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Authentic Questions of INI-CET with Finest Explanations and References from Standard Textbooks

COVID-19 Updates added

Updated from Harrison 20/E, Bailey and Love 27/E, Sabiston 20/E, Schwartz 11/E, Gray's 41/E, Ganong 25/E, Guyton 13/E, Harper 30/E, Robbin's 10/E, Katzung 14/E, Park 25/E, Nelson 20/E and latest editions of Premium Textbooks

Pritesh Singh

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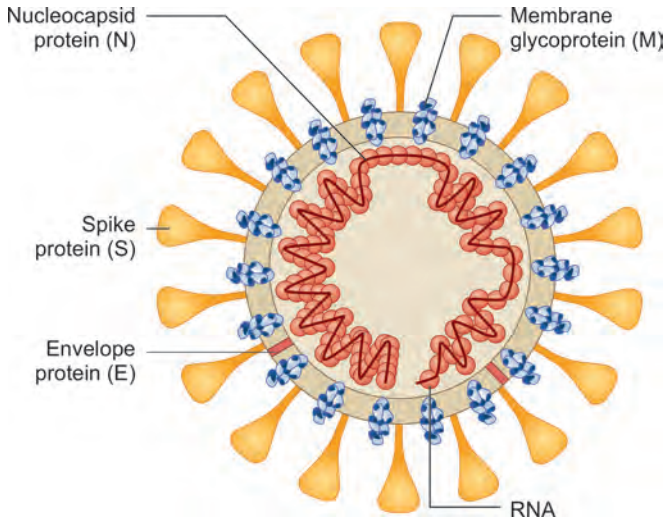
Coronavirus



SARS-CoV-2 (Causative Pathogen of COVID-19)

CORONAVIRUSES

- **Coronaviruses** are a family of **enveloped**[Q] viruses & contain a **genome of single-stranded positive-sense RNA**[Q] that is the **largest genome among RNA viruses**[Q] and infects **animal species (mainly the bats) & humans**[Q].
- They have distinctive **club shaped spikes on their surface** giving the appearance of "**solar corona**".
- Coronaviruses primarily cause **respiratory & intestinal infections**[Q] in **animals and humans**.
  - Coronaviruses exhibit a **high frequency of mutation during each round of replication**[Q], including the **generation of a high incidence of deletion mutations**[Q].
  - Coronaviruses undergo a **high frequency of recombination during replication**; may **contribute to evolution of new virus strains**[Q].
- **Important coronavirus members**: Viruses responsible for **common cold**, **severe acute respiratory syndrome coronavirus** (**SARS**), **Middle East respiratory syndrome-related coronavirus** (**MERS**), & **severe acute respiratory syndrome coronavirus 2** (**SARS-CoV-2**, the **causative pathogen of COVID-19**[Q]).
- **COVID-19**: **Co**rona**Vi**rus **D**isease of 20**19**

Important Properties of Coronaviruses	
Virion	• **Spherical**, 120–160 nm in diameter, **helical nucleocapsid**[Q]
Genome	• **Single-stranded RNA, linear, non-segmented, positive-sense**, 27–32 kb, **capped & polyadenylated, infectious**[Q]
Proteins	• **Two glycoproteins & one phosphoprotein**[Q] • Some viruses contain a **third glycoprotein** (**hemagglutinin esterase**)
Envelope	• Contains large, widely spaced, **club- or petal-shaped spikes**[Q]
Replication	• **Cytoplasm**; particles mature by **budding into endoplasmic reticulum & Golgi apparatus**[Q]

History & Origin of Coronaviruses:

- **Outbreak** of **Novel coronavirus disease** (**COVID-19**) was first noticed in a **seafood market in Wuhan city in Hubei Province of China**[Q] in **mid-December, 2019**.
- **Pneumonia of unknown cause** detected in **Wuhan**, China was first reported to the **WHO Country Office in China** on **31st December 2019**[Q].
- Outbreak was declared a "**Public Health Emergency of International Concern**" by WHO on **30th January, 2020**[Q].
- WHO declared **COVID-19** a **pandemic** on **11th March, 2020**[Q].

Definition of COVID-19 Case:

- **Confirmed Case**: A person with **laboratory confirmation of COVID-19 infection**, **irrespective of** clinical **signs & symptoms**[Q].

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Epidemiology:

- **Causative virus (SARS-CoV-2)** has a **zoonotic source,** closely related to **bat-origin SARS-like coronavirus**[Q].
- It is an **enveloped RNA beta coronavirus** related to **Severe Acute Respiratory Syndrome (SARS) virus**
- **Cell binding via viral S protein** to host receptor **angiotensin-converting enzyme 2 (ACE2)**, which is expressed by **epithelial cells of lung, intestine, kidney & blood vessels**[Q].
- **Main source of infection**: **Infected persons by novel coronavirus**[Q]**.**

Mode of transmission
• **Direct person-to-person transmission** occurs through **close contact**[Q]
• **Aerosolized droplets**[Q] generated through coughing, sneezing or breathing
• **Direct contact with patient** & their **body fluids** including feces[Q]
• **Indirect contact** with **surfaces & fomites**[Q] (if a person **touches an infected surface** and then **touches his or her eyes, nose, or mouth**[Q])

- **Incubation period**: **5 days**[Q] **(2-14 days)**
- **Period of infectivity:** Starts **2 days prior to onset of symptoms** & **lasts up to 8 days**[Q]

Life cycle of SARS-CoV-2 in Host Cells:

- **SARS-CoV-2 primarily infects respiratory tract** (**nasal epithelial cells, pneumocytes & alveolar macrophages**[Q]) & **GIT (enterocytes**[Q]**)**.
- **Virus enters** though **direct interaction between viral S protein** & **cellular receptor angiotensin-converting enzyme 2**[Q] **(ACE2)**.
- Following entry, **viral genome** is **released & translated into viral replicase polyproteins PP1a & PP1ab**, which are **cleaved into functional proteins by viral proteases**[Q].
- **Viral genome replication** is mediated by **viral replication complex**, which includes **RNA-dependent RNA polymerase** (**RdRp**), **helicase, exonucleaseN** & other accessory proteins[Q].
- **Viral nucleocapsids** are assembled from packaged viral genomes & translated viral structural proteins and **released through exocytosis**[Q].
- **Assembly of viral nucleocapsids** from packaged viral genomes & translated viral structural proteins **occurs at the endoplasmic reticulum-Golgi intermediate compartment**, with **infectious virions** then **released** from the cell **through exocytosis**[Q].

Pathophysiology:

- **Most patients predominantly** have **respiratory tract infection** associated with **SARS-CoV-2 infection**[Q]
- In a small proportion of cases, it can progress to a **more severe & systemic disease** characterized by **acute respiratory distress syndrome** (ARDS), **sepsis** & **septic shock, multiorgan failure**, including **acute kidney injury & cardiac injury**[Q].

Risk Factors for Severe & Systemic Disease	
• **Advanced age** (**age >60 years**[Q])	• Hypertension
• **Immunosuppression**[Q]	• Cardiac disease
• **Chronic lung disease**[Q]	• Cerebrovascular disease
• **Diabetes**[Q]	• Cancer
• **Chronic kidney disease**[Q]	

Clinical Features

- **Common signs & symptoms**: **Fever**[Q]**, cough**[Q]**, sore throat**[Q]**, shortness of breath**[Q]**, fatigue, expectoration, myalgia, rhinorrhea, diarrhea, loss of smell (anosmia**[Q]**)** or **loss of taste** preceding the onset of respiratory symptoms.
- As per data from **Integrated Disease Surveillance Programme** (IDSP), **common signs & symptoms** reported are (as on **11/06/2020**): **Fever**[Q] **(27%) >Cough**[Q] **(21%) >Sore throat**[Q] **(10%) >Breathlessness**[Q] **(8%) >Weakness**[Q] **(7%)> Running nose**[Q] **(3%); Others (24%)**

Clinical presentation according to Severity of Cases

Mild	Moderate		Severe
• **Uncomplicated upper respiratory tract infection** with **mild symptoms** such as **fever, cough, sore throat, nasal congestion, malaise & headache**	• **Pneumonia** with **no signs of severe disease**		• **Severe pneumonia**[Q]
	Adult or Adolescent	• Presence of **dyspnea** or **hypoxia** • **Fever, cough** & **SpO_2 (90-94%)** on **room air**[Q] • Respiratory rate (**RR**) **≥ 24 breaths/min**[Q]	• **Acute respiratory syndrome**[Q]
	Child **1–5 years**	• RR **≥40** breaths/min[Q]	• **Sepsis**[Q]
	Child **2–11 months**	• RR **≥50** breaths/min[Q]	• **Septic shock**[Q]
• **Without evidence of breathlessness or hypoxia** (normal oxygen saturation)	Child **<2 months**	• RR **≥60** breaths/min[Q]	

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CORONAVIRUSES

Laboratory Diagnosis:

- **Nodal laboratory** designated for coronavirus testing **in India: National Institute of Virology, Pune**
- **Coronavirus antigens** in cells in respiratory secretions may be **detected using the ELISA test** if a high-quality antiserum is available.
- **Antigen tests** target **spike protein on the surface of coronavirus**[Q] (**not the viral genome or RNA**). **Antigen tests detect current infection**[Q], typically have **high specificity**[Q] (99.3-100%) & **low sensitivity**[Q] (50.6-84%).

COVID-19 NAAT Positivity Rates	
Type of Specimen	**Positive**
Bronchoalveolar lavage fluid[Q]	**93%**[Q]
Sputum[Q]	**72%**
Nasopharyngeal swab[Q]	63%
Oropharyngeal swab[Q]	32%
Feces[Q]	29%
Blood[Q]	**1%**[Q]

- **Polymerase chain reaction (PCR) assays** are the **preferred methods to detect coronavirus nucleic acid in respiratory secretions & in stool samples**[Q].
- **Gold standard for diagnosis: RT-PCR**[Q]
- **Enteric coronaviruses** can be detected by **examination of stool samples by electron microscopy**[Q].
  - Up to **5th day, IgM starts coming** and **IgM gets detectable on 7th day**[Q].
  - **IgG gets detectable around 14-15 days** and **peaks around day 28**[Q].
- **Antibody tests: SARS-CoV-2 antibody tests** are **not recommended, for diagnosis of current infection with COVID-19**

Specimen Collection
• **Preferred sample: Throat & nasal swab** in **viral transport media** & **transported in cold chain**[Q]
• **Alternate: Nasopharyngeal swab, bronchoalveolar lavage (BAL) or endotracheal aspirate** which has to be **mixed with the viral transport medium** & **transported in cold chain**[Q]

- **Patterns of COVID-19 on Chest X-ray:** Reverse batwing, multifocal lower lobe consolidation, peribronchial rounded consolidation, ball pattern or round pneumonia, bilateral symmetrical diffuse lung involvement[Q]

Atypical CT Findings in COVID-19	
• **Mediastinal lymphadenopathy**[Q]	• **Tree-in-bud appearance**[Q]
• **Pleural effusion**	• **Pneumothorax**
• **Multiple tiny pulmonary nodules**[Q]	• **Cavitation**[Q]

Poor Prognostic Signs	
• **Neutrophil:Lymphocyte ratio ≥3.13**	• **Bilateral infiltrates & ground-glass opacities** in **chest X-ray**[Q]
• Development of **acute kidney injury**	• **Type 1 respiratory failure** in ABG or **PaO_2/FiO_2 ratio <300**[Q]
• **Raised serum ferritin, d-dimer & IL-6 levels**[Q]	

Management of COVID-19	
Mild Cases	• **No definitive treatment** available • **Mainstay of treatment:** Isolation, symptomatic management (Paracetamol) for fever and pain, adequate nutrition & rehydration) & supportive care • Follow-up on daily basis for temperature, vitals & oxygen saturation (SpO_2) • **Tab. hydroxychloroquine** may be considered for **patients with risk factors** under strict medical supervision[Q]
Moderate Cases	**In addition** to intervention provided for mild cases: • **Oxygen support: Target SpO_2- 92-96%** (**88-92%** in **COPD**) • Daily 12-lead ECG • **CRP, D-dimer** & **ferritin 48-72 hourly**[Q] • CBC with differential count, absolute lymphocyte count, LFT & KFT daily • Tab. **Hydroxychloroquine 400 mg BD** on **day 1** followed by **200 mg 1 BD** for **next 4 days**[Q] (after ECG Assessment) • Consider **IV methylprednisolone 0.5-1 mg/kg for 3 days** (preferably **within 48 hours of admission** or **if oxygen requirement is increasing**; if **inflammatory markers** are **increased**[Q]) • Prophylactic dose of **LMWH &** control of comorbid condition

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Severe Cases

Early supportive therapy & monitoring	Management of hypoxemic respiratory failure & ARDS	Management of septic shock
• **Supplemental Oxygen**: Initiate **O_2 therapy at 5 L/min**[Q] & titrate flow rates to reach **target SpO_2 ≥90%** in **non-pregnant** adults[Q] & **SpO_2 92-96% in pregnant** patients[Q] • **Children with emergency signs**[Q] (**obstructed or absent breathing, severe respiratory distress, central cyanosis, shock, coma B convulsions**) should **receive O_2 therapy** during resuscitation to **target SpO_2 ≥94%**[Q] • Use **conservative fluid management**	• **High-Flow Nasal Cannula Oxygenation** (HFNO) or **noninvasive mechanical ventilation**[Q] • **Endotracheal intubation & mechanical ventilation** may be required[Q] • In **severe ARDS**, **prone ventilation for >12 hours/day**[Q] is recommended • Application of **prone ventilation**[Q] is **strongly recommended for adult & pediatric patients** with **severe ARDS**	• **Early recognition of septic shock**[Q] • **Adults**: At least **30 mL/kg of isotonic crystalloid** in **first 3 hours** shall be given[Q] • **Children: 20 mL/kg rapid bolus** followed by **40-60 mL/kg** in **first hour**[Q] • **Crystalloids** include **normal saline & Ringer's lactate**[Q] • Use of **hypotonic crystalloids, starches, or gelatins** for resuscitation is **not recommended**[Q] • **Vasopressors**[Q]**: If shock persists** during or after fluid resuscitation • **Inotrope (dobutamine**[Q]**):** If signs of poor perfusion & cardiac dysfunction persist despite fluid resuscitation & use of vasopressors

Specific COVID-19 Treatment & Clinical Research:

- There is **no current evidence from multiple randomized controlled trials** (RCTs) **to recommend any specific treatment**[Q] for suspected or confirmed patients with COVID-19.
- **No specific antiviral agents** are **recommended for treatment of COVID-19** due **lack of adequate evidence from literature**[Q].

Investigational Therapies for COVID-19	
Remdesivir	• **Inhibits viral RNA-dependent, RNA polymerase**[Q] • **Inhibitory activity** against **SARS-CoV** & **Middle East respiratory syndrome (MERS-CoV**[Q]**)** • **Remdesivir** (under emergency use authorization) may be considered in **patients with moderate disease (Dose: 200 mg IV on day 1** followed by **100 mg IV daily for 5 days**[Q])
Convalescent plasma	• **Convalescent plasma** may be considered in patients with **moderate disease** who are **not improving despite use of steroids**[Q] **(**Dose: **4-13 mL/kg**)
Tocilizumab	• **Tocilizumab** is **humanized anti IL-6 receptor monoclonal antibody**, **binds specifically to IL-6 receptors**[Q] (**IL-6** is a **pro-inflammatory cytokine**) • **Tocilizumab** may be considered in **patients with moderate disease** with **progressively increasing oxygen requirements** and in **mechanically ventilated patients not improving despite use of steroids**[Q] • **Dose: 8 mg/kg** (maximum 800 mg at one time) given slowly **in 100 mL NS over 1 hour**[Q]
Hydroxychloroquine	• **Inhibit endosome maturation**[Q] • **Dose**: **400 mg BD on day 1** followed by **400 mg daily for next 4 days**[Q] • **Contraindications: Children <15 years, known history of retinopathy** & **hypersensitivity**[Q]

Discharge Criteria	
• **Asymptomatic, afebrile for 72 hours**[Q] • **Normal & stable vitals**[Q] • Other organ parameters normal/satisfactory	• **Chest X-ray: No abnormality** detected[Q] • **Viral clearance in respiratory samples after two specimens test negative** for SARS-CoV-2 **within a period of 24 hours**[Q]

Follow-up:

- As per **Chinese Centers for Disease Control and Prevention (CDC)**, after discharge the patient may be **home quarantined for a period of 14 days**[Q].
- **Post-discharge follow-up** for clinical assessment may be **carried out after 2 weeks & 4 weeks**[Q]**.**

Infection Prevention Control Practices:

- **At triage**: Give suspected patient a **triple layer surgical mask**[Q] and direct patient to a **separate area** or an **isolation room** if available
- **Apply standard precautions**[Q]**:** It includes use of **personal protective equipment** (PPE), **appropriate patient placement**, **prevention of sharp injury, safe biomedical waste management**, **cleaning & disinfection** of equipment and environment.
- **Apply droplet precautions**[Q]
- **Apply contact precautions**[Q]
- **Apply airborne precautions**[Q] when performing an aerosol generating procedure.

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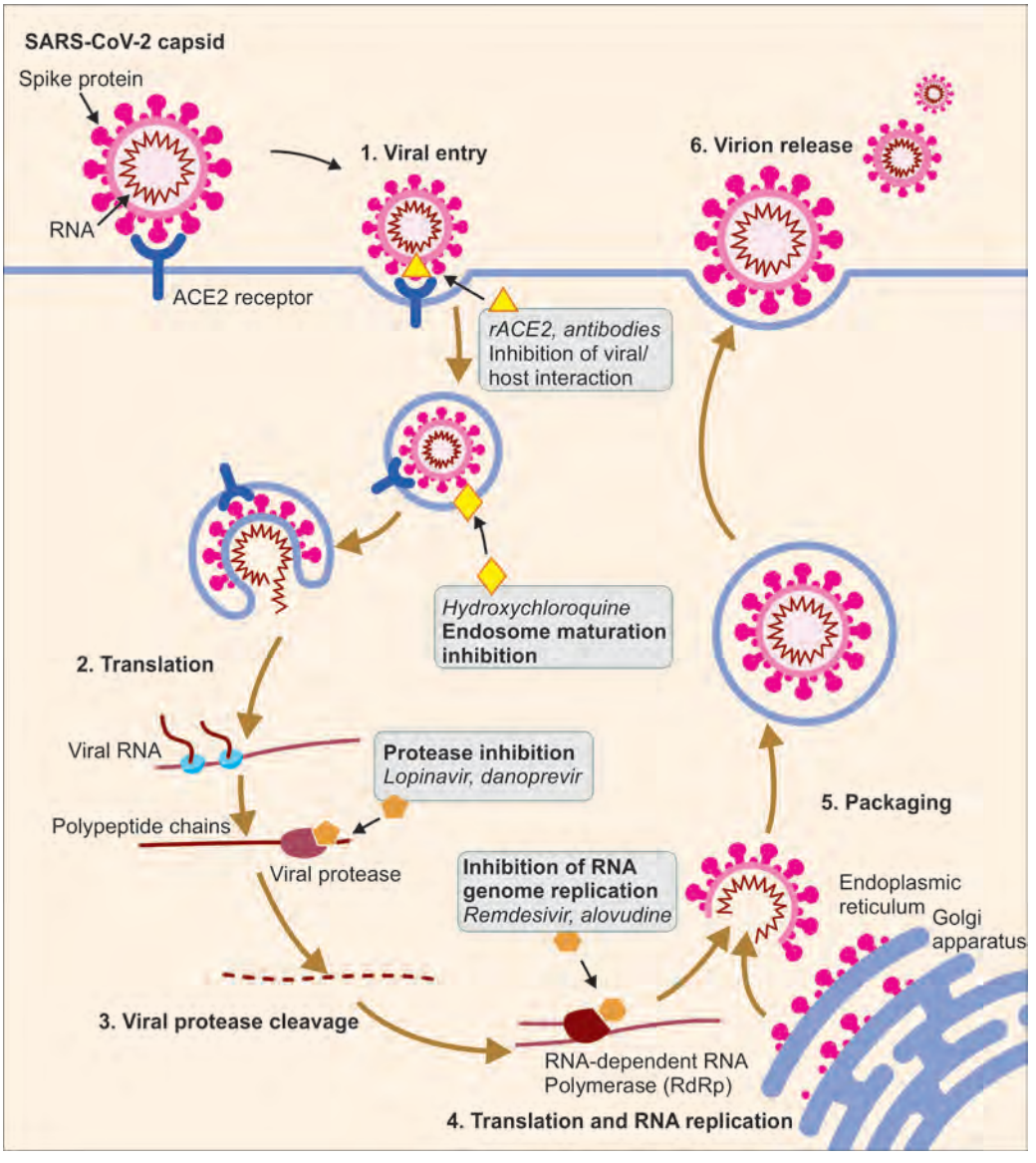
CORONAVIRUSES
• Commonly used in **walk-through-disinfectant-tunnels** for COVID19: **1% sodium hypochlorite**[Q] • **COVID19 biomedical waste guidelines:** – **N95 mask, head cover/cap, shoe cover, disposable linen gown should be disposed in yellow bag**[Q]. – **Viral transport media, plastic vials, vaccutainers, Eppendorf tubes, plastic cryovials, pipette tips should be disposed in red bag**[Q]. • **MOHFW** of India recommends **14 days quarantine**[Q] from the time of exposure for COVID19. • **ICMR Delhi &National Institute of Virology, Pune** has developed an **indigenous ELISA test kit for COVID19 antibody detection** known as **Kavach ELISA**[Q].



Life cycle of SARS-CoV-2 in Host Cells

Potential targets and postulated mechanism of action for antiviral interventions are shown: blocking virus/host cell interaction through the use of antibodies/nanobodies (and convalescent plasma therapy) or recombinant ACE2 protein; use of hydroxychloroquine (based on** *in vitro* **data) to inhibit endosome maturation; use of protease inhibitors to inhibit viral/endosome membrane fusion or viral polypeptide maturation; nucleoside/nucleotide analogues to inhibit viral genome replication.

Sequence for Putting on Personal Protective Equipment (PPE)

The type of PPE used will vary based on the level of precautions required, such as standard and contact, droplet or airborne infection isolation precautions. The procedure for putting on and removing PPE should be tailored to the specific type of PPE.

1. **Gown**
   - Fully cover torso from neck to knees, arms to end of wrists, and wrap around the back
   - Fasten in back of neck and waist

2. **Mask or respirator**
   - Secure ties or elastic bands at middle of head and neck
   - Fit flexible band to nose bridge
   - Fit snug to face and below chin
   - Fit-check respirator

3. **Goggles or face shield**
   - Place over face and eyes and adjust to fit

4. **Gloves**
   - Extend to cover wrist of isolation gown

Use Safe Work Practices to Protect yourself and limit the Spread of Contamination

- Keep hands away from face
- Limit surfaces touched
- Change gloves when torn or heavily contaminated
- Perform hand hygiene

How to Safely Remove Personal Protective Equipment (PPE)

There are a variety of ways to safely remove PPE without contaminating your clothing, skin, or mucous membranes with potentially infectious materials. Here is one example. Remove all PPE before exiting the patient room except a respirator, if worn. Remove the respirator after leaving the patient room and closing the door. Remove PPE in the following sequence:

1. Gloves

- Outside of gloves are contaminated!
- If your hands get contaminated during glove removal, immediately wash your hands or use an alcohol-based hand sanitizer
- Using a gloved hand, grasp the palm area of the other gloved hand and peel off first glove
- Hold removed glove in gloved hand
- Slide fingers of ungloved hand under remaining glove at wrist and peel off second glove over first glove
- Discard gloves in a waste container

2. Goggles or face shield

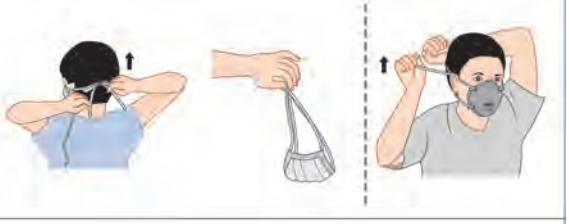
- Outside of goggles or face shield are contaminated!
- If your hands get contaminated during goggle or face shield removal, immediately wash your hands or use an alcohol-based hand sanitizer
- Remove goggles or face shield from the back by lifting head band or ear pieces
- If the item is reusable, place in designated receptacle for reprocessing; otherwise, discard in a waste container

3. Gown

- Gown front and sleeves are contaminated!
- If your hands get contaminated during gown removal, immediately wash your hands or use an alcohol-based hand sanitizer
- Unfasten gown ties, taking care that sleeves do not contact your body when reaching for ties
- Pull gown away from neck and shoulders, touching inside of gown only
- Turn gown inside out
- Fold or roll into a bundle and discard in a waste container

4. Mask or respirator

- Front of mask/respirator is contaminated—DO NOT TOUCH!
- If your hands get contaminated during mask/respirator removal, immediately wash your hands or use an alcohol-based hand sanitizer
- Grasp bottom ties or elastics of the mask/respirator, then the ones at the top, and remove without touching the front
- Discard in a waste container



5. **Wash hands** or use an alcohol-based hand sanitizer immediately after removing all PPE

Perform Hand Hygiene between Steps if Hands become Contaminated and Immediately after Removing all PPE

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Salient Features

- Authentic questions with exact language and options including all image-based questions
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Dr Pritesh Singh, graduate from Maulana Azad Medical College and postgraduate from Lady Hardinge Medical College, New Delhi, India, is an excellent teacher and has been taking awe inspiring classes in various countries since 2009. He is amongst the best faculty and is very popular with students because of his spellbinding classes. He is a renowned educationist and author of SURGERY ESSENCE, which needs no introduction and AIIMS ESSENCE, NEET ESSENCE, INI-CET ESSENCE, QUICK REVIEW OF SURGERY and DPG entrance examination books. The students all over the country admire the way he teaches. He is not just a source of inspiration for his pupils rather he is their role model, as he is young and dynamic. He sets a positive example with his style of teaching, courtesy, cooperation and professionalism. Some students say he is a magician who keeps his students spellbound throughout his class. His performance speaks volumes about his knowledge and precision.

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