HbA1c Control

Patients with type 2 diabetes who formed part of a healthcare plan and used a computer and/or an app on a mobile device to access a portal with tools for diabetes management were found to adhere more with prescription refills and had improved A1c levels, revealed a 33-month study.

The improvements appeared to be greater in patients who did not previously use the portal and began using it through a mobile device app as well as computer, in comparison with a computer only. The greatest improvements were seen in patients with poorly controlled diabetes (A1c >8%) who started using the portal by both means. The study was published online in *JAMA Network Open*.

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Medtalks with Dr KK Aggarwal

Possible Scenarios: Coronavirus

- Hit and run virus and will disappear in 6 months.
- Join the flu on the listing of the world's winter illnesses—that will be routinely vaccinated against.
- Might take the form of a global pandemic, killing millions of people.

Hit and run virus

Travel restrictions and quarantine were imposed in Hubei province and elsewhere over millions of people. Coronavirus is believed to have an incubation period of up to 14 days.

Deadly outbreak is tamped down by quarantines and hospitalization.

It appears that asymptomatic infections do not drive the outbreak, based on other coronaviruses. Four common coronaviruses are already endemic in people which seem to cause about 10-30% of colds, and pneumonia, as well as the more dangerous Middle East respiratory syndrome (MERS) and severe acute respiratory syndrome (SARS), with SARS being the closest genetic match to 2019-nCoV or COVID-19.

Will become endemic like another seasonal flu

It may go on to have seasonal behavior, with flare-up in winter like the flu. This pattern has been seen in at least two of the common coronaviruses.

This would mean that it would reappear next winter. Such a thing happened with the 1918 Spanish flu pandemic that hit the world in two seasonal waves. However, this will give us time for clinical trials to test the effectiveness of antiviral drugs including remdesevir and development of a new vaccine.

Deadly global pandemic: Unlikely

The relatively few cases appearing in several countries may flare up worldwide in the coming months with deadly consequences. This was seen in 1957, when a flu pandemic killed 1.1 million people worldwide, and again in 1968, when another flu strain killed about 1 million people.

As per WHO, it has not seen an outbreak in doctors and nurses outside of Wuhan.

The Spanish flu outbreak of 1918 had a death rate of 2.5% and affected the young.

The new coronavirus mortality rate is lower than 2%, owing to unreported milder cases. A Chinese National Health Commission official said that the death rate in provinces except Hubei was 0.16%. That's still higher than influenza, which has about a 0.03% death rate.

Nearly 82% of COVID-19 cases are mild, 15% are severe, and 3% are critical.

Acts Applicable to COVID-19

Indian public health system

India has a constitutional division of legislative responsibilities between the Central government and the States. Both the Central government and the State governments are constitutionally empowered to legislate on matters of public health.

Central Acts

1. **Epidemic Diseases Act 1897**

   The preamble states that its objective is to provide for better prevention of the spread of dangerous epidemic diseases.

   It empowers the State governments and the Central government to take measures as required to control the further spread of disease.

   When a State government is satisfied that any part of its territory is threatened with an outbreak of a dangerous disease, it may adopt or authorize all measures, including quarantine, to prevent the outbreak.

   Likewise, the Central government, when satisfied that there is an imminent threat of an outbreak of an epidemic disease and that the provisions of the law are insufficient to prevent the outbreak, may take measures and prescribe regulations enabling inspection of any ship or vessel leaving or arriving at any port and for the detention of any person arriving or intending to sail.

   Any person who disobeys any regulation or order made under the 1897 Act may be charged with an offence under Section 188 of the Indian Penal Code.

   188. Disobedience to order duly promulgated by public servant.—Whoever, knowing that, by an order promulgated by a public servant lawfully empowered to promulgate such order, he is directed to abstain

from a certain act, or to take certain order with certain property in his possession or under his management, disobeys such direction, shall, if such disobedience causes or tends to cause obstruction, annoyance or injury, or risk of obstruction, annoyance or injury, to any person lawfully employed, be punished with simple imprisonment for a term which may extend to one month or with fine which may extend to two hundred rupees, or with both; and if such disobedience causes or trends to cause danger to human life, health or safety, or causes or tends to cause a riot or affray, shall be punished with imprisonment of either description for a term which may extend to six months, or with fine which may extend to one thousand rupees, or with both. Explanation.–It is not necessary that the offender should intend to produce harm or contemplate his disobedience as likely to produce harm. It is enough that he knows of the order which he disobeys, and that his disobedience produces, or is likely to produce, harm. Illustration–An order is promulgated by a public servant lawfully empowered to promulgate such order, directing that a religious procession shall not pass down a certain street. A knowingly disobeys the order, and thereby causes danger of riot. A has committed the offence defined in this section.

Such offence, at the discretion of the trial magistrate, may be tried summarily. No suit or legal proceeding lies against any person or authority for anything done, or in good faith intended to be done, under this Act.

Some of the issues that require revisiting - the "definition of epidemic disease, territorial boundaries, ethics and human rights principles, empowerment of officials, [and] punishment." National Centre for Disease Control is developing a "Public Health Emergencies Act".

2. **Indian Penal Code: Section 270:** *Malignant Act likely to spread infection of disease dangerous to life.—Whoever malignantly does any act which is, and which he knows or has reason to believe to be, likely to spread the infection of any disease dangerous to life, shall be punished with imprisonment of either description for a term which may extend to two years, or with fine, or with both.*
3. **MCI Ethics Regulations 2.2:** *Patience, Delicacy and Secrecy: Patience and delicacy should characterize the physician. Confidences concerning individual or domestic life entrusted by patients to a physician and defects in the disposition or character of patients observed during medical attendance should never be revealed unless their revelation is required by the laws of the State. Sometimes, however, a physician must determine whether his duty to society requires him to employ knowledge, obtained through confidence as a physician, to protect a healthy person against a communicable disease to which he is about to be exposed. In such instance, the physician should act as he would wish another to act toward one of his own family in like circumstances.*
4. **MCI Ethics Regulation 7.14:** *The registered medical practitioner shall not disclose the secrets of a patient that have been learnt in the exercise of his/her profession except – i) in a court of law under orders of the Presiding Judge; ii) in circumstances where there is a serious and identified risk to a specific person and/or community; and iii) notifiable diseases. In case of communicable/ notifiable diseases, concerned public health authorities should be informed immediately.*
5. **Quarantine of Visitors:** For people entering India from abroad, a health officer appointed by the Central government is posted and empowered at the port of entry.

   The health officer may ask for the aircraft journey logbook, which shows the places the aircraft visited. He may also inspect the aircraft, its passengers, and its crew, and subject them to medical examinations upon arrival.

   The officer should follow specific precautions about communicable diseases requiring a period of quarantine (such as yellow fever, plague, cholera, smallpox, typhus and relapsing fever) and other infectious diseases that do not require a period of quarantine.

   He has the authority to prohibit the embarkation on any aircraft of any person showing symptoms of any quarantinable disease and any person whom the health officer deems likely to transmit infection.

   Airline staff need to report any suspected cases or passengers who in their opinion, from observations made in flight, may be suffering from symptoms of a quarantinable disease.

   With Ebola, in August 2014, the Health Ministry announced that "mandatory self-reporting is required at immigration."
6. **Right to move free**

   Quarantine affects the fundamental right "to move freely throughout the territory of India." However, this right is subject to reasonable restrictions that the state may impose in the interest of public health.

7. **Right to privacy**

The Supreme Court of India has found that the right of privacy is an essential component of the right to life, but it is not absolute and may be restricted to prevent crime or disorder, or to protect health, morals or the rights and freedom of others.

State Acts

Punjab Vaccination Act makes primary vaccination and revaccination of children compulsory throughout the state.

Epidemic Diseases Act gives wide ranging powers to the states.

The states, in such emergencies, assign some of the powers to the deputy commissioners in the districts through State Health Acts or Municipal Corporation Acts.

State and Municipal Governments

A State government can take measures and prescribe regulations for the inspection, vaccination and inoculation of persons traveling by road or rail, including their segregation in a hospital, temporary accommodation or otherwise, if they are suspected by the inspecting officer of being infected with any such disease.

A State government, by general or special order, may authorize a deputy commissioner to exercise, in relation to his district, all the powers under Section 2 of the 1897 Act that are exercisable by the State government in relation to the state, other than to determine the manner in which and by whom any expenses are to be defrayed.

Many of these powers are prescribed in Municipal Corporation Acts governing the major municipal areas, or Public Health Acts that also provide municipal-level commissioners or collectors with quarantine or other powers. These can be in relation to removal of a person to separate premises for medical treatment, cleansing or disinfecting any building or part of any building or any articles, taking special measures in case of the outbreak of dangerous or epidemic diseases.

Civil Rights

The extent of Section 2 of the Epidemic Diseases Act is wide enough to allow a state or a lower functionary in the administration, in dealing with an emergency caused by the outbreak of a dangerous disease, to seek or require the cooperation of the public or corporate bodies in the public or private sectors. If the desired cooperation is not forthcoming, a regulation may be imposed. Failure to obey or comply with restrictions imposed by such a regulation constitutes a punishable violation.

Judiciary

The judiciary in India ensures transparency in government actions and executive orders. A judicial review of executive orders and regulations can be sought. The Parliament of India has also enacted a Freedom of Information Act, requiring transparency in government actions.

International Regulations

PHEIC: mandates reporting to WHO about disease in question.

The Epidemic Diseases Act

2. Power to take special measures and prescribe regulations as to dangerous epidemic disease:

(1) When at any time the [State Government] is satisfied that [the State] or any part thereof is visited by, or threatened with, an outbreak of any dangerous epidemic disease, the [State Government], if [it] thinks that the ordinary provisions of the law for the time being in force are insufficient for the purpose, may take, or require or empower any person to take, such measures and, by public notice, prescribe such temporary regulations to be observed by the public or by any person or class of persons as [it] shall deem necessary to prevent the outbreak of such disease or the spread thereof, and may determine in what manner and by whom any expenses incurred (including compensation if any) shall be defrayed.

(2) In particular and without prejudice to the generality of the foregoing provisions, the— [State Government] may take measures and prescribe regulations for— (*b*) the inspection of persons traveling by railway or otherwise, and the segregation, in hospital, temporary accommodation or otherwise, of persons suspected by the inspecting officer of being infected with any such disease. **[2A. Powers of Central Government.—**When the Central Government is satisfied that India or any part thereof is visited by, or threatened with, an outbreak of any dangerous epidemic disease and that the ordinary provisions of the law for the time being in force are insufficient to prevent the outbreak of such disease or the spread thereof, the Central Government may take measures and prescribe regulations for the inspection of any ship or vessel leaving or arriving at any port in [the territories to which this Act extends] and for such

detention thereof, or of any person intending to sail therein, or arriving thereby, as may be necessary.]

3. **Penalty**—Any person disobeying any regulation or order made under this Act shall be deemed to have committed an offence punishable under Section 188 of the Indian Penal Code (45 of 1860).
4. **Protection to persons acting under Act**—No suit or other legal proceeding shall lie against any person for anything done or in good faith intended to be done under this Act.

COVID-19 Challenges: Why is It More Contagious at Some Places?

The way COVID-19 has spread in local clusters, onboard Diamond Princess and in a church in Korea, has opened questions about its contagiousness.

- It is a droplet infection: Passes through droplets from coughing or sneezing. When these droplets carrying the virus from an infected person reach the nose, eyes or mouth of another person, they can transmit the virus.
- High viremia in early illness.
- It is infectious in both upper respiratory tract infection (URTI) and lower respiratory tract infection (LRTI) stage: Respiratory illnesses can be segregated into two categories: upper respiratory infections - involving the nose, pharynx or larynx (common cold and seasonal influenza); and lower respiratory illnesses - like pneumonia, which affect the lungs.

  The original 2003 SARS virus was a lower respiratory infection: It replicated in the cells within the lungs and caused pneumonia. People also appeared to spread the virus days into their illness. Thus, it was more difficult to transmit SARS to others and the task of containing the virus became easier.

  COVID-19 appears to be different. While it can also lead to pneumonia, by replicating in the lung cells, it can replicate in the upper respiratory tract as well, even when people don't have any symptoms or just begin to feel sick.

  In a paper published in the *New England Journal of Medicine*, German researchers isolated the virus from patients' upper respiratory tract even before they began to show any symptoms. This provides additional evidence for asymptomatic spread of the virus from the nose and throat.
- The virus might also spread through feces: In a paper from the Chinese Center for Disease Control and Prevention (CDC), researchers could isolate live virus from stool samples of COVID-19 patients. This suggests that the disease could spread when there's suboptimal hygiene. China CDC has therefore recommended measures to stop the spread of the virus through this route. The advice includes: maintaining environmental health and personal hygiene; drinking boiled water, avoiding raw food consumption and implementing separate meal systems in epidemic areas; frequently washing hands and disinfecting surfaces of objects in households, toilets, public places and transportation vehicles and disinfecting the excreta and environment of patients in medical facilities to prevent water and food contamination from patients' stool samples.

  More research is needed to understand the significance of fecal-oral route in the spread of this disease.
- Airborne transmission: During the first SARS outbreak, a large Hong Kong housing estate became ground zero when more than 300 people were infected with the disease through airborne transmission.

  Such a condition arises when the residue from evaporated, virus-containing droplets gets suspended in the air and goes on to infect those who breathe it in. This is not droplet transmission, since droplets are too large to float through the air and need to be sprayed directly on someone's eye, nose, or mouth in order to infect them.

  In this particular case of transmission, it was later found that SARS was capable of going airborne, spreading through the building's faulty plumbing and ventilation systems to the people who lived on the estate.

  Vito Iacoviello, chief of the vision of infectious diseases at Mount Auburn Hospital in Cambridge, Massachusetts, has noted that the US CDC is recommending people admitted with COVID-19 to be put in an airborne isolation room. That is the precaution used for TB, measles and chickenpox.
- The super-spreader: The R_0 value of the individual may be more that the R_0 value of the virus or the person has more viruses than the others. It has been seen that an HIV-positive person sheds less virus than HIV + STI-positive person. We may need to find out the additional factor which intensifies the spread.
- Contact period: The virus may survive on the surface longer than thought. Similar viruses have been surviving for up to a week.

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Annual Conference of Endocrine Society of India (ESICON 2019)

21ST-24TH NOVEMBER, 2019 | HOTEL LE MERIDIEN, NAGPUR

GENETICS OF GLUCOSE DYSREGULATION IN NEWBORN

Dr Sudha Rao, Mumbai, Maharashtra

- Gluconeogenic and glycogenolytic enzymes are immature *in utero*.
- The maximum risk of hypoglycemia is in the first 24 hours of life and definitely not after 72 hours unless the baby is an "at-risk group" baby.
- Glucose dysregulation in newborn (Hypo-/hyperglycemia) is segregated into transitional, transient, permanent and syndromic.
- Transitional hypoglycemia is quite common even in normal babies; resolves within 24-48 hours of life.
- Refractory hypoglycemia accounts for 3-7% of cases of hypoglycemia.
- Causes of refractory hypoglycemia – Congenital hyperinsulinism (CHI), metabolic, endocrine, accelerated starvation and transient.
- Eleven genes have now been implicated in monogenic CHI (ABCC8, KCNJ11, GL UD1, GCK, HADH1, UCP2, MCT1, HNF4A, HNF1A, HK1, PGM1).
- Neonatal hyperglycemia is rare and often transient.
- Neonatal diabetes mellitus (NDM) is defined as persistent hyperglycemia occurring in the first 6 months of life that lasts for more than 2 weeks and requires insulin for management. It is rare – 1 in 1,00,000-5,00,000 live births. It is monogenic in origin. More than 10 genes have been identified so far.
- Both CHI and NDM are a very heterogeneous spectrum of glucose dysregulation disorders.
- Genotype characterization not only helps in appropriate treatment but also in prenatal counseling and antenatal diagnosis. This may also have implications on other family members.

All babies suspected to have glucose dysregulation disorder (CHI/NDM) should undergo genetic testing, as appropriate.

CONGENITAL HYPOTHYROIDISM – INDIAN GUIDELINES FOR SCREENING, DIAGNOSIS AND MANAGEMENT

Dr Sadish Kumar Kamalanathan, Puducherry

Universal newborn screening (NBS) for congenital hypothyroidism (CH) is the need of the hour in India. Recall for rescreening and subsequent venous confirmatory testing. Hearing test and clinical evaluation for other congenital malformations are to be performed for all babies with CH. Universal hearing screen and regular hearing assessment throughout childhood should be part of any NBS program along with CH. Treatment is required till 3 years of age followed by reassessment for CH permanence and etiology. Checking for permanence of CH alone – Dose tapered by one-third for 2-3 weeks and thyroid-stimulating hormone (TSH) level rechecked; TSH >10 mIU/L – permanence confirmed and treatment to be continued; If TSH does not rise, dose may be further tapered, stopped and then retested; in babies with proven agenesis or ectopic thyroid, reevaluation is unnecessary.

Screening with either cord blood or Day 3-5 heel prick dried blood spot filter paper testing is advised.

HOW TO PLAN AND IMPLEMENT BASIC SCIENCE RESEARCH? MY EXPERIENCE AS A CLINICIAN

Dr Sujoy Ghosh, Kolkata, West Bengal

- Problems of basic science research – A clinician has no formal training; He/she has no set up; He/she becomes sample provider; He/she has insight into meaningful/clinically relevant questions; Seek help of basic scientist to find answers; We need basic science workshops for clinicians.
- What a clinician does? – Clinical service/patient care; Identifies knowledge gaps; Unravels unmet needs; Clinical meta-data very important; Creation of cohorts essential; Try to understand your strengths and weakness; Take small steps; Identify collaborators.
- It is important to have the right mindset. Team work is important. Take one step at a time. Create cohorts.

DPP-4 INHIBITORS: EFFECTS BEYOND GLYCEMIC CONTROL

Dr Sanjay Kalra, Karnal, Haryana

- Dipeptidyl peptidase 4 (DPP-4) inhibitors play a role in simplifying diabetes management and are featured in international guidelines.
- DPP-4 inhibitors are associated with a low risk of hypoglycemia, are weight-neutral, have proven cardiovascular safety, have few interactions with co-medication, have no timing or dosing issues and are associated with good compliance.
- DPP-4 inhibitors have higher efficacy in Asian patients.
- Glucological approach – DPP-4 inhibitors are given as second-line drug after metformin; as first-line if metformin is contraindicated or not tolerated; and as third-line after metformin + sulfonylurea.

Advantages of DPP-4 inhibitors – The 6E Rubric: Efficacy – effective reduction in HbA_{1c}; Ease of use – no dose titration; Error free – safe; Extra-glycemic effect – reduction in progression of albuminuria and cardiac safety; Elementary investigations – minimum investigations required at screening; Elasticity – can be prescribed at any time of the day.

PREVENTION OF TYPE 2 DIABETES: INDIAN PERSPECTIVE

Dr Abhay Kumar Sahoo, Bhubaneswar, Odisha

The prevalence rates of diabetes are rising rapidly both in urban and rural India. Education is the cornerstone of diabetes care (WHO). Indian Diabetes Prevention Programs prove that Indians with impaired glucose tolerance (IGT) respond to lifestyle modification. Early improvement in glucose tolerance (normoglycemia in 6 months) significantly reduces risk of diabetes development. Spending on noncommunicable diseases (NCDs) accounts for 5.17% of household expenditure in India. Delivery of NCD screening services at home by trained community health workers is feasible. UDAY, a 5-year initiative, aims to reduce the risk of diabetes and hypertension and improve management by informing policymakers on the most appropriate community and health system-based approaches.

Both lifestyle modification and metformin significantly reduce the incidence of diabetes in Asian Indians with IGT.

MEDLEGAL ISSUES

Adv Mahendrakumar Bajpai, New Delhi

- Law and medicine are two different sciences. Medicine is therapy/indication specific.
- Law is specialty neutral. It has nothing to say on the science of medicine/therapy/indication. Law is merely there to ensure that healthcare practitioners follow the "Accepted Medical Practice". Understand law as lawyers, not doctors.
- The Indian Medical Council (Professional Conduct, Etiquette and Ethics) Regulations, 2002, published in Part III, Section 4 of the Gazette of India, dated 6th April, 2002 – Always keep an updated copy; Read it at least once in a year.
- Improper Consent and Improper Documentation – SOPs/Advisories from professional bodies is the need of the hour.
- Minor mistakes made – Not writing on appropriate stationery; Not writing in continuity; Not attesting notes; Leaving designated spaces/columns blank.
- Recent Significant Changes – Experience of doctor is specifically taken into account; Allegations of medical negligence only to avoid payment of fees are increasing alarmingly; Patients increasingly suing 'only' hospitals not doctors; Allegations relating to diagnosis have doubled; Selection of the other consultant for referral is also becoming contentious.

DIAGNOSTIC CHALLENGES IN CUSHING'S SYNDROME

Dr Rama Walia, Chandigarh, Punjab

- Diagnosis of Cushing's syndrome is enigmatic.
- Clinical, biochemical and radiological features may not go hand-in-hand.
- 0800 h cortisol is not employed for establishing hypercortisolism. It is used for documenting adrenal insufficiency.
- Intermediate adrenocorticotropic hormone (ACTH) values should be reconfirmed.
- Pituitary incidentaloma is not uncommon: Bilateral inferior petrosal sinus sampling (BIPSS) is complimentary to MRI.
- Lysine vasopressin can be used as an alternative to human corticotropin-releasing hormone (hCRH) for BIPSS.
- Ga^{68} corticotropin-releasing hormone (CRH) PET/CT represents a novel noninvasive integrated functional and anatomical imaging in patients with ACTH-dependant Cushing's syndrome.

Urinary free cortisol is the best screening test followed by late-night plasma cortisol.

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News and Views

Getting Plenty of Exercise Linked with Lower Risk of Kidney Disease

People who get plenty of physical activity may have lesser odds, than their more sedentary peers, of developing chronic kidney disease (CKD), suggests a recent study.

Investigators assessed nearly 2,00,000 Taiwanese adults without kidney disease for up to 18 years. Compared to those who were least active, individuals who got the most exercise were 9% less likely to develop kidney disease over the study period. The study was published in the *British Journal of Sports Medicine*… (*Reuters*)

Walking 10,000 Steps a Day not Enough to Prevent Weight Gain, Says Study

No amount of walking can prevent weight gain by itself, according to a study published in the *Journal of Obesity*. The study suggests that the widely practiced standard of pacing 10,000 steps a day to lose weight may not be solely effective.

Researchers assessed 120 college freshmen over their first 6 months of college who participated in a step-counting experiment. Researchers evaluated if exceeding the recommended count of 10,000 steps a day would minimize weight and fat gain. According to the study, the students gained weight even if they walked more than even 15,000 steps. "Exercise alone is not always the most effective way to lose weight," said study lead author Bruce Bailey, Professor of Exercise Science at Brigham Young University… (*The Indian Express - PTI*)

Pembrolizumab-Enfortumab Vedotin-ejfv Combo Promising in Advanced Bladder Cancer

Patients with cisplatin-ineligible advanced bladder cancer were found to achieve durable objective responses with the combination of pembrolizumab and a newly approved antibody-drug conjugate (ADC), revealed new data from a phase I trial.

Thirty-three of 45 patients responded to pembrolizumab and enfortumab vedotin-ejfv, and all but three of the 45 patients had some degree of tumor shrinkage. The findings were presented at the Genitourinary Cancers Symposium (GuCS).

Mediterranean Diet Improves Microbiome

A new study published in the BMJ journal *Gut* suggested that eating Mediterranean diet for just 1 year altered the microbiome of elderly people in ways that improved brain function and would aid in longevity.

The diet was shown to inhibit the production of inflammatory chemicals that can result in the loss of cognitive function, and prevent the development of chronic diseases such as diabetes, cancer and atherosclerosis… (*CNN*)

No Prenatal Vitamin D Protection for Asthma by Age 6, Suggests Follow-up Study

Prenatal supplementation with high-dose vitamin D was noted to have no impact on asthma and persistent wheezing in 6-year-olds in follow-up of a study that suggested protection at age 3.

Data from the Vitamin D Antenatal Asthma Reduction Trial (VDAART) had shown a reduction in recurrent wheezing in 3-year-olds associated with being born to mothers who took high-dose (4,400 IU daily) vitamin D supplementation during pregnancy. The follow-up study, published in the *New England Journal of Medicine*; however, revealed that there was no effect of taking vitamin D during pregnancy on either asthma or recurrent wheezing at age 6. The findings suggested that the previously reported benefit associated with high-dose supplementation was not sustained beyond 3 years of age.

World Failing to Provide Healthy Life and Climate Fit for the Future to Its Children: WHO-UNICEF-Lancet Commission

No country is providing the requisite protection to its children's health, their environment and their futures, suggests a landmark report by a Commission of child and adolescent health experts from across the world. The Commission was convened under the auspices of the World Health Organization (WHO), UNICEF and The Lancet. The report, A Future for the World's Children?, suggests that the health and future of the world's children and adolescents is being threatened by ecological deterioration, climate change and exploitative marketing practices that promote processed fast food, sugary drinks, alcohol and tobacco to children… (*WHO*)

Inactive Teens More Likely to Develop Depression

Sedentary teenagers may be more inclined than their active counterparts to be depressed, and even light exercise, like walking, might decrease this risk, suggests a new study published in *The Lancet Psychiatry*.

Investigators followed over 4,000 young people ages 12-18, and noted that physical activity levels declined as kids got older. Those who were the most sedentary between ages 12 and 16 were the most likely to have symptoms of depression at 18. Those maintaining or increasing light physical activity reported the lowest depression risk at age 18… (*Reuters*)

Screen for Cervical Cancer Every 3 Years

A unique study from New Mexico suggests that screening every 3 years can potentially reduce the rate of cervical cancer.

The study revealed that 3 years represents a safe interval, and that more frequent screening does not improve detection rates. Researchers stated that many women are being screened more frequently, which is a waste of healthcare resources. The study was published in the *International Journal of Cancer*.

GI Events Common with Colchicine Treatment

A meta-analysis published online in *Arthritis Research & Therapy* has revealed that the most common adverse events (AEs) associated with colchicine treatment include diarrhea and other gastrointestinal (GI) problems.

In an analysis of 19 studies, the estimated relative risk for diarrhea among patients given colchicine was 2.44 (95% confidence interval [CI] 1.62-3.69, $p < 0.001$) compared to the comparator groups. Additionally, among patients in 29 studies, the relative risk for any GI event, including diarrhea, nausea, constipation, and abdominal pain, was 1.74 (95% CI 1.32-2.30, $p < 0.001$).

Landmark Smoking Excise Bill in Ethiopia

The Ethiopian Parliament has passed landmark legislation in order to curb smoking in the country. Ethiopia has introduced a mixed-excise system on cigarettes in accordance with the recommendations of the WHO. There is a 30% tax rate on the cost of cigarette production, besides a specific excise rate of eight Ethiopian Birr (ETB) (USD$ 0.25) on each individual packet.

"…This ground-breaking new law will significantly reduce cigarette smoking among Ethiopians and save lives. It is a powerful example of how the government, civil society and WHO can work together to enact meaningful change," said Dr Boureima Hama Sambo, WHO Representative for Ethiopia… (*WHO/Africa*)

COVID-19 Virus More Contagious Than SARS or MERS: Chinese CDC Study

A comprehensive study of over 72,000 confirmed and suspected cases of the novel coronavirus, conducted by experts at the Chinese Center for Disease Control and Prevention (CDC), has revealed that the novel coronavirus is more contagious in comparison with the related viruses which cause SARS and MERS. The disease, COVID-19, is not as fatal on a case-by-case basis, yet its greater spread has resulted in a higher number of deaths than its related coronaviruses. The study was published in the *Chinese Journal of Epidemiology*… (*CNN*)

Assisted Reproductive Technology (Regulation) Bill Approved

New Delhi: The Union Cabinet has approved the Assisted Reproductive Technology (Regulation) Bill which proposes that a national registry and registration authority be created for all clinics and medical professionals serving in the field. The Bill recommends strict punishment for those practicing sex selection and sale of human embryos or gametes. Union Minister Smriti Irani stated that the Bill seeks to protect the reproductive rights of the commissioning couple as well as the lady who will be part of the process… (*ET Healthworld – PTI*)

Exposure to Cleaning Products may Harm Infants' Lungs

Early exposure to household cleaning products could have adverse effects on young children, suggests a Canadian birth cohort study.

Infants who were more frequently exposed to household cleaning products (frequent use reported by caregivers) at the age of 3-4 months were at increased risk for asthma and recurrent wheeze at 3 years of age when compared with infants whose caregivers reported less frequent use of such products. The findings were published online in the *CMAJ*.

Association Between Persistent Antisocial Behavior and Brain Structure

Individuals who exhibit antisocial behavior over a lifetime have been shown to have a thinner cortex

and smaller surface area in key brain regions when compared with their counterparts who do not engage in antisocial behavior, suggests new research published online in *Lancet Psychiatry*. However, there were no widespread structural brain abnormalities in those who exhibited antisocial behavior only during adolescence.

Common Antibiotics Tied to Increased Risk of Birth Defects, Says Study

Taking some of the common antibiotics during the first trimester of pregnancy seems to be associated with an increased risk of birth defects, suggested a new study.

The study, published in *BMJ*, noted that there was an increased risk of birth defects in the children of women taking macrolides during the first 3 months of pregnancy compared to mothers taking penicillin. Macrolide prescription to pregnant women during the first trimester heightened the risk of major malformations to 28 of 1,000 births, compared with 18 per 1,000 births with penicillin… (*CNN*)

IL-31 Drug Effective for Prurigo Nodularis

Nemolizumab, an investigational monoclonal antibody targeting interleukin-31 (IL-31) receptor A, seems to improve the symptoms of moderate-to-severe prurigo nodularis (PN), suggests a small randomized trial published in the *New England Journal of Medicine*.

After a period of 4 weeks, PN patients given subcutaneous nemolizumab had a significant reduction in pruritus score compared with patients given placebo. Peak pruritus score on the numerical rating scale declined by 53% for those on nemolizumab, compared to a 20% reduction for those on placebo (-32.8% difference, 95% CI -46.8% to -18.8%, $p < 0.001$).

Crohn's Disease Increases Risk of Death from Colorectal Cancer

Individuals with Crohn's disease (CD) have a greater risk of developing and dying of colorectal cancer (CRC) in comparison with the general population, revealed the first population-based study of CRC-specific mortality in these patients.

Overall, 499 of the 4,7035 CD patients in national registers were diagnosed with CRC over a 48-year period. Of these, 296 died over a median follow-up of 10 years. This amounts to a 40% increased relative risk of CRC diagnosis and a 74% increased relative risk of CRC death in patients with Crohn's disease between 1969 and 2017, noted researchers in *The Lancet Gastroenterology & Hepatology*.

Simple Urine Test could Help with Early Detection of Bladder Cancer, Says WHO Study

A study by WHO researchers has revealed that it is possible to detect bladder cancer mutations in urine up to 10 years before clinical diagnosis of the disease.

The test detects mutations in the telomerase reverse transcriptase (TERT) gene, which represent the most common mutations in bladder cancer, reports the WHO's International Agency for Research on Cancer (IARC) and international partners. The new evidence is published in *The Lancet*… (*UN*)

Long-term Changes in Gut Microbial Metabolite can Predict CHD Risk

New data, from a study published in the *Journal of the American College of Cardiology*, highlight the role that the gut microbial metabolite trimethylamine N-oxide (TMAO) can play to predict coronary heart disease (CHD). The study also puts forward the potential for diet to modify its deleterious effects. Changes in TMAO over 10 years were found to be significantly associated with CHD incidence among healthy women, even after accounting for multiple cardiovascular risk factors and dietary patterns. An unhealthy diet was found to significantly bolster the association between TMAO and CHD while a healthy, or plant-based, diet weakened it.

Hydration not Required to Prevent Contrast-enhanced Nephropathy

A new study has suggested that the common practice of hydration with sodium bicarbonate before contrast-enhanced CT imaging seems to have no benefit with regard to renal safety in comparison with withholding hydration in patients with stage 3 CKD.

The multicenter study had 523 patients with stage 3 CKD. The primary endpoint was mean relative increase in serum creatinine level 2-5 days after contrast administration. In comparison with baseline values, the mean increase in the prehydration group was 3.5% (SD, 10.3) vs. 3.0% (SD, 10.5) in the no prehydration group (mean difference, 0.5%; 95% CI, −1.3 to 2.3; $P < .001$ for noninferiority). No significant differences could be noted in the secondary outcomes of post-contrast AKI. The findings were published in *JAMA Internal Medicine*.

Eating Fruits, Vegetables Tied to Decrease in Menopause Symptoms

A diet rich in fruits and vegetables can potentially decrease various menopause symptoms, suggested a new study.

Assessing previous studies, scientists noted that the consumption of fruits or a Mediterranean-style diet, characterized by a high content of vegetables, fruits, cereals and nuts, is linked to fewer menopause symptoms and complaints. While certain subgroups of fruits and vegetables were inversely associated with menopause symptoms, an increased intake of other subgroups was linked with more urogenital problems. The study was published in the journal *Menopause*… (*The Indian Express*)

Severe Infection Linked with Substance-induced Psychosis

A new research has found a link between severe infection and an increased risk of substance-induced psychosis and later conversion to schizophrenia.

The large, population-based study revealed that any infection was associated with a 30% increased risk for substance-induced psychosis. Hepatitis was most strongly linked to psychosis, with more than three times increased risk of substance-induced psychosis, and the only infection associated with conversion to schizophrenia. The study was published online in the *American Journal of Psychiatry*.

FDA Approves Weekly Contraceptive Patch

The US Food and Drug Administration (FDA) recently approved levonorgestrel and ethinyl estradiol transdermal system as a contraceptive method in women with body mass index (BMI) <30 kg/m^2 for whom a combined hormonal contraceptive is suitable. The contraceptive patch can be applied weekly to the abdomen, buttock, or upper torso (excluding breasts), and delivers a daily dose of 30 μg ethinyl estradiol and 120 μg levonorgestrel… (*Medscape*)

Nonstatin Drug Approved to Treat High Cholesterol

The US FDA has given approval to a drug to treat high cholesterol that has a different action than statins, as per the maker of the drug. Bempedoic acid, a once daily oral drug, has been approved by the FDA for use with a healthy diet and the maximum tolerable dose of statins. The new drug has been shown to reduce low-density lipoprotein cholesterol. The drug acts by inhibiting cholesterol production… (*CNN*)

Decreased Levels of Specific Gut Bacteria in Infants Tied to Later Anxiety

New research, published online in *EBioMedicine*, has suggested that lower levels of a specific gut bacteria in infants are linked with the development of anxiety in toddlers.

Researchers noted that levels of Prevotella in fecal samples at 12 months of age were associated with anxiety-like behaviors at 2 years of age. Recent exposure to antibiotic use was the key predictor of having decreased levels of Prevotella.

Longer Breastfeeding Linked to Lower Type 2 Diabetes Risk after Gestational Diabetes

Among women with a history of gestational diabetes mellitus, a longer duration of breastfeeding has been found to be associated with a decreased likelihood of developing type 2 diabetes, and was tied to a more favorable glucose metabolic biomarker profile.

Women who breastfed for 2 years or more had a 27% lower risk compared to those who did not breastfeed, even after adjusting for age, ethnicity, family history of diabetes, parity, age at first birth, smoking, diet quality, physical activity and prepregnancy BMI. The findings were published in *Diabetes Care*. (*Medscape*)

First Generic of ProAir HFA Approved: FDA

The US FDA has approved the first generic of ProAir HFA (albuterol sulfate) Inhalation Aerosol for treatment or prevention of bronchospasm for patients aged 4 years and above with reversible obstructive airway disease and for the prevention of exercise-induced bronchospasm in patients 4 years and above… (*FDA*)

Antibiotics Reduce COPD Exacerbation Treatment Failures

Antibiotic therapy has been shown to be associated with significantly reduced treatment failure in chronic obstructive pulmonary disease (COPD) patients with mild exacerbations, in a systematic review and meta-analysis.

Among patients with moderate-to-severe exacerbations, antibiotics and systemic corticosteroids were linked with improved symptoms and less treatment failure in comparison with placebo or treatment without antibiotics. Antibiotics given for 3-14 days were found to be associated with increased exacerbation resolution and less treatment failure, with the findings being independent of exacerbation severity or treatment as outpatient or inpatient, reported researchers in *Annals of Internal Medicine*.

FDA Approves First Quadrivalent, Adjuvanted Flu Vaccine for Older Adults

The US FDA has given approval for the first quadrivalent, adjuvanted influenza vaccine for adults aged 65 years or older for protection against seasonal influenza.

The approval is supported by data from several clinical studies showing the safety and efficacy of the quadrivalent version in adults 65 years or older against influenza strains included in the vaccine… (*Medscape*)

Gefapixant may Help Relieve Long-term Cough, Says Study

A new agent, gefapixant, appears promising in relieving chronic cough, even when the cough has prevailed for more than 15 years, suggested a phase 2b trial.

In the current study, 253 patients with unexplained cough for an average 14.5 years were randomized to receive either gefapixant (7.5 mg [n = 64], 20 mg [n = 63], or 50 mg [n = 63]) or placebo (n = 63) twice a day, for 84 days. Following 12 weeks treatment period, patients given placebo coughed 18 times/hour and those receiving 50-mg dose coughed 11 times/hour, with the percentage reduction relative to placebo being –37.0%, a reduction from baseline of 57.6%. The study was published online in *The Lancet Respiratory Medicine*.

Serum Urate Tied to Atherosclerosis in Men

A new research has found high levels of serum urate to be associated with the presence of coronary artery calcification in men, but not in women.

In a multivariate analysis, the odds ratio for coronary artery calcification being detected in men with serum urate levels in the highest quartile was found to be 2.3 (95% CI 1.2-4.4, p = 0.01). Odds ratios were increased in men for the second quartile (OR 2.2, 95% CI 1.2-4, p = 0.008) and third quartile (OR 1.9, 95% CI 1-3.6, p = 0.04) as well. The findings were published online in *Arthritis Research & Therapy*.

High-dose Vitamin D in Pregnancy may Improve Kids' Bone Health

High-dose vitamin D supplementation during pregnancy seems to improve bone health in the offspring compared to the standard recommended dose, suggested new research published online in *JAMA Pediatrics*. Some experts have; however, expressed caution about introducing such high doses. In comparison with a standard dose of 400 IU/day, maternal supplementation with 2,800 IU/day, starting from Week 24 of pregnancy to Week 1 postpartum, yielded overall improvement in bone mineralization in the offspring through age 6. The effect was most robust among mothers with baseline vitamin D insufficiency and among children born during the winters, reported researchers.

ACIP Votes to Recommend Ebola Vaccine for Healthcare Workers with Exposure Risk

The CDC's Advisory Committee on Immunization Practices (ACIP) has unanimously voted in favor of recommending vaccination against Ebola for some healthcare and laboratory workers, including those responding to outbreaks.

In a 14-0 vote, pre-exposure vaccination was recommended for adults 18 years or older with potential risk of exposure to *Zaire Ebolavirus* who are responding to an outbreak of Ebola, work as healthcare personnel at federally-designated Ebola Treatment Centers across the US, work as laboratorians or other staff at US biosafety-level 4 facilities… (*Medpage Today*)

WHO Accelerates Action to Improve Access to Safe Blood

The WHO has devised a new action plan to boost universal access to safe blood and blood products. The action plan integrates existing recommendations and recommends new improved ways of working. It is the beginning of a 4-year collaborative effort to advance blood transfusion and blood-based therapies in all countries… (*WHO*)

FDA OKs Amisulpride for Post-op Nausea and Vomiting

The US FDA has given approval to amisulpride injection for the prevention and treatment of postoperative nausea and vomiting (PONV) in adults. This is the first and only antiemetic that has been approved for the rescue treatment of PONV for patients in whom previous prophylaxis with current standard of care has failed. For prevention of PONV, amisulpride can be used either alone or in combination with another antiemetic of a different class… (*Medscape*)

■■■■

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Indian Journal of Clinical Practice, Vol. 30, No.10, March 2020

The Deeper Meaning of Lord Shiva

KK AGGARWAL

Many of us are devout followers of Shiva. But, we worship Him without understanding the deeper meaning of Shiva.

In Hindu mythology, Shiva is one of the three forms (trimurtis) of God, Brahma, Vishnu and Mahesh, the Hindu Triumvirate.

The Parmatama or spirit or what is called as God can be classified as a mixture of three forces representing Generator (creator or Brahma), Organizer, (maintainer or Vishnu) and Destroyer (completing or Mahesh or Shiva). These three similar forces come into play in our body to perform any work. They can be denoted as: Idea generation or creation, maintaining or organizing the contents of the idea, and then destroying or completing, so that new work can be undertaken through Ganesha, the Lord of new beginnings.

One must understand and implement the principles of Lord Shiva in day-to-day life. This can be done by understanding the meaning of the form of Shiva.

Classically, Shiva is worshipped in a sitting meditating pose, sitting on a deer's skin with a background of white Himalayas and blue sky (akash). Shiva is also depicted with ashes from graveyard smeared on his body, a snake around his neck, Ganga flowing out of his hair, three eyes, blue neck, trishul in one hand and damru in his other hand.

All these symbolic representations have a deep spiritual meaning and tell us about Shiva's principles of success.

Of the three eyes of Shiva, the left eye indicates love; the right eye signifies justice and the third eye, wisdom or intelligence. To work effectively, one must use both eyes, i.e. doing every work with love and justice. Any work done with love and without justice will lead to pampering, and justice without love will lead to rudeness. The third eye should be used in times of difficulty. The message here is: whenever you are in difficulty, use your intelligence and wisdom. The opening of the third eye means the disappearance of ignorance (darkness or pralaya).

The half open-eye meditating pose teaches us that in daily life, one should be as calm as if you are in the meditation pose. Being calm or practicing calmness helps in achieving better results.

The snake around the neck represents ego. And, the downward posture of the head of the snake indicates that ego should be directed towards the consciousness and not outwards. The ego should be kept under control and not let it overpower you.

The blue color symbolizes sin or negative thoughts. Shiva as Neelkanth (blue neck) teaches us that the negative emotions should never be expressed nor suppressed; instead they should be altered or modified. This indicates that the poison is neither to be drunk nor to be spitted out but to be kept in the throat by making it a part of the life. For example, an episode of anger should neither be expressed nor suppressed. Suppressed anger releases chemicals in the body causing acidity, asthma, angina, diarrhea, etc. Expressed anger creates an unhealthy social environment. The only way is to alter or modify the anger by wilful cultivation of opposite positive thoughts in the mind. Therefore, the process of silently passing on love to any individual can take away the angry thoughts from the mind (love is opposite of anger).

The ash on the body of Shiva reminds that everything in the universe is perishable and nothing is going to remain. The message here is that "you have come in this world without anything and will go back without anything, then why worry".

The trishul in one hand represents control of three factors, i.e., mind, intellect and ego. It also represents controlling the three mental gunas; i.e., sattva, rajas and tamas.

The damru, the hollow structure, represents "taking all your ego and desires out of the body".

The blue Akash represents vastness and openness; the white mountains represent purity and truthfulness.

It is customary to fast on Shivaratri. Fasting does not simply mean missing a meal or not eating that day; it

Group Editor-in-Chief, IJCP Group

also means fasting or abstaining from all negativities "see no evil, hear no evil and speak no evil". Fasting also indicates controlling the desires for eating foods (like fermented, sweet, sour and salt) and controlling the negative thoughts both in the mind as well as in action.

By adopting these principles, one will attain a free flow of knowledge, which is represented by the Ganga coming out of the hairs of the Lord Shiva. The matted hairs of Shiva represent tapas and signify that nothing in the universe is impossible without contemplation and repeated practice.

If one follows Shiva's principles in everyday life, one will find no obstacles in routine life as well as in the spiritual journey.

■■■■

Fictions and COVID-19

Normally introduction of a new vaccine takes at least 18 months and only in rare exceptional circumstances, it can be introduced in the market in 12 months.

Most pharmaceutical companies are scared that coronavirus will last in the circulation only for 6 months and will never come back like SARS and therefore, why spend billions of dollars in research.

There are postulations that COVID-19 is a part of bioterrorism or the virus was being manufactured in one of the Chinese laboratories.

These speculations basically come from Hollywood and Bollywood movies which show that the villain is ready to manufacture a virus and the hero of the film will produce an antivirus within no time to save the community.

But remember, these are fictions and not a reality.

If it was a reality, then the lab will make a vaccine first, both to commercially exploit it, and save their own people.

The Chinese government in this epidemic has locked down its own 5 crore people, all susceptible to get the disease. The expected deaths with the current rate of spread is 5000.

It doesn't make sense for any government or a terrorist body to make bioweapons without making an antidote for it.

Most of the WhatsApp's are spreading these messages for them to become viral.

People compare them with what has been written in the fiction stories in the past and any similarities are a mere coincidence.

Remember, viruses like SARS, smallpox are still in the labs and Bollywood and Hollywood movies will still go on making fiction stories on these viruses.

New York Times: China's critics seize on fringe theory of virus

Scientists dismiss it as there is no evidence for it. A rumor about the coronavirus has gained traction, that the outbreak was somehow manufactured by the Chinese government as part of a biowarfare program.

It's the kind of story that resonates with those who see Beijing as a threat to the West. The theory has gained an audience with the help of powerful critics of the Chinese government, including right-wing media outlets and a US senator, Tom Cotton of Arkansas, who later walked his claims back.

Reality: Experts dismiss the idea that the virus was created by human hands, saying it resembles SARS and other viruses that come from bats.

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Don't Sweat the Small Stuff

One day an expert in time management was speaking to a group of students and, to drive home a point, used an illustration those students will never forget.

As he stood in front of the group of high-powered overachievers, he said, "Okay, time for a quiz." Then he pulled out a one–gallon, wide mouthed Mason jar and set it on the table in front of him. Then he produced about a dozen fist-sized rocks and carefully placed them, one at a time, into the jar. When the jar was filled to the top and no more rocks would fit inside, he asked, "Is the jar full?"

Everyone in the class said, "Yes." Then he said, "Really?" He reached under the table and pulled out a bucket of gravel. Then he dumped some gravel in and shook the jar, causing pieces of gravel to work themselves down into the space between the big rocks.

Then he asked the group once more, "Is the jar full?" By this time the class was on to him. "Probably not," one of them answered. Good!" he replied. He reached under the table and brought out a bucket of sand. He started dumping the sand in the jar and it went into all the spaces left between the rocks and the gravel. Once more he asked the question, "Is the jar full?" No!" the class shouted. Once again he said, "Good!" Then he grabbed a pitcher of water and began to pour it in until the jar was filled to the brim. Then he looked at the class and asked, "What is the point of this illustration?" One eager student raised his hand and said, "The point is, no matter how full your schedule is, if you try really hard you can always fit some more things in!"

"No", the speaker replied, "That's not the point. The truth this illustration teaches us is: If you don't put the big rocks in first, you'll never get them in at all". What are the 'big rocks' in your life?

"Your children… Your loved ones… Your education… Your dreams… A worthy cause… Teaching or mentoring others… Doing things that you love… Time for yourself… Your health… Your significant other."

"Remember to put these BIG ROCKS in first or you'll never get them in at all. If you sweat the little stuff (the gravel, the sand) then you'll fill your life with little things to worry about that don't really matter, and you'll never have the real quality time you need to spend on the big, important stuff (the big rocks).

So, tonight or in the morning, when you are reflecting on this short story, ask yourself this question: What are the 'big rocks' in my life? Then, put those in your jar first." (*Source: Sermon Central*)

■■■■

FDA Oks New Treatment for Adults with Cushing's Disease

The US FDA has approved osilodrostat oral tablets for the treatment of adults with Cushing's disease who either cannot undergo pituitary gland surgery or have undergone the surgery but continue to have the disease.

Osilodrostat becomes the first FDA-approved drug to directly address cortisol overproduction by means of blocking the enzyme 11-beta-hydroxylase and preventing cortisol synthesis… (*FDA*)

Brain Aging Linked to Leisure Time Physical Activity

More leisure-time physical activity, such as walking, gardening, swimming or dancing, seems to be associated with larger brain volume in older adults, reported a cross-sectional study.

Adults with an average age of 75 who did the most physical activity had 1.4% larger total brain volume as compared to those with the least activity, reported researchers in an early-release abstract from the American Academy of Neurology annual meeting, scheduled to be held in April… (*Medpage Today*)

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Indian Journal of Clinical Practice, Vol. 30, No. 10, March 2020

Lighter Side of Medicine

HUMOR

Dentist: "You need a crown."

Patient: "Finally someone who understands me".

Why are eggs not very much into jokes? Because they could crack up.

What do you call the soft tissue between a shark's teeth?

A slow swimmer.

I went to see the doctor about my short-term memory problems. The first thing the bastard did was made me pay in advance.

Two snails are chatting on the sidewalk. "I'll have to cross the road," says one.

"Well, be careful," says the other one, "there's a bus coming in an hour."

What do you call a bull that likes taking a nap?

A bulldozer!

Why do bees hum?

They don't remember the text!

A woman complains to her mother, "I had this big fight with my husband Joe and at the end he just told me to go to hell."

Mother frowns, "Oh, and so you came to me, huh?"

Q: Did you hear about the baby born in the high tech delivery room?

A: It was cordless!

Q: Did you hear about the optometrist that fell into his lens grinding machine?

A: He made a spectacle of himself.

Q: Why did the cookie go to the hospital?

A: Because he felt crummy

Q: Why did Johnny throw the clock out of the window?

A: Because he wanted to see time fly!

Q: What did the policeman say to his belly button?

A: You're under a vest!

Q: What do you call a fake noodle?

A: An impasta

Q: What did one toilet say to the other toilet?

A: You look flushed

Q: What do lawyers wear to court?

A: Lawsuits!

Q: Why is there a gate around cemeteries?

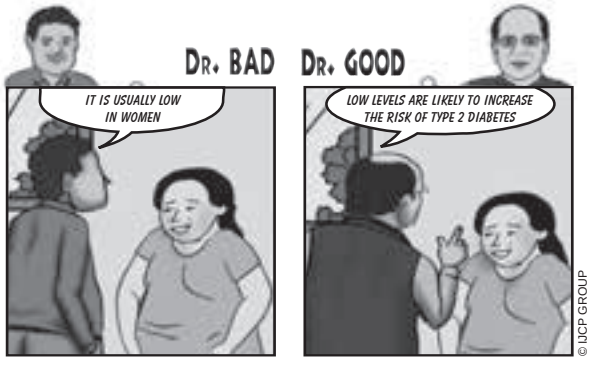
A: Because people are dying to get in!

Q: Why wouldn't the shrimp share his treasure?

A: Because he was a little shellfish

Dr. Good and Dr. Bad

SITUATION: A 44-year-old obese female had low total antioxidant capacity.



LESSON: The findings of a study have reported that total antioxidant capacity may play a vital role in reducing the risk of type 2 diabetes in middle-aged females. Moreover, an inverse link was observed between total antioxidant capacity and risk of type 2 diabetes in this study, which was linear up to 15 mmol/day and attained a plateau after that.

Diabetologia. 2018;61(2):308-16.

IJCP SUTRA: *"If you are anemic and you ordinarily eat meat, increasing the amount of meat you consume is the easiest way to increase the iron your body receives."*

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Dr KK Aggarwal
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Books

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

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