

Faculty/Presenter Disclosure

- Faculty: Dr M John Gill Financial affiliations:
 - HIV Advisory boards: ViiV, Gilead, Merck .
 - Grants, clinical trials: Amgen ,Merck,CHRR ,NIH
 - Patents, royalties: Nil
 - Investments in health organizations: Nil
 - Other influential affiliations: Nil

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Disentangling the message

- Mainstream media and social media in overdrive
- Lots of “papers” now published online before even reviewed
- “Science” may be correct but may jump to premature conclusions or worse be incorrect or incomprehensible and will/would never be published
- Even in top quality peer-viewed journals the articles may be premature / over interpreted / incomplete or without necessary caveats
- Why ? Authors, reviewers and journals are under immense pressure to be fast and first in publishing .
- Be careful

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Basic Viral Facts

- The SARS-CoV-2 is the virus causing COVID-19 infection.
- Single strand RNA virus in coronavirus family named from morphology .
- It is a respiratory virus (contact droplet **not** airborne transmission).
- Only a handful of coronaviruses cause human illness (mostly **respiratory** such as colds but include serious respiratory infections SARS and MERS).
- Uses human ACE 2 receptor(Angiotensin converting enzyme 2)
- **VERY high affinity** for receptor v SARS (i.e. very sticky to respiratory cells i.e. few viruses needed for infection)
- May be target for monoclonal antibody therapy or subunit vaccine .

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SARS -CoV-2

- SARS-CoV-2 likely originated from bats into intermediary animal host (likely pangolin) and then to humans.
- Virus not mutating significantly. So vaccine more possible but virus less likely to “flame out” or become less pathogenic.
- Variation is, however, enough for phylogenetic studies . <https://nextstrain.org/narratives/ncov/sit-rep/2020-03-27>
- IGG and IGM Antibody tests are close: Will be very useful for determining natural history and possible health care staffing
- No cross protection so No one is immune .

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Diagnosis of COVID 19 Infection

- A nasopharyngeal swab (NP) on good respiratory samples looking for viral genetic sequences (molecular testing) is only current diagnostic test. N95 not required for NP swab. BAL seldom indicated
- Two step process now identifies “e gene” coronavirus sequence then confirmed by SARS-CoV-2 “polymerase gene” sequence
- As with other tests, sampling and timing issues: Too early/bad sample limits sensitivity and do virus sequences found post-recovery mean active infectious virus?
- Severe global “reagent” shortage. Do not test asymptomatic!
- No serology testing yet, meaning we are unable to determine past asymptomatic exposures

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Natural History in Humans

- Proportion of asymptomatic infections unknown. May be low but critical for understanding possible transmission and HCW immunity.
- Incubation period after exposure likely 2-14 days (median ~5 days)
- 97.5% develop symptoms within 11 days
- Currently we believe of those diagnosed, 80% have self-limited mainly respiratory illness probably of ~ 14 Days duration
- 20% have more severe illness requiring medical care +/- hospitalization
- Risk in hospitalized is mainly respiratory then multi organ failure requiring ventilation and high risk of death
- Progression risk and rate down pathway below is unclear

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Diagnostic Clinical Challenges mostly unchanged

<u>Influenza-like-illness (ILI)</u>	<u>COVID-19</u>
<ul style="list-style-type: none">• New or changed cough AND one or more of the following:	<ul style="list-style-type: none">• Fever (98%)• Cough (76%)• Myalgia or fatigue (44%)• Anosmia/hyposmia/dysgeusia ?• Sputum production (28%)• Headache (8%)• Mild Diarrhea (? 3%)• Hemoptysis (5%)• Contact as no travel now
<ul style="list-style-type: none">• Fever (or history of fever in the last 24 hours)• Muscle aches• Severe exhaustion/weakness• Sore throat• Joint pain	

AHS Respiratory (ILI) algorithm JG April 1 2020

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Presenting symptoms

Symptom	Percentage
Fever	100%
Cough	76%
Dyspnea	64%
Malaise	33%
Myalgia	28%
Rhinorrhoea	8%
Headache	5%

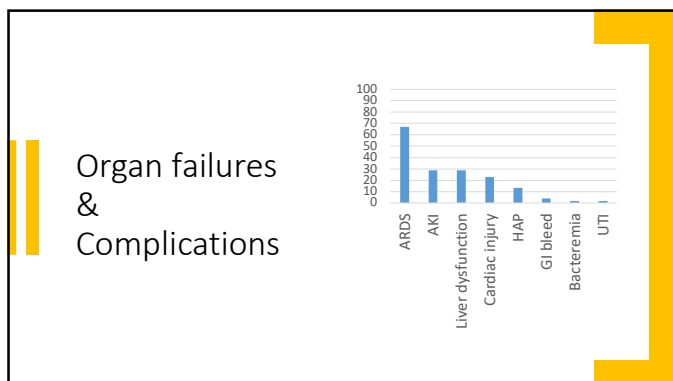
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Other tests

- Labs: WBC somewhat down and lymphopenia .
- Infrequent but may be abnormal elevated LFTS LDH CRP ESR .
- Only in critically ill are D Dimer IL6 elevated .
- Radiology :do not use as screening tool
- Early small infiltrates and interstitial changes peripherally then in some progression to ground glass and crazy paving .

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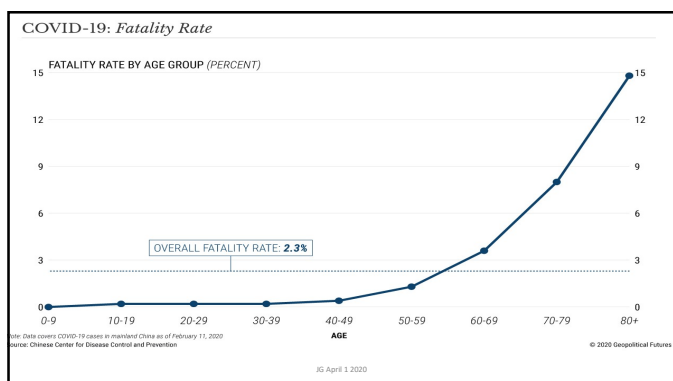
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Fatality rate

- Is it 0.5% or 10%?
- Difference driven in part by age of population and comorbidities (Korea v Lombardy)
- Stage of presentation
- Medical care available at time (i.e. overwhelmed)
- Duration of local epidemic (recent infections do not have endpoints)

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COVID 19 Infection treatment

- Supportive care
- Kaletra disappointing in a NEJM study published 10 days ago despite benefit in SARS
- Hydrochloroquine / azithromycin / chloroquine value unclear
- Awaiting many trial results (>500 listed as in progress)
- Until then <https://www.albertahealthservices.ca/assets/info/ppih/if-ppih-covid-19-recommendations.pdf>
- My main hope/interest is Remdesivir (unavailable in Canada)

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Americans Reportedly Turning To Mexico To Obtain Drug Trump Touts As Potential Coronavirus Cure.
The [Dallas Morning News](#) (3/23, Branham) reports that "Americans are making a mad dash south of the border in search of" hydroxychloroquine, a drug President Trump "calls a potential cure for the coronavirus, even as some health experts cast doubt on its effectiveness." The drug, an "anti-malaria medication known as Plaquenil, is a hot drug here, with more than a dozen pharmacies saying they've run out." Due to the high demand, pharmacists "said Monday and over the weekend that they're now requiring written prescriptions from doctors who must state the medicine is for patients with conditions that include lupus and malaria, conditions for which the drug is normally used."

Source: <https://www.dallasnews.com/news/public-health/2020/03/24/border-towns-see-run-on-drug-touted-by-trump-but-unproven-as-coronavirus-cure/>

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Scientific topics generating noise

- **Sex:** Why is COVID 19 infection mortality in men consistently twice that of women? Is it related to other factors e.g. smoking, or that immune genes reside on X chromosome?
- **Blood type A:** Are they more vulnerable? Some viruses do not infect people. Unclear here if that may be factor
- **NSAIDS contraindicated ??**
- **Pregnancy:** Unclear if risk to fetus but viremia not common in COVID 19
- **Does presence of viral genetic material match infectious virus?**

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The role of Angiotensin converting enzyme 2

- Increased rate of non-survival in ICU seen in CVD DM and high BP. Often these patients were on ACE inhibitors
- SARS-COV-2 enters cell by ACE 2 receptor which is expressed on epithelial cells in lung intestine kidney and blood vessels
- ACE 2 expression is increased in DM T 1 and 2 who are treated with ACE inhibitors and angiotensin II type 1 receptor blockers
- Calcium channel blockers do not increase ACE 2 expression

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The "Love Boat" : Season 2020

- The Diamond Princess, hosted 3,711 passengers/crew who underwent a two-week quarantine after a disembarked passenger was diagnosed with COVID-19
- Over 16 days, a total of 3,063 tests were conducted and **634 persons tested positive**. Of these, 476 (75.1%) of cases were ≥60 years old and 313 (49.3%) were female
- Of the 634 positive passengers, 306 (48.3%) were symptomatic and 328 (51.7%) were reported as asymptomatic at testing
- Using modeling it was estimated that 197 of the 328 (60.6%) asymptomatic cases would become symptomatic. As such, they estimate that **17.9% of infected cases would be truly asymptomatic** throughout their infection

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Therapeutic Trials

- CATCO
- Solidarity
- HOPE (outpatient early therapy)
- Post-exposure prophylaxis study for HCW
- Anti inflammatory studies in hospitalized patients: Colchicine
Tocilizumab (binds IL-6)
- Passive immunotherapy (antibody)

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In summary

- Prevention is easier than cure
- This poses many challenges to Public health and I p and C
- My final messages are

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If we are short of PPE can we reuse trusted PPEs from past pandemics ?

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