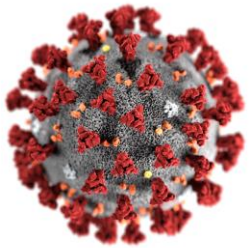
COVID 19 – Yesterday, Today, and Tomorrow



Rafael Pomales, Jr., MHS, PA-C, DFAAPA
Robert S. Smith, MS, DHSc, PA-C, DFAAPA

PA
AAPA CATEGORY 1 CME

Disclosures

Rafael Pomales, Jr., MHS, PA-C, DFAAPA

- I have no relevant relationships with ineligible companies to disclose within the past 24 months.

Robert S. Smith, MS, DHSc, PA-C, DFAAPA

- I have no relevant relationships with ineligible companies to disclose within the past 24 months.

Objectives

Learning Objectives:

- Discuss the history of COVID 19
- Identify the most common signs and symptoms of COVID 19
- Identify the most current treatment modalities in treating COVID 19 in family practice
- Identify the long-term effects of COVID 19, and how to treat those affects
- Apply presented materials in daily practice

Covid 19 – Epidemiology Yesterday

Brief History of the Pandemic

- December 12, 2019 – The first Covid-19 infection occurs in Wuhan, China with a patient getting sick with an unknown type of pneumonia, that quickly infects others. December 29, 2019, the total has increased to 59 cases – 169 people being monitored for this illness,
- December 31, 2019, Chinese Authorities report findings to World Health Organization (WHO) that they were dealing with an outbreak caused by an unknown virus.
- January 9, 2020, WHO announces a mysterious Coronavirus-related Pneumonia. Health care workers should be on the lookout for patients with respiratory symptoms traveling from Wuhan, China.

AJMC (2021)

Covid 19 – Epidemiology Yesterday

Brief History of the Pandemic

- January 21, 2020, First U.S. confirmed COVID-19 case – Washington state resident traveled from Wuhan, China on 15 January 2020. The patient died on 29 February 2020 thought to be the first, however 2 other patients had died earlier, but were not confirmed until months later.
- January 21, 2020, Zhong Nanshan, MD, a prominent Chinese scientist, confirmed that the mysterious coronavirus that has killed at least 4 people and infected more than 200 in China is capable of being transmitted from person to person.
- January 23, 2020, Wuhan, China – 13 more deaths in 2 days, 300 now sick. Wuhan, China quarantined along with surrounding communities within 30 miles (18 million people)
- January 31, 2020, WHO Issues “Global Health Emergency”, worldwide death toll >200 and more than 9800 cases. Human-to-human transmission found in the U.S., Germany, Japan, Vietnam, and Taiwan.

AJMC (2021)

Covid 19 – Epidemiology Yesterday

Brief History of the Pandemic

- February 2, 2020, Global air travel is restricted.
- February 3, 2020, U.S. declares public health emergency
- March 11, 2020, WHO Declares COVID-19 a Pandemic
- March 13, 2020, President Trump declares COVID-19 a “National Emergency”
- March 17, 2020, U.S. Lockdown begins. (2-week quarantine period for exposure)
- December 14, 2020, First COVID-19 Vaccine – Pfizer given to a Nurse – Sandra Lindsay (Black, female)

AJMC (2021

Covid 19 – Today
The Numbers

- Worldwide cases of Covid 19 - 323,864,201 with 5.52 million deaths and about 265,237,406 million recoveries (14 Jan 2022).
- The country with the highest number of new cases is the US (14 Jan 2022).
- U.S. case total is 65,976,500 and 871,333 deaths, 43 million recoveries – 2% of the resolved cases ended in death: twice as many as any other country the second-place country is India 36,849,474 cases and 485,780 deaths (14 Jan 2022)

World Health Organization, (14 Jan 2022) / CDC (14 JAN 2022)

Covid 19 – Today
The Numbers

- One (1) in 6 U.S. Residents have been confirmed infected and 1 in 487 have died from COVID -19 (Jan 2022).
- An average of 137, 931 people were hospitalized (14 Jan2022)
- 83% of the ICU beds in the U.S. occupied by COVID 19 Patients
- Majority of patients entering hospital for COVID 19 UNVACCINATED although can vary by region.

World Health Organization (14 Jan 2022) / New York Times (14 Jan 2022)

Covid 19 – Today
The Numbers

- Total U.S. Population - 328.2 million (2020)
  - White – 61.6% - 202,171,200 people
  - Hispanic or Latino – 18.7% - 61,373,400 people
  - Black – 12.4% – 40,696,800 people
  - Asian – 6.0% - 19,692,000 people
  - Native American and Alaska Native 1.1% - 3,610,200 people
  - Native Hawaiian and Other Pacific Islander .02% - 656,400

*These totals do not include other races or two or More Races

Multiple Races – Estimated to be about 2.8% or 9,189,600 of the total population.

U.S. Census 2020

Covid 19 – Today
The Numbers

As of 14 January 2022

Total U.S. Covid-19 Cases by Race/Ethnicity all age groups – Percentage of Cases

- Whites: 18,084,644 (54.8%)
- Latinos: 7,998,898 (24.2%)
- Blacks: 4,029,390 (12.2%)
- Asians: 1,139,239 (3.4%)
- Native American /Alaska Native: 332,035 (1%)
- Native Hawaiian/Pacific Islander: 101,310 (0.3%)
- Multiple / Other : 1,318,770 (4%)

Numbers extrapolated from data from cases that reported ethnicity (64%)

CDC, (14 Jan 2022 / Ndugga, Hill, and Artiga (2022)

Covid 19 – Today
The Numbers

As of 14 January 2022

Total U.S. COVID-19 deaths by Race/Ethnicity

- Whites: 384,386 (62.5%)
- Latinos: 104,445 (17%)
- Blacks: 82,852 (13.4%)
- Asians: 21,158 (3.4%)
- American Indian/Alaska Native: 6,806 (1.1%)
- Native Hawaiian/Pacific Islander: 1,492 (0.2%)
- Multiple /Other: 14,511 (2.4%)

Numbers extrapolated from data from cases that reported Race / Ethnicity (84%)

CDC (14 Jan 2022) / Ndugga, Hill, and Artiga (2022)

COVID 19 - VARIANTS

Like other RNA viruses, SARS-CoV-2 (COVID-19) is constantly evolving through random mutations. New mutations:

- Can potentially increase or decrease infectiousness and virulence.
- Can increase the virus' ability to evade adaptive immune responses from past SARS-CoV-2 infection or vaccination.
- May increase the risk of reinfection or decrease the efficacy of vaccines.
- Evidence that some SARS-CoV-2 variants have reduced susceptibility to plasma from people who were previously infected or immunized
- Reduced susceptibility to monoclonal antibodies (mAbs) that are being used for prevention and treatment.

NIH (2021)

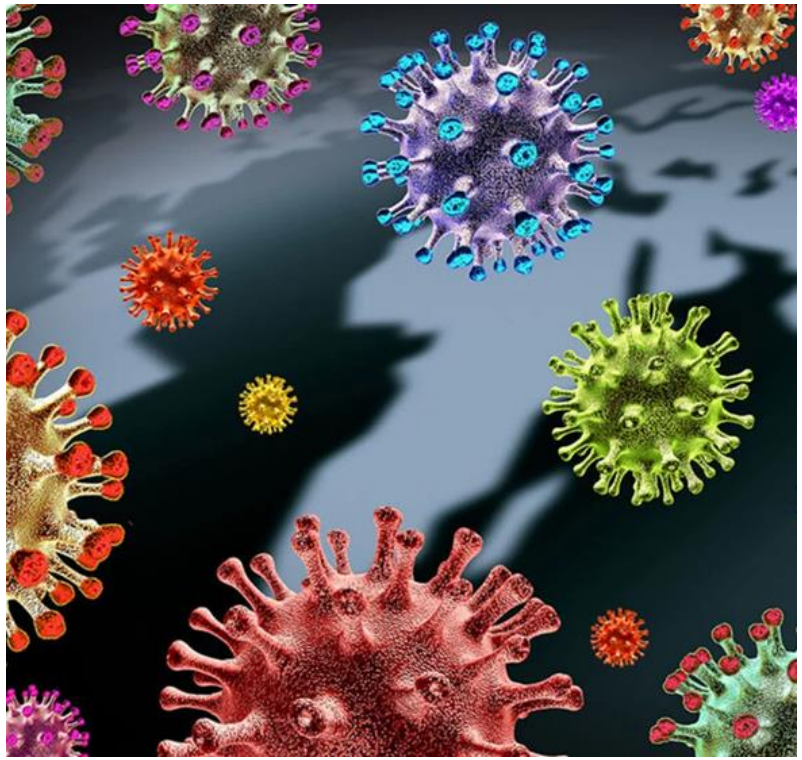
COVID 19 - VARIANTS

Since December 2020, the World Health Organization (WHO). Has assigned Greek letter designations and the SARS-CoV-2 variants are designated into categories based on certain characteristics

- **Variants of concern (VOC)**
- **Variants of interest (VOI)**
- **Variants being monitored (VBM)**

NIH (2021)

COVID 19 VARIANTS



Variants of Concern (VOC) - Increased transmissibility or detrimental change, increased virulence in clinical disease presentation, decreased effectiveness in social measures or available diagnostics or therapeutics

- Alpha – United Kingdom – 18 DEC 2020
- Beta – South Africa – 18 DEC 2020
- Gamma – Brazil – 11 JAN 2020
- DELTA – India – 11 MAY 2021
- Omicron – Multiple – 26 NOV 2021

WHO (2022)

COVID 19 VARIANTS

Variants of Interest (VOI) – Genetic Changes, increased transmissibility, severity, immune escape, diagnostic or therapeutic escape. Increasing prevalence, increasing risk globally

- Lambda – Peru – 14 JUN 2021
- MU – Columbia – 30 AUG 2021

WHO (2022)

COVID 19 VARIANTS

Variants under monitoring (VUM) - Genetic changes that are suspected to affect virus characteristics, some indication that may pose a future risk, evidence of phenotypic or epidemiological impact is currently unclear, requiring enhanced monitoring and repeat assessment pending new evidence.

- B.1.1.318 – Multiple Countries – 02 JUN 2021
- C.1.2 – South Africa – 01 SEP 2021
- IHU - B.1.640 – France / Cameroon – 22 NOV 2021

WHO (2021)

Covid 19 – Transmission

Viral Transmission

- Close contact of infected person – person – person via respiratory droplet
  - Through exposure of mucosal surfaces of the host - Eyes, nose, mouth
- Fomite Contact
  - Bedsheet, blankets, kitchen utensils, thermometers and stethoscopes
- Airborne Transmission (Limited)
  - Specific Circumstances
    - Endotracheal intubation, bronchoscopy, suctioning, nebulization with O2, bag-mask ventilation, tracheostomy and CPR.

Parasher (2021)

Covid 19 – Diagnostic Testing

Diagnostic Testing for SARS-CoV-2 Infection

- Testing should be completed on any patient who has symptoms that are consistent with COVID-19, as well as people with known high-risk exposures to SARS-CoV-2
- Testing should employ either a nucleic acid amplification test (NAAT) or an antigen test to detect SARS-CoV-2.
- Testing should also be performed for people who are likely to be at repeated risk of exposure to SARS-CoV-2, such as health care workers and first responders.
- Testing should also be considered for individuals who spend time in heavily populated environments (e.g., teachers, students, food industry workers) and for travelers.
- Testing requirements may vary by state, local, and employer policies.
- Travelers may need evidence of a recent negative test result to enter some states or countries;

NIH (2021)

Covid 19 – Diagnostic Testing

Numerous diagnostic tests for SARS-CoV-2 infection (e.g., NAATs, antigen tests) have received Emergency Use Authorizations (EUAs) from the Food and Drug Administration (FDA), but no diagnostic test has been approved by the FDA.

- Nasopharyngeal specimens remain the **recommended source** for samples for SARS-CoV-2 diagnostic testing, nasal (anterior nares or mid-turbinate)
- Oropharyngeal swabs have been found to be acceptable **alternatives.**
- Lower respiratory tract samples have a higher yield than upper tract samples (inpatient)
- Some tests that have received EUAs can be performed on saliva specimens, however ongoing studies are currently evaluating there use and their sample types, including stool samples.
- Home testing has received EUA's, there are concerns of false negatives due poor specimen collection

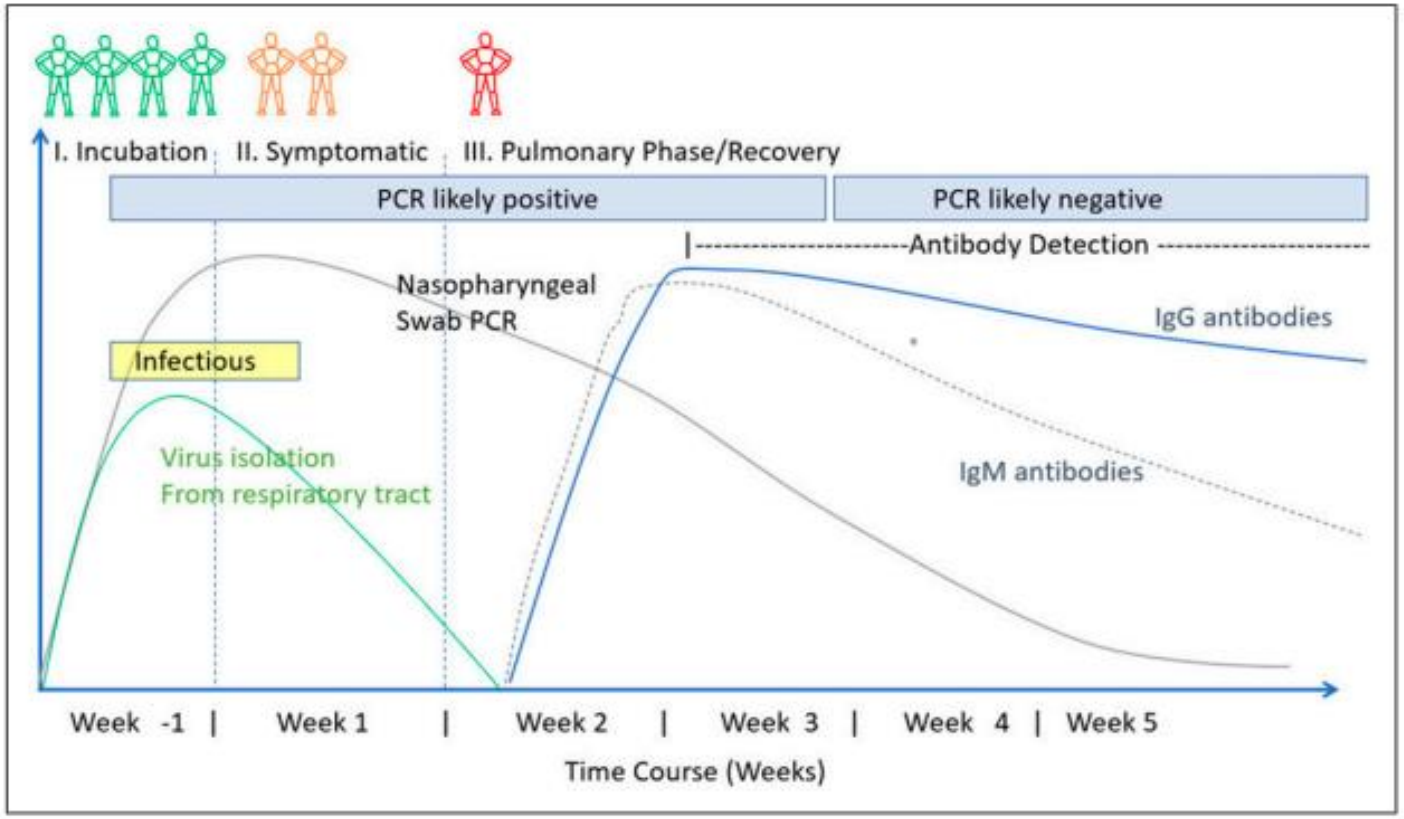
NIH (2021)

Covid 19 – Diagnostic Testing

Types of Tests

- Nucleic Acid Amplification Testing for SARS-CoV-2 **(PCR)**
  - Infection Reverse transcriptase polymerase chain reaction (RT-PCR)
    - Gold standard for detecting current SARS-CoV-2 infection. (Results consistent within 5-day exposure)
    - PCR test can detect virus >10 days in routine response or in severe disease >20 days is low
- Antigen Testing for SARS-CoV-2 **(Rapid Test)**
  - Infection Antigen-based diagnostic tests (which detect viral antigens) are less sensitive than RT-PCR-based tests, but they have similarly high specificity.
    - Antigen tests perform best early in the course of symptomatic SARS-CoV-2 infection,
    - Advantages of antigen-based tests are their low cost and rapid turnaround time.
    - Symptomatic patient with a negative test should receive PCR testing

NIH (2021)



Stages of COVID and time course of immune response.

Marik, Iglesias, Varon, Kory (2021)

Covid 19 – Diagnostic Testing

Types of Tests

Serologic or Antibody Testing for Diagnosis of SARS-CoV-2 Infection

- Unlike PCR (NAATs) and antigen tests (Rapid) for SARS-CoV-2, Serologic / Antibody testing can that detect the presence of the virus, recent or prior SARS-CoV-2 infection.
- Testing may take 21 days or longer after symptom onset for seroconversion to occur (i.e., the development of detectable immunoglobulin [Ig] M and/or IgG antibodies to SARS-CoV-2),21-26 the Panel does not recommend serologic testing as the sole basis for diagnosing acute SARS-CoV-2 infection.
- NAATs and antigen tests for SARS-CoV-2 occasionally yield false negative results, serologic tests have been used in some settings as an additional diagnostic test for patients who are strongly suspected to have SARS-CoV-2 infection.
- Using a serologic test in combination with a NAAT to detect IgG or total antibodies 3 to 4 weeks after symptom onset maximizes the sensitivity and specificity to detect past infection.
- No serologic tests for SARS-CoV-2 are approved by the FDA; some, but not all, commercially available serologic tests for SARS-CoV-2 have received EUAs from the FDA.

NIH (2021)

Covid 19 – Diagnostic Testing

Serologic Testing and Immunity to SARS-CoV-2 Infection

The Panel recommends against the use of serologic testing to determine whether a person is immune to SARS-CoV-2 infection and should not be used.

If SARS-CoV-2 antibodies are detected during a serologic test, the results should be interpreted with caution for the following reasons:

- **It is unclear how long antibodies persist following infection; and**
- **It is unclear whether the presence of antibodies confers protective immunity against future infection.**

NIH (2021)

Covid 19 – Clinical Spectrum of Infection

- *Asymptomatic or Pre-symptomatic Infection:* Patients who test positive for COVID-19 using a virologic test (PCR / Rapid) but who have no symptoms that are consistent with COVID-19.
- *Mild Illness:* Patients who have signs and symptoms of COVID-19 (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell) but who do not have shortness of breath, dyspnea, or abnormal chest imaging.
- *Moderate Illness:* Patients who show evidence of lower respiratory disease during clinical assessment or imaging and who have an oxygen saturation (SpO2) ≥94% on room air at sea level.
- *Severe Illness:* Patients who have SpO2 <94% on room air at sea level, a ratio of arterial partial pressure of oxygen to inspired oxygen (PaO2/FiO2)<300mm Hg, a respiratory rate >30 breaths/min, or lung infiltrates>50%
- *Critical Illness:* Individuals who have respiratory failure, septic shock, and/or multiple organ dysfunction.

NIH (2021)

COVID 19 - Pathophysiology

Asymptomatic Stage 1- 4 Days

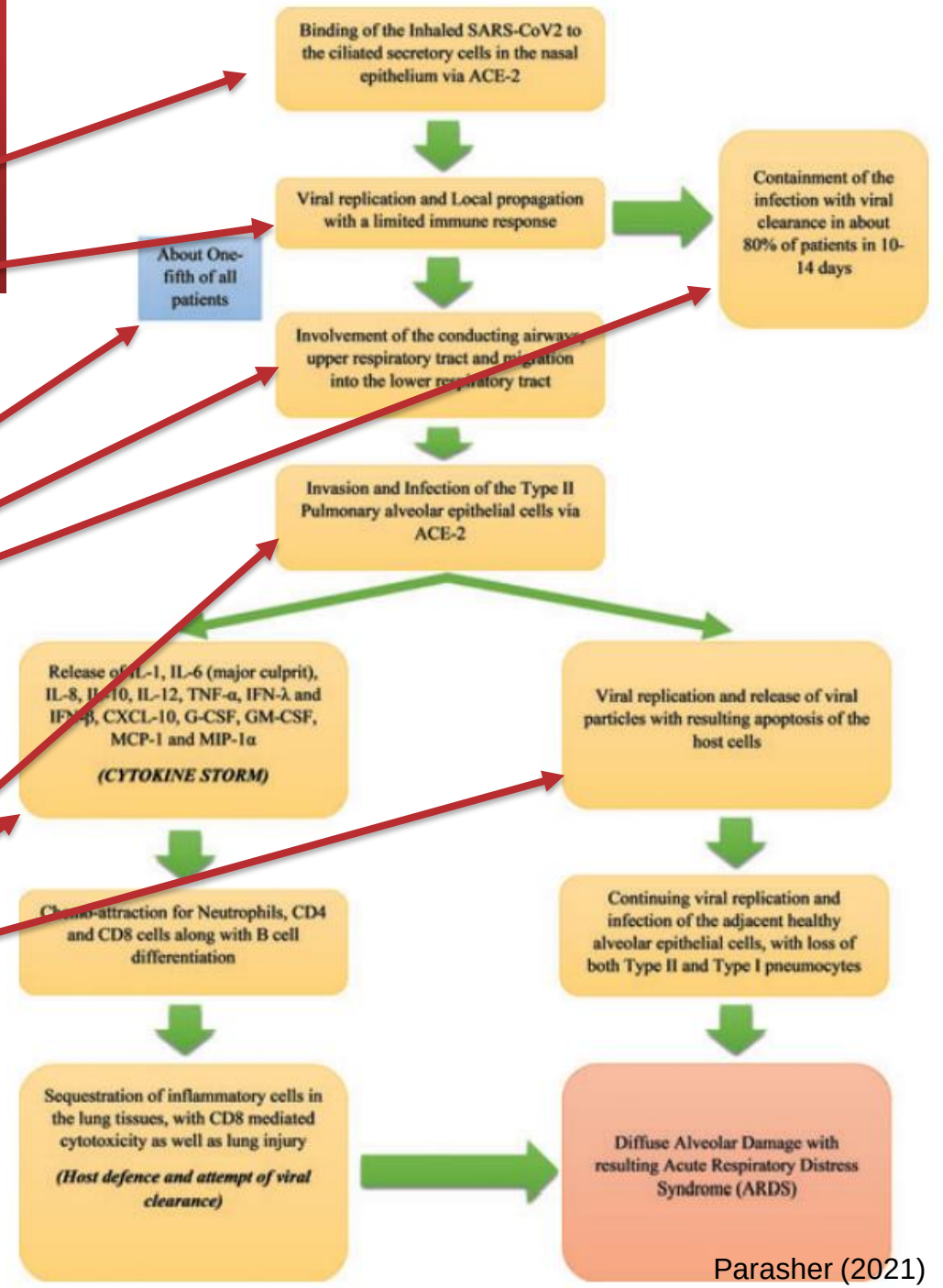
- Covid Virus invades nasal epithelial cells –
  - The receptor host is ACE-2 highly expressed in the adult nasal epithelial cells.
  - Local replication and infection of the ciliated cell in the conducting airways
  - Low viral load – highly infectious

Symptomatic State 2 – 14 Days

- Covid Virus migrates into the upper respiratory tract –
  - The disease starts manifesting symptoms
  - Greater Immune response – One in five clear at this point

Progression of Illness – Severe to Critical

- Covid Virus migrates into the lower respiratory tract –
  - Via ACE-2 into the Type 2 Alveolar epithelial cells and produce Nucleocapsids
  - Creating a Cytokine Storm causing inflammatory response leading to ARDS



Parasher (2021)

Parasher (2021)

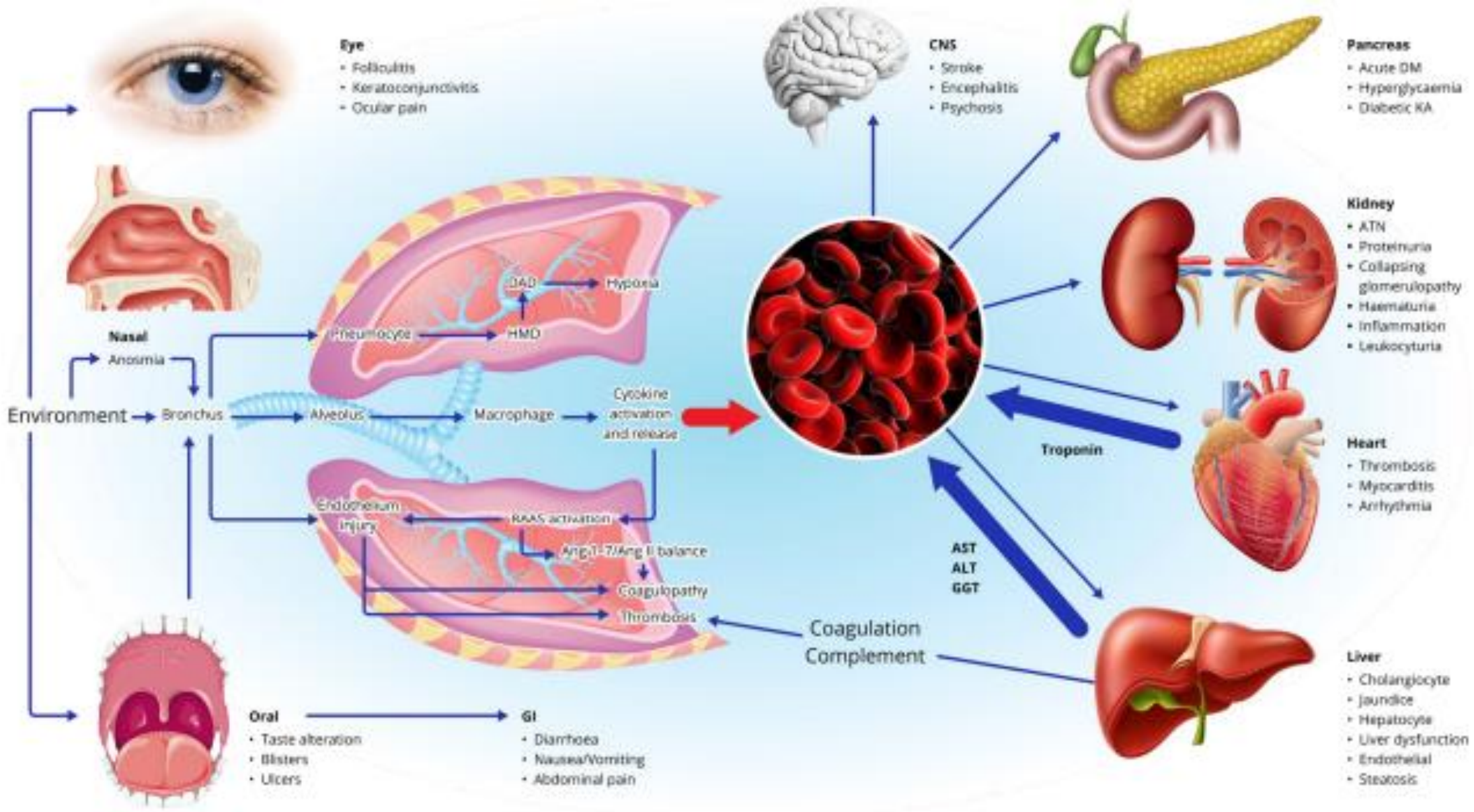
Covid 19 – Clinical Presentation

Incubation period 0 – 14 days with a median of 4 – 5 days. The spectrum can be asymptomatic to severe pneumonia with “Acute Respiratory Distress (ARDs)” and death.

- **Asymptomatic** – 1 - 4 days (may be asymptomatic the entire period)
- **Symptomatic** – 2–14 typically day 4-5 with Viral Syndrome / Flu type presentation
  - Fever, headache, body aches and pains, dizziness
  - Malaise and fatigue
  - Congestion, rhinorrhea, sore throat,
  - Dry cough, dyspnea on exertion / tightness in the chest / shortness of breath / hypoxia
  - Loss of smell (anosmia) and taste (ageusia)
  - ABD pain, nausea, vomiting, diarrhea, anorexia

NIH (2021)

Covid 19 – Clinical Presentation



Sridhar, Nicholls (2021)

Covid 19 – Physical Exam / Diagnosis

Clinical Exam should include

- Vital Signs – Temp, Height, Weight, B/P, HR, RR, SpO2
- EENT evaluation
- Respiratory
- Cardio
- ABD exam
- Cursory exam of the extremities for edema / cyanosis

- Clinical testing: PCR / Rapid Tests / Strep / Flu A/B … CBC / Chest X-ray – other as indicated.

Diagnosis – Based on clinical findings / Covid Test Results

NIH (2021)

Covid 19 - Treatment

Asymptomatic or Pre-symptomatic Infection

- Close exposure Asymptomatic– Negative test – No treatment – Observe recommend vaccination if not vaccinated. RTC with symptoms
- Close exposure Asymptomatic – Positive test – No treatment – Quarantine x 5 days (Wear mask 10 days (Vaccinated) Non-Vaccinated – Quarantine x 10 days, retesting is not necessary to return to work. RTC with symptoms

NIH (2022)

Covid 19 - Treatment

- Mild Illness – Patients who have signs and symptoms of COVID-19 (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell) but who do not have shortness of breath, dyspnea, or abnormal chest imaging.
    - Close exposure Symptomatic – Negative test – Treat symptomatically - Observe recommend vaccination if not vaccinated. RTC with increase symptoms – Consider comorbidities
    - Close exposure Symptomatic – Positive test – Treat symptomatically – Quarantine x 5 days (Wear mask 10 days (Vaccinated). Non-Vaccinated – Quarantine x 10 days, retesting is not necessary to return to work. RTC with increase symptoms. Consider comorbidities and treat appropriately.
- No imaging or specific laboratory evaluations are routinely indicated in otherwise healthy patients with mild COVID-19. Older patients and those with comorbidities are at higher risk health care providers should monitor these patients closely until clinical recovery is achieved.

Symptomatic treatment: Includes using over-the-counter antipyretics, analgesics, or antitussives, or other prescribed medications for fever, headache, myalgias, URI and cough.

NIH (2022)

Covid 19 - Treatment

Moderate Illness – Positive - Patients who show evidence of lower respiratory disease during clinical assessment or imaging and who have an oxygen saturation (SpO2) ≥94% on room air at sea level.

- Close exposure Symptomatic – Negative test – Treat symptomatically - Observe recommend vaccination if not vaccinated. RTC with increase symptoms – Consider comorbidities
- Close exposure Symptomatic – Positive test – Treat symptomatically – Quarantine x 5 days (Wear mask 10 days (Vaccinated). Non-Vaccinated – Quarantine x 10 days, retesting is not necessary to return to work. RTC with increase symptoms. Consider comorbidities and treat appropriately.

- Be **aware** of **Multisystem Inflammatory Syndrome in Children** (**MIS-C**) who are COVID-19 positive.

NIH (2022)

Covid 19 - Treatment

Moderate Illness

- **Symptomatic treatment**: Includes using over-the-counter antipyretics, analgesics, or antitussives, or other prescribed medications for fever, headache, myalgias, URI and cough.
- Consideration for escalating treatment of COVID 19 infection, are based on clinical signs and the high risk of clinical progression to severe illness.
  - The use of Monoclonal Antibodies (anti-SARS-COV-2 mABs to prevent progression should be started as soon as possible and within 10 days of symptom onset (EUAs). Shown to be effective Gamma, Beta and Delta, not shown to be effective in patients with Omicron
    - Bamlanivimab plus estesevimab or
    - Casirivimab plus imdevimab or
    - Sotrovimab

NIH (2022)

Covid 19 - Treatment

Moderate Illness

- Dexamethasone (outpatient use)
  - The use of dexamethasone or other systemic glucocorticoids to treat outpatients with mild to moderate COVID-19 who do not require hospitalization or supplemental oxygen is not recommended.
  - There is currently a lack of safety and efficacy data on the use of these agents, and systemic glucocorticoids may cause harm in these patients.

- Remdesivir
  - Only FDA approved drug for treatment of COVID-19. Inpatient use only, continuation after inpatient discharge is not recommended after discharge.

NIH (2021)

Covid 19 - Treatment

Moderate Illness

- Baricitinib – Not recommend in outpatient care
- Paxlovid – Recently given EUAs approval.  2085 patients in the clinical trials
  - (Nirmatrelvir 300mg (2-150mg tabs) plus Ritonavir 100mg – Every 12 hours x 5 days
    - Ritonavir-boosted nirmatrelvir (Paxlovid) has significant and complex drug-drug interaction potential. Has numerous serious adverse drug to drug interactions in commonly used medications and OTC supplements.
    - Significant potential future inhibition and resistance of HIV protease inhibitors in patients with uncontrolled or undiagnosed HIV infections.
    - Not indicated in patients under the age of 12.
    - Not indicated in pregnancy or potential of childbearing – Use contraception

NHI (2022)

Covid 19 - Treatment

Moderate Illness

- Molnupiravir 200mg - 900 patients in the clinical trials --
  - Molnupiravir 200mg (4 capsules) Every 12 hours x 5 days
    - No contraindications identified
    - No known drug to drug interactions
    - Not indicated for use in patient under 18 years - Bone and Cartilage toxicity
    - Not indicated in pregnancy or childbearing potential – Use contraception

NIH (2021)

Covid 19 - Treatment

Moderate Illness - Other agents that have been studied or are under investigation for use in outpatients with COVID-19

- ***Not recommended for the treatment of COVID-19***
  - Chloroquine or hydroxychloroquine with or without Azithromycin
  - Doxycycline / Levaquin or another antibiotic – (Prevention)
  - Lopinavir/Ritonavir and other HIV protease Inhibitors
  - Interferons (beta, alfa or lambda)
  - Antiviral agents
  - Ivermectin and Nitazoxanide

NIH (2021)

Covid 19 - Treatment

Moderate Illness - Other agents that have been studied or are under investigation for use in outpatients with COVID-19

- ***Not recommended for the treatment of COVID-19***
  - Convalescent plasma
  - Immunomodulators
  - Colchicine
  - Fluvoxamine
  - Cell– Based Therapy (Mesenchymal Stem Cells)
  - Antithrombictic Therapy
  - Zinc (Above dietary recommendations)

NIH (2021)

Covid 19 - Treatment

- *Severe Illness:* Patients who have SpO2 <94% on room air at sea level, a ratio of arterial partial pressure of oxygen to inspired oxygen (PaO2/FiO2)<300mm Hg, a respiratory rate >30 breaths/min, or lung infiltrates>50%
- *Critical Illness:* Individuals who have respiratory failure, septic shock, and/or multiple organ dysfunction.

Off to the races!

NIH (2021)

Covid 19 – Treatment – Post Infection

- Follow up care

Asymptomatic or mildly to moderately ill patient with COVID-19 may develop new, continued, or worsening symptoms and conditions following their acute infection.

  - Follow up appointments should occur 3-4 weeks from initial infection
    - Post COVID conditions can be clinically diagnosed based on history and physical examination.
    - Many diagnostic tests, post COVID may reveal uninformative information in the first 4-12 weeks, however delaying testing in an acute situation that potentially could cause harm is not recommended.
    - Coordinated care with OT, PT and social worker can help maximize improvement and rehabilitation.
    - Ongoing follow up visits, timely referrals, ongoing communication with consultants and the patient will facilitate the patient's recovery.

NIH (2022)

Covid 19 – Treatment Post Covid Conditions

Suggested Workup for Post-COVID Conditions

Patient History – Present illness, disease course, severity and treatments received

- Dyspnea or increased respiratory effort
- Fatigue
- Post-exertional malaise and/or poor endurance
- “Brain fog,” cognitive impairment
- Cough
- Chest pain
- Headache
- Palpitations and/or tachycardia
- Arthralgia
- Myalgia
- Paresthesia
- Abdominal pain
- Diarrhea
- Insomnia and other sleep difficulties
- Fever
- Lightheadedness
- Impaired daily function and mobility
- Pain
- Rash (e.g., urticaria)
- Mood changes
- Anosmia or dysgeusia
- Menstrual cycle irregularities
- Post-exertional malaise (PEM) is the worsening of symptoms following even minor physical or mental exertion, with symptoms typically worsening 12 to 48 hours after activity and lasting for days or even weeks.

NIH (2021)

Covid 19 – Treatment Post Covid Conditions

Suggested Workup for Post-COVID Conditions

Healthcare providers should consider a broad spectrum of conditions and multiple system affects.

Body

- **Conditions (subject to change and not mutually exclusive)**
- **Cardiovascular -** Myocarditis, heart failure, pericarditis, orthostatic intolerance (e.g., postural orthostatic tachycardia syndrome (POTS))
- **Pulmonary -** Interstitial lung disease, reactive airway disease
- **Renal -** Chronic kidney disease
- **Dermatologic -** Alopecia
- **Rheumatologic -** Reactive arthritis, fibromyalgia, connective tissue disease
- **Endocrine -** Diabetes mellitus, hypothyroidism

System

- **Neurologic -** Transient ischemic attack/stroke, olfactory and gustatory dysfunction, sleep dysregulation, altered cognition, memory impairment, headache, weakness, and neuropathy
- **Psychiatric -** Depression, anxiety, and post-traumatic stress disorder (PTSD), psychosis
- **Hematologic -** Pulmonary embolism, arterial thrombosis, venous thromboembolism, or other hypercoagulability
- **Urologic -** Incontinence, sexual dysfunction
- **Other -** Weight loss, dysautonomia, vitamin D deficiency, allergies and mast cell activation syndrome, reactivation of other viruses, pain syndromes, and progression of comorbid conditions

NIH (2022)

Covid 19 – Treatment Post Covid Conditions

Suggested Workup for Post-COVID Conditions

Physical examination and vital signs

- Post-COVID conditions involve multiple organ systems
  - A thorough physical examination should be completed.
    - vital signs (i.e., blood pressure, heart rate, respiratory rate, pulse-oximetry, body temperature) and body mass index,
    - Consider ambulatory pulse-oximetry for individuals presenting with respiratory symptoms, fatigue, or malaise.
    - Orthostatic vital signs for individuals reporting postural symptoms, dizziness, fatigue, cognitive impairment, or malaise.

NHI (2022)

Covid 19 – Treatment Post Covid Conditions

Suggested Workup for Post-COVID Conditions

Laboratory Testing

There are no specific tests to definitively distinguish post-COVID conditions. Testing guided by ongoing symptoms

CATEGORY	LAB TESTS
Blood count, electrolytes, and renal function	Complete blood count with possible iron studies to follow, basic metabolic panel, urinalysis
Liver function	Liver function tests or complete metabolic panel
Inflammatory markers	C-reactive protein, erythrocyte sedimentation rate, ferritin
Thyroid function	TSH and free T4
Vitamin deficiencies	Vitamin D, vitamin B12

NHI (2022)

Covid 19 – Treatment Post Covid Conditions

Suggested Workup for Post-COVID Conditions

More specialized diagnostic laboratory testing

CATEGORY	LAB TESTS
Rheumatological conditions	Antinuclear antibody, rheumatoid factor, anti-cyclic citrullinated peptide, anti-cardiolipin, and creatine phosphokinase
Coagulation disorders	D-dimer, fibrinogen
Myocardial injury	Troponin
Differentiate symptoms of cardiac versus pulmonary origin	B-type natriuretic peptide

NHI (2022)

Covid 19 – Treatment Post Covid Conditions

Suggested Workup for Post-COVID Conditions

Evaluation Tools

CATEGORY	TOOLS
Functional status and/or quality of life	Patient-Reported Outcomes Measurement Information System (PROMIS) (e.g., Cognitive Function 4a) Post-Covid-19 Functional Status Scale (PCFS) EuroQol-5D (EQ-5D)
Respiratory conditions	Modified Medical Research Council Dyspnea Scale (mMRC)
Neurologic conditions	Montreal Cognitive Assessment (MoCA) Mini Mental Status Examination (MMSE) Compass 31 (for dysautonomia) Neurobehavioral Symptom Inventory
	NHI (2022)

Covid 19 – Treatment Post Covid Conditions

Suggested Workup for Post-COVID Conditions

Evaluation Tools

CATEGORY	TOOLS
Psychiatric conditions	General Anxiety Disorder-7 (GAD-7) Patient Health Questionnaire-9 (PHQ-9) PTSD Symptom Scale (PSS) Screen for Posttraumatic Stress Symptoms (SPTSS) PTSD Checklist for DSM-5 (PCL-5) Impact of Event Scale-Revised (IESR) Hospital Anxiety and Depression Scale (HADS
Other conditions	Wood Mental Fatigue Inventory (WMFI) Fatigue Severity Scale Insomnia Severity Index (ISI) Connective Tissue Disease Screening Questionnaire

NHI (2022)

Covid 19 – Treatment Post Covid Conditions

Suggested Workup for Post-COVID Conditions

Evaluation Tools

CATEGORY	TOOLS
Exercise capacity	1-minute sit-to-stand test 2-minute step test 10 Meter Walk Test (10MWT) 6-minute walk
Balance and fall risk	BERG Balance Scale Tinetti Gait and Balance Assessment Tool
Other	Tilt-table testing (e.g., for POTS) Orthostatic HR assessment

NHI (2022)

Covid 19 – Treatment Post Covid Conditions

Suggested Workup for Post-COVID Conditions

Medical Management

The goal of medical management of post-COVID conditions is to optimize function and quality of life.

- Develop a comprehensive management plan based on their patients' presenting symptoms, underlying medical and psychiatric conditions, personal and social situations,
- Ongoing consultation and coordinated treatment, as necessary.
- Medications as necessary to address identified health issues.

NHI (2022)

Covid 19 – Multisystem Inflammatory Syndrome in Children (MIS-C) Treatment Post Covid Conditions

Multisystem Inflammatory Syndrome in Children (MIS-C)

Clinical Presentation of MIS-C

- Kawasaki disease-like features: conjunctivitis, red eyes; red or swollen hands and feet; rash; red cracked lips, swollen glands. In some children, coronary artery enlargement and/or aneurysms have been described. Some children presenting with Kawasaki disease-like syndrome have been noted to have a broader age range and presentation with more gastrointestinal (abdominal pain or diarrhea) and neurologic (headaches/meningitis) manifestations.
- Gastrointestinal symptoms such as abdominal pain, diarrhea, nausea/vomiting (patients have presented with colitis, hepatitis, and questionable appendicitis).
- Toxic shock syndrome-like features with hemodynamic instability and poor heart function.
- Cytokine storm/macrophage activation or hyperinflammatory features.

NHI (2022)

Covid 19 – Multisystem Inflammatory Syndrome in Children (MIS-C) Treatment Post Covid Conditions

Clinical Presentation of MIS-C

- Thrombosis or acute kidney injury.
- Shortness of breath suggestive of congestive heart failure or pulmonary embolism.
- Respiratory symptoms typically reported in adults with COVID-19 may or may not be present in pediatric patients with MIS-C.

Common laboratory findings

- An abnormal level of inflammatory markers in the blood, including elevated ESR/CRP and ferritin, LDH.
- Lymphopenia <1000, thrombocytopenia <150,000, neutrophilia.
- Elevated B-type natriuretic peptide (BNP) or NT-proBNP (pro-BNP), hyponatremia, elevated D-dimers.

NHI (2022)

Covid 19 – Multisystem Inflammatory Syndrome in Children (MIS-C) Treatment Post Covid Conditions Diagnosis Criteria

Multisystem Inflammatory Syndrome in Children (MIS-C) – Typically diagnosed inpatient

- A patient <21 years presenting with fever*, laboratory evidence of inflammation**, and evidence of clinically severe illness requiring hospitalization, with multisystem (≥2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological); AND
- No alternative plausible diagnoses; AND
- Positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or exposure to a suspected or confirmed COVID-19 case within the 4 weeks prior to the onset of symptoms.
- *Fever ≥38.0°C for ≥24 hours, or report of subjective fever lasting ≥24 hours
  **Including, but not limited to, one or more of the following: an elevated C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), fibrinogen, procalcitonin, d-dimer, ferritin, lactic acid dehydrogenase (LDH), or interleukin 6 (IL-6), elevated neutrophils, reduced lymphocytes and low albumin

Patient will be referred to the PCP for follow up care.

NHI (2022)

Multisystem Inflammatory Syndrome in Children (MIS-C)

- Follow up
  - Patients with a diagnosis of MIS-C should have close outpatient follow-up, including pediatric cardiology follow-up starting 2 to 3 weeks after discharge.
  - Patients who receive steroid therapy or treatment with biologics should receive follow-up with the pediatric rheumatologist following discharge.
  - Patients with a history of MIS-C should consider delaying vaccination until after they have recovered from illness (including return to normal cardiac function) and for at least 90 days following their diagnosis of MIS-C. Currently, there are limited data about the safety and efficacy of COVID-19 vaccine in patients with a history of MIS-C
  - Patients who have received monoclonal antibodies or convalescent plasma as part of their treatment should wait at least 90 days prior to receiving COVID-19 vaccine

Covid 19 – Prevention

Vaccines

Pfizer – BioN Tech

Moderna

Messenger RNA, or mRNA, was discovered in the early 1960s; research into how mRNA could be delivered into cells was developed in the 1970s, technology primarily used to treat disease – Cancer

Johnson & Johnson

Are created using the traditional model that all existing vaccines currently use employed by using the genetic information of the disease to create antibodies in the body.

COVID -19 Vaccinations

Vaccines Given Global – 9.37 Billion (14 Jan2022)

- Fully Vaccinated Global 3.92 Billion – 49%
  - First Dose given Global 4.63billion - 50%
  - Booster given Global 524,536,616 – 6.7%
  - Booster US - 18,745,803 - 44.1%

CDC (14 Jan 2022)

U.S. COVID -19 Vaccinations

Total U.S. Vaccines Given - 524 million doses (14 Jan 2021)

Total Population Fully Vaccinated: 208,791,862 – 77.2%

- White – 91,897,091 – 57.%
- Latino / Hispanic – 31,137,135 – 19.3%
- Black – 15,899,486 – 9.9%
- Asian – 10,950,633 – 6.8%
- Native American / Alaska Native – 1,356,285 – .8%
- Native Hawaiian / Pacific Islander – 518,443 – 0.3%
- Multiple / Other – 9,412,058 – 5.8%

CDC (14 Jan 2022)

U.S. COVID -19 Vaccinations

Received at Least One Dose : 248,338,448 – 73.7%

- White – 102,930,839 – 55.9%
- Latino / Hispanic – 37,035,040 – 20.2%
- Black – 18,396,434 – 10%
- Asian – 12,319,266 – 6.7%
- Native American / Alaska Native – 1,320,554 – 1.0%
- Native Hawaiian / Pacific Islander – 587,060 – 0.3%
- Multiple / Other – 5,701,748 – 4.5%

CDC (14 Jan 2022)

U.S. COVID -19 Vaccinations

Barriers to COVID 19 Vaccination

- False information – Social Media / Family / Other – Cost of Vaccine?
- Distrust of the Medical System
- Income / Poverty / Housing / Food / Employment / Education
- Daily Lifestyle – i.e., Hourly Worker / Self employed / Underemployed
- Definition of “Essential Workers”
- Access to Health Care – Care / Testing / Immunization Sites
- Structural Racism - Bias / Discrimination
- Language Barriers
- Undocumented – No benefits / No Unemployment Aid or Stimulus Checks

COVID-19 – Future Vaccines

- According to the WHO's COVID-19 vaccine tracker, there are 137 vaccines currently in clinical development an additional 194 in pre-clinical development. These will be available 1st Qtr. 2022.
  - Valneva – French – Vero-cell platform
  - Novavax – USA - Genetic sequence vaccine
  - Sanofi and GSK - USA – Recombinant adjuvanted vaccine
  - Medicago and GSK- Canada - Plant-based vaccine
  - Curevac – Germany – Second generation mRNA
  - University of Melbourne – Australian - mRNA
  - SK bioscience – South Korea – Protein subunit
  - EnGeneIC – Australian – Non-living Nano-cells

Arthur (2021)
NHI (2022)

COVID-19 – Future Therapeutic Options

Future COVID-19 Treatments in Development

- The list of new and repurposed drugs being investigated for possible treatment of COVID-19 is lengthy. There are currently over 4,000 studies on ClinicalTrials.gov, including 331 vaccine studies, 1,387 drug studies, and 516 mapped drug names. Preclinical data and clinical trial results emerge for new experimental therapeutics regularly. The World Health Organization (WHO) maintains an exhaustive list of COVID-19 clinical trials. The U.S. FDA Coronavirus Treatment Acceleration Program (CTAP) also features an overview of the types of drugs being studied for the treatment of COVID-19 which include:
  - Antiviral drugs
  - Immunomodulators
  - Cellular and gene therapies
  - Neutralizing antibodies

Arthur (2021)
NHI (2022)

Questions and Answers

Thank you for this opportunity.

Rafael Pomales Jr., MHS, PA-C, DFAAPA

Robert S. Smith, MS, DHSc, PA-C, DFAAPA

rsspac1958@gmail.com

References

- Arthur, R. (2021). COVID-19 vaccine development: What the next wave of vaccines in 2022 could look like. *BioPharma.* Retrieved from https://www.biopharma-reporter.com/Article/2021/12/22/The-next-wave-of-COVID-19-vaccines-December-2021
- AJMC (2021). A timeline of COVID-19 Developments in 2020. American Journal of Managed Care. Retrieved from https://www.ajmc.com/view/a-timeline-of-covid19-developments-in-2020
- Bloomberg (2022). COVID-19 Tracker. Retrieved from https://www.bloomberg.com/graphics/covid-vaccine-tracker-global-distribution/
- CDC (2022). Center of Disease Control and Prevention, COVID Data Tracker, Demographic Trends of COVID-19 cases and deaths in the US reported to CDC. Retrieved from https://covid.cdc.gov/covid-data-tracker/#demographics
- CDC (2022). Center of Disease Control and Prevention, COVID Data Tracker, Health Equity Data. Retrieved from https://covid.cdc.gov/covid-data-tracker/#health-equity-data
- New York Times (2022) Coronavirus in the U.S. Latest Map and Case Count. Retrieved from https://www.nytimes.com/interactive/2022/us/covid-cases.html

References

- Center of Disease Control and Prevention, First Travel –related Case of 2019 Novel Coronavirus detected in the United States. Retrieved from https://www.cdc.gov/media/releases/2020/p0121-novel-coronavirus-travel-case.htm
- Marik, P.E., Iglesias, J., Varon, J., Kory, P. (2021). A scoping review of the pathophysiology of COVID-19. International Journal of Immunopathology and Pharmacology 35,1-16. https:// doi: 10.1177/20587384211048026
- Ndugga, N., Hill, L., and Artiga, S. (2022) Latest Data on COVID-19 Vaccinations by Race/Ethnicity. Kaiser Family Foundation. Retrieved from https://www.kff.org/coronavirus-covid-19/issue-brief/latest-data-on-covid-19-vaccinations-race-ethnicity/
- NIH (2021). COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. National Institutes of Health. Retrieved from https://www.covid19treatmentguidelines.nih.gov/
- NYC Health (26 Aug 2021). COVID-19 Data. Retrieved from https://www1.nyc.gov/assets/doh/downloads/pdf/epi/databrief123.pdf

References

- Parasher, A. (2021). COVID-19: Current understanding of its pathophysiology, clinical presentation and treatment. Postgrad Med J. (97)312–320. https://doi:10.1136/postgradmedj-2020-138577
- Sridhar, S., Nicholls, J. (2021). Pathophysiology of infection with SARS-CoV-2—What is known and what remains a mystery. Respirology, 26(7), 652-665. https://doi.org/10.1111/resp.14091
- U.S. Census (2021). Race and Ethnicity in the United States: 2010 Census and 2020 Census. Retrieved from https://www.census.gov/library/visualizations/interactive/race-and-ethnicity-in-the-united-state-2010-and-2020-census.html
- World Health Organization (2022). Tracking SARS-CoV-2 variants. Retrieved from https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/