


46 – What Could Be on the Exam About COVID


Speaker: Roy Gulick, MD



What Could Be on the Exam About COVID

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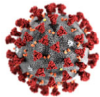


Disclosures of Financial Relationships with Relevant Commercial Interests

- None

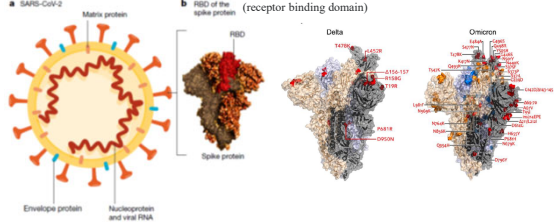
Outline – COVID-19

- Virology
- Clinical
- Treatment
- Prevention

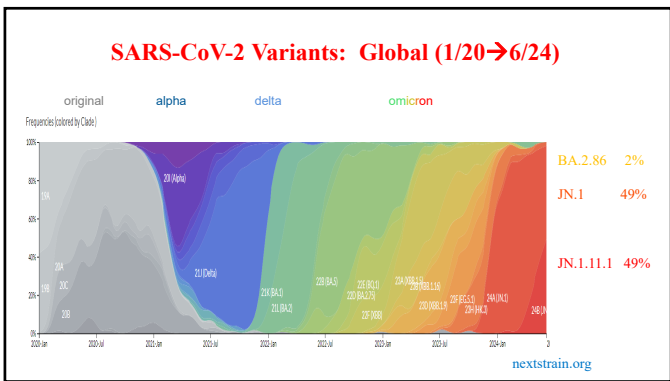


Virology

COVID-19 Structure



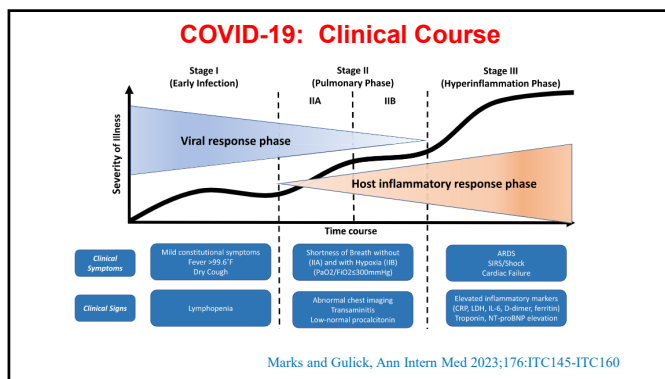
Krammer Nature 2020;586:516-527
 Annavajhala Nature 2021;597:703-708



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Clinical



What's the strongest risk factor for progression of COVID-19 to severe disease?

1. Older age
2. Diabetes, heart disease, or other comorbidities
3. Race/ethnicity
4. Vaccine status
5. Being infected with an omicron variant

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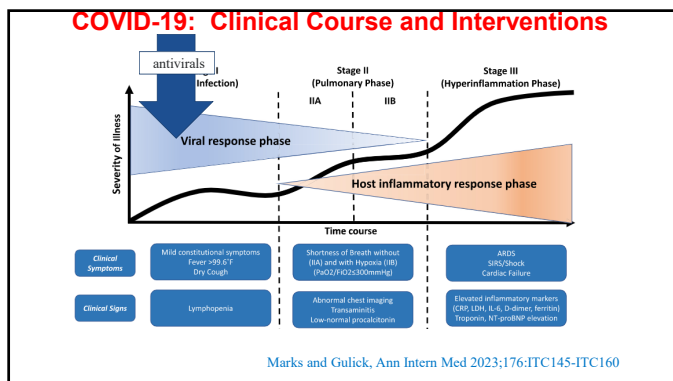
U.S. CDC: Risk for Severe COVID-19

- **Older age** remains the strongest risk factor
 - Compared with age 18-29, risk of death (vaccinated/unvaccinated individuals in 2020-2022) is:
 - 25X ↑ for age 50-64
 - 60X ↑ for age 65-74
 - 140X ↑ for age 75-84
 - 340X ↑ for age >85
- **Comorbidities** 1.3-2.9X ↑
- **Racial/ethnic minorities**, compared to Non-Hispanic Whites, have ↑ SARS-CoV-2 infections, hospitalizations, ICU admissions, death
- **Unvaccinated or not up-to-date with vaccines** www.cdc.gov (4/15/24)
- Risk ↓ with omicron variants

Treatment

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NIH COVID-19 Treatment Guidelines – Outpatients (2/29/24)

All Patients

- Symptom management should be initiated for all patients (AIII).
- The Panel **recommends against** the use of **dexamethasone**⁶ or other systemic corticosteroids (AIIb), unless these agents are being used to treat an underlying condition (AIII).

Patients Who Are at High Risk of Progressing to Severe COVID-19^{6,d}

Preferred therapies. Listed in order of preference:

- Ritonavir-boosted nirmatrelvir (Paxlovid)⁷ (AIIa).** Start as soon as possible and within 5 days of symptom onset. See footnote on drug-drug interactions.¹
- Remdesivir⁸ (BIIa).** Start as soon as possible and within 7 days of symptom onset.

Alternative therapy. For use when the preferred therapies are not available, feasible to use, or clinically appropriate⁹

- Molnupiravir⁹ (CIIa).** Start as soon as possible and within 5 days of symptom onset.

<https://www.covid19treatmentguidelines.nih.gov/>

Nirmatrelvir/ritonavir: Drug Drug Interactions

- Ritonavir inhibits CYP3A during rx (5 days) and 2-3 days after rx
- Some medicines **should not be coadministered**: e.g. rivaroxaban, amiodarone, rifampin, tadalafil (for pulmonary hypertension)
- Others may need to be **dose-reduced** or **temporarily stopped**: e.g., atorvastatin, rosuvastatin

Useful resources:

- NIH COVID-19 Treatment Guidelines
- IDSA Management of Drug Interactions: Resource for Clinicians
- University of Liverpool COVID-19 Drug Interaction Checker

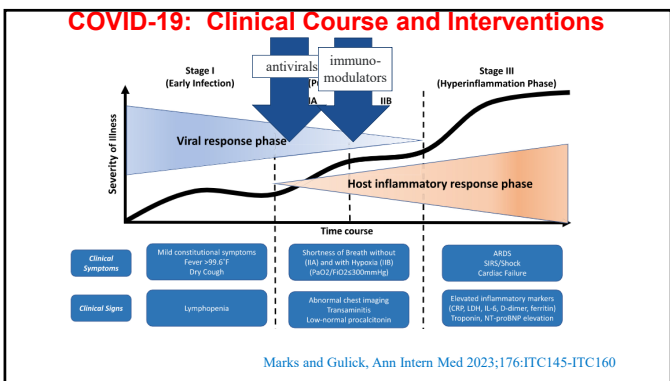
<https://www.covid19treatmentguidelines.nih.gov/>
<https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management/management-of-drug-interactions-with-nirmatrelvirritonavir-paxlovid/>
<https://www.covid19-druginteractions.org/>

What's the treatment of choice for COVID-19 with hypoxia?

- Nirmatrelvir-ritonavir
- Remdesivir
- Dexamethasone
- 1 and 2
- 2 and 3

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NIH COVID-19 Treatment Guidelines – Inpatients (2/29/24)

Hospitalized and Requires Conventional Oxygen

Clinical Scenario	Antiviral or Immunomodulator Therapy Recommendation
Patients who require minimal conventional oxygen	Remdesivir[®] (BIIa)
Most patients	Use dexamethasone[®] (BIIa) if remdesivir cannot be obtained, use dexamethasone (BII) .
Patients who are receiving dexamethasone and who have rapidly increasing oxygen needs and systemic inflammation	Add 1 of the following immunomodulators ^a Preferred • PO baricitinib (BIIa) • IV tocilizumab (BIIa) Alternatives (Listed in Alphabetical Order) • IV abatacept (CIIa) • IV infliximab (CIIa)

<https://www.covid19treatmentguidelines.nih.gov/>

NIH COVID-19 Treatment Guidelines – Inpatients (2/29/24)

Hospitalized and Requires MV or ECMO

Clinical Scenario	Antiviral or Immunomodulator Therapy Recommendation
All patients	Dexamethasone should be administered to all patients (AII). If not already initiated, promptly add 1 of the following immunomodulators ^a Preferred • PO baricitinib (AII) Preferred Alternative • IV tocilizumab (BIIa) Additional Alternatives (Listed in Alphabetical Order) • IV abatacept (CIIa) • IV infliximab (CIIa) Add remdesivir to 1 of the options above in certain patients (for examples, see footnote). ^a See footnote.

<https://www.covid19treatmentguidelines.nih.gov/>

Prevention

COVID-19 Vaccines

Krammer Nature 2020;586:516-527

RNA Vaccines

RNA vaccines consist of RNA encoding the spike protein and are typically packaged in LNPs

moderna
BIONTECH
Pfizer
FDA APPROVED

Viral Vector Vaccines

Replication-incompetent vector vaccines cannot propagate in the cells of the vaccinated individual but express the spike protein within them

Janssen
Novartis
May 2023

Protein Subunit Vaccines

Recombinant spike-protein-based vaccines

NOVAVAX
FDA APPROVED

COVID-19 Vaccines

Billions of vaccine doses given globally
 Benefits of vaccination outweigh risks; serious adverse events are rare

Side Effects

- **Most common:** fever, HA, fatigue, myalgias, pain at injection site X 1-2 days
- **Myocarditis / pericarditis:** rare (~1/5000-1/100,000)
 - more common in men: late teens-early 20s
 - mild; most recover fully
- **Anaphylaxis:** rare (1/200,000)
 - related to PEG/polysorbate(?)
 - more common in women, 80-86% had history of allergies, 24% had history of anaphylaxis
 - most within 15 minutes (one outlier at 20 hours)

www.CDC.gov 9/12/23

- **Uptake remains suboptimal** (2023-4 vaccine: 23% of US adults; 42% >65 yo as of 5/24)


- COVID-19: 5 Questions They Could Ask**
1. What leads to SARS-CoV-2 variants? MUTATIONS IN THE SPIKE PROTEIN
 2. What are important risk factors for COVID-19 progression? ↑AGE and IMMUNOSUPPRESSION
 3. What characterizes severe COVID-19? HYPOXIA
 4. Who should receive outpatient treatment for COVID-19? PEOPLE WITH RISK FACTORS FOR SEVERE DISEASE
 5. What is the preferred outpatient regimen for COVID-19? NIRMATRELVIR-RITONAVIR

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COVID-19: 5 MORE Questions They Could Ask	
6. What drugs interact with nirmatrelvir-ritonavir?	DRUGS METABOLIZED THROUGH CYTOCHROME P450 3A4 ENZYMES (E.G. AMIODARONE, RIFAMPIN)
7. What is the preferred regimen for inpatients with COVID-19 and hypoxia?	DEXAMETHASONE + REMDESIVIR
8. How do you manage a patient with rapidly progressive hypoxia or needing mechanical ventilation?	DEXAMETHASONE + A SECOND IMMUNOMODULATOR (BARICITINIB OR TOCILIZUMAB)
9. How do COVID-19 mRNA vaccines work?	MRNA TRANSCRIBED TO SPIKE PROTEIN THAT PROVOKES AN EFFECTIVE IMMUNE RESPONSE
10. What's the most important serious side effect of COVID-19 mRNA vaccines?	MYOCARDITIS

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