



COVID-19

DIAGNOSIS AND MANAGEMENT

PART I

Editors:

Neeraj Mittal
Sanjay Kumar Bhadada
O. P. Katare
Varun Garg

Bentham Books

COVID-19: Diagnosis and Management-Part I

Edited by

Neeraj Mittal

*Department of Endocrinology
Postgraduate Institute of Medical Education and Research
Chandigarh-160012
India*

Sanjay Kumar Bhadada

*Department of Endocrinology
Postgraduate Institute of Medical Education and Research
Chandigarh-160012
India*

O. P. Katare

*University Institute of Pharmaceutical Sciences
UGC Centre of Advanced Studies
Punjab University
Chandigarh-160014
India*

&

Varun Garg

*Department of Medical Affairs
Cadila Healthcare Limited
Ahmedabad 382421
Gujarat
India*

COVID-19: Diagnosis and Management-Part I

Editors: Neeraj Mittal, Sanjay Kumar Bhadada, O. P. Katare and Varun Garg

ISBN (Online): 978-1-68108-808-2

ISBN (Print): 978-1-68108-809-9

ISBN (Paperback): 978-1-68108-810-5

© 2021, Bentham Books imprint.

Published by Bentham Science Publishers – Sharjah, UAE. All Rights Reserved.

BENTHAM SCIENCE PUBLISHERS LTD.

End User License Agreement (for non-institutional, personal use)

This is an agreement between you and Bentham Science Publishers Ltd. Please read this License Agreement carefully before using the ebook/echapter/ejournal (“**Work**”). Your use of the Work constitutes your agreement to the terms and conditions set forth in this License Agreement. If you do not agree to these terms and conditions then you should not use the Work.

Bentham Science Publishers agrees to grant you a non-exclusive, non-transferable limited license to use the Work subject to and in accordance with the following terms and conditions. This License Agreement is for non-library, personal use only. For a library / institutional / multi user license in respect of the Work, please contact: permission@benthamscience.net.

Usage Rules:

1. All rights reserved: The Work is 1. the subject of copyright and Bentham Science Publishers either owns the Work (and the copyright in it) or is licensed to distribute the Work. You shall not copy, reproduce, modify, remove, delete, augment, add to, publish, transmit, sell, resell, create derivative works from, or in any way exploit the Work or make the Work available for others to do any of the same, in any form or by any means, in whole or in part, in each case without the prior written permission of Bentham Science Publishers, unless stated otherwise in this License Agreement.
2. You may download a copy of the Work on one occasion to one personal computer (including tablet, laptop, desktop, or other such devices). You may make one back-up copy of the Work to avoid losing it.
3. The unauthorised use or distribution of copyrighted or other proprietary content is illegal and could subject you to liability for substantial money damages. You will be liable for any damage resulting from your misuse of the Work or any violation of this License Agreement, including any infringement by you of copyrights or proprietary rights.

Disclaimer:

Bentham Science Publishers does not guarantee that the information in the Work is error-free, or warrant that it will meet your requirements or that access to the Work will be uninterrupted or error-free. The Work is provided "as is" without warranty of any kind, either express or implied or statutory, including, without limitation, implied warranties of merchantability and fitness for a particular purpose. The entire risk as to the results and performance of the Work is assumed by you. No responsibility is assumed by Bentham Science Publishers, its staff, editors and/or authors for any injury and/or damage to persons or property as a matter of products liability, negligence or otherwise, or from any use or operation of any methods, products instruction, advertisements or ideas contained in the Work.

Limitation of Liability:

In no event will Bentham Science Publishers, its staff, editors and/or authors, be liable for any damages, including, without limitation, special, incidental and/or consequential damages and/or damages for lost data and/or profits arising out of (whether directly or indirectly) the use or inability to use the Work. The entire liability of Bentham Science Publishers shall be limited to the amount actually paid by you for the Work.

General:

1. Any dispute or claim arising out of or in connection with this License Agreement or the Work (including non-contractual disputes or claims) will be governed by and construed in accordance with the laws of the U.A.E. as applied in the Emirate of Dubai. Each party agrees that the courts of the Emirate of Dubai shall have exclusive jurisdiction to settle any dispute or claim arising out of or in connection with this License Agreement or the Work (including non-contractual disputes or claims).
2. Your rights under this License Agreement will automatically terminate without notice and without the

need for a court order if at any point you breach any terms of this License Agreement. In no event will any delay or failure by Bentham Science Publishers in enforcing your compliance with this License Agreement constitute a waiver of any of its rights.

3. You acknowledge that you have read this License Agreement, and agree to be bound by its terms and conditions. To the extent that any other terms and conditions presented on any website of Bentham Science Publishers conflict with, or are inconsistent with, the terms and conditions set out in this License Agreement, you acknowledge that the terms and conditions set out in this License Agreement shall prevail.

Bentham Science Publishers Ltd.

Executive Suite Y - 2

PO Box 7917, Saif Zone

Sharjah, U.A.E.

Email: subscriptions@benthamscience.net



CONTENTS

FOREWORD	i
PREFACE	ii
LIST OF CONTRIBUTORS	iv
CHAPTER 1 HISTORY OF PANDEMICS	1
<i>Sunishtha, Govind Singh and Sanju Nanda</i>	
INTRODUCTION	1
THE ATHENIAN PLAGUE	3
PLAGUE OF JUSTINIAN	4
THE BLACK DEATH	4
SPANISH FLU	4
AIDS	5
SMALLPOX	5
SARS	6
SWINE FLU OR H1N1 PANDEMIC	6
EBOLA	6
COVID-19	7
ORIGIN OF CORONAVIRUS	7
TYPES OF CORONAVIRUSES	8
DISEASE ASSOCIATED WITH CORONAVIRUSES	11
MURINE HEPATITIS VIRUS (MHV)	11
Central Nervous System	11
Hepatitis	12
Pneumonitis	12
BOVINE CORONAVIRUS	12
HUMAN CORONAVIRUS	12
ABBREVIATIONS	13
CONSENT FOR PUBLICATION	13
CONFLICT OF INTEREST	13
ACKNOWLEDGEMENTS	14
REFERENCES	14
CHAPTER 2 INTRODUCTION TO COVID-19	18
<i>Hitesh Malhotra, Anjoo Kamboj and Peeyush Kaushik</i>	
INTRODUCTION	18
GENOMIC STRUCTURE OF CORONAVIRUS	21
STRUCTURAL PROTEINS	21
Spike Protein	22
Small Membrane Protein	23
Membrane Protein	24
Hemagglutinin-Esterase	24
Nucleocapsid and Internal Proteins	24
Replicase Protein	25
VIRAL CYCLE	25
OUTBREAKS OF CORONAVIRUS	27
Porcine Coronavirus	27
Avian Coronavirus	28
Feline Coronavirus	28
Bovine Coronavirus	28

Murine Coronavirus	29
Human Coronavirus	29
SARS-CoV	29
MERS-CoV	31
COVID-19	32
Introduction	32
Chronology of COVID-19	33
Symptoms	34
Transmission	36
Treatment	36
LIST OF ABBREVIATIONS	37
CONSENT FOR PUBLICATION	39
CONFLICT OF INTEREST	39
ACKNOWLEDGEMENTS	39
REFERENCES	39
CHAPTER 3 COVID-19: EPIDEMIOLOGY	42
<i>Kamya Goyal, Shammy Jindal, Tarun Kumar, Jugnu Goyal, Reena Sharma,</i> <i>Ravinder Singh and Samir Mehndiratta</i>	
INTRODUCTION	43
GEOGRAPHICAL DISTRIBUTION	44
GLOBAL EPIDEMIOLOGY OF COVID-19	45
Effect of Age, Sex and other Factors on Covid-19-Related Deaths	54
COVID-19 CASE COMPARISONS IN DIFFERENT REGION OF WORLD (WORLD HEALTH ORGANIZATION, 2020)	55
COVID-19 IN INDIA	58
REPORT BY ICMR ON COVID-19 ABOUT CONTAINMENT ZONE IN INDIA	60
NATIONAL RESPONSES ON COVID-19 WORLDWIDE	61
Asia	61
China	62
South Korea	63
Middle Eastern	64
<i>Iran</i>	64
<i>Europe</i>	65
<i>Spain</i>	65
<i>France</i>	66
<i>North America</i>	66
<i>United States</i>	67
<i>South America</i>	68
<i>Africa</i>	68
<i>Oceania</i>	69
EFFECT OF LOCKDOWN ON COVID-19 CASES IN TOP TEN MOST AFFECTED COUNTRIES OF WORLD	69
THE ROLE OF WHO AND INGOS FOR PROVIDING DATA IN COVID-19	73
OUTCOMES FROM SOME PUBLISHED REPORTS ON COVID-19 EPIDEMIOLOGY	74
Herd Immunity-COVID-19	76
CONCLUSION	77
LIST OF ABBREVIATIONS	77
CONSENT FOR PUBLICATION	77
CONFLICT OF INTEREST	77
ACKNOWLEDGEMENTS	77

REFERENCES	78
CHAPTER 4 PATHOPHYSIOLOGY	83
<i>Anirban Ghosh and Shamsher Singh</i>	
INTRODUCTION	83
TRANSMISSION OF COV	84
Virus Life Cycle	85
Role of Structural Proteins in The Pathogenesis	86
<i>A. Spike Protein</i>	86
<i>B. Hemagglutinin-Esterase (HE) Protein</i>	88
<i>C. Membrane (M) Protein</i>	89
<i>D. Small Envelop (E) Protein</i>	91
<i>E. Nucleocapsid (N) Protein and Internal (I) Protein</i>	92
<i>F. Replicase Proteins</i>	93
<i>G. CoV Associated Protein</i>	99
Pathophysiology from a Cell Biology Perspective	100
<i>Phase I. Asymptomatic Stage (First 1-2 Days of Infection)</i>	100
<i>Phase II. Upper Airway and Conducting Airway Response (Next Few Days)</i>	101
<i>Phase III. Hypoxia, Ground-glass Infiltrates, Progression to ARDs</i>	102
CONCLUSION	104
LIST OF ABBREVIATIONS	104
CONSENT FOR PUBLICATION	105
CONFLICT OF INTEREST	105
ACKNOWLEDGEMENTS	105
REFERENCES	105
CHAPTER 5 CLINICAL PRESENTATION AND COMORBIDITIES	117
<i>Jasleen Kaur, Baljinder Singh, Bikash Medhi and Gurpreet Kaur</i>	
INTRODUCTION	118
CLINICAL PRESENTATIONS OF COVID-19 INFECTION	118
INTER-INDIVIDUAL VARIATIONS IN CLINICAL PRESENTATIONS DUE TO DIFFERENTIAL SUSCEPTIBILITY TOWARDS COVID-19	120
Neonates or Newborns (Upto 1 Month); Infants (1 Month-2 Years), Children (2-10 Years)	120
Adolescent (11-19 Years), Young (20-35 Years) and Middle Aged (36-59 Years) Patients	128
Elderly (>60 Years) and Older (>80 Years) Patients	143
ACE2	148
Gender	149
Blood Group	150
Previous Immunization	151
COMORBIDITY	152
CONCLUSION	152
LIST OF ABBREVIATIONS	153
CONSENT FOR PUBLICATION	154
CONFLICT OF INTEREST	154
ACKNOWLEDGEMENTS	154
REFERENCES	154
CHAPTER 6 DIAGNOSIS	164
<i>Richa Deshpande, Aishwarya Joshi, Nikunj Tandel and Rajeev K. Tyagi</i>	
COVID-19: A PANDEMIC DISEASE	165
COVID-19: EARLY DETECTION BASED ON SYMPTOMS	166
Clinical Analysis	166

Hematological Analysis	167
Chest CT	168
COVID-19: MOLECULAR DETECTION OF VIRUS	169
RT-PCR Based Assays	170
Loop Mediated Isothermal Amplification (LAMP)	172
CRISPR-Isothermal Amplification Based Assays	174
Microarrays	175
Metagenomic Sequencing Based Methods	175
Gold Nanoparticles-Based Colorimetric Assay	176
COVID-19: SERIOLOGICAL AND IMMUNOLOGICAL BASED DETECTION	179
BIOMARKER IDENTIFICATION: APPROACH OF SERIOLOGICAL PLATFORM	181
Antibody Biomarkers	181
Antigen Biomarkers	182
Procalcitonin and Interleukin-6 as Prognostic COVID-19 Biomarkers	183
SEROLOGICAL AND IMMUNOLOGICAL ASSAYS	184
Enzyme-linked Immunosorbent Assay (ELISA)	184
Lateral Flow Immunoassay	185
Neutralization Assays	187
Luminescence-based Immunoassays	188
Biosensor Tests	188
Rapid Antigen Tests	189
CONCLUDING REMARKS	190
LIST OF ABBREVIATIONS	191
CONSENT FOR PUBLICATION	192
CONFLICT OF INTEREST	192
ACKNOWLEDGEMENTS	192
REFERENCES	193
SUBJECT INDEX	422

FOREWORD

It is my proud privilege to introduce the book “COVID-19: Diagnosis and Management”, which is authored by a group from PGIMER, Chandigarh. The timing of this monograph is very apt as it has been about 9 months since the start of the COVID-19 pandemic, and it is now that we are starting to unravel the various mechanisms of disease pathogenesis and treatment modalities for this viral infection which has infected 29 million people, out of which about 1 million have died till date globally.

It has been the need of the hour to come up with a treatment for this pandemic disease. Moreover, it is of utmost importance that all the information related to COVID -19 should be compiled in one place, a goal which this book will fulfill.

Though the tests for diagnosis of the infection have been developed in the start of the pandemic, there are still some issues in diagnosis, including the sensitivity of the best test available, *i.e.*, Real-Time Polymerase Chain Reaction.

The book is very well organized and has been divided into two parts; each part is comprised of 6 chapters and covers all the aspects of COVID-19 from the history to the treatment of the disease. Based on the best scientific studies available, the editors and authors have used their vast professional experience to discuss the all clinical aspects of COVID-19, including clinical presentation to diagnosis in the first part and treatment of COVID-19 in the second part, and I am very sure that this compendium will become the benchmark to refer to for any information required on COVID-19.

Whenever we write books, we must have in our minds, as clearly as possible, the affirmation of Carlyle Guerra de Macedo, who was the Director of Pan American Health Organization, relative to the responsibility of what is being published: “It must be remembered that behind each table, every report or material examined, there are lives, there are people, there is suffering, waiting for our efforts and human solidarity.” Both the parts of the book are very well organized, and the readers will get a mine of information available to date on COVID-19 in one place, and it would be helpful to both the clinicians and the lab professionals for day-to-day guidance in various matters. The monograph is comprehensive but is written in a lucid manner that is easy to grasp, and even complex topics are made simple for understanding.

I am also sure that as the knowledge of the virus evolves further, the authors will certainly keep updating the work from time to time, further adding to the importance of the book. I would like to congratulate the editors/authors for this tremendous effort, and I am very sure that this book will surely be of use to readers around the world and help them in the diagnosis and management of patients with COVID-19 and will also go a long way in the efforts to help fight the pandemic, which is being faced by the humanity now.

Prof. R. Sehgal
Department of Medical Parasitology
Chairperson Group D Departments
Postgraduate Institute of Medical Education & Research
Chandigarh-160012
India

PREFACE

The coronavirus disease 2019 (COVID-19) outbreak has spread throughout the globe and has been declared as a pandemic by the World Health Organization (WHO) on 11th March 2020. To date, *i.e.*, 1st September 2020, there are more than 25, 327, 098 confirmed cases of COVID-19 worldwide, and around 848, 255 deaths have been reported. Clinicians and scientists across the globe need all the information on this pandemic disease on one platform. This book, “COVID-19: Diagnosis and Management”, is a concise and visual reference for this viral disease. This book has been divided into two parts I and II.

Part I will provide a comprehensive knowledge which will cover all the aspects related to COVID-19, such as: 1) History of coronaviruses, 2) epidemiology of COVID-19 3) clinical presentation of this viral disease, 4) how to diagnose it, whereas part II of the book covers the prevention and treatment methodology of this communicable disease.

Key Features:

1. Chapter wise description and segregation of all the areas from pathophysiology to diagnosis and management of COVID-19 in two different parts of the book.
2. Six chapters in the first part that begin with the history of the coronaviruses and their introduction.
3. Multiple tables and figures which summarize and highlight important points.
4. Covering all the aspects of COVID-19, making this a perfect textbook for virologists and medical students.
5. A summary of the current standards for the evaluation and diagnosis of COVID-19.
6. A detailed list of references, abbreviations, and symbols.

This book is an essential reference for practicing and training virologists, pulmonologists, medical students, scientists working in various research labs, pharmaceutical and biotechnology industries on COVID-19.

Neeraj Mittal

Department of Endocrinology
Postgraduate Institute of Medical
Education and Research,
Chandigarh-160012
India

Sanjay Kumar Bhadada

Department of Endocrinology
Postgraduate Institute of Medical
Education and Research,
Chandigarh-160012
India

O. P. Katare

University Institute of Pharmaceutical Sciences
UGC Centre of Advanced Studies
Panjab University
Chandigarh-160014
India

Varun Garg

Department of Medical Affairs
Cadila Healthcare Limited
Ahmedabad 382421
Gujarat
India

List of Contributors

Aishwarya Joshi	Institute of Science, Nirma University, Ahmedabad, Gujarat, India
Anirban Ghosh	Department of Pharmacology, ISF College of Pharmacy, Moga, Punjab, India
Anjoo Kamboj	Chandigarh College of Pharmacy, Landran, Mohali, Punjab, India
Baljinder Singh	MM School of Pharmacy, MM University, Sadopur, Ambala, Haryana, India
Bikash Medhi	Department of Pharmacology, PGIMER, Chandigarh, India
Govind Singh	Department of Pharmaceutical Sciences, Maharshi Dayanand University, Rohtak, India
Gurpreet Kaur	Department of Pharmaceutical Sciences and Drug Research, Punjabi University, Patiala, Punjab, India
Hitesh Malhotra	Chandigarh College of Pharmacy, Landran, Mohali, Punjab, India
Jasleen Kaur	Department of Pharmaceutical Sciences and Drug Research, Punjabi University, Patiala, Punjab, India
Jugnu Goyal	Swami Dayanand Institute of Pharmaceutical Sciences, UHS, Rohtak, Haryana, India
Kamya Goyal	Laureate Institute of Pharmacy, Kathog, Distt, Kangra, India
Nikunj Tandel	Institute of Science, Nirma University, Ahmedabad, Gujarat, India
Peeyush Kaushik	Chandigarh College of Pharmacy, Landran, Mohali, Punjab, India
Rajeev K. Tyagi	Department of Medicine, Vanderbilt University Medical Center, Nashville, TN, USA Biomedical Parasitology and Nano-immunology Lab, CSIR Institute of Microbial Technology (IMTECH), Chandigarh, India
Ravinder Singh	Department of Chemistry, National Taiwan University, Taipei, Taiwan
Reena Sharma	Agricultural Biotechnology Research Center, Academia Sinica, Taipei, Taiwan
Richa Deshpande	Institute of Science, Nirma University, Ahmedabad, Gujarat, India
Samir Mehndiratta	School of Pharmacy, University of Southern California, Los Angeles, USA School of Pharmacy, Taipei Medical University, Taipei, Taiwan
Sanju Nanda	Department of Pharmaceutical Sciences, Maharshi Dayanand University, Rohtak, India
Shammy Jindal	Laureate Institute of Pharmacy, Kathog, Distt- Kangra, H.P., India
Shamsher Singh	Department of Pharmacology, ISF College of Pharmacy, Moga, Punjab, India
Sunishtha	Department of Pharmaceutical Sciences, Maharshi Dayanand University, Rohtak, India
Tarun Kumar	Department of ECE, Deenbandhu Chhotu Ram University of Science and Technology, Haryana, India

CHAPTER 1

History of Pandemics**Sunishtha¹, Govind Singh¹ and Sanju Nanda^{1,*}**¹ Department of Pharmaceutical Sciences, Maharshi Dayanand University, Rohtak, India

Abstract: Pandemic is the term coined for the widespread of a disease or infection on a very large scale and across borders. COVID-19, an outcome of the spread of coronavirus, reportedly started from China and spread to almost all the countries of the world. Though it is not for the first time that there was an outbreak of a disease at such a high magnitude but the duration for which it has continued to grapple the world with its virulence and contagious nature, it has become important to take a peek into the history of other pandemics of the world too. Before COVID -19, about 20 major outbreaks of infectious diseases took place and claimed millions of lives in a sweep. The awareness of government bodies, WHO, and non-government organizations grew better with every pandemic. Understanding the role of basic hygiene, self-immunity, social distancing, living in coherence with other living and non-living components of the planet are some positive outcomes of these pandemics. These pandemics also necessitated the need for discovering new drugs and vaccines.

This chapter describes the major pandemics in the history of mankind, the origin and types of coronaviruses, the association of different types of coronaviruses with the ranges and severity of infections, and the origin of COVID-19.

Keywords: AIDS, Black Death, Contagious, Corona, COVID-19, Ebola, Epidemic, Flu, H1N1, Host, Outbreaks, Pandemic, Plague, SARS, Swine flu, Vaccine, Virulence, WHO, Yellow fever.

INTRODUCTION

The terms pandemic, epidemic, outbreak are primarily categorized based on the number of cases of a condition often used to describe infections. These terms have described the comparison of the expected number of cases in a particular time and how far-off cases have spread in the geographical area. Some conditions, such as cancer, hypertension, violence, beneficial behaviors, or even positive behaviors, can also be defined in the same way (Morens *et al.*, 2009).

* **Corresponding author Sanju Nanda:** Department of Pharmaceutical Sciences, Maharshi Dayanand University, Rohtak, India; E-mail: sn_mdu@rediffmail.com

The term ‘pandemic’, has its origin derived from the Greek words *pan* (meaning “all”) and *demos* (meaning “the people”). Pandemic refers to a spread of contagious illness that spreads across the countries or world, usually affecting a larger area than an ‘epidemic’. It is important to note that a disease that is affecting a large number of people or widespread cannot be said to be a pandemic till it is contagious (Fig. 1). For example, cancer kills many people, but it is not a contagious disease, so not included as a pandemic (WHO, 2011).

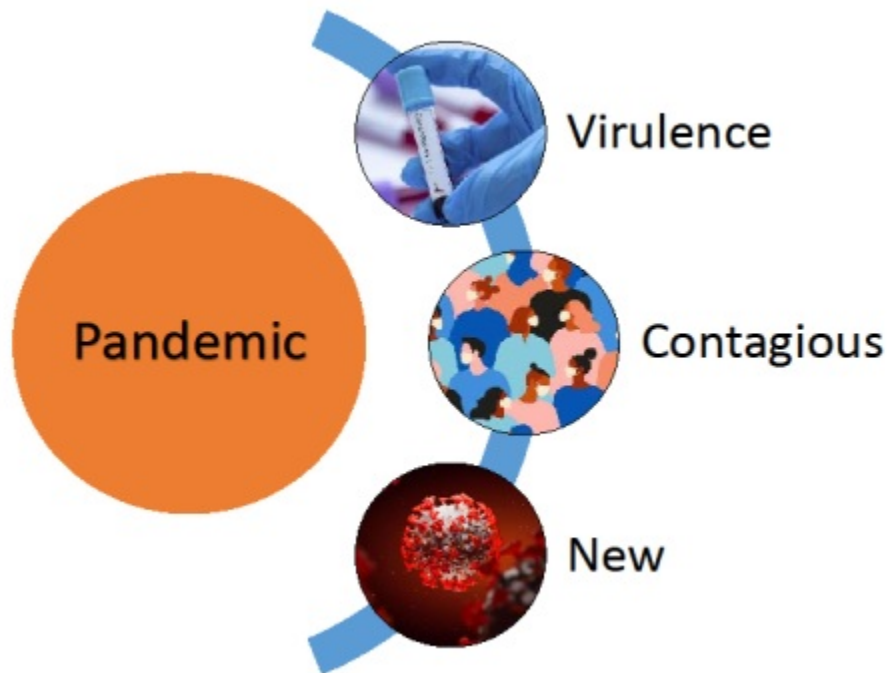


Fig. (1). The essentials of a pandemic.

The word “epidemic” is derived from the two Greek words *epi* meaning “upon or above”, and *demos* “the people”. An *epidemic* is an outbreak of disease that rapidly spread to a large population in a short period of time. For example, severe acute respiratory syndrome (SARS) took the lives of approx. 800 people worldwide during the epidemic of 2003 (Morens *et al*, 2009). An *outbreak* is an increase beyond expectation in the number of cases of a disease or condition occurring among a specified population in a limited geographic location and period of time (Gregg, 2002). The multi-state outbreak of *Salmonella Muenchen* in 1981 is an example of the outbreak.

Evidence suggested that the human population has suffered from many pandemics throughout history, be it the earlier form of smallpox or Spanish flu or the recent

incidence of Ebola or Covid. In world history, we can see a number of significant pandemics like cholera, dengue, plague, smallpox, AIDS, tuberculosis, influenza, West Nile disease, and severe acute respiratory syndrome (Rear *et al.*, 2015; Qiu *et al.*, 2016). In 1999, WHO issued a printed paper on pandemic readiness overview, which was further revised in 2005 and 2009 while planning for an influenza pandemic. In this guidance, WHO defined different phases of pandemic and required appropriate actions for each phase. The revision includes the explanation of a pandemic and declaration of its leading phases (WHO, 2011). There have been many pandemics declared at different times as enlisted in Table 1.

THE ATHENIAN PLAGUE

The plague has been responsible for three pandemics in history, including the 6th, 14th, and 19th centuries. The Athenian plague occurred during 430–26 B.C. It originated from Ethiopia, after that, it was distributed in Egypt and Greece. It is a well-known infectious disease primarily affecting rodents. *Yersinia pestis* bacteria is a causative agent of Athenian plague that is related to the Enterobacteriaceae family. It is transferred in humans from rodents through skin-piercing by infected fleas. Transmission of bacteria in an uninfected person is possible by droplet contact, direct or indirect contact with infected material (Huremovic *et al.*, 2017). Initial observed symptoms of the plague were headache, conjunctivitis, rashes on the whole body, and fever. After that patients showed severe symptoms like cough up blood, severe stomach cramps along with vomiting, and attacks of “ineffectual retching”. Generally, on the seventh or eighth-day infected persons die (Thucydides, 2017). Approximately 75000 to 100000 people died due to the plague of Athens (Littelman *et al.*, 2009).

Table 1. Chronology of pandemics.

Serial No.	Name of Pandemic Event	Year	Origin
1	Plague of Athens	430 B.C.	Ethiopia
2	Antonine Plague	165-190 A.D.	Italian peninsula
3	Justinian Plague	541-750 A.D.	Egypt
4	Japanese Smallpox	735-737 A.D.	Japan
5	Black Death	1347-1351	China
6	Aztecs Disease	1519-1520	Aztecs, America
7	London Plague	1665-1666	London
8	The Great Plague	1738	Central and Eastern Europe
9	Cholera 6 Outbreak	1817-1923	India

Introduction to COVID-19

Hitesh Malhotra^{1,*}, Anjoo Kamboj¹ and Peeyush Kaushik¹

¹ Chandigarh College of Pharmacy, Landran, Mohali, Punjab, India

Abstract: In the mid 20th century, virologists identified a new category of the virus, which has a fringe of projections on its surface that appears like a crown and named coronavirus. Coronavirus belongs to the family of pleomorphic spherical viruses recognized by bulbous surface projection and ssRNA. As the virus belongs to the family of RNA-virus, the chances of mutation are very high, which further increases its pathogenicity. The coronavirus mainly attacks the respiratory tract and ultimately leads to respiratory failure. Recent outbreaks of coronaviruses are severe acute respiratory syndrome and the Middle East respiratory syndrome, which cause a great threat to human health with a high mortality rate. Later on, in late 2019, a new form of coronavirus appears in Wuhan, China where numbers of people are recognized with pneumonia-like symptoms. The condition was entitled with COVID-19 by WHO on Feb 2020, which was declared to be pandemic by the same agency in Mar 2020. The COVID-19 is considered to be originated from bats, which then transmit to humans due to the consumption of contaminated animal raw. The virus is highly contagious and spread at a very high rate, which produces global health risks. Further various existing treatment is used for treating the infection but still the precise and accurate treatment yet to be investigated.

Keywords: ACE-II, Air droplets, Breathlessness, China, Chronology, Coronavirus, COVID-19, Genome, Helicase, Membrane protein, MERS, Pneumocytes, Pneumonia, Replicase, Respiratory distress syndrome, SARS, Structural proteins, Virus, World, Transmission.

INTRODUCTION

The coronavirus belongs to a family of viruses that mainly affects the respiratory tract infection with prime symptoms, such as hyperthermia, pneumonia, breathlessness, and acute or chronic pulmonary infections. The coronavirus mainly affects animals, but recent investigations in the late 20th century reported some human cases. In 1930, the first coronavirus case was reported in chickens recognized by pneumonia-like symptoms and termed as avian infectious bronchitis virus. Further, in late 1960, the first human coronavirus case was

* Corresponding Author Hitesh Malhotra: Chandigarh College of Pharmacy, Landran, Mohali, Punjab, India; Tel: 98 9637 1903; E-mail: hiteshmalhotra03.hm@gmail.com

reported (Pyrce *et al.*, 2007). In 1968, electron microscopy of the virus was done and termed as “**Coronavirus**” due to its crown-like appearance, clearly depicted in Fig. 1(A & B). Later on, in 1975, the International Committee on the Taxonomy of Viruses introduced a family Coronaviridae. In 2005, the family Coronaviridae was further split into two subfamilies, the Coronaviruses, and the Toroviruses (Tyrrel *et al.*, 1968).

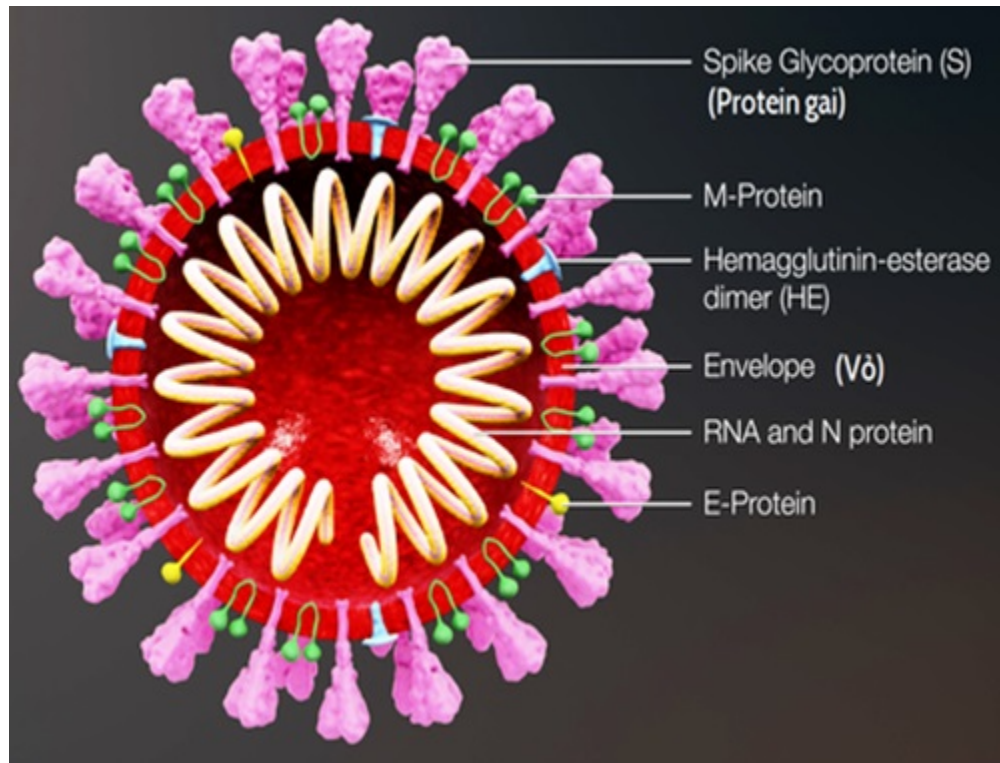


Fig. (1). Structure of Coronavirus (A) Electron Microscopy and (B) Model of CoV.

Based on serological reactions, the coronavirus is divided into three groups or genera *i.e.* Group-I, Group-II, and Group-III (McIntosh *et al.*, 1974). Group-I includes viruses that cause infection in animals only, like the Porcine epidemic diarrhea virus and feline infectious peritonitis virus. It also includes the viruses that produce respiratory infections in humans, such as Human Coronavirus 229E (HCoV-229E) and KHU1. The Group-II viruses are Porcine hemagglutinating encephalomyelitis virus, bovine coronavirus, and equine coronavirus, which shows pathogenicity in animals, while HCoV-OC43 and HCoV-NL63 produce pneumonia-like conditions in humans. Group-II viruses that cause infections in rodents are murine hepatitis virus (MHV) and Rat sialodacryoadenitis CoV, which produce enteritis, hepatitis, and encephalitis in addition to respiratory infections.

Lastly, infectious bronchitis virus (IBV), Turkey coronavirus, and pheasant coronavirus are classified under Group-III viruses. Table 1 summarizes the types of CoV (Cavanagh *et al.*, 2020). All the CoV possess some common characteristics, which are as follows:

1. The shape of coronavirus is spherical with an average size of 80-220 nm.
2. The virus is covered with an envelope having club-shaped peplomers.
3. It all contains a tubular nucleocapsid structure with helical symmetry.
4. All are composed of single-stranded RNA with a genomic size of 27-32 kb.
5. The coronavirus contains numerous structural proteins, but some are present in all, such as nucleoprotein, peplomer glycoprotein, a transmembrane glycoprotein, and hemagglutinin esterase.
6. While some non-structural proteins are also present in CoV, such as RNA dependent RNA polymerase.
7. The newly-formed viruses *i.e.* virions are generally assembled in the endoplasmic reticulum and Golgi cisternae.
8. The mutation is very common in CoV and due to this reason, a diverse host range was exhibited (Enjuanes *et al.*, 2000).

Table 1. Different types of coronavirus.

Group	Virus	Host	System Affected
I	229E	Human	Respiratory Infection
	TGEV	Pig	Respiratory & Enteric Infection
	PRCoV	Pig	Respiratory Infection
	Canine coronavirus	-	Enteric infection
	FeCoV	-	Enteric infection
	FIPV	Cat	Respiratory, enteric & neurologic infection
	NL-63	Human	Respiratory Infection
II	OC43	Human	Respiratory & enteric infection
	MHV	Mouse	Intestinal & neurological infection
	Sialodacryoadenitis CoV	Rat	Neurological infection
	Hemaagglutinating encephalomyocarditis virus	Pig	Respiratory, enteric & neurological infection
	BCoV	Cow	Enteric infection
	HKU1	Human	Respiratory infection
	SARS-CoV	Human	Life-threatening respiratory infection
III	IBV	Chicken	Respiratory infection, Hepatitis
	Turkey CoV	Turkey	Respiratory & Enteric infection

COVID-19: Epidemiology

Kamya Goyal^{1,2,#}, Shammy Jindal^{1,#}, Tarun Kumar³, Jugnu Goyal⁴, Reena Sharma⁵, Ravinder Singh⁶ and Samir Mehndiratta^{7,8,*}

¹ *Laureate Institute of Pharmacy, Kathog, Distt- Kangra, H.P., India*

² *Chitkara College of Pharmacy, Chitkara University, Chandigarh-Patiala National Highway, Rajpura, Patiala, Punjab, India*

³ *Department of ECE, Deenbandhu Chhotu Ram University of Science and Technology, Murthal, Haryana, India*

⁴ *Swami Dayanand Institute of Pharmaceutical Sciences, UHS, Rohtak, Haryana, India*

⁵ *Agricultural Biotechnology Research Center, Academia Sinica, Taipei, Taiwan*

⁶ *Department of Chemistry, National Taiwan University, Taipei, Taiwan*

⁷ *School of Pharmacy, University of Southern California, Los Angeles, USA*

⁸ *School of Pharmacy, Taipei Medical University, Taipei, Taiwan*

Abstract: In the history, the year 2019 will be remembered as the year that has witnessed the beginning of a pandemic, primarily affecting the respiratory tract and then, spreading from human to human. A total of 25.18 million reported cases and 0.84 million deaths, as of 30th August 2020, and still counting, were caused by a novel coronavirus named COVID-19 that originated in Wuhan, China. By the beginning of the year 2020, this virus spread to several countries like Singapore, South Korea, Japan, Italy, Spain, Germany, the United Kingdom, and the United States of America. Between January 2020 and March 2020, the disease took a paradigm shift and started to affect the majority of European countries like Italy, Spain, France, Germany and UK. In the majority of the patients with a competent immune system, this disease goes unnoticed or without symptoms, thus making them highly susceptible to spread this disease to whoever comes in their contact. Aged patients (>60 years) or patients with chronic health issues like heart diseases, cancer, diabetes, and weak immunity are at greater risk of developing the symptoms. In severe conditions, patients need hospitalization and respiratory support (respirators/ventilators), thus causing an overload on the health system of the world. This initiated the movement of “flattening the curve” by social distancing and isolation to decrease the burden on the health system and to decrease the spread of the disease.

* **Corresponding author Samir Mehndiratta:** School of Pharmacy, University of Southern California, Los Angeles, California, USA; School of Pharmacy, Taipei Medical University, Taipei, Taiwan; E-mail: d301100006@tmu.edu.tw

These authors contributed equally

Keywords: China, Confirmed Cases, *Cordon sanitaire*, Coronavirus, COVID-19, Curfews, Epidemiology, Geographical distribution, Global Epidemiology, Hotspots, Lockdown, National Responses, Non-essential, Outbreak, Pandemic, Person-to-person Transmission, Quarantines, SARS-CoV-2, WHO Region, Wuhan.

INTRODUCTION

The year 2019 has witnessed the beginning of a pandemic majorly affecting the respiratory tract; however, effects on the other body organs have also been reported (Singh *et al.*, 2020a). The pandemic has affected 25,182,329 people across the globe, with a total death toll of 846,936 registered up to 30th August 2020. The total recovered cases from the COVID-19 pandemic are 17,515,059 and the active cases till 30th August 2020 are 6,820,334. Half of the total affected population of the world resides in the USA, Brazil, and India. This disease spreads from human to human *via* air-borne droplets. This pandemic is not the first pandemic world has ever seen; however, it is one of the biggest of our times and the most vulnerable after World War II. The severity of this can be estimated from the fact that it is as destructive as the influenza pandemic in 1918, which emerged after World War I and caused deaths of tens of millions of people due to lack of antibiotics. Similarly, Acquired Immune Deficiency Syndrome caused by a retrovirus was equally lethal before it was controlled by using antiretroviral drugs (DiMaio *et al.*, 2020).

Broadly, pandemics are the epidemics that spread worldwide and thus are not confined to any particular geographical region. This current world epidemic originated in Wuhan, China is caused by a novel coronavirus and has been named coronavirus disease 2019 or COVID-19. Due to its similarity with SARS (Severe Acute Respiratory Syndrome), ICTV (International Committee on Taxonomy of Viruses) coined it as SARS-CoV-2 virus. COVID-19 was officially proclaimed as PHEIC Public Health Emergency of International Concern by WHO on 30th January 2020 with various countries starting to impose travel restrictions, issuing traveling warnings, and also exercising travel bans (Malviya *et al.*, 2020; Tang *et al.*, 2020). However, the lag between identification of the first case of COVID-19 infection to realizing its person to person transmission and to declare it as a world pandemic led it to spread to various countries and as of now at least 208 countries are infected with this infection (Hamid *et al.*, 2020).

Fortunately, due to previous exposure and understanding of coronavirus infections, such as SARS (Severe Acute Respiratory Syndrome) and Middle Eastern Respiratory Syndrome (MERS), this causative agent of SARS-CoV2 was quickly identified and its genome was rapidly sequenced to help researchers around the globe to develop potential drugs and/or vaccines. Fig. (1) shows various events and developments happened so far related to SARS-CoV-2.

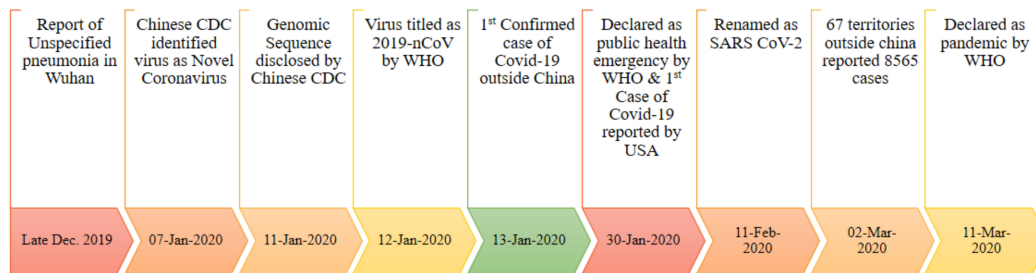


Fig. (1). Timeline of various developments in SARS-CoV-2 (Gennaro *et al.*, 2020; Park, 2020; Sun *et al.*, 2020; Srivastava *et al.*, 2020; Hamid *et al.*, 2020; Tang *et al.*, 2020).

In this chapter, we shall discuss the epidemiology of the COVID-19 pandemic. Basically, epidemiology is the study of various determinant factors of health and disease-related conditions or events in a sample population or globally, and the purpose of this study is to control the various factors related to disease and to control the spread of the disease. Therefore, from studying the epidemiology of COVID-19, one can conclude the frequency and pattern of this disease. In this chapter, the data has been collected and reported up to 12th June 2020. We shall discuss various determinants and factors like geographical distribution of the disease, patterns in the global spread of the pandemic, *etc.* Further, we shall discuss the comparison of the number of cases of COVID-19 in different WHO regions along with the effect of lockdown on the spread of the pandemic. Besides, the condition of the COVID-19 pandemic in India along with some published reports by clinicians/researchers will be discussed in the latter part of the chapter.

GEOGRAPHICAL DISTRIBUTION

On 13th January 2020, the first confirmed case of COVID-19 outside China was reported in Thailand. It made the situation clear that this virus is no longer confined to China or the provenances nearby Wuhan. Soon after, reports of confirmed cases started to emerge from different countries in Asia. In January 2020, this virus spread to many Asian countries like Thailand, South Korea, and Japan and also cases of patients affected by COVID-19 started to appear in the western part of the world, including Italy, Spain, Germany, the UK, and the USA. In early February, WHO realized that the occurrence of COVID-19 is very high and ranges between 2.24 to 3.38. From the end of January 2020 to March 2020, it took a paradigm shift and disease started to affect the majority of European

Pathophysiology

Anirban Ghosh¹ and Shamsher Singh^{1,*}

¹ Neuroscience Division, Department of Pharmacology, ISF College of Pharmacy, Moga, Punjab, India

Abstract: The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the causal pathogen of the novel coronavirus disease 2019. This novel Covid-19 has created a serious public health crisis throughout the world. The primary symptoms of coronavirus infection are common cold and influenza-like illness and with time it causes pneumonia. Although various studies are going on throughout the world, its actual pathophysiology is not very well clear to date. The Coronavirus is a positively charged single-stranded RNA virus. This virus gets easily transmitted from human to human. Numerous investigations have been found that the virus enters into the human body *via* its spike (S) proteins. The S-protein binds to ACE2 receptors and silently comes in contact with alveoli *via* blood. This entry hypersensitizes various receptors, epithelial cells, macrophages, T-cells, dendritic cells and thus implants pro-inflammatory cytokines and chemokines, resulting in stressful conditions. Studies found that Hemagglutinin-Esterase protein, Spike protein, Nucleocapsid protein, small envelope protein, internal proteins, group-specific proteins take part in viral pathogenesis, whereas, replication proteins (eIF4A, Cyclophilin, 3CLpro, RdRp) participates in Coronaviruses (CoVs) replication and translation phases, influencing both pathogenesis and pathophysiological conditions. In this chapter, we elaborate on viral pathogenesis, the various functions of proteins, structural, enzymatic, and accessory that are linked with the pathological conditions and will also highlight the correlation causing physiological alteration associated with this infection.

Keywords: ACE2 receptors, Covid-19, Hemagglutinin-Esterase protein, Life cycle, Membrane protein, Nsp1 protein, Nsp3 protein, Nsp8 primase, Nsp12 polymerase, Nsp13 helicase, Nsp14 protein, Nsp15 protein, Nsp16 protein, Nucleocapsid protein, Orf3b, Orf6, Orf7a, Pathogenesis, Pathophysiology, Spike proteins, Thrombosis, Transmission.

INTRODUCTION

Coronavirus (CoV) is a member of the Coronavirinae subfamily, which comprises a single positive-stranded RNA virus. The various endogenous proteins present in

* Corresponding author Shamsher Singh: Neuroscience Division, Department of Pharmacology, ISF College of Pharmacy, Moga, Punjab, India; Tel: +91 9779 9805 88; E-mail:shamshersinghbajwa@gmail.com

it are integral membrane (M), spike (S), nucleocapsid (N), envelope (E), and other accessory proteins, which not only facilitate its entry into the cells but also helps in replication (Fig. 1) (Garoff *et al.*, 1998). There are 3 different categories of CoVs- category 1, which includes human coronavirus 229e and transmissible gastric enteritis virus; category 2 includes human CoV-OC43, murine hepatitis virus, and bovine CoVs; class 3 comprehends avian infectious bronchitis virus (Fehr and Perlman, 2015). On 31st Dec 2019, China alerted WHO of a huge number of pneumonia-like cases in Wuhan city. After continuous investigations, Chinese scientists and WHO claimed the presence of a new strand of CoVs causing this pneumonia-like problem. CoV symptoms include- dry cough, shortness of breath, and respiratory distress. This virus has spread to almost every part of the world and costs about 469,587 lives worldwide till 23rd June 2020. From various investigations, WHO had declared that these CoVs are spreading through contacts by infected persons or patients. The S-protein of CoVs binds with ACE2 receptors and silently comes in contact with alveoli *via* blood. Initially, at the time of infection, the CoVs contaminates the epithelial cells, macrophages, T-cells, dendritic cells and execute pro-inflammatory cytokines and chemokines takes place, initiating stressful condition. In this chapter, we are discussing the viral pathology associated with proteins, enzymes, and accessory along with their roles in pathogenesis.

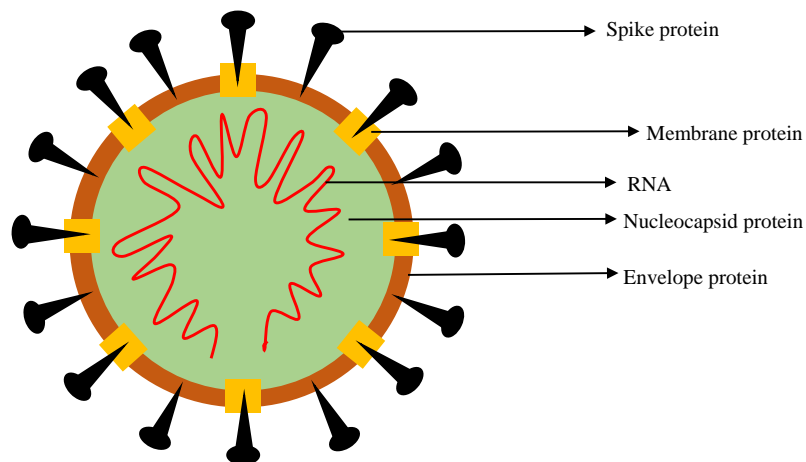


Fig. (1). Structure of CoV.

TRANSMISSION OF COV

Available reports have found that the CoVs are conveyed from animals to humans through close contact with animals like pigs, camels, and bats, are more susceptible to CoV infection, creating a reservoir (Mackay and Arden, 2015). At the early stage of CoV infection, the primary symptoms are not well expressed but as it gets matured and replication occurs CoVs slowly start to show their

symptoms. The incubation time of CoV infection is 2 to 14 days. It has been found that Covid-19 gets transmitted from an individual to another *via* cough, sneezing, hands shaking and thus found to get settled themselves at the respiratory tract (Gunalan, 2011) (Fig. 2).

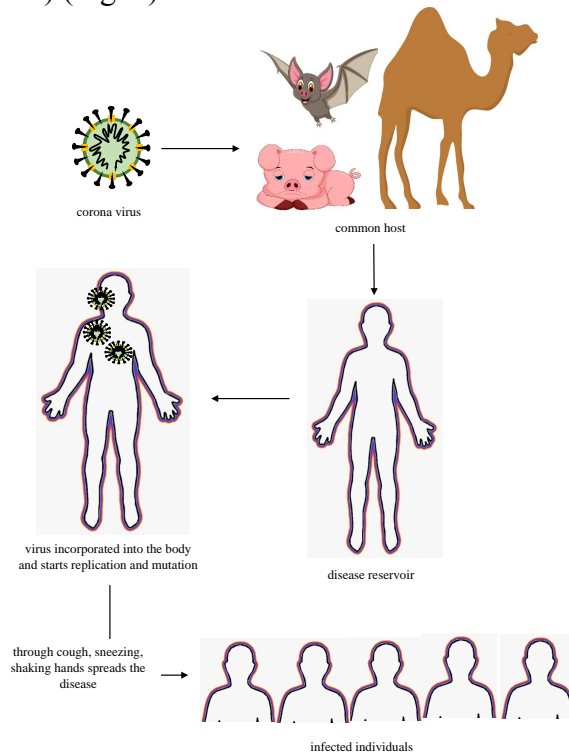


Fig. (2). Schematic representation of transmission of CoV.

Virus Life Cycle

The CoV life cycle has been summarized in this portion by discussing the various functions of viral proteins. It has been found that CoV with the help of the S-proteins gets attached with specific cellular receptors and thus initiates a conformational structural alteration of spike proteins, resulting in the liberation of the nucleocapsid into cells. After entering inside the cells, the 5' end of RNA, orf1a, and 1b gets translated to form pp1a and pp1ab. The orf1a represents the papain-like protease (PLpro) and a 3C-like protease (3CLpro), which acts to progress the pp1a and pp1ab to mature replicase protein (Lee *et al.*, 1991; Ziebuhr *et al.*, 2001). The orf1a X domain encodes the ADP-ribose¹-phosphatase activity (Ziebuhr, 2005; Snijder *et al.*, 2003), while the orf1b encodes a helicase and an RNA-dependent RNA polymerase (RdRp) which is processed by pp1ab (Gorbalenya, 2001). This orf1b also encodes various other enzymatic activities-

Clinical Presentation and Comorbidities

Jasleen Kaur¹, Baljinder Singh², Bikash Medhi³ and Gurpreet Kaur^{1,*}

¹ Department of Pharmaceutical Sciences and Drug Research, Punjabi University, Patiala, Punjab, India

² MM School of Pharmacy, MM University, Sadopur, Ambala, Haryana, India

³ Department of Pharmacology, PGIMER, Chandigarh, India

Abstract: Presently, the whole world is going through a historic yet a troublesome situation following COVID-19 outbreak. The clinicians have observed a wide variety of respiratory and non-respiratory clinical manifestations in COVID-19 patients. Accumulating reports revealed that the clinical features of COVID-19 may include asymptomatic/mild symptoms, neurological, cardiovascular complications, severe pneumonia and mortality. The most common features noticed are fever, dry cough, sore throat, shortness of breath, sputum production, fatigue, and myalgia. Recently, US health protection agency has also reported repeated shaking along with chills, loss of taste and smell in new case studies as additional symptoms. In addition to this, COVID-19 patients may show clinical signs like persistent pressure and pain in the chest, blue lips or face, confusion and GIT disturbances (diarrhea, nausea, vomiting and abdominal discomfort). The current ongoing pandemic has remarkably affected almost every age group of humans, starting from infants less than 3 months, adults, elder and older patients. Furthermore, the clinical presentations in these groups of COVID-19 infected patients were found to show considerable inter-individual variations. The findings also suggested that the comorbid conditions (heart injury, hyperglycemia, hypertension, neurodegenerative diseases) in elder/older patients further complicate the health of COVID-19 patients.

In the present book chapter, the clinical presentation of COVID-19 in pediatric, adults and geriatric group of population will be emphasized along with the higher susceptibility of COVID-19 in comorbid patients.

Keywords: ACE-2, Adolescents, Anosmia, Asymptomatic, Atypical symptoms, Comorbid, Comorbidity, Consolidations, Cutaneous, Dyspnea, Fatigue, Fever, Gastrointestinal, Ground glass opacities, Immunity, Incubation period, Neonates, Neurological, Pneumonia, Respiratory distress, Respiratory symptoms, SARS-CoV-2, Septic shock, Spikes, Vaccination.

* **Corresponding author Gurpreet Kaur:** Department of Pharmaceutical Sciences and Drug Research, Punjabi University, Patiala, Punjab, India, E-mail: kaurgpt@gmail.com

Neeraj Mittal, Sanjay Kumar Bhadada, O. P. Katare and Varun Garg (Eds.)
All rights reserved-© 2021 Bentham Science Publishers

INTRODUCTION

At the beginning of the COVID-19 outbreak, the clinicians have encountered a substantial diversity in the clinical presentations, such as different incubation periods among different age groups, noticeable variations in the onset of symptoms and degree of severity (moderate, serious and critical). Besides the most common respiratory symptoms, an array of complications has been found to be associated with Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) infection. Moreover, asymptomatic (transmit virus but never have symptoms) and presymptomatic (transmit virus and symptoms appear later) transmissions have also raised concerns. The present chapter elaborates the typical and atypical clinical features discerned in original clinical cases of COVID-19 patients. Besides, the factors (age, Angiotensin-Converting Enzyme 2 (ACE2), gender, blood group, previous immunization, comorbidity) responsible for the high inter-individual variations of clinical outcomes have also been discussed in detail.

CLINICAL PRESENTATIONS OF COVID-19 INFECTION

In COVID-19 patients, it is found that after exposure, the virus takes an incubation period of 2-14 days. According to the findings of clinical cases, the COVID-19 infection starts showing its mild symptoms after a median incubation time period of approximately 5.1 days (McIntosh, 2020). However, Lauer and his coworker estimated that 97.5% of COVID-19 infected patients presented severe symptoms by 11.5 days (Lauer *et al.*, 2020). The diverse respiratory and non-respiratory symptoms observed to date are compiled in Table 1.

Table 1. Respiratory and non-respiratory symptoms of COVID-19.

Respiratory Symptoms (Hassan <i>et al.</i> , 2020; Cascella <i>et al.</i> , 2020; Wang <i>et al.</i> , 2020)			
<p>Mild Cases</p> <ul style="list-style-type: none"> • Infection resides only in upper respiratory tract. • Fever, nasal congestion, dry cough, headache, sore throat and malaise. 	<p>Moderate Cases</p> <ul style="list-style-type: none"> • Respiratory manifestations include cough, shortness of breath, and tachypnea. 	<p>Severe Cases</p> <ul style="list-style-type: none"> • Patients are reported to have severe pneumonia. • Acute Respiratory Distress Syndrome (ARDS), $\text{PaO}_2/\text{FiO}_2 < 300$, $\text{SpO}_2 \leq 93\%$, tachypnea, severe dyspnea. • Fever can be absent or moderate. 	<p>Acute Respiratory Distress Syndrome</p> <ul style="list-style-type: none"> • It indicates worsening/failure of the respiratory system. • ARDS can be of different types on the basis of values of $\text{PaO}_2/\text{FiO}_2$. Severe ($\leq 100$ mmHg). Moderate (100-200 mmHg). Mild (200-300 mmHg).

(Table 3) cont....

<ul style="list-style-type: none"> • Dyspnea is absent. • Radiographic manifestations are not present. • Most of the cases have been found to be mild. • Mild cases may deteriorate into severe cases if precautions will not be acquired. 	<ul style="list-style-type: none"> • Severe symptoms are absent. 	<ul style="list-style-type: none"> • In critical cases, cardiac injury, RNAemia, respiratory failure or multiple organ dysfunction have also been found. • Comorbidities such as hypertension, diabetes, cancer, cardiovascular problems further increase the fatality rate in severe cases of COVID infection. 	<p>Its different values indicate different degrees of hypoxia.</p> <ul style="list-style-type: none"> • Deterioration of ARDS can also be correlated with altered AST (aspartate transaminase) and ALT (alanine transaminase) levels. • Ground Glass Opacity (GGO) (86%), bilateral (76%), peripheral (33%) distribution, consolidation (29%), crazy paving (19%) are the prominent features found in computed tomography (CT) scan.
Non-Respiratory Symptoms (unusual Manifestations)			
Neurological	Altered mental state, musculoskeletal disturbance, acute necrotising encephalopathy ischaemic stroke, headache, dizziness, Guillain-Barre syndrome.		
Ocular	<ul style="list-style-type: none"> • In China, 32% of infected patients showed ocular manifestations, for example, chemosis and conjunctival hyperaemia. • Tears and conjunctival seepage have shown the presence of COVID-19. • In severe COVID-19 cases, pseudomembranous and hemorrhagic conjunctivitis was also found. • Development of ptechia, tarsal pseudomembranous, mucous filaments in 63-year-old COVID-19 positive male. • External ocular infections could occur lately due to the spread of infection and physicians should take care if ocular complications exist for >2 weeks in COVID-19 patients (Navel, Chiambaretta and Dutheil, 2020). 		
Taste and Smell	<ul style="list-style-type: none"> • Olfactory dysfunction (Anosmia) is typically found to be present only in the most severe cases. • Bilateral obstruction in olfactory clefts due to inflammation; however no abnormalities were found in olfactory bulbs and tracts (Giacomelli <i>et al.</i>, 2020; Temmel <i>et al.</i>, 2004; Eliezer <i>et al.</i>, 2020). • Anosmia may persist with or without dysgeusia and manifest itself either in the early stage of progression or in patients with mild symptoms (Xydakis <i>et al.</i>, 2020; Carrillo-Larco <i>et al.</i>, 2020). 		
Cardiovascular	Heart failure, cardiac arrhythmias, pacemaker conduction defects, infections such as myocarditis and myopericarditis, chest pain (Yang <i>et al.</i> , 2020; Bonow <i>et al.</i> , 2020; Inciardi <i>et al.</i> , 2020; Driggin <i>et al.</i> , 2020; Wang <i>et al.</i> , 2020; Zhou <i>et al.</i> , 2020).		
Hematological Symptoms	Hypercoagulable state in COVID-19 patients increased the threat of thrombotic occlusion		
	Mediastinal lymphadenopathy was also found in patients with a severe form of COVID-19 (Valette <i>et al.</i> , 2020)		

Diagnosis

Richa Deshpande^{1,#}, Aishwarya Joshi^{1,#}, Nikunj Tandel¹ and Rajeev K. Tyagi^{2,*}

¹ *Institute of Science, Nirma University, Ahmedabad, Gujarat, India*

² *Biomedical Parasitology and Nano-immunology Lab, CSIR Institute of Microbial Technology (imtech), Chandigarh, India*

Abstract: Diagnosis of COVID-19 is supremely valuable in unraveling the complex dynamics involved in SARS-CoV-2 infection and in vaccine development. With an extremely high transmission rate, and initial symptoms similar to other human respiratory viruses, there has been a tremendous urge to develop and supply accurate and rapid procedures for testing the presence of SARS-CoV-2 in a plethora of patient specimens. Scientific and healthcare communities globally have been racing to develop critically needed test kits and ensure ample supply worldwide. Containing the spread of COVID-19 poses multiple challenges, including being able to correctly identify asymptomatic viral carriers that result in the silent spread of the virus, and diagnosing the infection at early stages. Current strategies employ molecular and serological testing techniques in lower and upper respiratory tract samples. The first type detects the presence of viral genetic material and can diagnose an active COVID-19 infection, whereas serological immunoassays detect viral antibodies, which can help identify individuals who have developed an adaptive immune response to the virus, as part of an active or prior infection. The newly authorized antigen tests are designed for the rapid detection of viral antigenic proteins. More elaborative diagnostic testing based on viral genomic sequencing can determine the rate and degree of mutational variability associated with SARS-CoV-2 and identifying newly emerging viral strains for more effective vaccine development. The chapter also highlights the role of rapid, easy-to-use point-of-care diagnostic tests in alleviating the challenge posed by the strain on the healthcare system and mitigating the cost of care for both individuals and the government.

Keywords: Antibody, Antigen, Biomarker, Biosensor, Chest CT, COVID-19, CRISPR, Cytokine, Detection, Diagnosis, ELISA, Hematological analysis, Immunoassay, Isothermal amplification, Microarray, POC tests, RT-PCR, SARS-CoV-2, Serology, Viral RNA.

* **Corresponding author Rajeev K. Tyagi:** Biomedical Parasitology and Nano-immunology Lab, Council of Scientific and Industrial Research Institute of Microbial Technology, Sector-39A, Chandigarh-160036, India; Tel: 91-172 6665278 (Off), 91-172-6665279 (Lab), 91-9899554047 (Cell); E-mail: rajeevtyagi@imtech.res.in and rajeev.gru@gmail.com

These authors contributed equally

COVID-19: A PANDEMIC DISEASE

With the current stage of the pandemic and the associated challenges presenting major hurdles, it is evident that highly sensitized and precise diagnostic measures for COVID-19 are paramount for rationalizing infection control initiatives, as well as for case identification and contact tracing (Chan *et al.*, 2020). There is an urgent necessity for rapid yet accurate SARS-CoV-2 diagnostic methods, with emphasis on what type of tests are available in the region, under what circumstances these tests can be used, and who should be tested (Patel *et al.*, 2020).

Similar to other infectious diseases, effective COVID-19 diagnosis relies on various parameters such as patient history, respective epidemiological conditions, clinical symptoms, and, radiological and hematological analysis. However, standard guidelines state two categories of COVID-19 tests; viral RNA tests (molecular tests) to detect the presence of SARS-CoV-2 in an active infection state, and serological tests to identify whether the subject (patient) has been exposed earlier/previously to the virus and the presence of virus-specific antibodies in the serum (Li *et al.*, 2020b). Some techniques are onerous and technically taxing, hence, there is an urgent need for rapid, cost-effective, and selectively diagnostic point-of-care (POC) tests for COVID-19 capable of providing quick yet accurate, results within a duration of possibly a few minutes (Moitra *et al.*, 2020). These POC tests allow medical diagnostic testing at the time and place of patient care while offering extra benefits of speed of diagnosis and ease of use. The current POC tests available in the market utilize the aforementioned diagnosis strategies of nucleic acid detection and analysis of antigen and/or antibodies in various sample specimens (mostly nasopharyngeal swabs). POC tests are pictured to supplement laboratory testing and enable testing to be available for remote communities and populations that lack readily accessible laboratory settings. In such secluded, crisis-struck locations, small and portable mobile POC platforms are optimal for deployment, although they are lower throughput and run one sample at a time in a specified time-frame of 5-30 minutes. They can be of great value to test moderately symptomatic patients outside clinical settings (Yang *et al.*, 2020). Higher throughput, facility-based POC platforms are also available for use in hospitals and medical centers for diagnosing top-priority specimens, such as that of frontline healthcare workers and critically-ill patients. Although POC tests are a handy component of the rapid diagnostic strategy to battle the ongoing outbreak, they are strictly recommended to be used only in conjunction with PCR-based detection. Laboratory testing undoubtedly remains the foremost testing mechanism because of the presence of complex technology specifically designed to perform a sizeable number of tests at a time. Thus, parallel use of these serology-based detection techniques alongside

molecular techniques is the way forward for mitigating the global, as well as regional load of the disease (CDC-Fact-Sheet, 2019).

COVID-19: EARLY DETECTION BASED ON SYMPTOMS

Clinical Analysis

Clinical presentation of COVID-19 is vague as symptoms coincide with other seasonal respiratory infections simultaneously circulating in the respective territorial population. It is observed that infected patients present with symptoms ranging in severity. Fever (37.5° C and above) must be carefully interpreted as even in severe cases; it can be present in moderation or even absent. Upper respiratory tract viral infection, noted as the leading symptom, was reported in more than 80% infected patients which also include mild fever, dry cough, soreness of the throat with probable nasal congestion, headache, fatigue, or malaise. Patients with moderate infection present symptoms like shortness of breath or tachypnea in children in addition to mild symptoms. On the other hand, highly infected patients are diagnosed with severe pneumonia, having fever associated with severe dyspnea, respiratory distress, cyanosis in children, tachypnea, and hypoxia (Casella *et al.*, 2020). Particularly, a chest computed tomography (CT) is the expert's recommendation for the severely infected individuals and works as an auxiliary tool alongside other standard diagnostic methods. The current pandemic status depicts that it has no age-limits as it affects the newly-born and the aged people; however, those who have crossed the age of 50 are at a relatively higher risk. Additionally, patients with a history of other comorbidities such as cardiovascular disease, diabetes, lung disease, and other types of immune suppression are also at the risk of getting an infection due to their compromised immune system. Despite measurements of the severity and other symptomatic conditions, the identification marks for the COVID-19 cases, epidemiological circumstances of the respective locations and other parameters may vary from place to place, other factors which affect the diagnosis and identification of the patients (Harapan *et al.*, 2020).

According to WHO, screening for the routine causes of respiratory illness, which delineates the season of the respective location, is the rudimentary step as and when the patient first appears with the symptoms. If a sample yields a negative result, it should be sent to a referral laboratory for SARS-CoV-2 detection. Real-time RT-PCR assay is the preferred molecular test for detecting SARS-CoV-2 infection in a clinical specimen, while serology-based techniques are used as adjunct tools. Specimen for testing must be collected from both the upper respiratory tract (*i.e.*, nasopharyngeal (NP) and oropharyngeal (OP) swabs) as well as the lower respiratory tract (*i.e.*, expectorated sputum, endotracheal

SUBJECT INDEX

A

Abdominal 117, 128, 143, 144
 discomfort 117
 pain 128, 143, 144
 Abnormalities 119, 140
 autonomic 140
 polymorphonuclear 140
 Acid(s) 24, 88, 89, 147, 167
 lactic 167
 reflux disease 147
 sialic 24, 88, 89
 Acquired immune deficiency syndrome 43
 Acute pancreatitis 136
 Acute 27, 30, 31, 33, 34, 74, 118, 119, 120,
 134, 143, 147, 148, 151
 respiratory distress syndrome (ARDS) 27,
 30, 31, 33, 34, 74, 118, 119, 143, 148,
 151
 thromboembolic disease 147
 tubular necrosis (ATN) 134
 urticaria 120
 Adenovirus 169
 Adjuvant immunotherapeutic agent 151
 Alanine aminotransferase 128, 167
 Alphacoronavirus 8, 9, 10
 Alveolar 168
 cavity 168
 septal capillary 168
 Amoxicillin 126
 Amplicon-based system 176
 Anemia 134
 Angiotensin 31, 87, 118, 148, 149
 converting enzyme 87, 118
 Anosmia 117, 119, 131, 146
 Antibodies 90, 91, 164, 165, 172, 180, 182,
 184, 185, 186, 187, 188, 189, 190
 monoclonal 90, 91, 189
 viral 164
 Anti FITC antibody 174
 Antigen, carcinoembryonic 183
 Apoptosis 24, 91, 92, 95, 97, 99, 100, 103

activation of 100, 103
 mitochondrial 97
 signaling pathways 99
 Aspartic acid glutamic acid-alanine-aspartic
 acid 96
 Aspirate 124, 167, 170
 endotracheal 170
 nasopharyngeal 124
 Assays 170, 171, 173, 176, 177, 179, 181,
 182, 184, 185, 186, 187, 188, 189, 190
 chemiluminescence 189
 colorimetric 176, 177
 developed LAMP-based 173
 direct ELISA 184
 immunological 184
 immunological/serological 181
 isothermal amplification 190
 qPCR-based 179
 rapid diagnostic test 186
 serum neutralization 187
 AtilaBioSystems 177
 ATP 96, 188
 binding 96
 dependent duplex RNA 96
 Aztecs disease 3

B

Bacillus Calmette-Guerin (BCG) 151
 Backward inner primer (BIP) 173
 Betacoronavirus 8, 10
 Bilateral 126, 142
 air space opacification 126
 patchy pulmonary infiltrates 142
 Biventricular hypertrophy 126
 Blood 3, 5, 6, 30, 83, 84, 141, 167, 170, 180,
 181
 clotting 103
 gas analysis 167
 oxygen, low 103
 Body mass index 145
 Bovine coronavirus 12

Subject Index

monitoring programs 12
transfer 12
Bradycardia 133
Breast cancer 146
Bronchiolitis 7, 29, 31
Bronchitis 11, 13
Bronchi tissue 28
Bronchoscopic biopsy 135
Bronchoscopy 135

C

Calcium homeostasis 183
Cancer 1, 2, 42, 45, 54, 119, 150
 high grade prostate 150
Canine coronavirus 20
Cardiac 34, 119, 126, 131, 134, 145, 151
 arrest 126
 arrhythmias 119, 131
 biomarkers 134
 complications 145, 151
 diseases 143
 injury 34, 119
 marker-creatine kinasemyocardial band 131
 myopathies 126
Cardiomegaly 126, 148
Cardiomyopathy 145
Cardiopulmonary 140, 146
 abnormality 140
 arrest 146
Cardiovascular 54, 119, 166
 disease 54, 166
 problems 119
cDNA 90, 172, 175, 176
 translation 90
Ceftriaxone 126
Cell(s) 21, 23, 25, 27, 28, 29, 83, 84, 85, 86,
 88, 89, 91, 92, 94, 96, 97, 100, 103, 137,
 173, 180, 187
 cycle arrest 96
 dendritic 83, 84, 91
 fusion 27, 88
 growth arrest 100
 hepatic 27, 29

COVID-19: Diagnosis and Management-Part I 201

intestinal 28
lysate 173
neuroglial 29
neuronal 92
proliferation 96
white blood 137, 180
Central nervous system 11
Cerebral 148
 arteriosclerosis 148
 stroke 148
Cerebrovascular disease 143
Chemiluminescent immunoassay 179
Chemosis 119, 120
Chest 74, 119, 123, 125, 128, 130, 136, 138,
 144, 147
 distress 128
 pain 74, 119, 130, 136, 138, 147
 radiographs 123, 125, 136, 139, 144
Chinese 62, 63
 embassies 63
 national health commission 62
Chromatography 185
Chronic 11, 45, 141, 143, 145, 146, 148
 coughs 143
 health problems 45
 kidney disease 141, 145, 146
 pancreatitis 148
 progressive neurologic disease 11
Ciliostasis 27
Clarithromycin 126
Clotting disorders, frequent 167
Clustered regularly interspaced short
 palindromic repeats (CRISPR) 164, 174
CNS 11, 25, 29, 89, 92
 demyelination 11
 disease 25
 infiltration 11
 pathogenesis 92
Cohort study 148
Colorimetric-based biosensing applications
 176
Colorimetric bioassays 176
Community 75, 76, 164, 169
 healthcare 164
Community transmission 33, 60, 65, 75, 180

- Comorbid diseases 133
 Comorbidities, cardiac 133
 Computerized tomography angiography (CTA) 138
 Confirmed cases of COVID-19 in India 59
 Congenital heart defect 131
 Conjugate, antibody-enzyme 185
 Conjunctival 6, 119, 120
 hyperaemia 119, 120
 secretions 6
 Conjunctivitis 3, 7, 29, 119
 hemorrhagic 119
 Consolidation 117, 119, 126, 129, 131, 134, 136, 138, 139, 143, 144, 145, 147, 148
 bilateral pulmonary 144
 Contagious diseases 2, 76, 121
 deadly 76
 Convalescent plasma (CP) 180
 Coronary 145, 148
 artery disease 145, 148
 heart disease 145
 Coronavirus 6, 7, 9, 10, 11, 18, 19, 20, 21, 27, 43, 44, 45, 83, 101, 102
 respiratory 9
 Coronavirus disease 7, 8, 11, 33
 Coronaviruse(s) 1, 7, 8, 9, 10, 11, 12, 13, 18, 19, 33, 36, 43, 68, 71, 73, 83, 170
 infection 43, 73, 83
 outbreak 71
 pandemic 68
 RNA 170
 Cough 7, 30, 32, 34, 35, 60, 117, 118, 125, 126, 127, 130, 131, 132, 133, 135, 136, 137, 141, 142, 143, 144, 145, 146, 147, 148, 166, 168
 dry 30, 32, 117, 118, 127, 130, 133, 136, 137, 143, 146, 147, 166, 168
 etiquette 32
 persistent 148
 productive 145, 146
 CoV associated protein 99
 COVID-19 44, 65, 66, 67, 68, 74, 118, 124, 125, 126, 127, 130, 131, 138, 143, 150, 152, 178, 180
 co-infections 127
 Coronavirus 178
 disease symptoms 180
 epidemiology 44, 74
 infection 65, 66, 67, 68, 118, 124, 125, 126, 127, 130, 131, 138, 143, 150, 152
 PCR test 54, 141
 related deaths 54
 situation in Africa 68
 COVID-19 pandemic 43, 44, 45, 60, 66, 73, 75, 77, 143, 152
 in France 66
 in Germany 73
 in India 44, 60
 CoV 84, 85, 86, 88, 91, 97, 100, 102, 104
 infection 84, 85, 86, 88, 91, 97, 100, 102, 104
 proteins 97
 C-reactive protein (CRP) 128, 134, 142, 167
 and procalcitonin 142
 CRISPR 174, 190
 associated assays 190
 isothermal amplification based assays 174
 Crohn's disease 145
 Cystic fibrosis 124
 Cytokine 141, 168, 183, 184
 mediated lung damage 183
 storm 141, 168, 184
- D**
- Deltacoronaviruses 8
 Dengue virus 189
 Detection 164, 165, 167, 170, 173, 174, 176, 177, 178, 179, 181, 182, 184, 186, 188, 189, 190
 biosensor-mediated 189
 luminescence 188
 nucleic acid 165
 qPCR-based 179
 respiratory virus 190
 systems 188
 Diabetes mellitus 136, 141, 143, 145, 146, 148
 and hyperlipidemia 136
 Diaphoresis 136, 140

Subject Index

Diarrhea 27, 28, 30, 32, 35, 125, 130, 136, 143, 144, 146
Dipeptyl peptidase 32
Disease 1, 2, 4, 5, 11, 12, 30, 31, 33, 42, 44, 45, 73, 76, 169, 180, 183
 epidemiology 180
 modulation 183
 related conditions 44
Distress syndrome 18, 27, 30, 31, 33, 45, 74, 118
 acute respiratory 27, 30, 31, 118
 developed acute respiratory 74
 respiratory 18
 severe respiratory 33
Dizziness 119, 135
DNA amplification 173
Droplets, respiratory 6, 7
Dyslipidemia 141
Dyspnea 117, 118, 119, 125, 126, 130, 135, 136, 138, 142, 143, 144, 145, 146, 147, 166
 acute 147
 progressive 142
 severe 118, 166

E

Ebola virus 6
EBV and COVID-19 co-infections 127
Echocardiography 126
Edema 5, 30, 168
 hemorrhagic 5
 interstitial 168
Effective screening methods 64
Electrochemical 188, 189
 biosensors 188
 impedance spectroscopy (EIS) 188, 189
Electro-chemiluminescence Immunoassay 179
ELISA assays 184
Emergency, national 67
Encephalitis 11, 19, 29, 135
Encephalomyelitis 9
Encephalopathy 137
Encode ACE2 protein 149

COVID-19: Diagnosis and Management-Part I 203

Endonuclease 94
Endoribonuclease 25, 86
Enteric 9, 20, 27, 28
 infection 9, 20
 systems 27, 28
Enteritis 19, 27, 28
 viral 27
Enterocytes 148
Enzyme-linked immunosorbent assay (ELISA) 164, 172, 179, 184, 185, 189
Enzymes 25, 27, 84, 93, 94, 148, 167, 172, 174, 184, 185
 muscle 167
 myocardial 167
 proteolytic 27
 reverse transcriptase 172
 transmembrane 148
Enzyme-substrate reaction 184
Epidemic 1, 2, 32, 43, 62, 76
Epithelial cells 27, 28, 83, 84, 100, 101, 103, 148
 alveolar 27
 regeneration of 103
Epstein-Barr virus (EBV) 127
Erythrocyte sedimentation rate (ESR) 167
Esterase 20, 24, 87, 88, 89
 activity 89
 domain 87
 hemagglutinin 20, 24
Eukaryotic translation initiation factor 96
Exonuclease 25, 86

F

Factors 11, 25, 44, 54, 60, 103, 118, 120, 150, 166, 167, 181
 basic fibroblastic growth 167
 colony-stimulating 167
 epithelial growth 103
 immune response 25
 inflammatory 167
 platelet-derived growth 167

Fever 1, 4, 117, 118, 120, 123, 125, 126, 131, 135, 140, 142, 143, 144, 145, 146, 147, 148, 151, 166

low-grade 120, 126
mild 166
yellow 1, 4, 151

Flu 1, 4, 6, 30
swine 1, 4, 6

Focal status epilepticus 147

Functions 21, 83, 85, 93, 94, 100, 130, 180
haematopoietic 130
viral 180

Fusion, mediating membrane 88

G

Gastroenteric disease 12

Gastroenteritis 7, 123

Gastroesophageal reflux 123

Gastrointestinal symptoms 144

Gene 21, 170

accessory 170
replicase 21

Genome 8, 18, 21, 24, 25, 28, 43, 89, 170, 174
respiratory virus 174

single-stranded RNA 170

Genomic 36, 44, 92, 93

analysis 36
sequence 44

Global epidemiology 43, 45

Glomerulopathy, collapsing 141

Glucose-6-phosphate dehydrogenase
deficiency 146

Glutathione S-transferase 94

Glycoprotein 20, 21, 22, 24, 27, 86, 88
glycosylated 27

peplomer 20
receptors 24, 88

Glycosylated polypeptide 24

Gold nanoparticles-based colorimetric assay
176

Ground glass opacity (GGO) 119, 122, 123, 128, 130, 134, 136, 139, 143, 144, 145, 146, 147, 148

Grover disease 146

Guillain Barne syndrome (GBS) 145

H

Headache 3, 34, 60, 74, 118, 119, 128, 132, 135, 140, 144

Head CT scan 127

Health 42, 45, 73, 169

circumstances 73
emergencies, global 169
system 42, 45

Healthcare 65, 68

facilities, standard 68
professionals 65

Health risk 18, 104

factors 104
global 18

Heamglutinin esterase protein 21

Helicase 18, 21, 25, 85, 95, 170

Hemaagglutinating encephalomyocarditis
virus 20

Hemagglutinin 24, 88, 170

esterase 24, 88, 170
esterase protein 24

Hematological 119, 164, 165, 167

analysis 164, 165, 167
symptoms 119

Hematology reports for total white blood cell
125

Hemoperfusion 134

Hemoptysis 34, 138

Hemorrhagic 6, 132, 147

fever 6
infarct 132
rash 147
venous infarct 132

Hepatic infection 9

Hepatitis 11, 12, 19, 20, 25, 29, 92, 93, 97, 142, 150

C virus (HCV) 97
chronic 142

developed acute 12

Hepatocytes 183

Subject Index

Herpes simplex virus (HSV) 137, 147
Human 5, 36, 97, 104, 136, 137, 169, 170, 175
 immunodeficiency virus (HIV) 5, 97, 137
 pancreatitis 136
 transmission 36
 viruses 104, 169, 170, 175
Human respiratory 9, 11, 20
 coronaviruses 11
 infections 9, 20
Hygiene, basic 1
Hyperglycemia 117
Hyperlipidemia 136, 147
Hyperplasia 141
Hypertension 1, 34, 117, 119, 141, 142, 143,
 145, 146, 147, 148, 149
 arterial 145, 148
Hypertensive 143, 148
 cardiopathy 148
 nephropathy 143
Hyperthermia 18, 30, 32, 34
Hypoproteinemia 148
Hypotension 134
Hypothyroidism 145
Hypoxemia 35, 142

I

Illness, contagious 2
Immature immune systems 121
Immune 28, 101
 markers, preliminary 101
 -mediated pathology 28
Immune cells 5, 29, 31, 32
 innate 32
Immune reaction 27
 innate 27
 virus-mediated 27
Immune responses 29, 98, 101, 103, 164, 180,
 183, 190
 acquired 103
 adaptive 164
 antiviral 98
 innate 183

COVID-19: Diagnosis and Management-Part I 205

Immune system 5, 29, 31, 34, 42, 45, 66, 77,
 120, 121, 151, 152, 181
 compromised 166
 innate 120
 weak 45
Immunity 29, 76, 117, 121, 151, 181, 190
 acquired 121
 adaptive 97
 cell-mediated 29
 post-infection 181
Immunoassays 164, 179, 181, 186, 188, 189
 colorimetric enzyme 189
 serological 164, 181
Immunodeficiency 76
Immunoglobulins 31, 181, 186
Immunosuppressant 92, 127
Indian council of medical research (ICMR) 60
Infection 1, 11, 18, 20, 28, 29, 30, 31, 32, 34,
 60, 65, 66, 69, 72, 73, 76, 91, 102, 118,
 119, 121, 150, 151, 152, 167, 179, 181,
 183, 190
 acute 11, 29
 bacterial 167
 chronic pulmonary 18
 conducting airways 102
 corona 65, 66
 hospital-acquired 34
 intestinal 30
 invasive bacterial 183
 neurologic 20
 respiratory virus 121
 severe systemic 28
 transmission 73
Infectious 1, 3, 9, 18, 20, 23, 28, 84, 165
 bronchitis virus (IBV) 9, 18, 20, 23, 28, 84
 diseases 1, 3, 165
Inflammation 28, 97, 119, 135, 183
 indicated patchy chronic 135
Inflammatory pathologies 183
Influenza virus 5, 190
Interferon(s) 25, 27, 91, 92, 96, 99, 100, 101,
 167
 activation 99
 release 27
 signaling 99, 100

synthesis 96
 International non-government organizations
 (INGOs) 73, 74
 Intracellular signaling cascades 97

L

Left ventricular ejection fraction (LVEF) 145
 Lesions 11, 168
 outspread demyelinating 11
 Liver 11, 25, 30, 91, 92, 93, 127, 167
 damage 25, 92
 enzymes 167
 transplantation 127
 Load, viral 31, 100, 187
 Lockdown 44, 61, 62, 63, 64, 65, 68, 69, 70,
 71, 72, 73, 77
 effect of 44, 69
 national 71
 nationwide 72
 measures 73
 partial 63
 period 71
 restrictions 73
 Long-chain fatty acid 188
 Luminescence-based immunoassays 188
 Luminescent immunoassay 188
 Lymphopenia 30, 34, 92, 126, 143

M

Malignancy 146
 Maltose-binding protein (MBP) 94
 Mediastinal lymphadenopathy 119
 Membrane 27, 30, 185
 hyaline 27, 30
 nitrocellulose 185
 Membrane protein 18, 21, 23, 24, 26, 27, 83,
 87, 90
 Mengovirus 152
 Metabolic acidosis 146
 Metagenomic 175
 approaches 175
 sequencing based methods 175

Methyltransferase 86
 Microcytic anemia 132
 Middle East respiratory 4, 10, 11, 13, 18, 31,
 33, 35, 43, 177
 syndrome (MERS) 4, 10, 11, 13, 18, 31, 33,
 35, 43, 177
 virus 31
 MinION sequencing technique 175
 Ministry of health and family welfare
 (MoHFW) 72
 Mitochondrial antiviral signaling protein 99
 Mitogen-activated protein kinase 100
 Mobile analysis platform (MAP) 175
 Monocyte chemo-attractant protein 167
 Mounier-Kuhn Syndrome (MKS) 143
 mRNA 25, 26, 86, 93, 95, 96, 97
 genomic 86
 subgenomic 93
 synthesis 25, 26, 86
 viral 96, 97
 Murine 9, 11, 13, 19, 20, 23, 24, 27, 29, 38, 84
 coronavirus 11, 29
 hepatitis virus (MHV) 9, 11, 13, 19, 20, 23,
 24, 27, 29, 38, 84
 Musculoskeletal disturbance 119
 Mutations 18, 20, 89, 91, 94, 95, 149, 175,
 176
 unglycosylated M-protein 91
 viral gene 176
Mycobacterium bovis 151
 Myocarditis 31, 119
 Myopericarditis 119

N

Neurodegenerative diseases 117
 Neurological disorders 28
 Neurologic complications 132
 Neuropathogenesis 89
 Neutralization assays 187
 Nikolaidis 103
 Non-small cell lung cancer (NSCLC) 145, 146
 Nucleic acid 124, 170
 amplification assays 124

Subject Index

tests 170
Nucleic acid detection 170
 kits 170
 strategies 170
Nucleocapsid 21, 24, 25, 27, 32, 83, 84, 85,
 87, 92, 97, 166, 167, 170, 182
 protein (NP) 21, 24, 25, 27, 32, 83, 87, 97,
 166, 167, 170

O

Obstructive sleep apnea 145
 syndrome 145
Olfactory dysfunction 119
Organ 31, 119
 dysfunction, multiple 119
 failure 31
Organisms, pathogenic 176

P

Pain 117, 136, 141, 143, 144, 145, 147
 epigastric 136, 143, 147
 hip 145
 muscle 136
Painel coronavirus 71
Pancytopenia 130, 134
Pandemic(s) 1, 2, 3, 4, 5, 6, 7, 31, 32, 33, 42,
 43, 44, 61, 65, 66, 77, 165
 corona 66
 disease 165
 infectious 77
 influenza 3, 43
 real plague 4
Papain-like protease (PLP) 25, 85, 95
Parainfluenza virus 130
Pathogenesis 7, 25, 83, 86, 88, 89, 151
 influenza 25
 viral 83, 88
Pathogenic 23, 169
 agents 169
 phenotype 23
Pathogens 13, 33, 121, 173, 175, 176, 187,
 188

COVID-19: Diagnosis and Management-Part I 207

infectious 173
 respiratory 13
Pathophysiology of coronavirus 102
PCR-based 165, 173, 179
 detection 165
 methods 173
 techniques 179
Personal protective equipment (PPE) 68
Placental transmission 36
Plaque reduction neutralization assays
 (PRNA) 187
Pneumonia 7, 11, 13, 18, 29, 31, 32, 34, 117,
 118, 127, 130, 143, 146, 147, 151, 152,
 166
 acute 31
 interstitial 127, 147
 life-threatening 7, 32
 severe 117, 118, 130, 166
Pneumonitis 12, 31
Poliovirus 93
Polymerase 20, 21, 25, 170, 172, 176, 186
 chain reaction (PCR) 170, 172, 176, 186
 dependent RNA 20, 25
Processed recombinant proteins 94
Processing precursor proteins 93
Prognosis 120, 184
Properties 10, 23, 24, 94, 95, 98, 151
 endo-ribosomal 94
 entero-pathogenic 24
 immunomodulatory 151
 interferogenic 24
 phylogenetic 10
 pneumo-protective 23
Protease 21, 23, 25, 85, 88, 90, 93, 95, 98,
 182, 183
 activity 95
 cellular 88
 cysteine 98, 182
 enzyme 23
Proteins 21, 23, 24, 25, 26, 27, 83, 84, 85, 86,
 87, 88, 89, 90, 91, 92, 93, 94, 95, 97, 99,
 104, 178, 179, 182
 accessory 21, 84
 cellular 97
 endogenous 83

- endosomal 104
 - fibrinogen-link 92
 - hemagglutinin-esterase 83, 87
 - maltose-binding 94
 - viral 26, 85, 86, 99, 104, 182
 - Protein synthesis 96, 97, 100
 - cellular 100
 - Proteolytic degradation 27
 - Public health 5, 67, 83, 169
 - crisis 83
 - emergency 67
 - interventions 169
 - officers 5
 - Pulmonary 103, 135, 146, 147
 - disease 135
 - embolism 146, 147
 - toxin 103
- R**
- Rapid 172, 189
 - antigen detection tests 189
 - detection test 172
 - Real-time RT-PCR assay 166
 - Receptor binding domain (RBD) 23, 31, 86, 87, 179, 182
 - Receptor-binding motif (RBM) 87
 - Recombinant viruses 99
 - Red blood cells (RBCs) 151
 - Renal 54, 137, 141
 - disease 54
 - functions deteriorate 141
 - injury 137
 - Renal failure 31, 143
 - chronic 143
 - Renin-angiotensin system 23, 88
 - Replicase 18, 25, 26, 93
 - proteins 25, 93
 - Replication proteins 83
 - Resin-angiotensin system 88
 - Respiratory 29, 37, 84, 117, 126, 131, 137, 127, 144, 145, 146, 166, 183
 - alkalosis 146
 - arrest 137
 - complications 127
 - distress 29, 37, 84, 117, 126, 131, 144, 145, 146, 166
 - dysfunction 183
 - Respiratory disease 6, 7, 8, 12, 13, 54
 - bovine 12
 - Respiratory illness 6, 7, 12, 124, 166
 - contagious 7
 - viral 6
 - Respiratory infections 19, 20, 28, 29, 151, 166, 169
 - acute 169
 - Respiratory syndrome 10, 18, 29, 83, 186
 - coronavirus, severe acute 83, 186
 - Respiratory tract infection 18, 32, 124
 - lower 32
 - upper 124
 - RNA 20, 21, 25, 27, 85, 86, 92, 93, 94, 96, 99, 176, 190
 - and DNA duplex 94
 - modification enzymes 21
 - genetic 86
 - multiple sub-genomic 25
 - small nucleolar 94
 - subgenomic 25
 - RNAemia 34, 119
 - RNA binding 24, 95
 - motif 95
 - protein 24, 95
 - RNA-dependent 85, 93, 96, 170
 - ATPase activity 96
 - RNA polymerases 85, 93, 170
 - RT-LAMP-VF assay 174
 - RT-PCR 100, 134, 171, 175
 - real-time 175
 - assays 171
 - for viral RNA 100
 - test of nasopharyngeal swab 134
- S**
- Sandwich ELISA 184
 - SARI infections 59, 60
 - SARS-associated coronavirus 6

Subject Index

SARSCoV-2 infection 168
SARS-CoV-2 23, 142, 149, 171, 173, 175, 181, 189
 infection, symptomatic 171
 proteins 181
 RNA 142, 171, 175
 S1 protein 189
 detection rates and LAMP assay sensitivity 173
 genomic mutations 175
 infection 23, 149
 spike protein 23
SARS disease 6
Senile heart valve disorders 148
Septic shock 37, 117, 126, 142, 143
 managing 37
Severe acute respiratory 1, 2, 3, 4, 6, 11, 18, 23, 24, 29, 30, 31, 32, 33, 43, 59
 infection (SARI) 59
 syndrome (SARS) 1, 2, 3, 4, 6, 11, 18, 23, 24, 29, 30, 31, 32, 33, 43
Sickle cell disease 134
Signs of anicteric cholestasis and cytolysis 127
Single nucleotide polymorphisms (SNP) 175
Sjogren-syndrome 141
Sleep-disordered breathing (SDB) 142
Spike proteins 21, 22, 23, 24, 25, 26, 27, 83, 85, 86, 87
Surface plasmon resonance (SPR) 97, 176, 188

T

Tachycardia 137
Techniques 164, 165, 166, 169, 170, 171, 172, 173
 efficient sampling 171
 non-PCR-related 170
 novel nucleic acid amplification 172
 nucleic acid amplification 173
 reliable laboratory detection 169
 serological testing 164
 serology-based 166

COVID-19: Diagnosis and Management-Part I 209

 serology-based detection 165
Techniques-chromatography 188
Technology, surface plasmon resonance biosensor 97
Therapy 130, 145, 172, 180, 187
 convalescent plasma 180, 187
 oxygen 37
 radiation 145
Thoracic malignancy 145
Throat 30, 32, 35, 60, 74, 117, 118, 122, 128, 131, 133, 139, 144, 166, 168
 sore 30, 32, 35, 60, 74, 117, 118, 128, 131, 133, 139
 swab 122, 168
Thrombosis 83, 103, 132, 146
Thrombotic 142, 151
 complications 142
 disorders 151
Time-resolved fluorescence immunoassay 179
Traction bronchiectasis 172
Transcriptional regulatory sequences (TRS) 89, 92
Transmembrane 20, 88, 89, 150
 glycoprotein 20
 motifs 89, 90
 protease/subfamily 88
 serine protease 150
Transmembrane proteins 23, 148, 170
 integral 23
Transmissible 6, 27
 disease 6
 gastroenteritis virus 27

V

Vaccination 5, 76, 117, 121, 152
Vaccines 1, 5, 12, 31, 36, 43, 76, 77, 104, 151, 152, 175
 killed 12
Vaginal secretions 5
Vascular endothelial growth factor-A (VEGFA) 167
Venous thrombo embolism (VTE) 132

Viral 32, 34, 61, 66, 86, 88, 89, 92, 95, 96, 97, 98, 100, 135, 164, 166, 171, 173, 179, 182, 183, 184, 187
diseases 32, 100
genetic material 164
genome translation 95
infections 61, 66, 88, 89, 92, 96, 97, 166, 173, 179, 183, 187
invasion 34
key proteinase 98
load kinetics 171
memory 182
pathology 84
RNA 86, 100, 135, 164, 171
Viral RNA 165, 171
load 171
tests 165
Virions 20, 21, 23, 24, 25, 26, 27, 89, 90
Virulence factors 95, 99
Virus 5, 7, 9, 11, 12, 18, 19, 20, 21, 23, 24, 25, 27, 28, 29, 31, 33, 44, 64, 83, 84, 86, 89, 90, 91, 92, 97, 100, 104, 137, 149, 152, 169, 179
diarrhea 9
encephalomyocarditis 152
human immunodeficiency 5, 97
infectious 92
infectious bronchitis 9, 18, 20, 84
infectious peritonitis 19
like particles (VLPs) 86, 90, 91
live attenuated 12
measles 97
murine hepatitis 11, 19, 84
porcine hemagglutinating encephalomyelitis 19
recurrent Herpes Simplex 137
single positive-sense RNA 7
single positive-stranded RNA 83
single-stranded positive RNA 104
smallpox 5
transmissible gastric enteritis 84
Vomiting 117, 123, 125, 126, 127, 130, 133, 136, 139, 141, 144

W

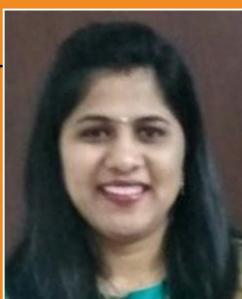
White 10, 125, 137, 167, 180
blood cell (WBC) 125, 137, 167, 180
eye coronavirus 10
World health organization (WHO) 1, 2, 3, 6, 7, 8, 31, 33, 34, 44, 55, 65, 68, 73, 84

X

Xenopus laevis 94

Z

Zika virus 169
Zinc finger configuration 94



Neeraj Mittal

Dr. Neeraj Mittal works as a scientist B at the Department of Endocrinology, PGIMER, Chandigarh. She completed her M. Pharmacy and PhD (Pharmaceutics) from the Department of Pharmaceutical Sciences and Drug Research, Punjabi University, Patiala. She has worked as a research fellow in DST-funded projects during her doctorate degree. Dr. Neeraj has 7 years of research experience. She has more than 12 publications in national and international journals. Dr. Neeraj has research interests in nanotechnology, bioadhesive drug delivery systems, and other novel drug delivery systems.



Sanjay Kumar Bhadada

Prof. Sanjay Kumar Bhadada (MD, DM (Endocrinology and Metabolism), FICP, FRCPI, and MNAMS) is a professor and the head at the Department of Endocrinology, PGIMER, Chandigarh, which is a premier medical institute of the country, known for its research and patient care worldwide. Currently, he is the National Executive and Ex-Secretary of the Indian Society for Bone and Mineral Research (ISBMR). He is a regular speaker at annual conferences of RSSDI, Endocrine Society of India (ESI), and ISBMR. He has more than 250 publications in highly reputed journals, 14 book chapters, 6 edited books, and 2 patents. He has guided 18 PhD/DM students and 20 MD/MS/MCh students. He has given more than 200 invited talks. Dr. Bhadada has research collaboration with international institutes like Henry Ford Hospital, Detroit, USA and Antwerp University, Belgium, and national institutes. He is the section editor of the ESI Manual of Endocrinology. He has contributed a chapter in the 14th Edition of Williams textbook of Endocrinology. He has received prestigious awards like Prof. Survir Singh Visiting Professorship by Association of Physicians of India, PN Shah and Subash Mukherjee Oration awards by Endocrine Society of India. He also received prestigious M N Sen Oration and Om Prakash Kunti awards by ICMR. He created a social support group for type 1 DM individuals called "ADITI."



Om Prakash Katare

Prof. Om Prakash Katare is currently working as a professor at the University Institute of Pharmaceutical Sciences, Panjab University, Chandigarh. He has published >250 publications, 20 book chapters, 5 edited books, and 19 patents. He has guided 25 PhD students and 50 post-graduate students. He is also working as a reviewer for reputed professional journals. Dr. Katare has an active association with different societies and academies around the world. He has given >150 invited talks. Dr. Katare made his mark in the scientific community with his contributions, gaining wide recognition from honorable subject experts around the world. Dr. Om Prakash Katare has received several awards for the contributions to the scientific community. He has successfully transferred and commercialized 3 novel pharmaceutical products like Psorisome™, Lipotar™ S, and Lipotar™ SS.



Varun Garg

Dr. Varun Garg completed his PhD in Pharmaceutics from the School of Pharmaceutical Sciences, Lovely Professional University. He has published 27 papers in international journals and authored 2 book chapters. He has presented 12 papers at national and international conferences. He has developed himself with a unique profile involving an interplay of research, technical, and medical skills. He has experience of 7 years in medical affairs and has worked with Biocon and Zydus Cadila. Apart from his academic activities, he is actively involved in presenting his research work at different national and international scientific forums.