COVID-19 Update
January 13, 2021

Jorge Mera, MD

Whitney Essex, APRN

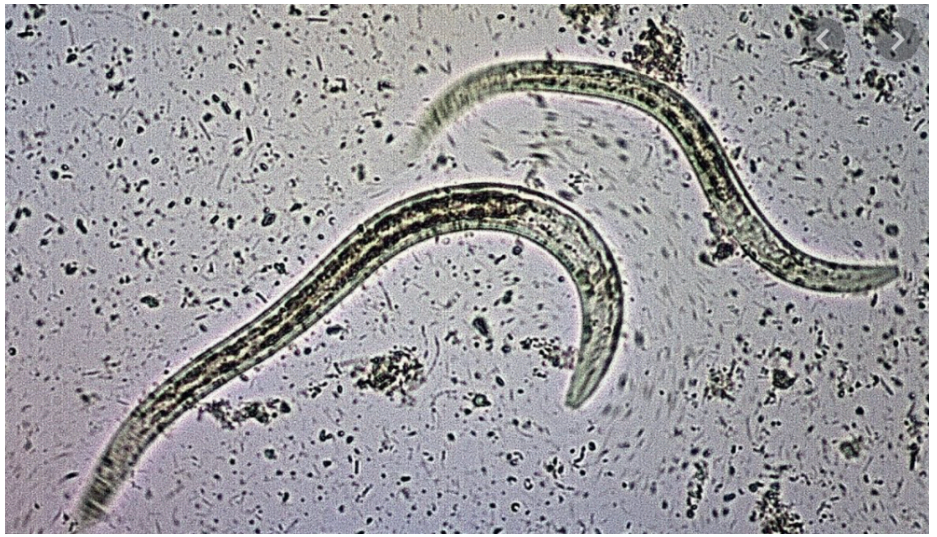
Ivermectin for COVID-19

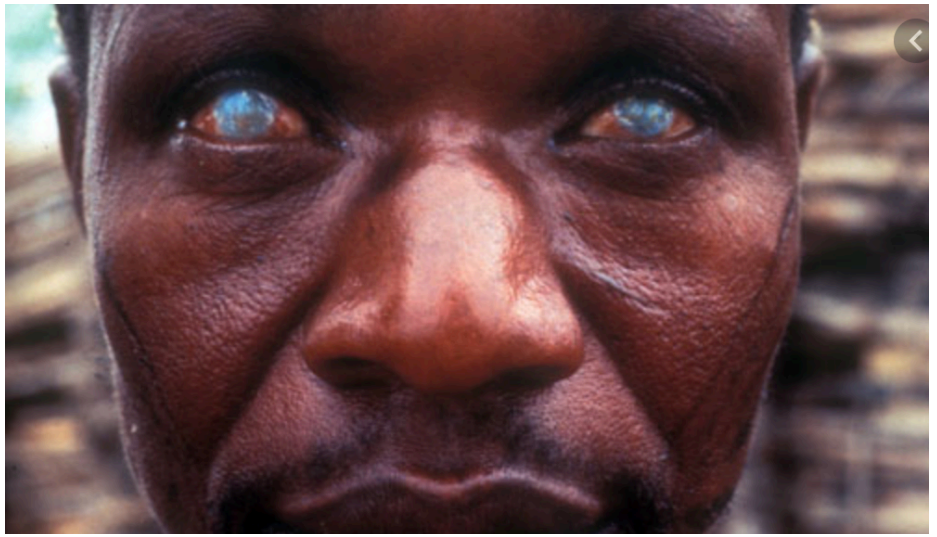
- Outpatient COVID-19 treatments are lacking
- There is a need for something safe, easy to take as a pill, and inexpensive, given within a short time after diagnosis, to a highly contagious person.
- A group called the Front Line COVID-19 Critical Care Alliance made up of predominantly critical care clinicians. Devotes much of its organization's homepage to ivermectin's promise for COVID-19 treatment

Paul Sax, Journal Watch, January 2020

What do We know about Ivermectin?

- It is licensed for use against strongyloidiasis and Onchocerciasis (river blindness)
- Also used off-label use for scabies and head lice
- Used in veterinary medicine for pet owners as a common de-worming agent.





How does Ivermectin Work Against SARS-CoV-2?

- Importins, a type of karyopherins, exemplify a major class of soluble transport receptors which are involved in nucleo-cytoplasmic transit of various substrates.
- The speculated inhibitory action of ivermectin on importin α/β mediated transport system, Based on this conjecture, the role of ivermectin in eliminating Covid-19 can be assumed.

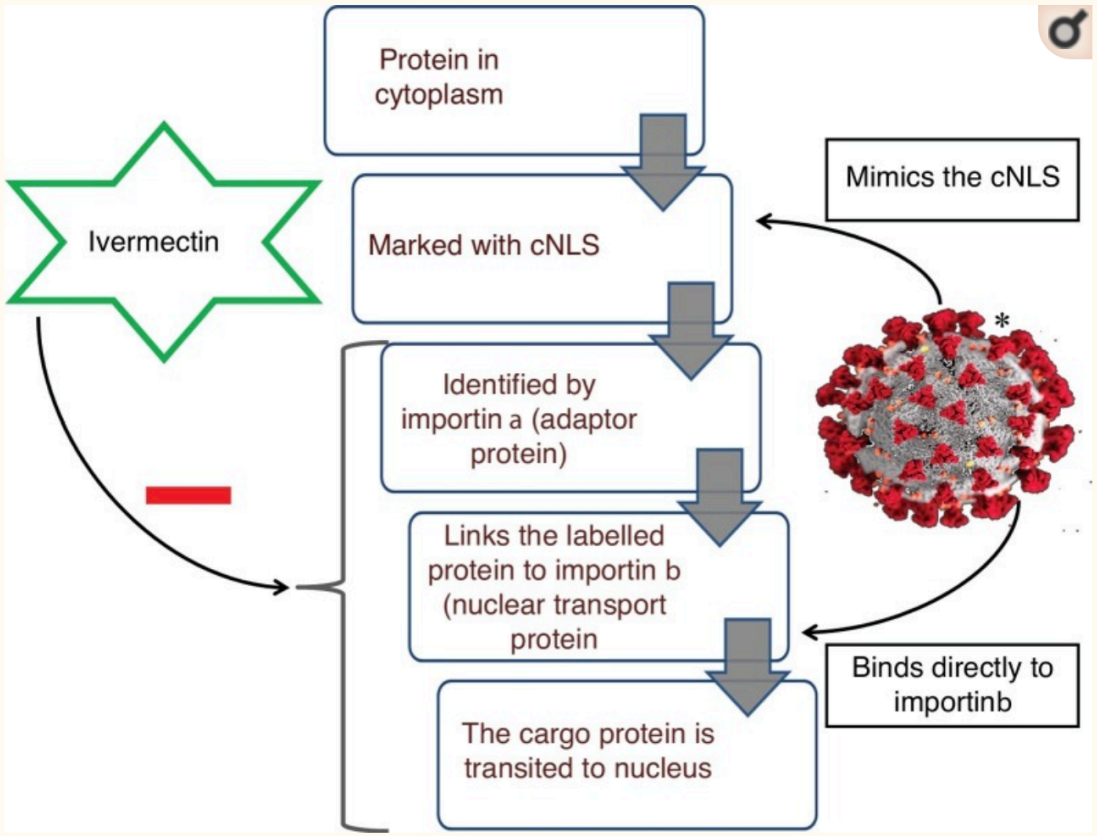
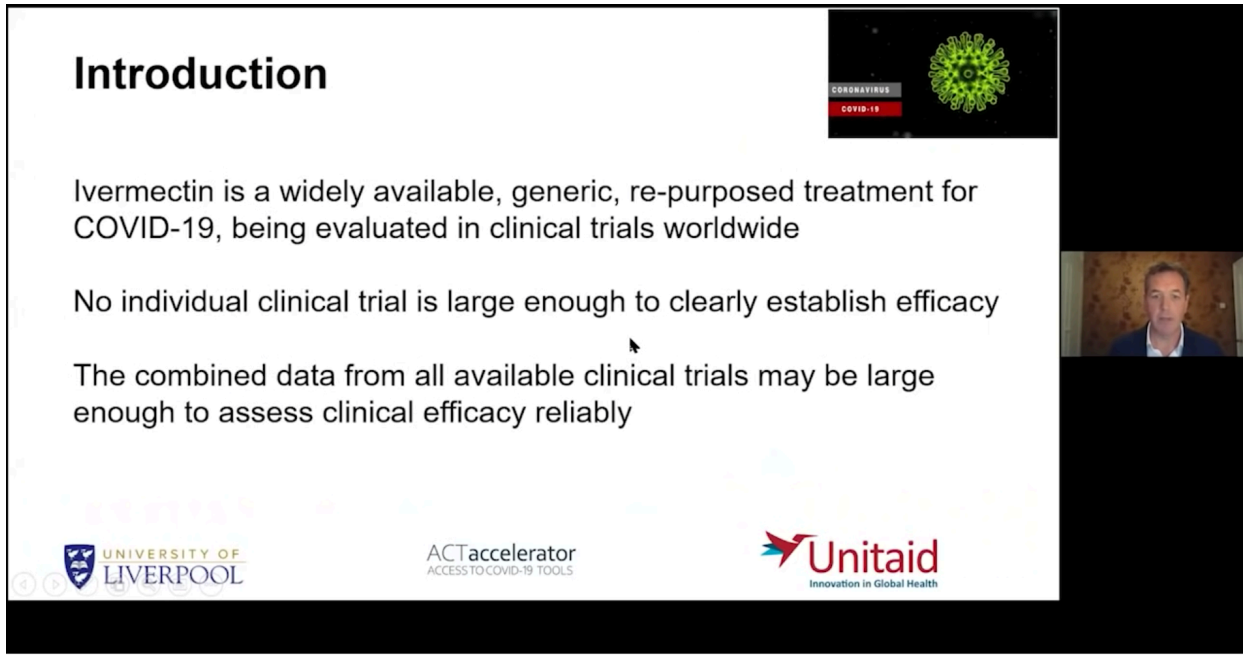


Fig. 1

Mechanism of ivermectin induced inhibition of importin α/β mediated coronavirus proteins transport. cNLS : classical Nuclear Localization Signal. ***Image courtesy: CDC/Alissa Eckert, MS; Dan Higgins, MAMSA.**

Braz J Infect Dis. 2020 July-August; 24(4): 369–371.

What do We know about Ivermectin and COVID-19?



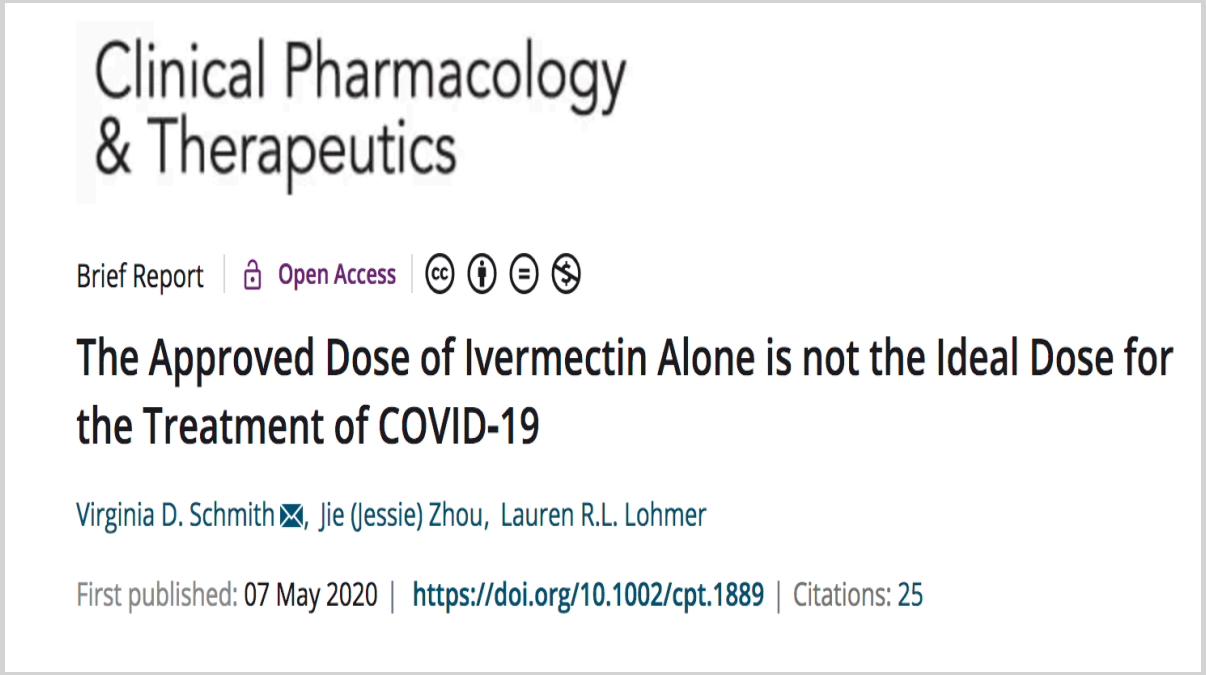
Ivermectin meta-analysis by Dr. Andrew Hill

https://www.youtube.com/watch?v=yOAh7GtvcOs&feature=youtu.be

- **Metanalysis**
  - The risk-ratio for mortality with ivermectin was 0.17 (95% confidence interval 0.08, 0.35), an 83% reduction in risk of dying .
  - Outcomes for other endpoints (time to viral clearance, time to clinical recovery, duration of hospitalization) also favored treatment over controls.
- **Limitations**
  - incompleteness of the data
  - Some of the studies were open label,
  - Difference in dosing regimens and endpoints.
  - Publication bias may play a role
  - None of these trials have yet been published in peer-reviewed journals.

What do We know about Ivermectin and COVID-19?

- Pharmacokinetic (PK) data on ivermectin's antiviral activity.
  - PK studies don't always correlate with clinical activity, and ivermectin may have anti-inflammatory activity



Clinical Pharmacology & Therapeutics

Brief Report | Open Access

The Approved Dose of Ivermectin Alone is not the Ideal Dose for the Treatment of COVID-19

Virginia D. Schmith, Jie (Jessie) Zhou, Lauren R.L. Lohmer

First published: 07 May 2020 | https://doi.org/10.1002/cpt.1889 | Citations: 25

"Ivermectin is unlikely to reach the IC_{50} of 2 µM in the lungs after single oral administration of the approved dose (predicted lung concentration: 0.0873 µM) or at doses 10× higher that the approved dose administered orally (predicted lung concentration: 0.820 µM"

Ivermectin for COVID-19 Recommendations

- The clinical trials data for ivermectin look stronger than they ever did for hydroxychloroquine, but we're not quite yet at the "practice changing" level.
- Results from at least 5 randomized clinical trials are expected soon that might further inform the decision.
- NIH treatment guidelines still recommend against the use of ivermectin for the treatment of COVID-19

Paul Sax, Journal Watch, January 2020

Ivermectin for COVID-19

“But we have to guard against two important biases here.

First, that because we were burned by hydroxychloroquine means that all other repurposed antiparasitic drugs will fail too.

Second, that studies done in low- and middle-income countries must be discounted because, well, they weren’t done in the right places. That’s not just bias, it’s also snobbery.”

Paul Sax, Journal Watch, January 2020

Early High-Titer Plasma Therapy to Prevent Severe Covid-19 in Older Adults

- **BACKGROUND**
  - Therapies to interrupt the progression of early Covid-19 remain elusive
  - Convalescent plasma administered to hospitalized patients has been unsuccessful

- **METHODS**
  - Randomized, double-blind, placebo-controlled trial of convalescent plasma with high IgG titers against SARS-CoV-2 in older adult patients within 72 hours after the onset of mild Covid-19 symptoms

  - The primary end point was severe respiratory disease, defined as:
    - Respiratory rate of 30 breaths per minute or more, an oxygen saturation of less than 93% while the patient was breathing ambient air, or both.

NEJM, January 6, 2021
DOI: 10.1056/NEJMoa2033700

Early High-Titer Plasma Therapy to Prevent Severe Covid-19 in Older Adults

- **RESULTS**
  - A total of 160 patients underwent randomization.
    - In the intention-to-treat population, severe respiratory disease developed in 13 of 80 patients **(16%)** who received convalescent plasma and in 25 of 80 patients **(31%)** who received placebo
      - Rrelative risk, 0.52; 95% confidence interval [CI], 0.29 to 0.94; P=0.03), with a relative risk reduction of 48%.
  - No solicited adverse events were observed.

- **CONCLUSIONS**
  - Early administration of high-titer convalescent plasma against SARS-CoV-2 to mildly ill infected older adults reduced the progression of Covid-19.

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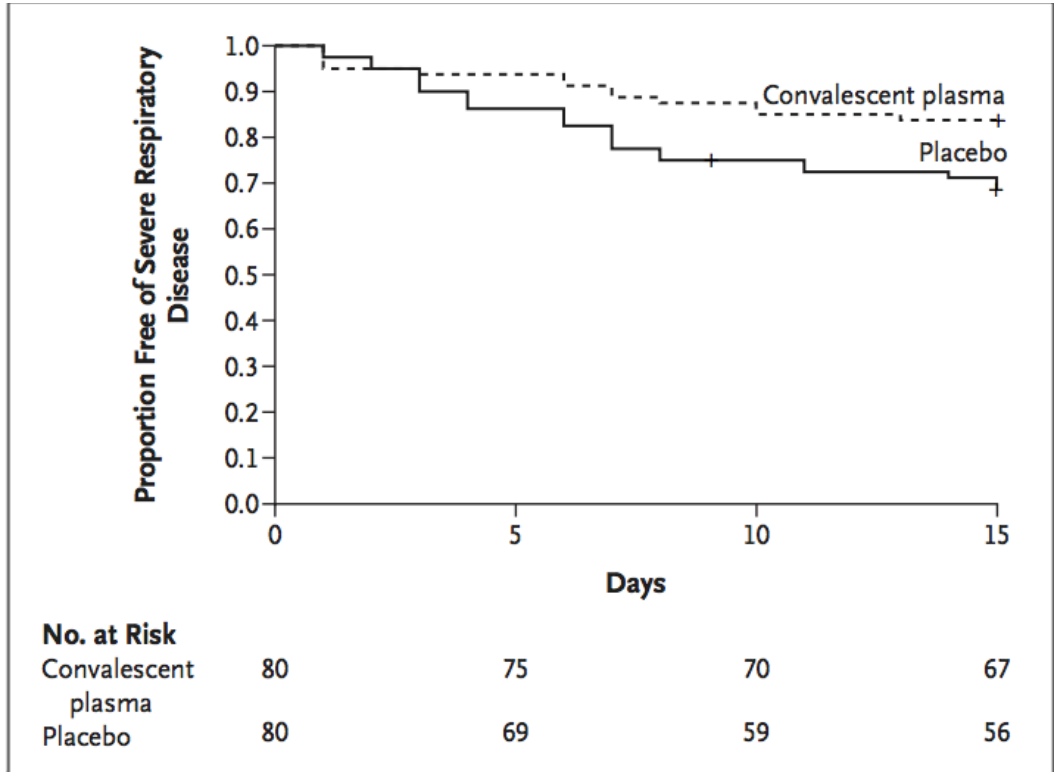
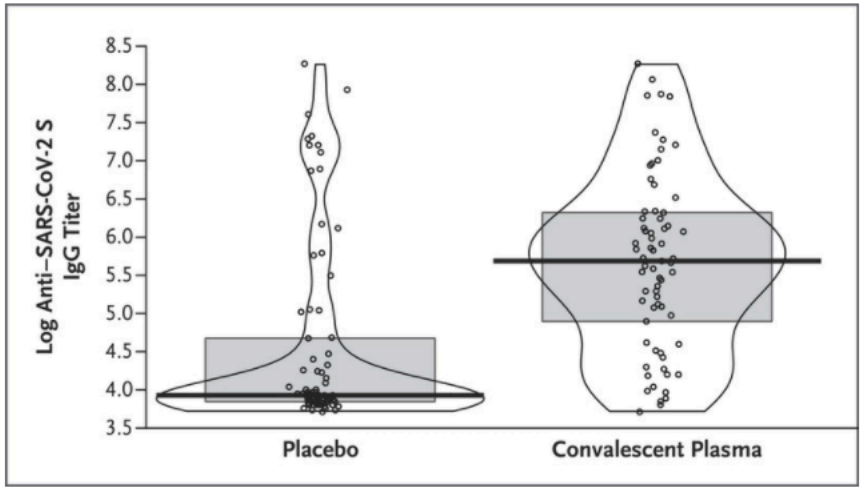


- **Time to the Development of Severe Respiratory Disease Due to Coronavirus Disease 2019, According to Trial Group in the Intention-toTreat Analysis**.
- Shown are Kaplan–Meier estimates of the time from the intervention (administration of convalescent plasma or placebo) to the development of severe respiratory disease. The tick marks on the curves represent the interquartile range in the Kaplan–Meier time-to-event analysis in the convalescent plasma and placebo groups

Early High-Titer Plasma Therapy to Prevent Severe Covid-19 in Older Adults



SARS-CoV-2 Serum Titers, According to Trial Group.

Table 3. Primary End Point, According to Donor SARS-CoV-2 S IgG Titer.

Patient Group	Patients with Severe Respiratory Disease	Relative Risk (95% CI)	Relative Risk Reduction
	no./total no. (%)		*percent*
Placebo group	25/80 (31)	1.00	
Recipient of SARS-CoV-2 S IgG in donor plasma*			
At a titer at or above median concentration	3/36 (8)	0.27 (0.08–0.68)	73.3
At a titer below median concentration	9/42 (21)	0.69 (0.34–1.31)	31.4

* The median concentration is a SARS-CoV-2 S IgG titer of 1:3200.

NEJM, January 6, 2021
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Q&A

- *Is there is any guidance on use of COVID-19 vaccines and immunosuppressive medications for patients that are taking such medications?*

- Any updates on the doctor who passed away two weeks after receiving the vaccine?