

PRACTITIONERS' GUIDANCE SERIES – XV

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President's Remarks



Mankind has witnessed many diseases becoming epidemics, and pandemics since ages. Some epidemics have taken toll of a lot of population and were responsible for famine and migration of people. The outbreak of diseases is responsible for economic recession, travel restrictions and job losses globally. Bacterial diseases such as cholera, plague have been controlled after discovery of antibiotics like tetracycline.

Smallpox was eradicated after successful mass vaccination programme. Similarly, polio eradication might become reality because of effective pulse polio programme. influenza epidemics is to some extent controlled by vaccination. Due to antigenic drift, vaccine strains have to be prepared for recent strains. H1 N1 which is covered to some extent in this vaccine.

At present World is living in fear of Coronavirus epidemics. Corona viruses like SARS, and MERS have taken some toll in the past. Recent virus COVID-19 has caused a panic situation globally. Partly media is also responsible for this situation. Once herd immunity develops, effective preventive measures with global cooperation in place, disease will be brought under control. Vaccine development may ease the situation.

Because Corona virus is prevalent in almost eighty countries, this topic is covered in detail for the benefit of practitioners. Other topics like adjustment disorders, family medicine and general practice which are useful topics for the practitioners are also included. There is also a writeup on Zika virus infection which made its appearance in our country.

The Book is edited by eminent editor and writer Dr. P.S. Shankar and it has good layout and pictures. I thank our editorial team members immensely for their excellent work in bringing out this book in practitioner's series.

H. Veerabhadrappa

President



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Editorial



I am happy to place before you the 15th Practitioners' Guidance Series which covers 4 topics such as Coronavirus diseases, Management of adjustment disorders, Career in Family Medicine and General Practice, and Zika virus infection.

Dr P S Shankar has written on **Coronavirus diseases**. Coronavirus infection has drawn the attention of everyone all over the world. The infection which began in China has spread over 80 countries and mankind is worried about the disease caused by the virus. Most of the human coronavirus infections have been recognised in the last two decades. The illness has ranged from common cold to more severe pandemics such as Severe acute respiratory syndrome, Middle-east respiratory syndrome and a novel coronavirus disease (COVID-19) from a new strain of virus that had not been previously identified in humans. Coronaviruses are zoonotic and are transmitted between animals and humans. They appear to jump easily between species, and spread from human-to-human. The infection presents with respiratory symptoms such as fever, cough, shortness of breath and breathing difficulties. In more severe cases the infection can cause pneumonia, severe acute respiratory syndrome. Kidney failure and even death. The treatment is symptomatic and there is no vaccine to prevent the infection. Every effort is to be made to prevent spread of infection by regular hand washing, covering mouth and nose while coughing and sneezing, avoid close contact with persons coughing and sneezing, and thorough cooking of meat and eggs.

Dr C R Chandrashekar has discussed with five examples of different situations presenting with **adjustment disorders in clinical practice**. Adjustment disorder refers to development of emotional or behavioural symptoms in response to an identifiable stressor(s) occurring within a month of onset of stress(s). They present with marked distress, impairment of personal, social, educational and occupational functioning. These symptoms get relieved once the stress is relieved.

Adjustment disorders are very common. There is no way to predict which person is likely to get it under the influence of same stressor. The condition has grown as a 'modern epidemic'. There are 7 subtypes of adjustment disorders. They have to be managed on the basis of major symptoms. With the

pharmacologic therapy and counselling the symptoms get relieved and there is improvement leading to adaptation.

Every medical graduate has an intention of studying postgraduate course and become a specialist. However, there are many limitations for them to pursue it. **Dr Ravish** has advised them to study **Family Medicine and General Practice**. It will allow them to set up their practice. This specialty focuses on many of the common illnesses in all age groups and it gives an opportunity to them to provide comprehensive health care in community setting. He has stated that it is a patient-centred, evidence-based, family-focussed, and problem-oriented, requiring the ability to observe, understand and manage. They provide health care services which are personalised for each patient, coordinated with the family and friends.

National Board of Examinations (NBE) is offering courses in family medicine as an independent academic discipline and specialty. The family physician can develop his reputation on affability, availability and ability. He should develop the essential qualities of general practitioner and family physician. They are compassion, ethics, professionalism, knowledge, confidence, humility and passion. The writeup has highlighted the secrets of a successful general practitioner.

Dr P. S Shankar has written about Zika virus infection which made in our country in 2017. Zika virus belongs to the family of flavivirus. The virus recognized in Uganda caused its outbreak in 2007 and spread to Central America, Caribbean islands and South America particularly Brazil. The outbreak assumed a pandemic proportion during 2014-15. The causative agent is closely related to Dengue virus and is transmitted by the bite of tiger mosquito. The mosquito is highly domestic and breeds near human habitat in the standing water collected in containers. The symptoms are self-limiting. However, the potential teratogenic and neurological complications are causing concern. Infection in pregnancy may result in pregnancy complications and neurodevelopmental abnormalities in the new born. There is no specific treatment. The treatment is symptomatic. Prevention from mosquito bites, and vector control are essential. Attempts are made to produce a vaccine.

The above topics have been described in detail to make the Practitioners aware of the currently prevailing COVID-19 infection. It also highlights Zika virus infection which had made its appearance in our country. There are details about adjustment disorders seen in clinical practice. The article on Family Medicine and General Practice will be of great help to the Practitioners.

P.S. Shankar
Editor-in-Chief

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CORONAVIRUS DISEASES

CORONAVIRUS

Introduction

Coronaviruses (CoV) are a large family of diverse group of RNA viruses belonging to the family of Coronaviridae and the order Nidovirales that can infect birds and mammals, including humans. They are divided in 4 genera: alpha, beta, gamma and delta that cause disease in human and animals (1). Most human coronavirus infections that have been recognized in the last two decades have caused illness ranging from the common cold to more severe pandemic such as Severe Acute Respiratory Syndrome (SARS-CoV), Middle-East Respiratory Syndrome (MERS-CoV) and a novel coronavirus disease (COVID-19) from a new strain of virus that had not been previously identified in humans. In addition, there are 4 more different serotypes such as OC43 and HKU1 belonging to alphacoronavirus and 229E and NL63, belonging to betacoronaviruses responsible for mild respiratory symptoms similar to common cold (1). These cold viruses have not jumped from animals to human beings, and they utilise humans as their primary hosts. It is worth noting that those coronaviruses which have jumped from animals to humans appear to cause more severe illness in human. Coronaviruses get transmitted between humans through respiratory droplets that are expelled when the infected person breathes, coughs or sneezes.

Structure

Coronaviruses are enveloped, non-segmented, particles. They are spherical and the core beneath the greasy surface contains matrix protein enclosed within which is a single strand of positive-sense RNA. The genetic material in the core can inject into vulnerable cells to infect them. There are spiky glycoprotein projections on the outer surfaces of the envelope, resembling the points of a crown or a halo. The viruses are named coronaviruses because of the crown-like (or 'corona' in Latin) appearance of their virus particles when seen under an electron microscope. The spikes bind and fuse with host-cell receptors and facilitate the entry of the virus into the host cell. On entry into the cell it

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gets uncoated and the genome gets transcribed and then translated to the new host and begins to replicate. The genetic material of the virus becomes host cell's internal machinery. The cells are converted into a factory. New virions bud from host cell membrane.

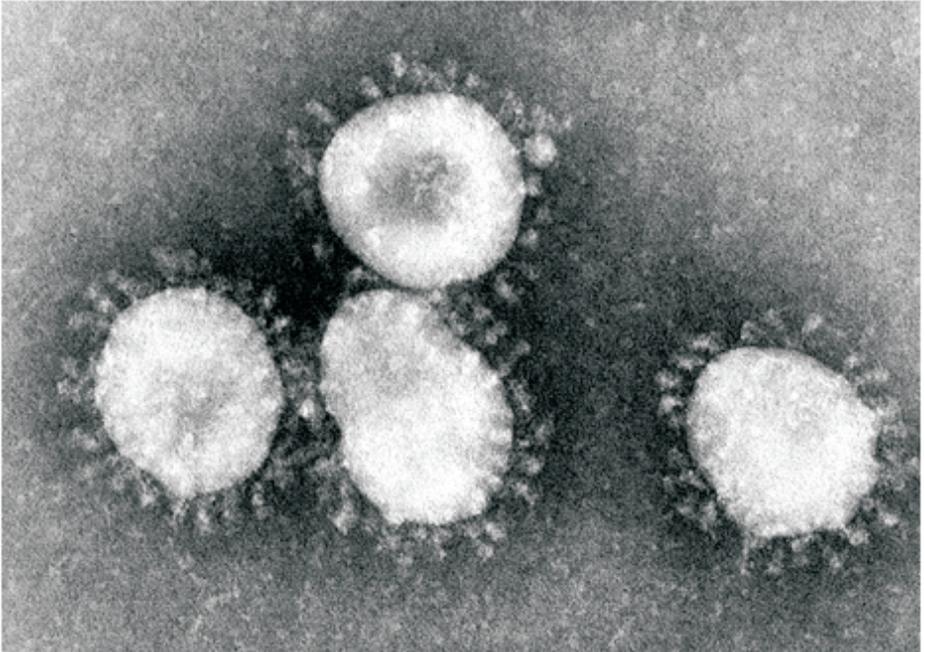


Fig.1: Coronaviruses with crown-like spikes on their envelope
Courtesy: CDC/Dr Fred Murphy

Transmission

Coronaviruses are zoonotic and are transmitted between animals and humans. They appear to jump easily between species. Investigations have suggested that the virus has passed through an intermediate animal before infecting humans. SARS-CoV has jumped from bats to civet cats (small nocturnal mammal) on its way to humans and MERSCoV from Arabian (dromedary) camels to humans. There are still many coronaviruses circulating in animals which have not infected humans.

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Coronaviruses cannot survive for more than a few hours on surfaces outside a human host. However, persons can pick up the virus from a contaminated surface for a short period of time.

Clinical features

Common signs of infection include respiratory symptoms such as fever, cough, shortness of breath and breathing difficulties. In more severe cases, infection can cause pneumonia, severe acute respiratory syndrome, kidney failure and even death.

Treatment and Prevention

The treatment is symptomatic and there is no vaccine to prevent the infection. Every effort is to be made to prevent spread of infection by regular hand washing, covering mouth and nose while coughing and sneezing, avoid close contact with persons coughing and sneezing, and thorough cooking of meat and eggs.

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SEVERE ACUTE RESPIRATORY SYNDROME (SARS)

Introduction

A mysterious form of highly contagious pneumonia was reported in Guangdong province in Southern part of People's Republic of China in late 2002 and subsequently spread to parts of South-east Asia (Vietnam, Hong Kong Special administrative region, the Philippines, Singapore, Thailand, Taiwan, Indonesia) and Canada during early months of 2003. There were reports of treating suspected cases in Germany, Switzerland, France, United States, Australia, Slovenia, UK, Ireland, Malaysia, Italy, and Romania. There were small outbreaks that have ceased since 2004. This illness has been referred to as 'Severe Acute Respiratory Syndrome' (SARS). The disorder causes flue-like symptoms initially, rapidly to be followed by respiratory problems, often serious leading to higher mortality. The apparent speed or ease of transmission associated with SARS led to international concern. The disease may be acquired in laboratory and the infection presumably may be transmitted from animal reservoir (1). China and its surrounding countries witnessed the greatest numbers of SARS-related cases and death.

According to the World Health Organization (WHO), as of July 2003, a total of 8,437 people worldwide became ill with SARS and 813 died. No outbreaks or epidemics have been reported since 2004.

Aetio-pathology

The aetiology of this highly infectious disease appears to be of viral origin from a virus-a corona ('crown like' appearance) virus (CoV), a relative of one of the many viruses that cause the common cold-possibly a strain never before identified in human beings or animals, is responsible for the outbreak (Fig.1 & 2). The SARS-associated

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coronavirus (SARS-CoV) is neither a mutant of any known coronavirus nor a recombinant of known coronaviruses. It is a previously unknown coronavirus, probably from a nonhuman host, that somehow acquired the ability to infect humans (2, 3). It looks like a species jump from wild animals to human beings. The genome of the SARS coronavirus is 29,727 nucleotides in length and the genome organization is similar to that of other coronaviruses. SARS coronavirus consists of a silver of genetic material wrapped in an overcoat of fat that is spiked with finger-like proteins that bind to receptors on host cells and fuse the viral envelope with host cell membranes. This enveloped RNA virus mutates more easily. The Coronavirus Study Group of the International Committee on Taxonomy of Viruses has announced the official name for the virus- 'severe acute respiratory syndrome coronavirus 2' or 'SARS-CoV-2'.

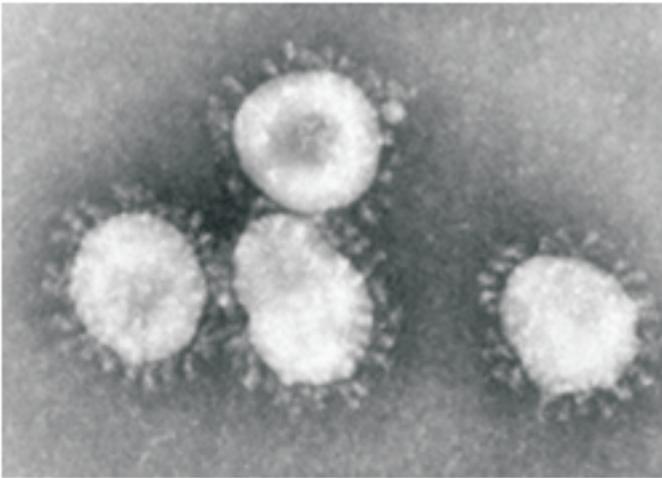


Fig. 1: SARS-associated coronavirus
Photo courtesy: the Centers for Disease Control-Dr Fred Murphy

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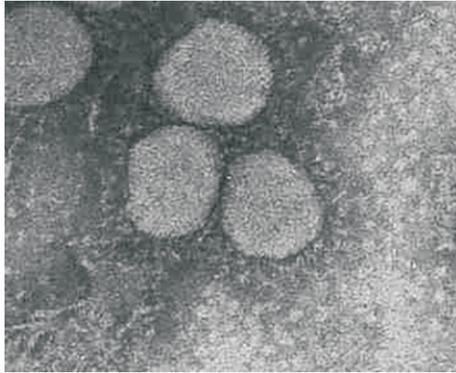


Fig. 2: Thin section electron micrograph negative stained Coronavirus from SARS isolated in FRhK-4 cells.

Source: Department of Microbiology, The University of Hong Kong and the Government Virus Unit, Department of Health Hong Kong SAR China

SARS-CoV has the ability for rapid adaptation to new hosts, a feature of Coronaviruses, and it adapts to replicate in the human lung. Adaptation involves changes in the surface glycoprotein, substance responsible for binding to the host-cell entry receptor, and in proteins taking part in viral replication.

Pathologically there is diffuse alveolar damage with varying degrees of organization (4). In the acute phase, there is hyaline membranes, interstitial and intra-alveolar oedema, mild interstitial infiltrates of inflammatory cells and vascular congestion. In the organization phase there is interstitial and airspace fibroblast proliferation and type II cell hyperplasia. The fibroblastic proliferation is mostly seen in the alveolar septum (Fig.3).

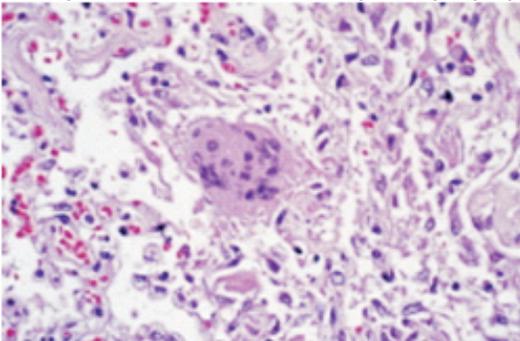


Fig.3: Lung tissue showing pathologic architectural changes suggestive of diffuse alveolar damage.

Note presence of a multinucleated giant cell without presence of conspicuous viral inclusions.

Courtesy: The Centers for Disease Control-Dr SherifZaki

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The median time from exposure to onset of symptoms is nearly one week. The SARS-CoV appears to be transmitted by close contact with aerosolized droplets and bodily secretions from an infected person (5). Transmission is facilitated by face-to-face contact. Most early cases were reported among health care workers and family members of affected persons. The disease spreads around the World by international air-travelers. The condition has been a threat to traveler by air to those affected regions.

The viral RNA concentration in sputum is high, suggesting that shedding of the virus from the respiratory tract could be the primary route of transmission (2). There is a long viraemic phase and the replication of SARS virus also occurs outside the respiratory tract. There is shedding of the virus in faeces and may be an additional source of spreading provided the virus is stable in such an environment.

Human leucocyte antigen (HLA-B 4601) is likely to be a risk factor for more severe viral infection. Angiotensin-converting enzyme 2 may also act as a cellular receptor for severe respiratory syndrome-associated coronavirus.

Risk factors: The risk factors that can lead to development of SARS include

1. Exposure to an infected person
2. Male sex
3. Traveling in a SARS-related outbreak
4. Having co-existent medical problems
5. Being a health care worker in a SARS outbreak area

Clinical features

The illness affects adults aged 25 through 70 years. Children appear to be relatively protected from severe illness. It begins with a high fever, dry, non-productive cough, and severe breathlessness. Systemic manifestations like headache, chills or rigors, muscular stiffness, malaise, loss of appetite, rash, and confusion may be noted. Fever followed by rapidly progressive respiratory compromise are the key complex of signs and symptoms from which the syndrome derives its name (6). Lower respiratory symptoms such as cough, shortness of breath typically begin 2 to 7 days of the onset of symptoms. Gastrointestinal symptoms

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including nausea, diarrhea and vomiting occur with variable frequency. Tachycardia and tachypnoea form the most common signs at presentation. Crackles may be audible at the bases of the lung symmetrically or asymmetrically.

The disease is often reported as a biphasic or triphasic illness: an initial acute febrile phase followed by a lower respiratory tract illness phase. Acute lung injury (ALI) is the most common severe organ dysfunction and occurs in nearly 16% of all patients with SARS, and in 80% of critically ill patients with SARS (7).

A person could be considered to have the infection if he/she exhibits the following four features:

1. high fever ($> 38^{\circ}$ C)
2. one or more respiratory-related symptoms such as cough, shortness of breath, and difficult breathing
3. close-contact (a situation of having cared for, having lived with, or having had direct contact with respiratory secretions and/ or body fluids of a patient suspected of having SARS) with a person who was known to suffer from SARS within the past 10 days.
4. travel within the past 10 days of onset of symptoms to places which have reported cases of the disease.

Investigations

There is evidence of moderate leucopaenia, lymphopaenia, and thrombocytopaenia. There is elevation in liver enzymes especially alanine aminotransferase. The level of lactate dehydrogenase (LDH) and creatine kinase (CK) are elevated. Severe case exhibit hypoxaemia.

Chest radiograph does not typically show abnormalities during the initial phase of the illness but becomes progressively abnormal during the lower respiratory tract illness phase. It is characterized by air-space shadowing which is predominantly peripheral in distribution, ground-glass opacities, focal consolidation or patchy consolidation suggestive of pneumonia or bilateral widespread pulmonary infiltrates suggestive of acute respiratory distress syndrome (Fig.4). There is no interstitial pattern on the chest radiographs. During the initial phases of infection,

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the virus causes pauci-inflammatory alveolar and interstitial edema that result in imaging abnormalities dominated by ground glass opacities (GGO) (Fig.4). Severe SARS cases can develop radiologic and pathologic findings of diffuse alveolar damage. Although radiologic evidence of acute bronchiolitis is absent, SARS-CoV also infects ciliated airway epithelium, probably accounting for respiratory transmissibility of the virus (8).

Computed tomography reveals subpleural focal consolidation with air bronchograms and ground-glass opacities (Fig.5). When compared to the chest radiographic changes, auscultatory signs are disproportionately mild. Air space opacification progresses within a few days of presentation, increasing in size, extent, and severity. The extent of lung opacities seen on chest radiograph correlate with the deterioration in respiratory function.

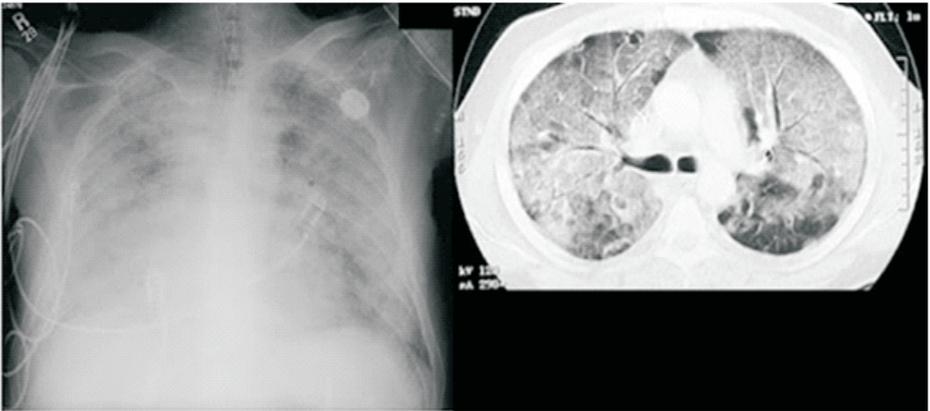


Fig 4, Chest X ray showing dominant ground-glass opacities bilaterally suggesting ARDS. Fig 5. CT scan showing focal consolidation with air bronchograms and Ground glass opacity Courtesy: meddean.leu.edu

Neutralizing antibodies against SARS may be demonstrated between five to 14 days following infection (SARS diagnostic test). Blood, serum, nasopharyngeal swabs or washings, sputum, tracheal aspirate and broncho-alveolar lavage fluid collected within 72 hours after the onset of symptoms can be inoculated onto number of continuous (Vero E)

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cell lines to grow the virus. The presence of SARS-related coronavirus brings about cytopathic effect (5). A rapid diagnosis of SARS using molecular technique of polymerase chain reaction (PCR), reverse transcriptase (RT)-PCR, and real-time PCR help in identification of SARS-CoV RNA and it is necessary for infection control measures and potential treatment.

Diagnosis

Clinically, the condition has to be distinguished from influenza. Influenza makes a sudden onset with fever, generalized aches and pains. However, breathing difficulty and pneumonia are less frequent though they can occur as a complication. SARS characteristically exhibits absence of upper respiratory symptoms. There is presence of dry cough. The auscultatory findings of the chest are minimal even in presence of consolidation in chest radiograph.

Current case definition for SARS according to CDC is as follows (9):

Clinical criteria

- Asymptomatic or mild respiratory illness
- Moderate respiratory illness
- Temperature greater than 39° C and one or more clinical findings of respiratory illness such as cough, shortness of breath,
- Difficult breathing
- Severe respiratory illness
- Same findings as with moderate respiratory illness plus
- Radiographic findings of either pneumonia or SARS or autopsy findings consistent with pneumonia or respiratory distress syndrome without an identifiable cause

Epidemiologic criteria

- Travel within 10 days of onset of symptoms to an area with current or recently documented or suspected community transmission of SARS
- Close contact within 10 days of onset of symptoms with a person known to be a suspected SARS

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Laboratory criteria

Confirmed

Detection of antibody to SARS-CoV RNA by RT-PCR

Isolation of SARS-CoV

Negative

Absence of antibody to SARS Co-V in a convalescent serum sample obtained

. >28 days after symptom onset

Laboratory testing either not performed or incomplete

Case classification

A probable case meets the clinical criteria for severe respiratory illness of unknown aetiology with onset since Feb 2003 epidemiologic criteria for exposure, and laboratory criteria confirmed or undetermined.

A suspect case meets the clinical criteria for or moderate respiratory illness of unknown aetiology with onset since Feb 2003, epidemiologic criteria for exposure, and laboratory criteria confirmed or undetermined.

Prognosis

8098 cases of this globe-trotting disease have been reported during outbreak of 2002-03. The worldwide case fatality rate among all SARS outbreaks is about 9.6% (10). Among those with SARS-related critical illness, 50% of patients died (7). Age plays an important role in the prognosis. Mortality is increased among older patients and may be increased in those with coexisting diabetes mellitus, hepatitis, lymphopaenia, leukocytosis, and high cytokine levels in the first week of infection (11). The risk factors associated with respiratory failure requiring intensive care ventilator support are (12):

older age

male sex

severe lymphopaenia

a high initial neutrophil count

raised level of alanine aminotransferase

a high lactate dehydrogenase level

a low sodium level

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delayed initiation of treatment with ribavirin and corticosteroids in presence of underlying diseases and tobacco smoking

Multivariate analysis has shown the factors that predict an adverse outcome are, advanced age, a high peak LDH level and a high absolute neutrophil count. Death rate from SARS is higher than that of influenza or other common respiratory tract infections. Complications include altered pulmonary functions, polyneuropathy and avascular necrosis.

Treatment

SARS is suspected if a person becomes ill with fever accompanied by cough, and difficulty in breathing. Recent travel in an area with documented or suspected community transmission makes the condition more likely. Such persons are advised not to continue with their travel until they have made complete recovery. These patients have to be kept isolated and they should undergo aggressive treatment, in a hospital so as to prevent its spread. They may require intensive care treatment and mechanical ventilation. Strict respiratory and mucosal barrier nursing is advocated. They should receive supportive care as there is no specific treatment for SARS. There is absence of response to empirical antimicrobial therapy commonly used in cases of atypical pneumonia such as beta-lactams, macrolides, or fluoroquinolones.

During the outbreak antiviral agents such as ribavirin, interferon (IFN)-alpha and protease inhibitors, and host immunomodulators such as systemic corticosteroids have been tried with variable success. None of them have proved their therapeutic effectiveness conclusively.

The ribonucleotide analog ribavirin exhibits a broad spectrum of antiviral activity in vitro, and induces lethal mutagenesis of RNA viral genomes. Oral and intravenous ribavirin has been widely used in different regions for treating patients with SARS. Ribavirin is administered intravenously in a dose of 8 mg/kg of body weight every 8 hours for 7-10 days (6). Oral ribavirin may be administered in a dose of 1.2 g every eight hours. Type 1 interferon inhibits SARS-CoV in vitro. A treatment regimen consisting of 3 million units of IFN-alpha daily for first 14 days has shown to be beneficial (13).

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High doses of corticosteroids are used to control the toxic features of SARS, and to cause immunomodulation. They are not indicated for routine use in patients with uncomplicated SARS (11). Glucocorticoids are recommended to patients with suspect SARS exhibiting persistent fever, worsening hypoxaemia, worsening dyspnoea or signs of radiographic progression. Pulse-doses (500-1000 mg) of methyl prednisolone intravenously each day for 2-3 days have to be given.

Supplementary oxygen should be administered in all hypoxaemic patients. The manifestations seen in patients with severe SARS developing hypoxaemic respiratory failure is indistinguishable from acute lung injury(ALI)/ Acute respiratory distress syndrome (ARDS). They need to be intubated and put on mechanical ventilation with a low tidal volume strategy (6 ml/kg predicted body weight (14).

Prevention

Persons in direct, close contact with persons who have had SARS are at greatest risk for infection, Prevention of SARS involves avoidance of close contact with SARS patients. Such close contact includes direct care of the patients, or direct contact with their respiratory secretions and body fluids. Persons suspected of having SARS must be isolated and should limit their interactions outside hospital settings. They should wear a surgical mask. Quarantine of patients before they spread disease, quarantine or close monitoring of all the people they had come in contact, and a clamp down of social gatherings and travel are important. Health workers and visitors should wear efficient filter masks, goggles, aprons, head covers and gloves when in close contact with the patient. Careful attention to hand washing or hand disinfection with an alcohol-based product after removal of gloves is necessary. Coronavirus can survive on environmental surfaces, and thorough hand washing is advocated. The protective measures contain the spread of this infection. There is necessity of grouping of exposed health care workers and it will help in minimizing the number of persons who are exposed. Similarly, the number of visitors should be limited as much as possible.

The World Health Organization (WHO) and Center for Disease Control and Prevention (CDC) have prepared guidelines to help in the prevention and spread of SARS. They are as follows:

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1. limit time outside of the home. People with SARS should not go to work, school, childcare facilities, or any public place until 10 days after their fever has subsided and their respiratory symptoms are improving
2. Wash the hands frequently with soap and hot water, and use an alcohol-based hand rub, or both, especially after being in contact with bodily fluids such as respiratory secretions or urine
3. Wear disposable gloves when in contact with bodily fluids from a person with SARS. After use, throw the gloves away immediately and thoroughly wash the hands
4. Wear a surgical mask
5. Cover the nose and mouth with a tissue when sneezing or coughing
6. Do not share eating utensils, towels, or bedding. Thoroughly wash these items with soap and hot water after use by a person who is infected
7. Use household disinfectant on any surface that may be contaminated, such as countertops or doorknobs. Wear disposable gloves while cleaning these surfaces
8. Follow these guidelines for at least 10 days after the symptoms have resolved.

2 potential SARS vaccines are undergoing trial on animals. Still it is premature to say whether the antibodies will effectively block the replication of the SARS virus. International experts in infectious disease and epidemiologists consider it likely that there will be a recurrent outbreak of SARS.

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Middle-East Respiratory Syndrome

Introduction

A deadly virus that struck Saudi Arabia in 2012-13, became a concern about the potential impact on Haj pilgrimage when millions of people from around the globe will head to and from Saudi Arabia. The first report was made on 24th Sept 2012 by Egyptian virologist Ali Mohamed Zaki in Jeddha, Saudi Arabia. The causative agent had killed 45 persons since its emergence in late 2012 (1). A total of 88 got infected from laboratory confirmed virus.

The disease though did not make a worldwide spread, cases have been reported from 27 countries since its outbreak in 2012. The countries include Saudi Arabia, Jordan, Qatar, Abu Dhabi, Bahrain, France, Germany, Italy, Tunisia, Algeria, Austria, China, Egypt, Greece, Iran, Kuwait, Lebanon, Malaysia, the Netherlands, Oman, Philippines, Republic of Korea, Thailand, Turkey, United States, Yemen, and Great Britain. Since the infection was noted in Middle-East, the disease acquired the name as Middle East Respiratory Syndrome (MERS). At the end of November 2019, a total of 2494 laboratory confirmed cases of MERS including 858 associated deaths have been reported globally

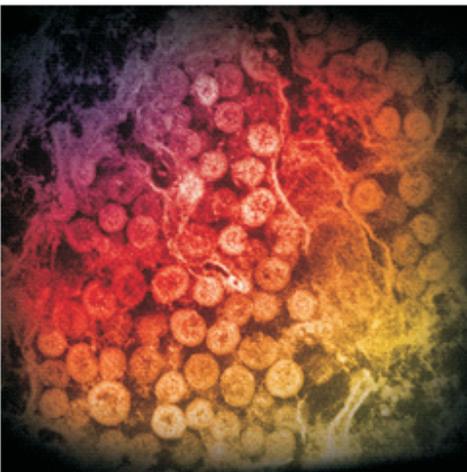


Fig. 1 An electron micrograph of a thin section of MERS-CoV, showing the spherical particles within the cytoplasm of an infected cell.

Source: Cynthia Goldsmith/AzaibiTamin

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(case-fatality rate of 34.4%). The majority of these cases were reported from Saudi Arabia. There were 2101 cases including 780 deaths with a case fatality rate of 37.1%.

Aetiology

MERS-CoV is a zoonotic virus. The virus is related to SARS (severe acute respiratory syndrome) CoV and belongs to same corona virus family (MERS-CoV). However, both viruses are distinct. (Fig. 1, 2).

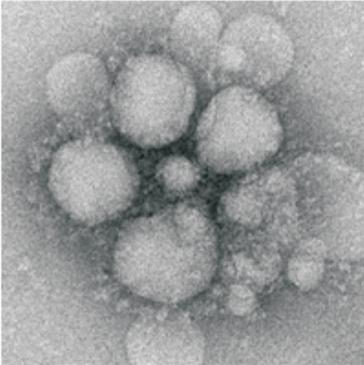


Fig. 2 MERS-CoV particles as seen by negative stain electron microscopy. Virions contain characteristic club-like projections emanating from the viral membrane. Source: Cynthia Goldsmith/Maureen Metcalfe/AzaibiTamin

These viruses use different receptors to infect cells in human airways. Reproduction number of infection (the average number of secondary cases \ from a single infective case will cause in a population without any immunity to the disease) is lower in MERS than SARS. MERS virus circulates more than a year in human population without mutating into a pandemic form. Health care-associated outbreaks have been noted in countries like Saudi Arabia, United Arab Emirates and the Republic of Korea. The virus is airborne spreading when an infected person coughs or sneezes, or touches contaminated surfaces. People with chronic diseases seem to be more vulnerable. However, the virus has not shown to spread in a sustained way in community (2). The largest outbreak outside of the Arabian Peninsula occurred in the Republic of Korea in 2015. It was linked to a traveler returning from the Arabian Peninsula.

It has been shown that humans are infected through direct or indirect contact with infected dromedary (Arabian) camels in several

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countries, including Saudi Arabia, Egypt, Qatar, and Oman. Though the origin of the virus has not been fully understood, it is believed to be originated in bats, and transmitted to camels later. Human-to-human transmission of the virus does not easily occur unless there is close contact, such as providing unprotected care to an infected patient. Cases have been reported from healthcare facilities with inadequate or inappropriate infection prevention and control practices. The virus does not pass easily from person-to-person unless there is close contact. More number of cases are reported among family members and health care workers (3)..Though route of transmission from dromedary camels to humans is not fully unravelled, strains of the virus identical to human strains have been isolated. Since the outbreak in 2012, 27 countries have reported cases of MERS, and nearly 80% of cases have been reported from Saudi Arabia. People can get infected from unprotected contact with infected dromedary camels or infected persons

There are evidences to think that dromedary camels are the major reservoir host for the virus. Thus, the infection has an animal source. Strains of MERS-CoV that are identical to human strains have been isolated from dromedaries in many countries. Still, the exact role of these camels in transmission of the virus and the exact route of transmission remain undetermined (2). Nearly 80% of human cases have been reported by Saudi Arabia. The infection spreads through unprotected contact with infected dromedary camels or infected persons. Cases recognized outside the Middle East are those who got infection in the Middle East and then travelled to areas outside the Middle East (4).

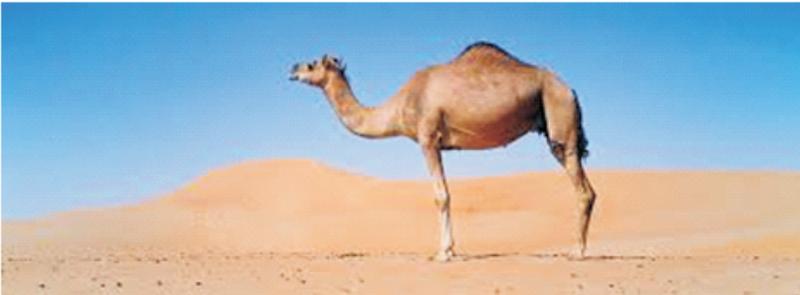


Fig.1 Dromedary camel (*Camelus dromedaries*)
Courtesy: pixels.com

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Those who work and handle live camels, or camel's meat or milk are at risk. It includes veterinarians and those who work at markets or race tracks, and those who slaughter, butcher, milk, and cook raw camel products. Cooked meat and pasteurized milk are safe to handle and consume. However, it must be noted that not all camels may transmit the disease; Bactrian (Mongolian) camel herds have not shown any infections with MERS..

Clinical features

The virus has an incubation period of 2-12 days. It has a strong tropism for non-ciliated bronchial epithelial cells. The tropism is unique in that most respiratory virus targets ciliated cells.

The clinical features of MERS-CoV infection may remain asymptomatic without any symptoms, or present with mild respiratory manifestations to severe acute respiratory features. Commonly the condition presents with flu-like symptoms (5). There is fever, cough and shortness of breath. Severe cases may present with features of pneumonia. Some patients may present gastrointestinal manifestations, including diarrhoea. In individuals with severe respiratory manifestations, the condition may progress to respiratory failure necessitating management in intensive care unit and mechanical ventilatory support. Severe disease is often noted in elderly persons and in persons with co-existent chronic diseases such as diabetes, chronic lung disease, heart disease, liver disease, chronic renal disease, cancer and weakened immune status (6).

Diagnosis

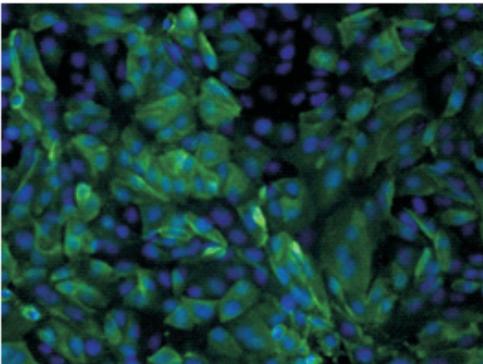


Fig. 4 Human serum antibodies react with MERS-CoV-infected Vero cells, indicating the patient has been infected with MERS-CoV.

Source: Jennifer L. Harcourt

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According to World Health Organization, (7)

confirmed case

a person with a positive lab test by "molecular diagnostics including either a positive PCR on at least two specific genomic targets or a single positive target with sequencing on a second.

probable case

- a person with a fever, respiratory infection, and evidence of pneumonia or acute respiratory distress syndrome, and testing for MERS-CoV is unavailable or negative on a single inadequate specimen, and the person has a direct link with a confirmed case.
- A person with an acute febrile respiratory illness with clinical, radiological, or histopathological evidence of pulmonary parenchymal disease (e.g. pneumonia or acute respiratory distress Syndrome) and an inconclusive MERS-CoV laboratory test (that is, a positive screening test without confirmation) and a resident of or traveler to Middle Eastern countries where MERS-CoV virus is believed to be circulating in the 14 days before onset of illness.
- A person with an acute febrile respiratory illness of any severity and an inconclusive MERS-CoV laboratory test (that is, a positive screening test without confirmation) and the person has a direct epidemiologic link with a confirmed MERS-CoV case.

Chest X-ray may show bilateral patchy infiltrates and the lower lobes tend to be more involved. Interstitial infiltrates are demonstrable on CT scan. Peripheral blood examination may show leucopaenia and lymphopaenia.

The condition is confirmed by RT-PCR assays for rapid identification of MERS-CoV from patient derived samples (Fig. 4). The samples obtained from the sputum, lower respiratory tract via bronchoalveolar lavage, and tracheal aspirate demonstrate the highest viral loads. Nasopharyngeal swabs are also used to demonstrate the virus. The physicians are to be on lookout for patients who get sick after visiting Middle-Eastern countries.

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Treatment

There is no vaccine available to prevent the disease. There is no specific treatment, and the treatment is supportive and it is based on the clinical manifestations exhibited by the patient.

Prevention

Persons visiting markets, farms or places where dromedary camels or other animals should follow general hygiene measures. They should undertake hand washing before and after touching animals, and should avoid contact with sick animals. The consumption of raw or undercooked animal products, including milk and meat carries high risk of the disease. Animal products that have been processed thoroughly by cooking or pasteurization are safe for consumption. Care should be taken to avoid cross contamination with uncooked food material. Countries should maintain a high level of vigilance, especially those with large numbers of travellers or migrant workers returning from the Middle East. Young men in Saudi Arabia who have contact with camels in cultural or occupational settings have the chance of getting infected with MERS-CoV.(8) It may go undetected and there are all chances of they introducing the virus to the general population in which severe illness may occur.

CDC has recommended the following measures to reduce the risk of acquiring the illness.

- Wash your hands often with soap and water for at least 20 seconds, and help young children do the same. If soap and water are not available, use an alcohol-based hand sanitizer.
- Cover your nose and mouth with a tissue when you cough or sneeze, then throw the tissue in the trash.
- Avoid touching your eyes, nose, and mouth with unwashed hands.
- Avoid personal contact, such as kissing, or sharing cups or eating utensils, with sick people.
- Clean and disinfect frequently touched surfaces and objects, such as doorknobs

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COVID-19 INFECTION

World Health Organization (WHO) has declared International Health Emergency following reports of a number of cases Pneumonia from Wuhan, China and subsequently in other countries. The condition is due to an infection from a corona (crown-like or hollow shape) virus (2019-nCoV) (Fig.1).

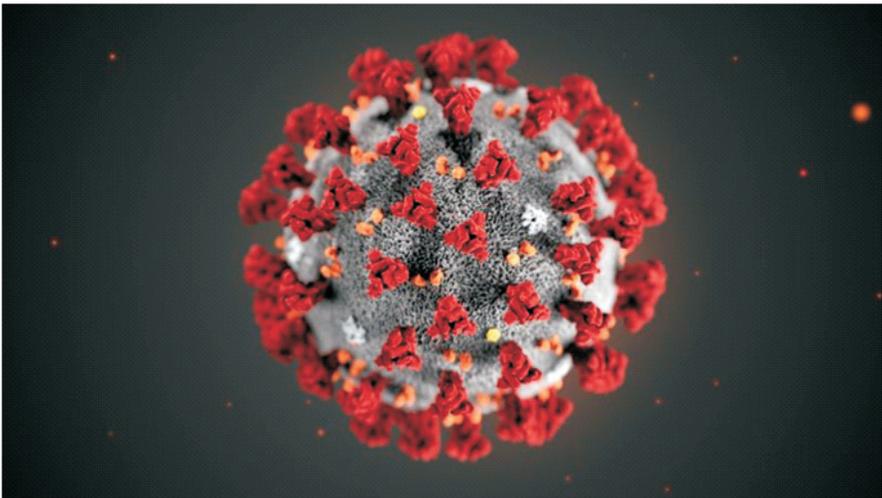


Fig. 1. Picture showing ultrastructural morphology exhibited by the 2019 novel coronavirus Credit: CDC/ Alissa Eckert, Dan Higgins.

Coronaviruses are a family of viruses that cause illness ranging from the common cold to more severe diseases such as severe respiratory distress syndrome (SARS) and Middle-East respiratory syndrome (MERS)

Aetiology

The causative agent is a virus that causes upper respiratory tract infection and pneumonia. It is an enveloped RNA virus found in birds, animals and human being. Under electron microscope, the image of the virus is a reminiscent of a solar corona. Earlier the World had witnessed

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outbreaks of two serious corona virus (CoV) infections, namely Severe acute respiratory syndrome (SARS-CoV) and Middle-East respiratory syndrome (MERS-CoV). The outbreak of SARS which made its appearance in Southern China in 2002 spread to 30 counties. It infected 8437 persons and killed 813 persons. MERS which appeared in Saudi Arabia in 2012 spread to 27 countries. There were 2492 confirmed cases of whom 858 died. MERS has been considered more deadly as there were deaths in 30% of cases who were infected. The current novel corona virus (nCoV) has emerged in Hubei province capital Wuhan (1)(Fig.2). The causative agent was identified on January 7, 2020 and

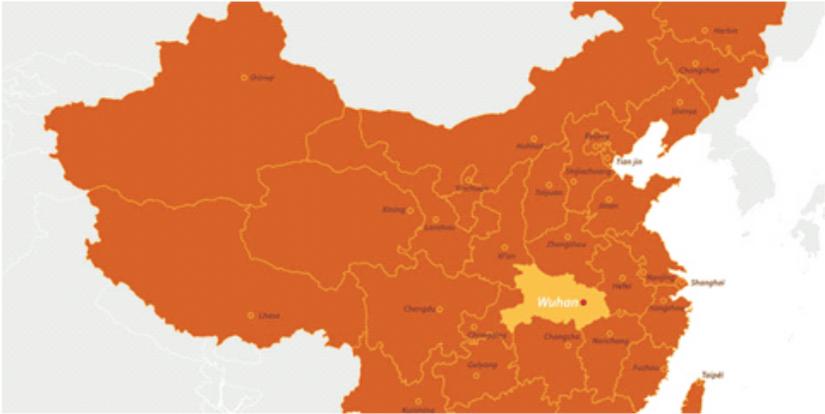


Fig 2. Map showing Wuhan in the State of Hubei, China

was named as 2019-nCoV, a new strain that had not been previously identified in humans (2). The current epidemic of 2019-nCoV is more widespread compared to the epidemic of earlier corona viruses. Coronavirus outbreak has a larger negative effect on the global economy than the SARS outbreak in 2003. This deadly coronavirus was named by WHO following a scientific approach as COVID-19, name of the disease caused by the novel coronavirus. The 'CO' in COVID stands corona, while 'VI' is for virus and 'D' for disease. The number 19 stands for year 2019, when the outbreak was first identified

The magnitude of the risk posed by this novel coronavirus is assessed by three parameters such as transmission rate (R_0) giving

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average number of newly infected people from a single case to a naïve population, case fatality rate (CFR) giving the percent of cases that result in death and to determine whether asymptomatic transmission is possible. On average every case of the nCoV is able to create 3 to 4 new cases indicating the infection is likely to spread. Case fatality rate for nCoV has been estimated to be 2% (for comparison, the case fatality rate for SARS was 10%, and for MERS 34%).

Attempts were made quickly in Wuhan and surrounding region in China, to contain the spread of the infection by suspending live animal markets throughout the country, cancelling the trains and flights out of the city, banning the movement of private cars, suspending the long-distance bus services, restriction of movement of people in the city, confining them in their houses, providing health care facilities by converting the exhibition grounds into make-shift hospitals, construction of hospitals to provide additional beds to take care of the patients (Fig 3-10).



Fig. 3 showing closed houses and barren street

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Fig. 4 picture showing empty shops



Fig. 5 Picture showing dead silence I
n the business centre



Fig.6 picture showing empty mall



Fig 7 Picture showing absence of
traffic on the roads

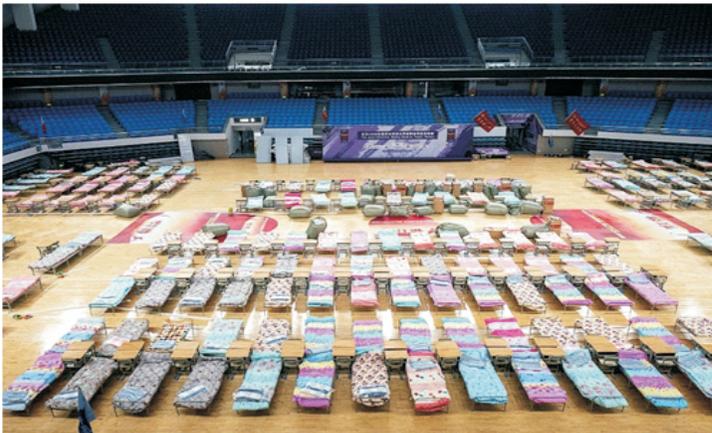


Fig. 8 Picture showing make-shift hospital in the exhibition ground

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Fig 9. Picture showing the make-shift health care facility



Fig 10. Construction of additional health care facility

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Epidemiology:

On December 31, 2019, China reported a cluster of Pneumonia cases of unknown aetiology, from Wuhan city ('China's thoroughfare, river city, The Chicago of China, Different everyday) in the Hubei Province. Within a week, it was found to be due to a novel Corona virus, labelled as 2019-nCoV, belonging to genus Beta-coronavirus found in humans, bats, and wild animals. The virus had 96% concordance with an already known bat-borne coronavirus. These viruses are zoonotic viruses and they are transmitted between animals to humans. SARS-CoV was transmitted from civet cats (small mammals) to humans and MERS-CoV from dromedary (Arabian) camels to humans. The natural animal host of nCoV-2019 is yet to be identified. The intermediate host responsible for its transmission to humans is not known. It most closely resembles coronaviruses from Chinese horseshoe bats. Environmental samples were positive for nCoV in human seafood Wholesale Market, where wild animals are traded in Wuhan city. It is noteworthy that some laboratory confirmed patients did not visit this market. Wuhan city is the epicenter of the current outbreak. Cases were being reported from other provinces of China. Within a month, 14,562 persons were reported to be infected this virus. 31,535 cases were reported worldwide, most of which belonged to China. They have been confirmed by laboratory tests. It included 17 healthcare workers. A total of 1,63,844 persons had been exposed to the infection in Hubei province. There were 636 deaths in Hubei province, including Li Wenliang (34), an Ophthalmologist, who tried to sound warning about the viral infection that ravaged China two decades ago. Philippines reported first death outside China, and Hong Kong reported one death. The victim had arrived from Wuhan. The virus spread within a month to 28 countries including India, the US, the UK, Russia, Japan, Australia, Thailand, Republic of Korea, Germany, Vietnam, Bangladesh, Sri Lanka, and United Arab Emirates. India, the US, Sri Lanka, Bangladesh and many other countries evacuated their nationals from Wuhan. India airlifted 654 persons including 7 Maldivians to Delhi and they were kept in quarantine facility at Manesar, near Delhi, to monitor the signs of

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infection for 2 weeks. 3 cases were reported positive from Kerala and they had returned from China.

On 5th March 2020, China reported 80,430 cases with 3913 deaths. Globally, there were 96,268 cases and 3,304 deaths. These confirmed cases had been reported from 81 countries and territories. South Korea (5,766), Iran (3,513) and Italy (3,089) were other countries which reported maximum number of cases outside China. Thus, the virus has exhibited pandemic potential. In South Korea more than 90 per cent of the new cases were in Daegu city and the neighboring North Gyeongsang province according to the Korea Centers for Disease Control and Prevention. 29 cases were reported from India, of which there were 15 Italian tourists. The cases were reported from Delhi, Rajasthan, UP, Kerala and Telangana.

Causative agent

SARS-CoV and COVID-19 share structural similarity and binding to the same receptor on the cells. Bats are considered to be the original host of SARS-CoV. COVID-19 appears to have jumped the species barrier possibly via close contact with infected animals, and may then be spread person-to-person. Changes in the surface protein may facilitate the virus to attach itself to the new host cell either by mutation or recombination. Similar to SARS-CoV, the spike protein of COVID-19, that is responsible for the disease, binds to the cellular receptor (angiotensin-converting enzyme 2, ACE2), serving as the entry point into the cells of human body. It is worth noting that both SARS-CoV and COVID-19 bind to the same receptor (ACE2) allowing virus to get deep into human lungs. Unlike SARS-CoV, the spike protein of COVID-19 binds to the cell receptor with much higher (10-to-20 fold) binding affinity. This characteristic is unique to COVID-19 and it explains high human-to-human transmissibility of the virus compared with SARS-CoV. COVID-19 might be spread even during the incubation period when the person is not exhibiting any symptoms.

Spread of infection

The role of environmental contamination in the transmission of COVID-19 is not yet clear. The infection spreads from person-to-person

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from close contact. The spread occurs via the respiratory tract through the droplets following cough or sneeze of the infected person. There is a suspicion that the infection can spread from fomites such as chair, door, utensils, door handle that have been touched by the infected persons. It must be noted that the spread can occur even when the person is asymptomatic. The residents of Wuhan city had been isolated and experienced frightening time. Most forms of traffic had been banned and 11 million people were shut up in their homes, to minimize the spread of the virus.

People of all ages are susceptible to COVID-19. Older persons and persons with pre-existing medical conditions such as heart disease, asthma, diabetes appear to be more vulnerable to becoming severely ill with the virus. According to China's National Health Commission, about 80% of those who died were over the age of 60 and 75% of them had pre-existing health conditions. The virus is contagious even when the patient is not displaying any symptoms.

Pathology

COVID-19 infects human respiratory epithelial cells through an interaction between the viral S protein and the angiotensin-converting enzyme 2 receptor on human cells. The causative viruses possess spiky projections on their outer surfaces that have a resemblance to the points of a crown (3). Beneath this exterior lie a greasy membrane and a round core. The core contains genetic material which the virus can inject into vulnerable cells to infect them. The spike proteins extend from within the core to the viral surface. When the spike engages its receptor on a host cell there is merger of the virus with the cell. This will facilitate the release of genetic material to take over the internal machinery of the cell and produce large number of viruses.

Post-mortem samples from a 50-year old male patient from Wuhan were taken from the lung, liver, and heart. Histological examination showed bilateral diffuse alveolar damage with cellular fibromyxoid exudates. The lung showed evidence of desquamation of pneumocytes

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and hyaline membrane formation, indicating acute respiratory distress syndrome (ARDS). Interstitial mononuclear inflammatory infiltrates, dominated by lymphocytes, were seen in both lungs. Multinucleated syncytial cells with atypical enlarged pneumocytes characterized by large nuclei, amphophilic granular cytoplasm, and prominent nucleoli were identified in the intra-alveolar spaces, showing viral cytopathic-like changes. No obvious intranuclear or intracytoplasmic viral inclusions were identified.

Clinical features

Huang and co-workers reported 41 cases of novel coronavirus infected pneumonia (NCIP) in which majority of patients gave a history of exposure to seafood wholesale market. There were 30 (73%) men and 13 (32%) had underlying diseases including diabetes, hypertension and cardiovascular disease. Median age was 49 years. They presented with fever, non-productive cough, dyspnoea, myalgia, and fatigue. They had lymphopaenia. All of them exhibited pneumonia and chest CT images showed bilateral ground=glass opacity. Complications included acute respiratory distress syndrome, anaemia, acute cardiac injury and secondary infection. There were six (15%) deaths. No antiviral treatment was found to be effective (4).

After giving details of 99 patients of NCIP from the same hospital at Wuhan, Chen et al came to the conclusion that 2019-nCoV infection is clustered within groups of humans in close contact. It had affected older men with comorbidities (5). The condition could progress to adult respiratory distress syndrome (ARDS).

In a retrospective study of 139 consecutive hospitalized patients with confirmed Novel Corona-virus infected pneumonia at Zhongnan Hospital of Wuhan University in Wuhan in the initial four weeks of January 2020 followed up to Feb 3, 2020 by Wang and co-workers, it was found the median age of the patients was 56 years(range 22-92 years) and 75 (54.3%) were men. Hospital-associated transmission was thought in 40 (29%) affected health professions and 17 (12.3%) hospitalized patients (6).

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They presented with fever (98.6%), fatigue (96.69%), dry cough (59.4%) and dyspnoea as the common features. Laboratory investigations showed lymphopaenia, prolonged prothrombin time and elevated lactate dehydrogenase(LDH). Chest computed tomographic scans showed bilateral patchy shadows or ground glass opacity in the lungs of all patients. The cases were confirmed by the study of throat swabs with real time reverse transcription polymerase chain reaction (RT-PCR).

The patients received antiviral (oseltamivir) or antibacterial therapy and glucocorticoid therapy. Due to complications such as acute respiratory distress syndrome (ARDS) (61%), arrhythmia, (44.4%) and shock (30.6%) the patients had to be shifted to intensive care unit (36 patients). These patients belonged to older age group (66 years) and had underlying comorbidities. There was 4.3% mortality.

The patients exposed to the corona virus infection may remain asymptomatic or seriously ill requiring treatment is intensive care unit (ICU). After an incubation period varying from 2 to 14 days, the condition presents with symptoms similar to any other upper respiratory tract infection such as running nose, sneezing, sore throat, cough, shortness of breath and sometimes fever. Many of these symptoms simulate flu or a common cold. Due to similarities of the symptoms from different viruses, it becomes difficult to identify the disease based on symptoms alone. The laboratory help is needed to confirm COVID infection. The infection can cause pneumonia, severe acute respiratory distress, impaired liver and kidney functions, and even death.

In a subset of individuals, including those with cardiopulmonary disease or a weakened immune system, the viral infection can progress to a more severe lower-respiratory infection. The novel coronavirus causes symptoms similar to those of other coronaviruses, triggering fever, cough and difficult breathing in most patients. Rarer symptoms include dizziness, nausea, vomiting and a runny nose.

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Case definition(7)

The Clinical management guidelines of COVID is based on case definition

Suspect case

- a. Patient with severe acute respiratory infection such as fever, cough, and requiring admission to the hospital, **and** with no other aetiology that fully explains the clinical presentation, **and** history of travel to or residence in China during the 14 days prior to symptom onset, **or**
- b. Patient with acute respiratory illness **and** at least one of the following during the 14 days prior to symptom onset;
 - i. Close contact with a confirmed or probable case of 2019-nCoV infection **or**
 - ii. Worked in or attended a health care facility where patients with confirmed or probable 2019-nCoV acute respiratory disease patients were being treated

Probable case

A suspect case for whom testing for 2019 nCoV is inconclusive or is tested positive using a pan-coronavirus assay and without laboratory evidence of other respiratory pathogens

Confirmed case

A person with laboratory confirmation of 2019 nCoV infection irrespective of clinical signs and symptoms

Close contact

1. Health care associate exposure, including providing direct care for nCoV patients, working with health care workers infected with nCoV, visiting patients or staying in the same close environment of an nCoV patient
2. Working together in close proximity or sharing the same classroom environment with a nCoV patient
3. Traveling together with nCoV patient in any kind of conveyance
4. Living in the same household as a NCoV patient

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Diagnosis

The infection has to be suspected in persons who have visited areas with the outbreak of infection. Three specimens of serum, respiratory secretions (sputum, bronchoalveolar lavage fluid, tracheal aspirate) and upper respiratory tract secretions (nasal or throat swabs) should be sent to the laboratory identify the cause of the infection

The samples are to be obtained from the lower respiratory tract, including sputum, bronchoalveolar lavage (BAL) and tracheal aspirate. In situations where the sample can't be obtained from the lower respiratory tract, samples from the upper respiratory tract (nasopharyngeal swab and oropharyngeal swab) can be used. The swabs should be kept and transported in the tube with viral transport medium. Samples should be kept refrigerated at 4-8° C and sent to the laboratory with molecular diagnostic facility. Real-time reverse transcriptase–polymerase chain reaction (RT-PCR) tests for COVID-19 nucleic acid is used to determine positivity of the sample and those positive are to be notified immediately (8).

In a retrospective analysis of serial chest CT scans of 81 patients with COVID-19 pneumonia in Wuhan hospital, the predominant pattern of abnormality observed was bilateral (79%), peripheral (54%), ill-defined (81%) and ground-glass opacification (65%) (8). It was concluded that chest imaging abnormalities are recognizable even in asymptomatic patients which get rapidly evolved from focal unilateral to diffuse bilateral ground-glass opacities within 1-3 weeks. The radiological evolution of COVID-19 pneumonia was consistent with the clinical course of the disease.

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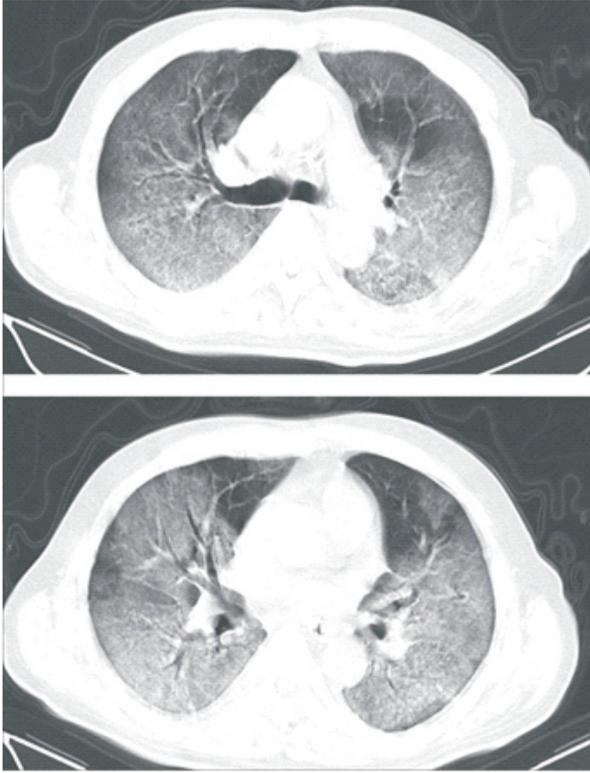


Fig. 11. High resolution image of transverse CT scan showing extensive ground glass opacities in both lungs giving a white lung appearance
Courtesy: Lancet Inf Dis Feb 24, 2020 [http://doi.org/10.1016/S1473.3099\)2-_30086](http://doi.org/10.1016/S1473.3099)2-_30086)

Most patients in the study cohort by Shi et al showed bilateral lung involvement, with lesions mainly located peripherally and sub-pleurally with diffuse distribution (9). The predominant pattern was ground-glass opacity, with ill-defined margins, air bronchograms, smooth or irregular interlobular or septal thickening, and thickening of the adjacent pleura (Fig.11).Some patients presented with pleural effusion, lymphadenopathy, and round cystic changes on CT

Analysing the CT abnormalities in COVID-19 lower respiratory tract infection, Kanne and colleagues have stated that the most common CT

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findings are bilateral, basal and peripheral predominant ground glass opacity, consolidation or both implying the presence of lung injury. These changes peak around 9-13 days and then slowly resolve (10).

Virus isolation is to be conducted with various cell lines, such as human airway epithelial cells, Vero E6, and Huh-7. Cytopathic effects (CPE) are observed within 96 hours after inoculation. Typical crown-like particles are observed under transmission electron microscope (TEM) with negative staining (Fig.12-14). The cellular infectivity of the isolated viruses could be completely neutralized by the sera collected from convalescent patients.

Real-time PCR (RT-PCR) assays on these samples are positive for pan-Betacoronavirus. Using Illumina and nanopore sequencing, the whole genome sequences of the virus can be acquired. Bioinformatic analyses indicated that the virus had features typical of the coronavirus family and belonged to the Betacoronavirus 2B lineage.

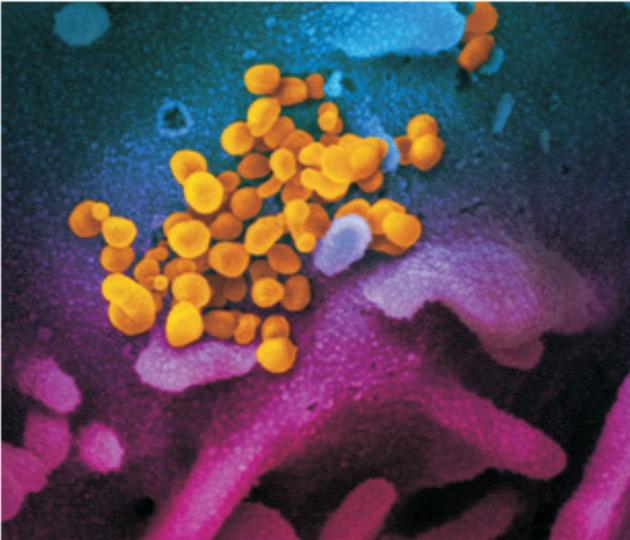


Fig. 12. A scanning electron microscope image of COVID-19 virus grown from a laboratory culture.

Credit: US National Institute of Allergy and Infectious Diseases-RMI

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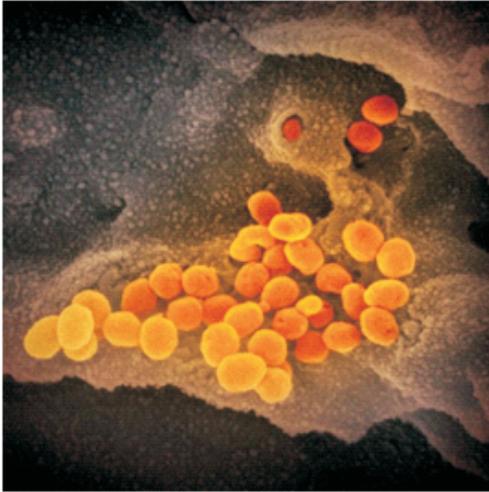


Fig. 13 A scanning electron microscope image of the CoVID-19 grown from a laboratory culture. It should be noted that electron microscopes utilise a beam of energy to take a detailed picture of the virus.

Credit: US National Institute of Allergy and Infectious Diseases-RMI

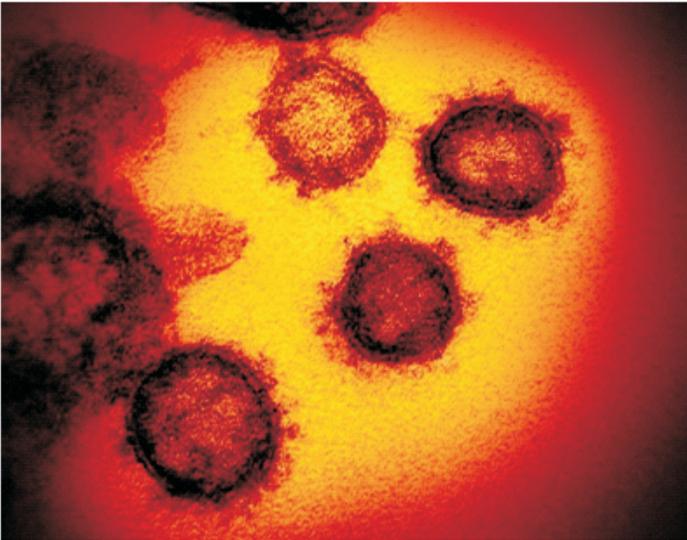


Fig. 14. A coloured transmission electron microscope image of the CoVID-19 grown from a laboratory culture

Credit: US National Institute of Allergy and Infectious Diseases-RMI

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Mortality

CoVID-19 is more contagious than the related viruses such as SARS-CoV and MERS CoV. Covid-19 appears to be not as fatal on a case-by-case basis, its greater spread has already led to an increased number of deaths than its related coronaviruses. Old age, male sex, and presence of comorbidities and progressive radiographic deterioration on follow-up CT might be risk factors for poor prognosis in patients with COVID-19 pneumonia.

Chinese Center for Disease Control and Prevention (CDC) has stated that of the 44,672 confirmed cases, there were 1,023 deaths, with a crude mortality rate of 2.3%. By comparison, SARS had a mortality rate of 9.6% during the 2003 outbreak, while MERS showed a case fatality of 35% (11). The highly contagious seasonal influenza which affects a large number of people has a mortality rate of around 0.1%.

Many of the deaths seen during the current outbreak of COVID-19 in China is among elderly persons and those with pre-existing conditions that make them more susceptible to serious illness from the viral attack. According to Chinese CDC the crude fatality rate is 14.8% among patients aged 80 and above. The fatality rate was 10.5% among those with pre-existing illness especially cardiovascular disease.

In retrospective, observational study of 52 critically ill patients with SARS-CoV-2 pneumonia, in Jin Yin-tan Hospital, Wuhan over a period of 28 days during January 2020, it was found they were of 59.7 years, 35 (67%) were men, and 21(40%) had chronic illness, 32(61.5%) had died at 28 days (12). Most patients had organ function damage, including 35(67%) with ARDS, 15(29%) with acute kidney injury, 12(23%) with cardiac injury, 15(29%) with liver dysfunction, and one (2%) with pneumothorax. The study concluded that older patients (>65 years) with comorbidities and ARDS are at increased risk of death. February 2020 DOI: [https://doi.org/10.1016/S2213-2600\(20\)30079-5](https://doi.org/10.1016/S2213-2600(20)30079-5)

Treatment

There is no specific antiviral treatment available for any human coronavirus infection. The individuals who are affected by a coronavirus usually recover on their own. The suspected cases are to be kept isolated

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at designated medical institutions and treated. The treatment is essentially symptomatic and supportive. They are advised staying at home to rest. The approach to contain this disease is to control the source of infection, use of personal protection to reduce the risk of transmission, and early diagnosis, isolation and supportive treatment for affected patients. Paracetamol and acetaminophen are given for the treatment of pain and fever. The patients are advised to drink plenty of fluids. Though antiviral agents, antibacterial agents and methylprednisolone have been given to these patients, no effective outcomes have been noted (5).

Convalescent plasma has been used as a therapeutic method. People who have recovered from COVID-19 disease would demonstrate the presence of antibodies against the virus. Infusing the antibodies to critically ill patients is expected to improve the chance of survival. The plasma that is transfused contains the antibodies. Patients who received plasma therapy showed an improvement in the clinical symptoms, 12-24 hours after administration of the therapy. Antibodies in the plasma bind to the virus and prevent them from entering the cells. But by the time it is given, many cells would have been infected. Hence, convalescent plasma therapy appears to be not very effective.

Chloroquine phosphate, an old remedy for malaria, has shown to have apparent efficacy and acceptable safety against COVID-19 associated pneumonia in multi-centre clinical trials conducted in China (13). The drug is recommended to be included in the Guidelines for the Prevention, Diagnosis, and Treatment of Pneumonia Caused by COVID-19 issued by the National Health Commission of the People's Republic of China for treatment of COVID-19 infection in larger populations in the future

1. Upper respiratory tract infection without lung infiltrates, positive PCR

Chloroquine phosphate 500 mg orally twice a day for 5 days

Oseltamivir 150 mg orally twice a day for 5 days

2. Treatment of COVID-19 pneumonia

Chloroquine phosphate 500 mg orally twice a day for 10 days

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Darunavir 800 mg /Cobicistat 150 mg orally for 2 weeks **or**
Atazanavir 400 mg once daily orally daily with food for 2 weeks,
and
Oseltamivir 150 mg orally twice a day with or without
Corticosteroids in the form of Methylprednisolone 40 mg
intravenously every 12 hours for 5 days

These medications disable viruses by interfering with their attempts to replicate in host cells. The 'protease inhibitors', have shown promise against coronaviruses as they help to alert the immune system to viral invaders. Potential broad-spectrum antiviral agents act by increasing activity of the endosomal pH required for virus/cell fusion as well as interfering with the glycosylation of cellular receptors of SARS COV. The anti-viral and anti-inflammatory activities of chloroquine may account for its potent efficacy in treating patients with COVID 19 pneumonia

Prevention of spread:

No vaccine is available for preventive use. In an attempt to prevent the spread of the infection, Chinese authorities effectively sealed off Wuhan, and placed restrictions on travel to and from several other cities. The move was to 'resolutely contain the momentum of the epidemic spreading' and protect lives. WHO Director General Tedros Adhanom Ghebreyesus has said that, "Every country must be ready for its first case, its first cluster, the first evidence of community transmission, and for dealing with sustained community transmission," Further he said, "We are not defenceless," he has urged that "every country and every person" to help ensure cases are detected early and that authorities are able to trace contacts, provide care and prevent widespread community transmissions.

Steps to stop the virus from spreading

The countries embarked to contain the spread of the virus, must detect cases early and isolate people who test positive for the virus. On detection of a case, the focus should be to trace the contact and treat them, if already infected. Immediate medical care has to be given once

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the symptoms are manifested. Spread can be stopped by avoiding mass gathering in enclosed spaces. People should avoid all non-essential travel to countries where community spread of the virus is reported especially to Singapore, South Korea, Iran and Italy. There is check on individuals travelling from China, Singapore, Thailand, South Korea, and Japan for a period of 28 days.

Discharge

The patients are discharged or quarantine discontinued if they fulfil the following criteria (14)

- normal temperature lasting longer than 3 days,
- resolved respiratory symptoms,
- substantially improved acute exudative lesions on chest computed tomography (CT) images, and

2 consecutively negative RT-PCR test results separated by at least 1 day

WHO's strategic objectives (15)

- Interrupt human-to-human transmission including reducing secondary infections among close contacts and health care workers, preventing transmission amplification events, and preventing further international spread;
- Identify, isolate and care for patients early, including providing optimized care for infected patients;
- Identify and reduce transmission from the animal source;
- Address crucial unknowns regarding clinical severity, extent of transmission and infection, treatment options, and accelerate the development of diagnostics, therapeutics and vaccines;
- Communicate critical risk and event information to all communities and counter misinformation;
- Minimize social and economic impact through multisectoral partnerships.

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Reduction of risk

WHO has suggested that people can help to reduce their risk of getting respiratory illnesses by following simple measures.

- Wash your hands often with soap and water for at least 20 seconds, and help young children do the same. If soap and water are not available, use an alcohol-based hand sanitizer.
- Cover your nose and mouth with a tissue when you cough or sneeze, then throw the tissue in the trash.
- Avoid touching your eyes, nose, and mouth with unwashed hands.
- Avoid personal contact, such as kissing, or sharing cups or eating utensils, with sick people
- Clean and disinfect frequently touched surfaces and objects, such as doorknobs

Scrupulous personal hygiene has to be maintained. The dirty hands must be washed with soap and water. It is advisable to keep the hands clean with alcohol-based hand rubs. Close contact should be avoided with person showing symptoms of respiratory illness such as coughing or sneezing. Persons having flu-like symptoms with fever, cough, running nose, sneezing or sore throat must seek medical help. The face especially nose and mouth are to be covered while sneezing and coughing. It is necessary to maintain social distancing. It is advised to maintain at least 1 meter (3 feet) distance between persons especially with those who are coughing, sneezing and have a fever. This will prevent breathing in the virus. Wearing a triple-layer surgical mask can help limit the spread of infection to some extent. There is need to avoid touching eyes, nose and mouth with contaminated hands as it can transfer the virus from the surface to the individual. It is necessary to avoid raw and uncooked animal products. One should avoid travel when he/she is feeling unwell. It is also necessary to avoid travelling to areas with outbreaks of infection. Recent travel history should be made available to the health care provider. It is necessary to keep track of all contacts of an infected person and keep them under surveillance. Since health care providers are under high risk, they have to take all personal protective measure.

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**MANAGEMENT OF ADJUSTMENT
DISORDERS IN CLINICAL
PRACTICE**

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CASE I:

Mr. Ram, PU student residing in a residential college, one day at 6 am screamed and started sobbing. His roommate Mr. Gopal approached him and found him nonresponsive. He informed the warden. Mr. Ram was shifted to a nearby hospital. He remained unconscious. Neurologist was summoned, ECG, brain scan was done which were normal. Mr. Ram opened his eyes and wanted to see his parents. He had one more attack in the hospital. Doctors made a diagnosis of 'functional attack'. Psychiatrist was called. On enquiry, Mr. Ram had a bad dream that morning in which his father died in an accident followed by his mother's death who developed heart attack. Mr. Ram reported that he was not comfortable staying in the residential college. He was missing his parents and family. He requested the doctors to recommend to his parents to shift



Case II:

Padma, 12-year-old, following the death of Rocky - the pet dog, became dull, withdrawn, stopped going to the school. She started showing anger and resentment towards her father who delayed taking the dog to the hospital. Last one week, she is not eating well. Her sleep is disturbed. She talks during sleep and says 'Rocky where are you. I don't want to be here. I can't live without you'. Most of the time she remains in the bed, weeping.

Case III:

Mr. Sunder was shifted to stores - section as punishment. He was a cashier and could not give account for Rs. 20,000. Manager accused him of swindling the money and made nasty comments on his integrity. Sunder was upset. His colleagues did not think that he was responsible for the loss. Mr. Sunder developed involuntary neck movements and severe headache with vomiting. All investigations were normal. He would weep and request his colleagues to convince the manager. He would pay the lost amount from his pocket, but nobody should doubt his honesty.

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Case IV:



Vidya found her friend Shantha's body hanging from the fan. She came out screaming and told others that Shantha had committed suicide. She was shaken and remained dazed. By evening she started reporting that a black shadow was seen by her room. She pleaded her parents to stay with her. She remained very fearful. A sacred thread was tied to her. People thought that she was haunted by the spirit of Shantha. Next day she became mute, did not identify her parents. She tried to run away from the house. When people held her, she showed anger and resentment. She was taken to a manthravadi. She did not cooperate for the rituals. When he talked, her voice was different and irrelevant. People did not know whether she was mentally ill or victim of the spirit.

Case V:



Mr. Sujeet, a married gentleman, working as a mechanic in a private factory. He was very energetic with high aspirations in life and a pleasant disposition. He lived in a nuclear family consisting of his wife

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and two daughters. One day while returning from his office, he met with an accident, during which he sustained a crush injury to his right leg. He was taken to a private hospital where the orthopedician and the vascular surgeon tried to do a restorative surgery. Unfortunately, gangrene set in after the emergency surgery. Hence the specialist decided to go in for a below knee amputation. The patient refused to give consent for the surgery but later on when left with no options, he agreed for it. Operations went on without any complications. Post-operative – period was uneventful, and he was discharged within a week.

A fortnight after the operation on follow-up, Sujeet was brought with complaints of feeling uneasy, having decreased sleep, multiple body aches, being withdrawn, irritability on trivial issues, anger outbursts, reporting fear at times, decreased interest in pleasurable activities and occasional crying spells. On one occasion, he expressed death wishes to his wife. The orthopedician did not find any post-operative complications. During the consultation Mr. Sujeet started crying and asked the orthopedician for some injection, which would put an end to his life without any pain. On hearing his suicidal ideation, the orthopedician referred the patient immediately for psychiatric consultation. Psychiatric evaluation revealed that his symptoms have increased since two days when he came to know from his colleague that he might lose his job. History of marital conflicts was also revealed. During the therapy he said, 'I can't return to my job, I am worthless. It is not fair that I am subjected to such punishment. I am a burden on my family. No one really cares for me'.

Adjustment Disorders:

The development of transient psychiatric symptoms in the context of stress is virtually a universal experience. An adjustment disorder is defined as development of emotional or behavioural symptoms in response to an identifiable stressor(s) occurring within a month of the onset of the stressor(s) and the duration of the symptoms usually does not exceed 6 months, except in the case of a prolonged depressive reaction. These symptoms or behaviours are clinically significant as evidenced by marked distress which is excess of what is expected from

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exposure to that stressor and there are significant impairment in personal, social, educational or occupational functioning. Once the stressor or its consequences have terminated, the symptoms do not persist for more than 6 months.

States of subjective distress and emotional disturbances, arising in the period of adaption to a significant life change or stressful life event. This would have affected the integrity of an individual's social network, social support and values

The common stressful events are

- i. Joining a new school / college / hostel / residential school / living in a PG away from family.
- ii. Series of physical illness, undergoing surgery, hospitalization.
- iii. Parental separation by divorce or death.
- iv. Breaking of relationship.
- v. Living in a new locality, migration to a new state or country.
- vi. Accident / Developing disability.
- vii. Physical / Sexual abuse.
- viii. Separation / Death of a pet animal.
- ix. Transfer / demotion / promotion / change of a job.
- x. Public insults, losing status and popularity.

Prevalence

Adjustment disorder is very common. Prevalence of adjustment disorder in general public is 1-2%. Depending upon the population studied, prevalence of adjustment disorder varies. Studies done on clinical population report a wide range of prevalence of adjustment disorder from 15-95%.

Adjustment disorder affects both genders equally. It can occur at any age. People are particularly vulnerable during normal transitional periods such as children, adolescence, mid-life and late life.

Pregnancy and puerperium are vulnerable periods in every woman's life. 4-8% have diagnosis of adjustment disorder during this period.

Adjustment disorder have been reported frequently in individuals

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with variety of medical disorders like vitiligo, psoriasis, cancer, diabetes, mellitus, heart attack, stroke, fractures, terminal illness etc.

Aetiology:

Adjustment disorders are reaction to stress but there is no way to predict the individuals who are likely to get an adjustment disorder, given the same stressor. Patients with adjustment disorder have increased vulnerability to stress. The vulnerability depends upon patient's life values, adaption level, personality, past stress experiences and coping skills. Diminished psychological defences and inability to cope with stressors on a cognitive level may lead to suicidal behaviour in patients with adjustment disorder. They may also develop conversion or dissociative disorder or somatoform disorder.

Stress, frequently described as 'black Plague' or 'the modern epidemic' has become an important feature and major problem of everyday life, threatening individual, organization and social health. Hans Selye, who is often referred to as 'father of stress research' has defined stress as the 'non-specific response of the body to any demand' the general Adaption Syndrome (GAS).

Lazarus (1966) postulated that an individual's perception of stress was significantly more important than the event per se in determining the impact of the stressor. Stressor also varies in duration, intensity and effect. Impact of stress of an individual is modified by a number of intrinsic factors (e.g. genetic vulnerability, premorbid personality) and extrinsic factors (e. g environment and social support). Currently there is no evidence available to suggest a specific biological factor that causes the adjustment disorders. We know that stress leads to various physical and mental illness as it is also been proved beyond doubt that stress leads to poor outcome of any physical illness and mental illness.

Clinical Features

The adjustment disorders in the ICD-10 have been placed in a cluster of stress related disorders. As per the diagnostic criteria.

- The onset of symptoms must occur within 1 month of exposure to

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an identifiable psychosocial stressor, not an unusual or catastrophic type.

- The individual manifests symptoms or behavior disturbances, which should not meet the criteria for any other unusual mental disorder.

People with adjustment disorders may have wide variety of symptoms. How those symptoms cluster depend on the particular subtype of adjustment disorder and on the individual's personality and psychological defences. Adjustment disorders have been classified depending upon the type of presentation.

There are 7 subtypes of adjustment disorders that are based on the type of the major symptoms experienced. The following are the most common symptoms of each of the subtype of adjustment disorder. However, each person may experience symptoms differently. Symptoms normally include some (but not all) of the following

1. Brief depressive reaction is a transient mild depressive state of duration not exceeding 1 month. Lack of interest in usual activities, withdrawal, inhibition including loss of appetite or interest in sex, hopelessness, sadness, crying, feeling of loss, suicidal ideas/attempt, guilt and self-doubt not severe enough to warrant diagnosis of psychiatric disease like depression, GAD (General Anxiety disorder)
2. Prolonged depressive reaction is a mild depressive state occurring in response to a prolonged exposure to a stressful situation but of duration not exceeding 2 years.
3. Mixed anxiety and depressive reaction is characterized by anxiety symptoms like breathing fast, numbness, heart pounding, excitement, fear, trembling, nausea, being easily startled by loud noises or sudden movements, worrying, feeling unreal, being isolated or detached from other people, problem with thinking, concentration or remembering things, preoccupation with the stressor, sleep problems including difficulty in getting sleep, waking in the middle of the night, dreams or nightmares. Both anxiety and depressive symptoms are prominent, but at levels no

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greater than those specified for mixed anxiety and depressive disorder or other mixed anxiety disorders.

4. With predominant disturbance of other emotions: The symptoms are usually several types of emotions such as anxiety, depression, worrying, tensions, loss of feelings, irritability and anger. This category should also be used for reactions in children in whom regressive behavior such as bedwetting or thumb sucking, clinging to mother, baby speech may be present.
5. With predominant disturbance of conduct: The disturbance is one involving conduct, an adolescent grief reaction resulting in aggression, irritability, dissocial behavior like violation of the rights of others or violation of normal societal behaviours and rules (truancy, destruction of property, reckless driving, fighting, lying, stealing etc.).
6. With mixed disturbances of emotions and conduct: Combinations of symptoms from all of the above subtypes are present (depressed mood, anxiety and conduct)
7. Other specific predominant symptoms: Like unexplained physical symptoms such as tense muscles, trembling or shaking, diarrhea, stomachaches, constipation, nausea, headaches, sweating, tiredness, remaining unresponsiveness/unconscious etc.

Diagnostic Guidelines

Diagnosis depends on a careful evaluation of the relationship between

- Form, content and severity of symptoms.
- Previous history and personality.
- Stressful event, situation or life crisis. The presence of this third factor should be clearly established and there should be strong, though perhaps presumptive evidence that the disorder would not have arisen without it. It is important to note that adjustment disorder in children includes grief reaction or hospitalization.

Grief and Bereavement

Loss is a universal experience. During life everybody has to cope with a series of losses, which may range in intensity from the minor loss of pet to the major loss of a spouse or child or parent or sibling.

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Bereavement is loss of loved person through death. Grief stands for the feelings and associated behaviour (e.g. crying) precipitated by this death. Mourning indicates the social expression of grief, including funerals, visitations and rituals.

Stages of normal grief

1. A first phase of shock, disbelief, numbness and denial followed by searching behaviour lasting for days or weeks
2. A second phase of acute anguish characterized by intense somatic distress, preoccupation with the deceased, anger, restlessness, bargaining, feeling of sadness, guilt and impairment in functioning, lasting for weeks.
3. A third phase of restitution and reorganization (acceptance) lasting for a few months.

Normal grief usually follows the above phases with possibility of some variation. It is important to identify abnormal grief, as if undetected, it could lead to various problems like non – acceptance of the death of the individual, avoidance of the mention of the deceased, avoidance of the funeral and other associated rituals, holding on to the belonging of the dead, preoccupation with thoughts of the deceased, a strong and continued feeling of the dead person's presence, illusions or hallucinations of the deceased for a long time.

Abnormal grief can be grossly classified into the following

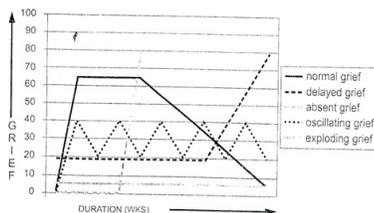
Delayed Grief

Absent Grief

Oscillating Grief

Exploding Grief

Graph depicting patterns of normal and abnormal grief



Management of Grief

In general, rituals associated with death serves the purpose of mourning. These rituals offer an opportunity for catharsis and reliving, which help the bereaved in getting over the loss. The judicious use of drug does not hinder grieving but helps in overcoming the abnormal/excessive emotions during abnormal grief. The drugs should be used cautiously depending upon the type of presentation.

The essence of treatment is however psychological intervention in the form of grief therapy. This essentially involve getting the individual talk about the deceased, recollecting the experiences receding and succeeding the death, ventilating his/her feelings both right and wrong towards the dead person and finally letting go of the deceased. During the sessions, the therapist plays a supportive role and helps in rationalizing the patients feeling towards the dead one. It would help to bear in mind that during the process of grief therapy, the depressive symptoms of the patients may escalate or worsen for a brief period indicating that the person is grieving. It is at this stage that the patient requires the support of the therapist most. Hence therapist should take care not to abort or digress from the therapy. Time limited, short-term group therapy is one of the successful approaches in complicated grief.

Course and prognosis

Adjustment disorder occurs in response to an identifiable stressor. The person's response to the stressor is either very strong and causes a great deal of distress (feeling suicidal after losing a limb in an accident) or results in impairment in functioning in either the persons occupational/education, social or interpersonal life. (i.e. missing work for a week after breaking up with a boy/girlfriend). Still others may not experience behavioural disturbances but will begin to suffer from physical illness. If someone is already suffering from a medical illness, that condition may worsen during the time of the adjustment disorder. Most people recover completely from adjustment disorders. People with no history prior psychiatric symptoms, who have stable environments and strong social support are likely to display no further psychological

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symptoms in the future. People with progressive or cyclic disorders (such as multiple sclerosis) may experience adjustment disorder with each exacerbation period.

Generally, it is reported a 76% recovery rate within a year which is maintained even after 10 years follow up. Adjustment disorder should be predicted as having relatively good outcome and most patients should be well at the follow up.

Management

The primary goal of the treatment is to relieve symptoms and assist with achieving a level of adaptation that is comparable to the affected person's level of functioning before the stressful event.

Pharmacotherapy

Most stress reactions will resolve without the use of medication. Doctor's empathetic reassurances are as effective as benzodiazepines, however if severe anxiety symptoms occur, consider using anxiolytic drugs for up to 10 days. If the patient has severe insomnia, use hypnotic drugs upto 10 days. Physicians should be especially careful of over prescribing possibly addicting medication for anxiety. Doses should be as low as possible.

Short acting benzodiazepines like Lorazepam in the doses of 1-4 mg/day can be prescribed. Long acting doses like Diazepam, Nitrazepam, Chlordiazepoxide have to be used with caution

Bupirone, acts as an anxiolytic without any side effects or addictive property like other sedatives. The usual adult dosage is 10 – 15 mg/day in three divided doses. Patients may benefit from dosage titration up to 30 – 60 mg/day. While medications have very limited value in the treatment of adjustment disorders, medication may be considered on a short-term basis if a specific symptom is severe and known to be responsive to medication.

Strong suicidal ideas or attempts

Suicidal ideas or attempts are one of the common presentations in adjustment disorder. It is a psychiatric emergency, calling for immediate psychiatric referral.

Psychosocial Intervention

Individual Psychotherapy / Counselling

Psychotherapy (counselling) is the treatment of choice for adjustment disorders, since the symptoms are understandable reaction to a specific stress. **Adjustment disorder responds better to psychotherapy than medication.** The type of therapy depends on the health professional, but it is usually short-term treatment that focuses on resolving the immediate problem.

Therapy should occur within a supportive, non-judgmental environment that encourages the client's growth through exploration of new behaviours and ideas. This therapy often takes the form of solution-focused therapy, to help the individual deal more effectively with the specific life problem. Often the therapist acts as a partner in therapy, helping and guiding the client towards finding these new coping mechanisms or finding a better understanding of issues and problems.

Adjustment disorder is a short-term difficulty that rarely goes beyond 6 months. Lingering feeling may occur beyond that time, those are natural, not likely to be severe enough to require additional attention or treatment. It often helps treatment progress (and is required in many agencies) to put together firm but realistic treatment plan, so that the patient can also see the short-term nature of the therapy. Clinicians should be careful not to lapse as an advice-giver to individuals who suffer from and adjustment disorder.

The exact content and type of therapy used will vary widely. Treatment will often emphasize the importance of social support within the client's life. Alternative activities to explore or to find meaning in, increasing a person's range and effectiveness of coping skill, learning better ways of dealing with stress etc.

Group Psychotherapy

Group psychotherapy is useful if similar group of patients are involved in the therapy. For example, group therapy done once in a month in patients undergoing treatment for early stages breast cancer was proved to be effective. Before approaching the concrete work of

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planning and organizing a psychotherapy group, the goals of the group must be clearly understood and developed by the leader. These in turn, depends on the setting, the population, the time available for treatment and the training and capacity of the leader to leader. Therapy groups can be organized with a variety of goals in mind like character change, supporting homogeneous patient populations, targeting certain symptoms, re-establishing premorbid levels of functioning etc.

A major advantage in group psychotherapy is that patients feel a sense of belonging. Most people enter group therapy feeling that their problems are uniquely shameful and that their pathology sets them apart from competent human beings. Group members come to recognize that their problems are more similar than different from those of others in the group, as they increasingly feel accepted and cared for.

Working with the family of the patient

Give essential information to the patient and family, regarding illness. Identify relatives, friends, community resources, who are able to offer support. Encourage the patient to acknowledge the personal significance of the stressful event. Short term rest and relief from stress may help the patient. Consider short-term sickness certification. Encourage return to usual activities within a few days to weeks.

Family therapy is often focused on making needed changes within the family system such as improving communication skills and family interactions as well as increasing family support among the family members. Family therapy may be appropriate for certain individuals, especially if the person presenting with the disorder is an adolescent. This type of therapy is also appropriate when the family is 'scapegoating' a particular family member, or there is a clear 'identified patient' when the actual problem is family-system related. Education related to the disorder is sometimes needed and the family can be reassured as to the nature and seriousness of the disorder, as well as its prognosis. Couple therapy is appropriate when the disorder is additionally negatively affecting the marital relationship.

Self-Help Groups

Self-help method for the treatment of this disorder are often overlooked by the medical profession because very few professionals are involved in them, often people with this disorder will get help from attending a group related to their specific problem. This could be anything ranging from someone who just divorced someone who was just diagnosed with cancer, to dealing with job loss etc. Many such support groups exist in communities across the nation. Therefore, finding an appropriate one may not be difficult. This allows for sharing of information and experiences, which can be vital in the road to recovery. Social support is also vital component of a self-help group and increased social support usually leads to better and quicker recovery.

As an adjunct to regular psychotherapy, people can also be encouraged to use a support group to try out new coping skills and express their feelings to others who have gone through similar experiences. This is usually very rewarding and helpful

Post-Traumatic Stress Disorder

An intense, prolonged, sometimes delayed reaction to an intensely stressful event.

The principal symptoms are:

- Hyper Arousal: Persistent anxiety, irritability, insomnia, poor concentration.
- Re-experiencing: Intrusive imaging, headaches and reoccurring distressing dreams.
- Avoidance: Difficulty in recalling stressful events at will, avoidance of reminders of the event, detachment, inability to feel the emotion (numbness), diminished interest in activities including self-care.

Treatment

Trauma focused cognitive behaviour therapy,
Reprocessing,
Emotional Support, Sadness/Anger management

MANAGEMENT OF ADJUSTMENT DISORDERS IN CLINICAL PRACTICE

Exposure to imagination and then VIVO to situations that are being avoided

Recall images of the events.

Medications

Anti-depressant drugs: SSRI, SNRI

(Escitalopram, Venlafaxine etc)

Benzodiazepines better avoided because of dependence on such tablets.

Conclusion

Since incorrect diagnosis may result in inadequate treatment, inappropriately conceptualizing a patient's problem as constituting an adjustment disorder may result in delays or inaccuracies in treatment planning. Misdiagnosis of other, more specific disorders when an adjustment disorder should appropriately diagnose is also a problem. When treating a patient, diagnosed to be suffering from adjustment disorders, one need to be aware that pharmacological interventions in this population should be used to augment psychological strategies rather than serving as the primary modality.

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FAMILY MEDICINE AND GENERAL PRACTICE: A GOOD CAREER TO REACH THE COMMUNITY

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FAMILY MEDICINE AND GENERAL PRACTICE: A GOOD CAREER TO REACH THE COMMUNITY

Medical profession is a respectable, stable and evergreen profession in India. Pursuing MBBS is just a 1st step in a successful medical career; there are numerous job opportunities available after that, and many wish to pursue specialization.

- In India, with 539 medical colleges is producing 70,000 fresh medical graduates every year, the scope for post-graduation is only for 32,753.
- In Karnataka; with 59 medical colleges producing about 7,000 medical graduates every year, only about 3,000 post-graduation seats are available for the medical graduates.

In the field of post-graduation also, that is as diverse as medicine and offers various opportunities and choices, there can be a sense of uncertainty regarding the post-graduation (PG)/ area of specialization and their future. Many, who actually get success at PG entrance test, only realize a few years later that they are in no better condition.

- Many PG qualifications only serve the purpose of ornamental title; adding little to clinical skills or employability, which renders them further vulnerable as non-practicing doctors.
- Even those with highly focused clinical skills; find themselves dependent on tertiary care hospitals for their practice.
- Many specialists realize later that, there are few available patients who would require or could afford their services.
- Also, there is paradoxical oversupply of specialists in the urban area leading to low demand and lower income.

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Therefore, family medicine and general practice is becoming popular among MBBS graduates; who don't want to pursue higher studies/ uncertain regarding the specialty and their future and want to set up their clinics; which not only promises financial freedom but also provides the space to work at their own place, pace and time.

I. Important aspects of general practice/ family medicine:

- General practice (GP)/ family medicine (FM) focuses on managing common illnesses in all age groups, focusing on their overall health and well-being; and be able to provide comprehensive health care in community setting.
- It is patient centred, evidence based, family focused and problem oriented, which requires refined abilities to observe, communicate, understand and manage.
- The physical, emotional, social, spiritual, cultural and economic aspects through patient-centred with their family approach are vital in any general practice/ family medicine.
- GPs/ FPs acquire and maintain a broad array of competencies that depend on the needs of the patients and communities they serve.
- GPs/ FPs possess unique attitudes, skills, and knowledge which qualifies them to provide continuing and comprehensive medical care and preventive services to each member of the family regardless of sex, age, or type of problem, be it biological, behavioural or social.

The scope of practice is not defined by diagnoses or procedures but by human needs and they do not treat diseases; they take care of people.

General practitioners/ Family physicians have an important role of promoting, preventing and treatment; as they are often the first point of contact for anyone with a health problem. Therefore, GP/ FM is the need of community and population; owing to recent developments in both public and private health sector.

National Health Mission (NHM) is emerging and private sector is also venturing into primary and community-based health care facilities with high-quality, affordable health care; which is increasingly a difficult

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challenge; due to complexities of health care services, investigations costs, quality, accessibility, delivery and organization of these services to reach the entire population across the country under Universal health Coverage.

The National Sample Survey (NSS) 2014, estimated that >70% (72% in rural and 79% in urban) spells of ailment were treated in the private sector. This inclination toward availing services from private sector is also corroborated from NFHS-4 report, which states that 56.1% and 49.1% of members of surveyed urban and rural households, respectively, sought private health care in times of sickness, while for public sector; it was only 42% and 46.4%, respectively.

Therefore, it showed that, the private sector has a significant potential for providing both preventive and curative public health services in fulfilling universal health coverage as:

- GPs/ FPs can provide health care services which are personalized for each patient, coordinated with family and friends on whom the patient relies should be involved, and care should provide physical comfort and emotional support.
- General practice has a distinct clinical approach that requires special skills to identify concerns, focus issues, negotiate plans and help solve problems. The recognition, integration and prioritization of multiple concerns and the synthesis of solutions are critical clinical competencies.

In this regard the National Board of Examinations (NBE), New Delhi, conducts family medicine residency programmes at various hospitals in India that it accredits and awards to the successful candidates, the post – graduate degree DNB (Family Medicine).

II. DNB - Family Medicine

Family medicine is an independent academic discipline and specialty that prepares medical graduate to be able to provide comprehensive health care in community setting. A family medicine-trained physician is perhaps the best person to start a clinic and work in community hospitals and health care facilities. Family physicians learn

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and demonstrate skills across a spectrum of clinical domains in order to provide initial, continuing, comprehensive and coordinated medical care for all individuals, families and communities and which integrates current biomedical, psychological and social understandings of health.

Specific Learning Objectives:

At the end of course, the physician should be able to acquire following competencies:

1. Effective management of common diseases within the limited resources and in particular socio-cultural setting, harnessing available community services.
2. Identification of complex health problems and their appropriate referral.
3. Promotion of health & prevention of diseases; support to the National Health Programmes.
4. Taking care for disadvantaged groups viz., Elderly, handicapped and others.
5. Use of behavioural sciences related to family practice.
6. Effective communication with patients, family, colleagues and others in the community.
7. Domiciliary care and palliative care.
8. Conducting research and writing the report.
9. Management of common medical emergencies with evidence-based medicine.
10. Cost effective use of investigations and ability to interpret the results of investigations.

Duration of Course

- For post MBBS candidates: **3 years**
- For post MBBS + PGDMCH/PGDGM (IGNOU) candidates: **2 years**

Course Details:

- **27 months of hospital-based postings**, in various departments as follows:

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Paediatrics (6 months), OBG (6 months), Internal Medicine including mental health (6 months), Emergency Services including ICU (3 months), General Surgery (3 months), Others (Orthopaedics, Ophthalmology, ENT, Dermatology, Psychiatry, etc) (3 months).

- **9 months of Field based mandatory rotational postings.**

Family Practice Centre (or a primary health centre), satellite clinics as served through outreach camps, Mass screenings, OPD's, Follow up OPD's, epidemiological surveys, immunization camps, Preventive & Promotional health camps, Disease Surveillance, etc.

They should possess the management, team work, leadership qualities and the ability to organize and actively engage in community care programmes, focusing on promoting and maintaining health of the community.

- **Availability of the course:**

DNB (Family Medicine) residency programs are presently ongoing at many of the corporate and other teaching hospitals; with most of them having 2 seats. The course is recognized by Medical Council of India. For more details, one may visit the website of NBE- <https://natboard.edu.in/>

III. Scope of Family Medicine:

1. Establish a good GP/ FP, as they would have obtained more skills for providing both preventive and curative public health services.
2. Manage any of the multi-speciality clinics/ Nursing home/ Hospital, as they acquire better leadership qualities and team work.
3. Work as a consultant in Preventive Medicine Clinics of corporate hospitals, as there is a trend of establishing these clinics in every corporate hospital.
4. Govern the MCH clinics, Well women clinics, well baby clinics, Immunisation clinics, etc in any of the hospitals.

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5. Handle the general OPDs in any of the polyclinics/ corporate/ general hospital.

IV. Need for general practice/family medicine:

The epidemiologic and demographic transition, as well as the consequences of globalization, urbanization and climate change, requires an effective health system based on primary care. This system should focus more on health promotion, disease prevention and continuity of care, to which family physicians/ general practitioners can significantly contribute.

Likewise, during past few decades, health care landscape has rapidly transformed and so have the Indian economy and the society. Health care has also become more technology centric, expensive and urban focused and privatized.

- Most metropolitan cities and tier 1 and 2 cities are flustered with corporate-owned tertiary care hospitals. However, rural population is largely uncovered from this boom and people have to travel long distances to get proper medical treatment.
- Even the urban communities are devoid of quality community-based health facilities and population is dependent on tertiary care hospitals for minor illnesses and primary health care needs; as an outcome, public sector hospitals are overburdened with patient load and are always short of resources.
- Although a section of society is able to afford treatment and medical care from flourishing private sector hospitals, a large chunk of urban population cannot afford their cost and these are the people in need of qualified general practitioners/ family practitioners.
- Most medical graduates are not aware that GPs/ FPs are capable of taking care of 90% of the clinical conditions in a given community.
- The decision to start their own medical practice and embrace the entrepreneurial path of being self-employed is a daunting exercise and a decision requiring careful planning and a

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considerable investment of time and money.

- For most, the decision to start their own practice is well and truly the biggest decision they will make in their career as a medical professional; especially considering that as a practice principle; they are not just responsible for themselves but also for the community they serve. The following are the important aspects of family medicine/ general practice:

V. 5 Keys to a successful medical practice start-up:

Starting up a medical practice is like building a new home; In order to build a solid foundation, it requires good planning and the right set of tools. viz.,

- Select a good place, accessible to all sections of people.
- Start in a simple way and build up your reputation.
- Be punctual and sincere to the practice.
- Respect the individuals and give time to listen to them.
- Be humble and respond to their queries.

VI. Fundamentals of building reputation as a General Practitioner/ family physician:

- **3 A's: Affability, Availability and Ability**

Affability is the quality of being easy to talk to, friendly and good-natured. As a service industry, with quality performance measures, affability is even more important as word of mouth still drives the referrals, so GPs/ FPs have to present accordingly.

In order to improve economic benefits, regular availability of the GP is another important issue; as people do not like to wait for a long time and they might as well see someone else. The only way to capture reimbursement revenue is to see the patient at the earliest & treat them well.

Lastly, the ability of the GP/ FP, since the present generation patients are techno-savvy and are capable of discovering the newest things in the field, whether or not they are based on science. Therefore, a GP/ FP should know the latest changes and innovations in the field and treat well.

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VII. Essential qualities for a General Practitioner (GP)/ Family Physician (FP)

- 1. Compassion:** Patients respond better to a physician, who is empathetic to their needs, so focus should be on exercising courtesy and compassion.
- 2. Ethics:** Having a strong work ethic means, dedicating 100% work every day. While this quality will help succeed in any field, it is especially essential to the practice of medicine, since every day brings a new challenge and should be readily faced and resolved at that point.
- 3. Professionalism:** Simply wearing a white coat and a stethoscope won't command respect from patients; it must be earned. As with all encounters, first impressions are of paramount importance and the patients will usually stick on, as long as they are treated well with respect. If the practitioner is inattentive, impatient or unkempt, the patient will feel unsatisfied and neglected and will most likely seek the care of another physician.
- 4. Knowledge:** Practicing physicians need to have medical knowledge that can be recalled at a moment's notice. They also have to stay on top of the latest medical news and trends, which could contradict something that was learned way back in medical school. In other words, as advancements are made in the field, new information that enhances or counters what was already committed to memory has to be learnt.
- 5. Confidence:** A successful physician with good knowledge must reinforce that with confidence. Patients want to trust their physicians as caregivers, but the lack of self-assurance communicates uncertainty. A physician with strong, healthy confidence will be listened to and respected by patients and colleagues alike.
- 6. Humility:** Humility and confidence work as a complementary pair. With patients and colleagues, you must be approachable and

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available. This means that despite time limitations and over-scheduling, the patient should never feel rushed; You must also be willing to admit when you're unsure about something and especially willing to ask questions. A physician is a lifelong learner and these situations should strengthen to resolve the unknown issues.

7. Passion: GPs/ FPs should take the profession with a passion for the study and practice of medicine. Their passion makes them disciplined and willing to sacrifice other opportunities to better their career. If you are dedicated to improving the lives of others and can spend long nights hovering over patient charts, then you've applied to the right profession.

Patient-centered care recognizes that listening to the patient's needs, values and preferences is essential to providing high-quality care.

General Practice/ Family Practice are also lucrative and good revenue generating and requires careful planning and a considerable investment of time and money.

VIII. Important Ways to boost medical practice revenue

For a successful medical professional, there are two important general financial tips:

Tip 1: Possessing adequate savings for the future: Any practitioner should chalk out a plan to save for the future while still earning. Make sure to save at least 50 - 60% of your income.

Tip 2: Make essential investments for business expansion: A clinic's expansion depends on a lot of factors. Installation of the latest technology, introducing new tools and equipment, hiring more skilled staff, opening a new branch, launching a website, initiating a digital marketing campaign, etc. are some of the significant investments GPs/ FPs can make. However, it has to be made sure to evaluate the requirements and present business condition to decide on the appropriate investment areas.

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IX. Important pillars for expanding General/ Private/ Family practice:

- 1. Finance:** There are many banks and finance companies ready to provide money to doctors. However, checking the terms and small print carefully is important and carefully to seek clarifications on any hidden information. If leasing for IT, medical supplies or furniture, make sure that your lease payments have no more than a 3 year term.
 - If the bank or finance company is willing to manage the escrow for start up invoices, make sure the costs are included in their fees.
 - When ready to drawdown the loan, make sure you take time to get the best possible deal.
 - As well as covering the setup costs make sure to borrow enough funds from the bank to cover operational costs for the first year.
- 2. Staff:** Staff can make or break your practice. Good staff embodies following characteristics:
 - Experienced, but no bad habits
 - Bubbly, but professional
 - Efficient, but not assertive
 - Great customer service skills, but not overly friendly
 - Excellent business skills, but not too expensive

Whilst the above criteria are good to know, the reality is that no matter what a person's resume and references look like, hiring can be hit and miss. To reduce the chances of hiring the wrong person; try best to hire people with the same philosophy. This means doing best to get to know people in an interview by letting them talk as much as possible about not just the role but their ambitions and values.

Keep in mind that hiring an experienced person is not always the answer; what is often a better indicator of success is hiring someone who is willing to work to the vision. Also, make sure you pay your staff

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appropriately. If you pay them too little, as soon as another job becomes available, they will leave you and you'll be forced to go back to recruiting, which will only cost you more time and money hiring and training.

- 3. Systems:** Systems take time to develop, but it is still a good idea to have a plan in place from day one to ensure professionalism and protect yourself and your staff from litigation.
 - Keep the practice registered under KMC and accreditation from day one.
 - Becoming member of the professional association such as IMA.
 - Professional indemnity insurance: Ask them about what systems you need to in place so they can protect you.
- 4. Service:** The fourth pillar to a well-established general practice is service. The service you provide to your patients is the most pivotal aspect of an operational practice. Quality of care is the name of the game. All these qualities can be accomplished gradually during the practice and should strive to improve throughout the career.

X. 10 secrets of successful General Practice; Try them yourself, and see how they work.

1. **Smile:** Everybody is attracted to happy, positive people. Many doctors walk around with a frown and are always irritable; no one wants to be around someone who is in a bad mood.
2. **Respect:** Every individual have their own respect, give respect to the individual as well as their culture and practices.
3. **Listen to their problems:** People have enough of their problems and they come to you for solving all their problems; try to listen completely and then give treatment/ advice.
4. **Consistent:** Try to go for practice at almost the same time each day; people will be waiting for your advice/ treatment and time is precious for all.
5. **View everyone as a potential patient:** Do not say anything about anybody, that isn't true or you wouldn't say to their face; since, you never know whom you'll have as a patient someday.

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Remember, no matter where you live; when you're in public, you represent yourself and your profession.

6. Do not criticize/ abuse other physicians: It is bad to always criticize/ abuse others, since you should know that, they may also do the same to you.
7. Stop needing to be right: Sometimes, it's best to let others be right, even though you could correct them. Nobody likes a know-it-all. If a family is convinced that it was the extra vitamins they brought cured their mother's pneumonia (while you had her on antibiotics), let it go. Be sure to ask which vitamins they used, so you can order that brand for your next pneumonia patient!
8. Give credit where it is due: Look for opportunities to give sincere compliments. Show appreciation; when they do well and you'll be appreciated in turn, many times over.
9. Patient-Centred: Patient-centred care recognizes that listening to the patient's needs, values, and preferences is essential to providing high-quality care. Health care services should be personalized for each patient, care should be coordinated, family and friends on whom the patient relies should be involved, and care should provide physical comfort and emotional support.
10. Don't try to impress: People expect physicians to be confident, decisive, and intelligent, but they especially appreciate the doctor who's down-to-earth and humble. You have nothing to prove, so relax a bit; maybe even dress down a tad. Don't wear suits and Rolex watches; many people resent that type of pretentious display.

XI. Remember-

- You have a lot to offer your own community. Start giving back to them and you'll find it's a great way to build up a reputation for your private family practice.
- General practice/ family medicine/ community based skilled medical practitioners, are capable of taking care of 90% of the clinical conditions in a given community.

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- General practice not only promises financial freedom, but also provides the space to work at your own pace and time.
- Medical practitioners who just have an air of positivity; convey a sense of "charisma" and are generally happy and engaged; which in turn is profitable to them.
- The more people locally who know and trust you, the more likely it is that they'll recommend you to their friends and family, because there's already a level of trust built-in to the relationship.. Referrals are always the best way to receive new business.
- Take a look at your practice and notice how people are responding to you, your employees, and the environment. If you see happy, relaxed people, you're doing something right. If you see chaos and frustration, changes need to be made quickly.
- Never assume your education in running a successful private medical practice is over. Keep learning, find sources you trust and like; follow their advice.

**RIGHT MEDICAL CAREER AND PRACTICE
MAKES ALL THE DIFFERENCE IN YOUR LIFE**

ZIKA VIRUS INFECTION

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ZIKA VIRUS INFECTION

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Introduction

Zika virus (ZIKV) belongs to the flaviviridae family has derived its name from the Zika (means 'overgrown' in Luganda language) forest near lake Victoria, Uganda where it was first identified in 1947 in rhesus monkey through a monitoring network of sylvatic yellow fever (1). Subsequent studies showed the presence of neutralizing antibodies against the virus in the human serum samples implying that the virus can infect humans in 1952 in Uganda, and Nigeria (2).

Countries with cases of Zika virus in the Americas



Source: WHO 17-23 Jan 2016

BBC

Fig.1. Countries with Zika virus infection in Americas

ZIKA VIRUS INFECTION

Epidemiology

The infection is known as Zika fever. It may remain asymptomatic or may cause only mild symptoms. It was known to be restricted to a narrow equatorial belt from Africa to Asia since 1950s. The first recorded outbreak of Zika virus disease was reported from the island of Yap (Federated States of Micronesia) in 2007. It was followed by a large outbreak of Zika virus infection in French Polynesia in 2013, and then to Easter island across Pacificocean in 1914 and in 2015 to Mexico, central America, Caribbean islands and South America with an epicenter in Brazil where the Zika outbreak assumed a pandemic proportion. World Health Organization has declared Zika virus disease to be a Public Health Emergency of International Concern (PHEIC) on 1st February, 2016.

Indian scenario

Since India provides fertile climate for the *Aedes aegypti* mosquito to grow and multiply, there is the potential of an outbreak situation in the country. 3 laboratory-confirmed cases of Zika in January 2017 from Bapunagar, Ahmedabad, Gujarat were reported in May 2017. Later in the same year in July, there were reports of Zika infection from Krishnagiri, Tamil Nadu and one man tested positive for the virus. An elderly women was diagnosed with Zika infection in September 2018 at Jaipur, Rajasthan. Since then 152 more individuals including 22 pregnant women have tested positive for the infection around Shastinagar area and Sindhi camp area... More than 100 persons have been tested positive for the Zika virus in seven districts of Madhya Pradesh. This includes 44 cases reported from Bhopal, 20 from Sehore, 29 from Vidisha, two each from Sagar and Hoshangabad, and one each from Narsinghpur and Raisen. With the presence of these confirmed cases, India has been included in WHO category 2. The spread appears to be due to local transmission and none of the patients were associated with travel history. It suggests that ZIKV might be present in India since long time (3). (which cause Dengue, Japanese encephalitis, tick-borne encephalitis, yellow fever and West Nile fever),

Zika virus

Zika virus is related to Dengue, Yellow fever, Japanese encephalitis (JE),

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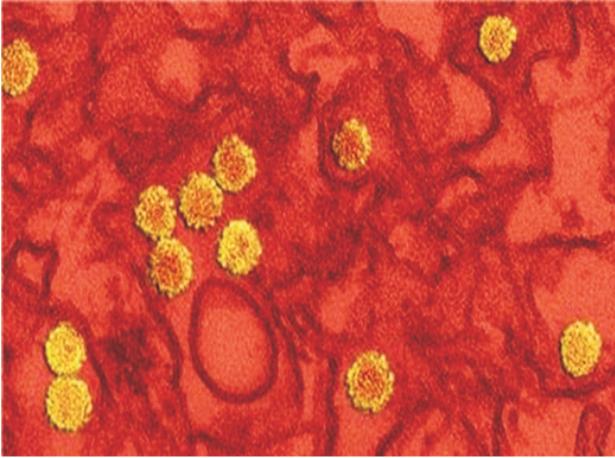


Fig. 2 Zika virus

tick[borne encephalitis, and West Nile fever (WNF). It is a non-segmented, single stranded RNA virus. The viral particles are 40 nm in diameter with an outer envelope and a dense inner core. It is an icosahedral virus of 18-45 nm in diameter. .Zika virus causes a zoonosis of the monkeys. Mosquitoes transmit the disease to humans. It is transmitted by day-time active *Aedes* mosquitoes (*A. aegypti*, *A. albopictus*) (4).

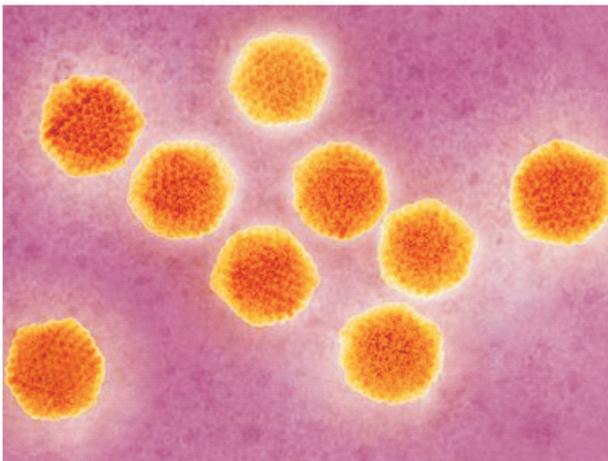


Fig. 3 Zika virus

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Transmission

Aedes aegypti forms the principal vector supported by secondary vector *Ae albopictus*. *Ae aegypti* is a native of Egypt, commonly known as yellow-fever mosquito. *Ae albopictus* is identified by its peculiar white-spotted body and legs, and it has been given the name, tiger mosquito. The mosquito is found in urban surroundings in domestic and peri-domestic areas.

The flight of mosquito is short. It is highly domestic and breeds near human habitat in standing water collected in containers such as old discarded tyres, cans, water storage jars, mud pots, plastic containers, abandoned shoes, coconut shells, uncovered overhead tanks, oil drums, drip-pans below refrigerators, air conditioners, empty tins, plastic containers, plastic trays under potted plants, water coolers, pots, latex collecting cup, and buckets (man-made habitats).. It has a flight range of only 100-200 m. It mostly rests indoors, though it could be in any cool shaded places inside or outside the house.

The female mosquito gets infected by Zika virus while feeding human blood having Zika infection. Peculiarly the mosquito is a daytime



Fig. 4 *Aedes aegypti*

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feeder and it bites many people to get its blood meal. It has a diurnal feeding pattern usually peaking mid-morning and late afternoon. Peculiarly its bite is imperceptible. It is capable of biting many people in a short period of time for one blood meal. Persons who stay indoors during the daytime are vulnerable to mosquito bites. Overcrowding, poor living conditions and lack of vector control facilitate the spread of infection. Epidemics are explosive.

There is a possibility of virus being transmitted sexually (3). Zika virus RNA has been detected in amniotic fluid and virus crosses the placenta and infect foetus. It can be transmitted through blood transfusion, organ transplantation and laboratory exposure. There is a possible link between Zika and microcephaly in new born babies by mother-to-child transmission (4, 5). There is likelihood of occurrence of miscarriages. The infected adults may present with neurological condition like Guillain-Barre syndrome (GBS) (6). The Governments of Columbia, Dominican Republic, Equator, El Salvador, Jamaica, and Center for Disease Control and Prevention (CDC), US have issued guidelines about precautions for women to postpone travel and even to postpone getting pregnant (7).

Pathogenesis

On entry the virus induces strong interferon responses in infected cells. Viremia is responsible for the non-specific symptoms initially. In pregnant woman, maternal viremia may cause foetal viremia. While in circulation, zika virus can infect foetal monocytes, which in turn can carry the infection to the developing nervous system, where the viral particles can proliferate inside the neural cells and cause neurovirulence. There is microglial activation and macrophage infiltration (8),

Clinical features

The incubation period of Zika virus disease appears to be 3-14 days. Many infected persons remain asymptomatic. About 1 in 5 people infected with Zika become ill.

The illness is usually mild with symptoms lasting for several days to a week. The most common symptoms are fever, rash, joint pain, malaise,

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and conjunctivitis. Other common symptoms include muscle ache and head ache. Thus the clinical features are non-specific. It should be noted that occurrence of rash, and conjunctival hyperaemia are more common with Zika compared to other viral illnesses. Zika virus usually remains in the blood of an infected person for about a week. The symptoms are similar to Dengue and Chikungunya which spread through the same mosquitoes that transmit Zika.

The symptoms are usually self-limiting and usually last for 2-7 days, . However the potential teratogenic and neurological complications are causing great concern. Teratogenic neurodevelopmental abnormalities may occur during the first two trimesters. The incidence of microcephaly may be as high as 1 per cent of pregnancies. There can be other congenital abnormalities in the developing foetus and newborn. Zika infection in pregnancy may result in pregnancy complications such as foetal loss, stillbirth and preterm birth. In addition, there may be occurrence of limb weakness, hearing deficits, ocular and skeletal abnormalities, cessation of development and



Fig. 5 Microcephaly

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cognitive and learning defects (9). In infected adults and older children, there is likelihood of development of Guillain-Barre syndrome and acute demyelinating encephalomyelitis.

Diagnosis

The infection with Zika virus may be suspected based on symptoms with residence or visit to an area which is known to be endemic. The manifestations of Zika infections simulated those of Dengue and Chikungunya infection. Fever and arthralgia are common in Chikungunya and Zika infections. Myalgia is noted in Dengue, Chikungunya and Zika infections. Conjunctivitis is noted in Zika infection. Occurrence of low platelet count is noted in Dengue.

Reverse transcriptase PCR is highly sensitive and specific for the diagnosis of Zika virus infection (ZIKV). It is a qualitative nucleic acid test to screen Zika virus RNA in the blood or other body fluids such as urine or saliva. Anti-Zika virus antibodies can be detected. Zika virus IgM antibody makes its appearance within the first week after the onset of symptoms and can be demonstrated 3-7 days following the clinical manifestations. Anti-Zika virus IgG antibody makes its appearance by the end of second week of illness. IgM antibodies persist up to 3 months and the IgG antibodies for months to years. IgM detection assays have to be interpreted with caution as there is cross-reactivity with other Flaviviruses such as dengue(10-12).

Effect of pesticides

Physicians in the Crop-Sprayed Towns in Brazil have put forward the theory that malformation of the skull and brain in children from pregnant women living in areas must be the effect of the pesticide, Pyriproxyfen which has been introduced into the drinking water supply. Pyriproxyfen is a chemical larvicide producing malformations in the developing mosquitoes by acting as a juvenile hormone (juvenoid).

Treatment

There is no specific treatment. The patients who have presented with mild features of Zika virus infection are to be treated with bed rest under mosquito net, antipyretic (acetaminophen, paracetamol) and fluid

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replacement either orally or intravenously to prevent dehydration. Administration of aspirin or non-steroidal anti-inflammatory drugs may be considered only after ruling out the condition of dengue fever.

Prevention

The patient must be prevented from mosquito bites. The patient is able to transmit the virus to a biting mosquito during the first week of illness. An infected mosquito can then transmit the virus to other people.

Vector control is essential in the prevention of Zika virus infection. The environment must be free of potential breeding sources as *Aedes* mosquitoes breed in small collections of water around homes, schools, and work places. It is important to eliminate these mosquito breeding sites. The containers such as old tyres, cans, jars, coconut shell, oil drums, flower pots and buckets, should not be left outside home as they can be filled with water and become breeding sites. The water containers should be kept covered. Public health authorities should undertake fogging operations on war footing, and clear the breeding grounds of mosquito.



Fig. 6 Fogging operation

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Fig. 7 Lemon Grass Oil

The best way of prevention of the infection is by protection against mosquito bites during the day and early evening. Special attention should be given to prevent mosquito bites among pregnant women, women of reproductive age and young children. Insect repellents are to be used and persons are advised to wear long sleeves and pants treated with permethrin. The clothes should preferably be light-colored and must cover the body as much as possible. There should be physical barriers in the house such as closed doors and windows and window screens, Lemon grass oil is given to poor pregnant women to help preventing them from getting bitten by mosquitoes. Lemon grass oil acts as a mosquito/insect repellent. It is advised to secure screens on windows and doors to keep mosquitoes out. The human cost of the disabling disease is very great and public health services have to respond to the challenge.

Zika virus can spread from a pregnant woman to her foetus. Pregnant women in any trimester should consider postponing travel to any area where Zika virus infection is spreading. Unprotected sexual contact is discouraged.

India is the first country in the world to have ready for testing of two vaccines against the virus that is causing nightmares in The

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Americas. A single dose vaccine has been prepared by Bharat Biotech which is ready for pre-clinical trial. The vaccine may be a 'recombinant' vaccine produced through recombinant DNA technology by inserting a bacterial surface protein to stimulate an immune response. or an 'inactivated' vaccine

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