The Daily COVID-19 Literature Surveillance Summary

October 07, 2020

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COVID-19 Daily Literature Surveillance

COVID19LST

Bringing you real time, distilled information for guiding best practices during the COVID-19 pandemic

LEVEL OF EVIDENCE

Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

Question	Step 1 (Level 1*)	Step 2 (Level 2*)	Step 3 (Level 3*)	Step 4 (Level 4*)	Step 5 (Level 5)
How common is the problem?	Local and current random sample surveys (or censuses)	Systematic review of surveys that allow matching to local circumstances**	Local non-random sample**	Case-series**	n/a
Is this diagnostic or monitoring test accurate? (Diagnosis)	Systematic review of cross sectional studies with consistently applied reference standard and blinding	Individual cross sectional studies with consistently applied reference standard and blinding	Non-consecutive studies, or studies without consistently applied reference standards**	Case-control studies, or "poor or non-independent reference standard**	Mechanism-based reasoning
What will happen if we do not add a therapy? (Prognosis)	Systematic review of inception cohort studies	Inception cohort studies	Cohort study or control arm of randomized trial*	Case-series or case-control studies, or poor quality prognostic cohort study**	n/a
Does this intervention help? (Treatment Benefits)	Systematic review of randomized trials or *n*-of-1 trials	Randomized trial or observational study with dramatic effect	Non-randomized controlled cohort/follow-up study**	Case-series, case-control studies, or historically controlled studies**	Mechanism-based reasoning
What are the COMMON harms? (Treatment Harms)	Systematic review of randomized trials, systematic review of nested case-control studies, *n*-of-1 trial with the patient you are raising the question about, or observational study with dramatic effect	Individual randomized trial or (exceptionally) observational study with dramatic effect	Non-randomized controlled cohort/follow-up study (post-marketing surveillance) provided there are sufficient numbers to rule out a common harm. (For long-term harms the duration of follow-up must be sufficient.)**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning
What are the RARE harms? (Treatment Harms)	Systematic review of randomized trials or *n*-of-1 trial	Randomized trial or (exceptionally) observational study with dramatic effect			
Is this (early detection) test worthwhile? (Screening)	Systematic review of randomized trials	Randomized trial	Non -randomized controlled cohort/follow-up study**	Case-series, case-control, or historically controlled studies**	Mechanism-based reasoning

*** Level may be graded down on the basis of study quality, imprecision, indirectness (study PICO does not match questions PICO), because of inconsistency between studies, or because the absolute effect size is very small; Level may be graded up if there is a large or very large effect size.**

**** As always, a systematic review is generally better than an individual study.**

How to cite the Levels of Evidence Table

OCEBM Levels of Evidence Working Group*. "The Oxford 2011 Levels of Evidence".
Oxford Centre for Evidence-Based Medicine. http://www.cebm.net/index.aspx?o=5653

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EXECUTIVE SUMMARY

Climate

- An article in Nature highlights concerns among the scientific community about current COVID-19 vaccine trials being run by AstraZeneca, Pfizer, and Moderna. In light of two reported cases of transverse myelitis in trial participants, some scientists urge for more transparency from the companies leading trials, others are concerned about public opinion of vaccine safety and worry about political pressure on the trials, especially during the U.S. election season, and some question the vaccine trials' goals of reducing cases of symptomatic COVID-19, and instead suggest focusing on reducing incidence of severe disease.

Epidemiology

- Members of the Max Planck Institute for Evolutionary Anthropology in Germany conducted a genetic analysis investigating previous findings of an association between severe COVID-19 disease (hospitalization and respiratory failure) and a six-gene region on chromosome 3 (49.4kb), asserting that the region has been inherited from Neanderthals, following analysis using the 1000 Genomes Project. The anthropologists report this haplotype is seen in 50% of South Asians and 16% of Europeans, which they believe directly contributes to increased susceptibility to severe disease.

Understanding the Pathology

- A review by molecular biologists found a higher prevalence of the G614 variant of SARS-CoV-2 is related to increased prevalence of chemosensory dysfunction due to expression of a spike protein with higher receptor binding domain affinity to h-ACE2 receptors, leading to enhancement of SARS-CoV-2 binding in the olfactory epithelium and increased chemosensory deficits.

Adjusting Practice During COVID-19

- Increased risk of COVID-19 infection among patients with a history of or current gynecologic cancer has led to the development and implementation of an algorithm for less invasive and more cost-effective surveillance with telemedicine-based, risk-stratified surveillance and a shared-decision making program for patient follow-up, suggesting the potential for reconsideration of healthcare delivery for these patients.

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CLIMATE

COVID-VACCINE RESULTS ARE ON THE WAY - AND SCIENTISTS' CONCERNS ARE GROWING

Mallapaty S, Ledford H.. Nature. 2020 Sep 25. doi: 10.1038/d41586-020-02706-6. Online ahead of print.
Level of Evidence: Other - Opinion

BLUF

A news article published in Nature highlights concerns among the scientific community about current COVID-19 vaccine trials being run by AstraZeneca, Pfizer, and Moderna. In light of two reported cases of transverse myelitis in trial participants, some scientists urge for more transparency from the companies leading trials. Others are concerned about public opinion of vaccine safety and worry about political pressure on the trials, especially during the U.S. election season. Finally, some researchers question the vaccine trials' goals of reducing cases of symptomatic COVID-19, and instead suggest focusing on reducing incidence of severe disease.

EPIDEMIOLOGY

FURTHER INFORMATION ON POSSIBLE ANIMAL SOURCES FOR HUMAN COVID-19

Opriessnig T, Huang YW.. Xenotransplantation. 2020 Sep 25:e12651. doi: 10.1111/xen.12651. Online ahead of print.
Level of Evidence: Other - Review / Literature Review

BLUF

A review by a multi-institutional team of veterinarians provide updates on COVID-19 spread to other animal species like Mustelidae (ferrets), Felinae (cats, tigers, lions), and Caninae (dogs), in addition to discussing how ferrets, Egyptian fruit bats, dogs, cats, golden Syrian hamsters, and macaques have been used in COVID-19 research (Table 2). The research has been focused on respiratory symptom replication, antibody titer loads, and studying interactions between the ACE2 protein and receptor binding domain (RBD) viral protein. Recently, there have been more reports of minks being infected with the COVID-19 virus. Overall, more research is needed on identifying animal reservoirs for COVID-19 given the widespread usage of animal products in medical treatments (e.g. grafts, xenotransplants).

FIGURES

Virus	Time of circulation	Laboratory confirmed cases	Deaths	Case fatality rate (%)	Country distribution
SARS-CoV[a]	2002-2003	8096	774	9.6	26
MERS-CoV[b]	2012-ongoing	2494	853	35	27
SARS-CoV-2[c]	2019-ongoing	25 602 665	852 758	3.3	Global pandemic

[a]Source: https://www.who.int/csr/sars/country/table2004_04_21/en/.
[b]Source: https://www.who.int/emergencies/mers-cov/en/.
[c]Source: https://covid19.who.int (Accessed 2020/09/03).

Table 1: Facts on high pathogenic human CoVs

			Experimental infection characteristics			Susceptibility			Serological surveillance	
Family	Species	Type of infection	Animal# (Reference)	Route	Dose[a]	None, low, high	Clinical signs	Transmission	Positive/total number tested	Reference
Suidae	Pigs	Experimental	9^{6} 5^{4}	Intra-nasal	10^{5} $TCID_{50}$ 10^{5} PFU	None	No	No	0/187	26
Poultry	Chickens	Experimental	17^{6} 5^{4} 10^{7}	Oculo-oronasal Intra-nasal	10^{5} $TCID_{50}$ $10^{4.5}$ PFU $10^{5.4}$ $TCID_{50}$	None	No	No	0/153	26
	Duck	Experimental	5^{4} 10^{7}	Intra-nasal Intra-choanal	$10^{4.5}$ PFU 10^{6} $TCID_{50}$	None	No	No	0/153	26
	Turkeys	Experimental	10^{7}	Intra-choanal	$10^{5.4}$ $TCID_{50}$	None	No	No	NA	
	Japanese quail	Experimental	10^{7}	Intra-choanal	$10^{5.4}$ $TCID_{50}$	None	No	No	NA	
	White Chinese geese	Experimental	10^{7}	Intra-choanal	10^{6} $TCID_{50}$	None	No	No	NA	
Ruminants	Cattle	NA							0/107	26
	Sheep								0/133	26
	Goats								NA	
Caninae	Dogs	Natural and experimental	5^{4}	Intra-nasal	10^{5} PFU	Low	No or mild	No	8/180 0/497	3 26
Felidae	Cats (domestic)	Natural and experimental	14^{4} 3^{27}	Intra-nasal NA	10^{5} PFU NA	High	No or mild	Yes	6/60 0/87	3 26
	Tigers and lions	Natural				High	Yes	Yes	0/8	26
Musteliadae	Ferrets	Experimental	10^{6} 9^{4}	Intra-nasal	10^{5} $TCID_{50}$ 10^{5} PFU	High	No or mild	Yes	0/2	26
	Minks (American minks, *Neovison vison*)	Natural				High	Yes	Yes, also mink-human	0/81	26
Pteropodidae	Egyptian fruit bats (*Rousettus aegyptiacus*)	Experimental	9^{6}	Intra-nasal	10^{5} $TCID_{50}$	High	No	Yes	NA	
Cricetidae	Golden Syrian hamsters	Experimental	4^{5} 9^{12} 15^{11} 13^{13}	Intra-nasal	6×10^{5} $TCID_{50}$ 8×10^{4} $TCID_{50}$ 10^{5} PFU 10^{5} PFU	High	No or mild	Yes	NA	
Old word monkeys Subfamily *Cercopithecines*	Macaques (*Macaca fascicularis* and *Macaca mulatta*)	Experimental	5^{15} 3^{16} 3^{16} 3^{16} 10^{18}	Intra-nasal Intra-nasal and intra-tracheal	10^{6} $TCID_{50}$ 1.1×10^{6} PFU 1.1×10^{5} PFU 1.1×10^{4} PFU	High	Yes	Yes	NA	

Abbreviation: NA, not available.
[a]Median tissue culture infectious dose ($TCID_{50}$) per animal or plaque forming unit (PFU).

Table 2: Summary of findings in animals to date (Adapted from OIE Technical Factsheet, Infection with SARS-CoV-2 in animals)

THE MAJOR GENETIC RISK FACTOR FOR SEVERE COVID-19 IS INHERITED FROM NEANDERTHALS

Zeberg H, Pääbo S.. Nature. 2020 Sep 30. doi: 10.1038/s41586-020-2818-3. Online ahead of print.
Level of Evidence: Other - Modeling

BLUF

Members of the Max Planck Institute for Evolutionary Anthropology in Germany conducted a genetic analysis investigating previous findings of an association between severe COVID-19 disease (hospitalization and respiratory failure) and a six-gene region on chromosome 3 (49.4kb), asserting that the region has been inherited from Neanderthals, following analysis using the 1000 Genomes Project. The anthropologists report this haplotype is seen in 50% of South Asians and 16% of Europeans (Figures 1 & 3), which they believe directly contributes to increased susceptibility to severe disease.

ABSTRACT

A recent genetic association study1 identified a gene cluster on chromosome 3 as a risk locus for respiratory failure upon SARS-CoV-2 infection. A new study2 comprising 3,199 hospitalized COVID-19 patients and controls finds that this is the major genetic risk factor for severe SARS-CoV-2 infection and hospitalization (COVID-19 Host Genetics Initiative). Here, we show that the risk is conferred by a genomic segment of ~50 kb that is inherited from Neanderthals and is carried by ~50% of people in South Asia and ~16% of people in Europe today.

FIGURES

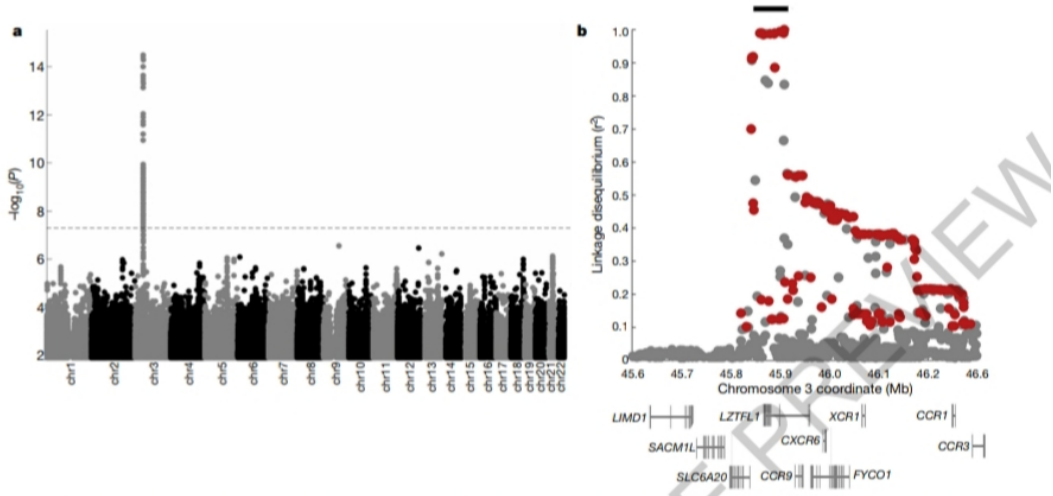

Figure 1: Genetic variants associated with severe COVID-19. A) Manhattan plot of a genome-wide association study of 3,199 hospitalized COVID-19 patients and 897,488 population controls. Dashed line indicates genome wide significance (p = 5e-8, i.e., threshold corresponding to Bonferroni correction for one million independent variants for a two-sided z-test). Data modified from the COVID-19 Host Genetics Initiative2 (https://www.covid19hg.org/). B)Linkage disequilibrium between the index risk variant (rs35044562) and genetic variants in the 1000 Genomes Project. Red marks genetic variants where alleles are correlated to the risk variant (r2>0.1) and the risk alleles match the Vindija 33.19 Neanderthal genome. The core Neanderthal haplotype(r2>0.98) is indicated by a black bar. Note that some individuals carry longer Neanderthal-like haplotypes. The x-axis gives hg19 coordinates.

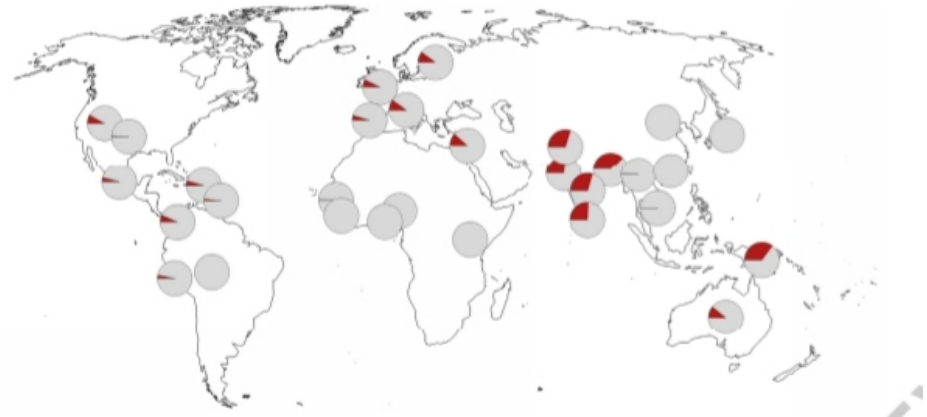

Figure 3: Geographic distribution of the Neanderthal core haplotype conferring risk for severe COVID-19. Pie charts indicate minor allele frequency at rs35044562. Frequency data from the 1000 Genomes Project22. Map source data from OpenStreetMap23.

CHEMOSENSORY DYSFUNCTION IN COVID-19: INTEGRATION OF GENETIC AND EPIDEMIOLOGICAL DATA POINTS TO D614G SPIKE PROTEIN VARIANT AS A CONTRIBUTING FACTOR

Butowt R, Bilinska K, Von Bartheld CS.. ACS Chem Neurosci. 2020 Sep 30. doi: 10.1021/acschemneuro.0c00596. Online ahead of print.

Level of Evidence: Other - Mechanism-based reasoning

BLUF

A review conducted by molecular biologists from Nicolaus Copernicus University in Poland and University of Nevada-Reno School of Medicine found a higher prevalence of the G614 variant of SARS-CoV-2 to be related to increased prevalence of chemosensory dysfunction (Figure 1). They hypothesize that this is due to it expressing a spike protein with higher receptor binding domain affinity to h-ACE2 receptors, leading to enhancement of SARS-CoV-2 binding in the olfactory epithelium and thus, increased chemosensory deficits. It was determined that the G614 variant does not increase disease severity; however, mild-moderate COVID-19 infections are associated with chemosensory deficits and increased infectivity/transmissibility between populations.

ABSTRACT

After several months of rapid pandemic expansion, it is now apparent that the SARS-CoV-2 coronavirus interferes with smell and taste sensation in a substantial proportion of COVID-19 patients. Recent epidemiological data documented intriguing differences in prevalence of chemosensory dysfunctions between different world regions. Viral genetic factors as well as host genetic factors appear to be relevant; however, it is not yet known which mutations or polymorphisms actually contribute to such phenotypic differences between populations. Here, we discuss recent genetic and epidemiological data on the D614G spike protein variant and assess whether current evidence is consistent with the notion that this single nucleotide polymorphism augments chemosensory impairments in COVID-19 patients. We hypothesize that this spike variant is an important viral genetic factor that facilitates infection of chemosensory epithelia, possibly acting together with yet to be identified host factors, and thereby increases smell and taste impairment. We suggest that the prevalence of chemosensory deficits may reflect the pandemic potential for transmissibility and spread which differs between populations.

FIGURES

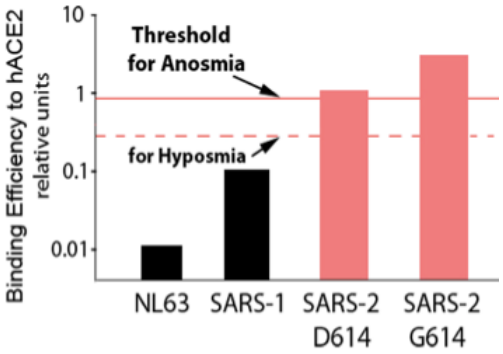

Figure 1. Schematic representation of the key role of the coronavirus spike protein-RBD binding efficiency to human ACE2 in the development of olfactory dysfunction. NL63, SARS-CoV-1, and SARS-CoV-2 are three human coronaviruses that use hACE2 to enter host cells. The RBD of spike proteins in NL63 and SARS-CoV-1 have lower affinity to hACE2 as compared to SARS-CoV-2. The D614G substitution, even though it is not located within the RBD (so it will not change the affinity of pure RBD to hACE2), changes the interprotomer spike energetics and enhances RBD exposure, thus favoring the likelihood of binding of the G614-spike protein to hACE2 as compared with the D614 variant.(11) Convincing alternative explanations have also been proposed, indicating that G614 results in spike protein stabilization and increased spike protein incorporation into pseudovirions, thus creating more ACE2-binding sites on the virion surface.(12) We propose that hyposmia and anosmia require virus binding in the olfactory epithelium above a certain threshold, and for this reason chemosensory dysfunctions did not occur with infections of the SARS-CoV-1 or NL63 viruses. Thresholds and binding efficiencies are approximations based on the literature for different cell lines and are not yet known for cells in the olfactory epithelium. RBD, receptor binding domain of the spike protein; hACE2, human ACE2 receptor, NL63, human coronavirus HCoV-NL63.

ADJUSTING PRACTICE DURING COVID-19

SURGICAL SUBSPECIALTIES

OTOLARYNGOLOGY

OCULAR PROTECTION NOT USED DURING ELECTIVE COCHLEAR IMPLANT AND MASTOID SURGERY DURING COVID-19 ERA

Jaiswal V, Fraser L, Wardrop P.. Laryngoscope. 2020 Oct 3. doi: 10.1002/lary.29150. Online ahead of print.
Level of Evidence: 2 - Expert Opinion

BLUF

A letter to the editor by the Scottish Cochlear Implant Centre at University Hospital Crosshouse discusses how they restarted elective surgery in May 2020 and found no COVID-19 infection among patients or surgeons involved in 24 cochlear implant procedures while using microscopes to assist in drilling without additional eye protection. They suggest that ocular transmission of SARS-CoV-2 is less likely due to lesser ocular expression of ACE-2 receptor mRNA and markedly reduced/absent corresponding cofactors (TMPRSS2 or Furin proteins) to allow binding to the ACE-2 receptor, especially in cases where patients are tested for COVID-19 preoperatively.

OBGYN

GYNECOLOGIC CANCER SURVEILLANCE IN THE ERA OF SARS-COV-2 (COVID-19)

Mancebo G, Solé-Sedeño JM, Membrive I, Taus A, Castells M, Serrano L, Carreras R, Miralpeix E.. Int J Gynecol Cancer. 2020 Oct 5:ijgc-2020-001942. doi: 10.1136/ijgc-2020-001942. Online ahead of print.
Level of Evidence: Other - Guidelines and Recommendations

BLUF

A review by members of the OBGYN and oncology departments of Universitat Autonoma de Barcelona, Spain discusses the increased risk of COVID-19 infection among patients with history of or current gynecologic cancer which led to the development and implementation of an algorithm (figure 1) for less invasive and more cost-effective surveillance with telemedicine-based, risk stratified surveillance and a shared-decision making program for patient follow-up. These findings suggest the potential for reconsideration of healthcare delivery for these patients, in order to make informed decisions about face-to-face and telemedicine surveillance protocols, in a multi-disciplinary approach to monitor for recurrence of gynecological cancer without increasing risk of COVID-19 infection.

ABSTRACT

The SARS-CoV-2 (COVID-19) pandemic has significantly impacted the management of patients with gynecologic cancers. Many centers have reduced access to routine visits to avoid crowded waiting areas and specially to reduce the infection risk for oncologic patients. The goal of this review is to propose a surveillance algorithm for patients with gynecologic cancers during the COVID-19 pandemic based on existing evidence and established guidelines. It is time to consider strategies based on telemedicine and to adapt protocols in this new era. We hereby propose a strategy for routine surveillance both during and beyond the pandemic.

FIGURES

Figure 1: Low-risk cervical cancer surveillance in the era of COVID-19. Gyn, gynecologic surgeon oncologist. #Patients who have undergone fertility-sparing treatment should have a yearly pap smear (PAP) and human papillomavirus (HPV) test with pelvic examination.

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