FADONA 2023



"Latest Updates in COVID Skin and Other Long-Hauler Issues

Presenter

Pamela Scarborough PT, DPT, CWS, FAAWC Vice President of Clinical Affairs Restorix Health

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OBJECTIVES

At the end of this presentation, participants should be able to:

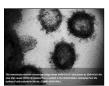
- 1. Describe multiple and varied skin manifestations related to COVID-19;
- Relate some of the COVID-19 skin disruptions to other skin manifestations that look similar to, but are NOT COVID-19 skin issues;
- 3. Describe COVID-19 disease affect on wound healing
- Define Post-Acute Sequelae of SARS CoV-2 infection and the proposed mechanisms leading to Long COVID
- 5. Describe the theory of why Post-Acute Sequalae of SARS-CoV-2 (PASC) develops in some people
- List proposed treatment and rehabilitation considerations for patients/residents with

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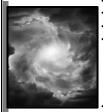
COVID-19 EPIDEMIC

- > COVID-19 pandemic caused by SARS-CoV-2
 - Primarily triggers respiratory tract infections

 - $\,\,igspace\,\,$ Spreads same way other coronaviruses do
 - Mainly through person-to-person contactInfections range from mild, moderate to
- severe to deadly outcomes
 Originally thought to be only respiratory disease
- Current research demonstrates significant extrapulmonary involvement
- > New variants appear to cause less pulmonary involvement for most people



CYTOKINE STORM & COVID-19



- Cytokines are part of immune system
- Causes acute hyperinflammatory response
- Immune cells spread beyond infected body parts
- Inflammatory response to infection
 - · Attacks healthy tissues
 - · Causes blood clots
 - Coagulopathy
 - · Creates decreased blood flow to organs
- Skin is largest organ
- Blood flow and inflammatory processes often manifest on skin and mucous membranes

CURRENT MOST COMMON SYMPTOMS OF XBB.1.5 OMICRON VARIANT

Fatigue

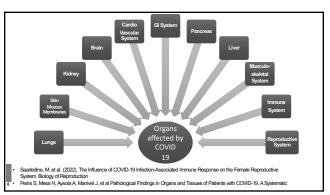
- Congestion
- Body or muscle aches
- Sore throat
- Runny nose
- Cough
- Headache
- Nausea/vomiting





Silent symptoms of COVID-19 include skin and mucocutaneous symptoms

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CURRENT PRIMARY STRAIN OF COVID-19 Subvariant XBB and XBB.1.5



- Labeled globally as Omnicron family subvariant currently responsible for bulk of new COVID-19 cases since October 2022
- > Combination of 2 different variants BA.2.10.1 and BA.2.75
- > Note: More than 50 COVID-19 variants across the globe
- > Most contagious Omicron mutation to date WHO & CDC
- > XBB.1.5 termed "Kraken" strain thought to be 5 times more contagious than earlier Omicron strains
- Has characteristics that allow it to spread easier among both vaccinated and recently COVID-19-recovered individuals
- Common symptoms associated with XBB.1.5 strain can be easily dismissed as seasonal illness or flu

https://www.valemedicine.org/news/omicron-xbb-kraken-subvariant

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WHO label	Lineage #	US Class %T	otal 95%PI	
Omicron	XBB.1.5	VOC 90.2%	87.4-92.4%	
	BQ.1.1	VOC 3.5%	2.5-4.9%	
	XBB	VOC 2.5%	1.5-4.1%	
XBB.1.5. Variant Responsible for 90% of New Coronavirus Infections through 3/18/23 https://covid.cdc.gov/covid-data-tracker/#variant-				
Accessed 3/19/23				

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COVID-19 Skin Manifestations

INITIAL COVID SKIN MANIFESTATIONS RECOGNITION IN HEALTHCARE COVID-19 DERMATOLO

April 2020 International League of Dermatological Societies and American Academy of Dermatology established international registry for COVID-19 dermatological manifestations



- \blacktriangleright At the same time, clinicians in LTC facilities reporting skin manifestations that looked like pressure injuries, but were NOT related to pressure
- ▶ Also, anecdotally, residents with wounds that HAD been improving began to stall or get worse after surviving COVID-19
- ► April 2020 the journey to learn about COVID skin manifestations began

https://www.aad.ore/member/practice/coronavirus/reeistry
Mantovani, A., Morrone, M.C., Patrono, C. et al. Long Covid: where we stand and challenges ahead. Cell Death Differ 29, 1891–1900 (2022).

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WHY IS KNOWLEDGE REGARDING **COVID-19 SKIN SYMPTOMS IMPORTANT?**

► Early detection of skin and mucosal symptoms can assist with early diagnosis of COVID-19









Livedoid/Necrotic lesions

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HOW DOES SARS-COV-2 VIRUS INFECT THE SKIN?

Direct Infection of Endothelial Cells	Indirect Infection of Endothelial Cells
 Small blood vessels in skin are targets for SARS-CoV-2 Lymphocyte skin infiltration in patients with COVID-19 Evidence that virus enters skin through blood vessels after systemic infection 	 Superficial layers of skin prevent viral entry with normal conditions Skin disruptions (e.g., wounds) May allow contamination of underlying tissues
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CLASSIFICATION OF HISTOPATHOLOGICAL FINDING IN THE SKIN OF COVID-19 CASES Endothelial Injury Endotheliitis Petechiae Dermal necrosis Dermo-hypodermal/superficial thrombi Coagulopathy associated abnormalities Deep dermis thrombi Vasculitis Purpura Subcutaneous lymphocytic vasculitis Lymphocytic infiltration of vessels · Possible cytopathic effects Intranuclear viral inclusions Multinucleated cells Intraepidermal vesicle Dyskeratosis Necrotic keratinocytes Pathological findings in organs and tissues of patients with COVID-19: A systematic review Crossref DOI link: https://doi.org/10.1371/JOURNAL.PONE.0250708; 4/28/21. Accessed 3/11/22

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SKIN RASHES PREDICTIVE SYMPTOM OF COVID-19

- Virus causes wide variety of skin symptoms
- · These skin changes may have diagnostic value for SARS-CoV-2 infections
- Support studies suggest that skin rash may be predictive symptom of COVID-19 infection

In nine percent of cases, dermatologists identified outbreaks of small blisters, commonly itchy, that appeared on the trunk of the body



Looks like shingles Is COVID-19

Bataille V, Visconti A, Rossi N, Murray B et. al. Diagnostic value of skin manifestations of SARS-CoV-2 infection.
Young S, Fernandez AP. Skin manifestations of COVID-19. In COVID-19 Curbside Consultants. Cleveland Clinic

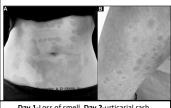
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WHAT IS THE DIAGNOSTIC VALUE OF NEW SKIN RASHES **IN SARS-COV-2 INFECTION?**

- Study. 336,847 UK users of the COVID Symptom Study app
- - > 8.8% (~30,000 patients) positive SARS-CoV-2 viral swab, reported a skin eruption
- ➤ Skin symptoms first: 15% 17%
- ➤ Skin symptoms during illness: 47%
- ➤ Skin symptoms after illness: **35% 39%**
- > Skin symptoms only: 21%
- > This site has a large library of high-quality photos: https://covidskinsigns.com

6	British Association of Darmandiagnos Audity atta for all	=
Cov	rid-19 Skin Patter	This is a second of the second
Acco Imag coll- to h	s website hus been created by ociation of Dermotologists to ges of possible skin signs of CI ected by the COVID Symptom relp increase our understandir size. Images are subject to cop	provide OVID-19, 1 Soutly App. ng of the

COVID-19 Cutaneous Manifestations



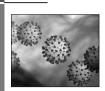


Day 1-Loss of smell, Day 2-urticarial rash,
Day 3-onset of fever

Nan Casas, C., Catala, K. C. H. G., Carretero Hernandez, G., Rodriguez-Jiménez, P., Fernández-Nieto, D., Rodríguez-Villa Lario, A., ... & cases. British Journal of Demandolow, 1881/1. 17-17.

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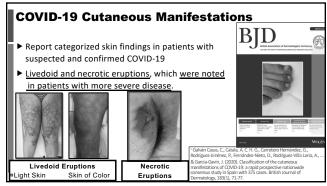
True Incidence of COVID-19 Related Skin **Injuries Currently Unknown**

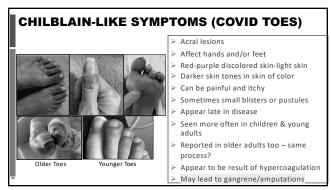


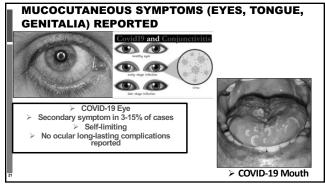
 Many of the skin changes mimic known dermatologic disorders including pressure injuries, Kennedy Terminal Ulcer, and arterial insufficiency wounds

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	COVID-	19 Skin	Manifes	tations	
Urticarial rash	Confluent erythematous/ maculopapular/ morbilliform rash	Papulovesicular exanthem	Chilblain-like acral pattern	Livedo reticularis/ racemosa-like pattem	Purpuric "vasculitic" pattern
Wheals Predominantly involved site: trunk, limbs	Erythematous macules - papules Predominantly involved site: trunk	Erythematous papules - vesicles Predominantly involved site: trunk	Enythematous- violaceous macules and patches Predominantly involved site: lower limbs, feet	Reticular erythematous- violaceous macules Predominantly involved site: lower limbs	Violaceous papules, ulceration Predominantly involved site: lower limbs
Photo permission: S. Karger AG	Associated with		io A, V: Skin Manifestations		







DIFFERENTIAL DIAGNOSIS

Deep Tissue Pressure Injury



- Usually avoidable
- Deep: Bone/Muscle interface

Kennedy Terminal Ulcer Skin Failure



Organ failure

- Unavoidable
- Superficial/Deep

COVID Skin Damage



- Coagulopathy
- Unavoidable
- Superficial

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OMICRON VARIANT SKIN SYMPTOMS

- ▶ Overall symptoms described as milder than earlier variants
- ► Symptoms similar to those of common cold in some people
- ► Omicron skin manifestations include:
 - Rashes
 - Dry lips
 - Grey/blue-tinged lips or nailbeds



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COVIC-19 RASH 1ST SYMPTOM IN 15 Y/0 JANUARY 2022 PCR POSITIVE FOR COVID-19 PROBABLY OMICRON VARIANT





- ➤ Skin manifestations reported with Omicron variant ➤ Similar to previous
- variants but fewer reports.

SKIN & MUCOUS MEMBRANE SYMPTOMS REPORTED WITH OMICRON VARIANT

- ► Chilblain-acral lesions-fingers/toes
- ► Chapped or sore lips
- ► Xerostomia (dry mouth)
- ► Oral lesions
- ► COVID tongue
- ▶ Dry skin
- ▶ Other rash-like symptoms



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DOCUMENTATION BY PROVIDERS AND WOUND SPECIALISTS FOR COVID SKIN/WOUND HEALING ISSUES

Dr. Vycki Nalls, PhD, GNP-BC, ACHPN, CWS

- "Wound healing: secondary effects from COVID-19 due to hypoxia, poor nutritional intake, and debility.
- Delayed wound healing expected due to these effects, and it would not be a surprise if the wound does not heal or declines further given patient's declining status."

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ICD-10 DOCUMENTATION FOR DR. NALLS' PATIENT

- L89.150 Pressure ulcer of sacral region, unstageable (HCC 158)
 - Unstageable pressure injury to sacrum, with delayed wound healing due to comorbid conditions of hypoxia, poor nutrition, debility, and overall decline from COVID-19 infection.
- U07.1 COVID-19
 - COVID positive patient with decline for aggressive management.
- D68.8 Other specified coagulation defects (HCC 48)
- Coagulopathy due to COVID-19.

ICD-10	CODES	FOR	COVID-DERM	MATOLOGIC
MANIF	ESTATIO	ONS		

- ➤ <u>Use U07.1</u> as first diagnosis for patients with confirmed COVID-19.
- Add an additional diagnosis for pneumonia or other conditions, or symptoms.
- D68.8 is a specific ICD-10 code to indicate a <u>diagnosis of other specified coagulation defect</u>. COVID toes/fingers (acral lesions)
- > L99 specifies a <u>diagnosis of other disorders of skin and</u> subcutaneous tissue in diseases classified elsewhere (rashes)

Post Acute Sequelae of SARS-CoV2

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LONG COVID NOMENCLATURE

- ▶ Post-acute sequelae of SARS-CoV-2 (PASC) new formal name
- ► Post-COVID Syndrome (PCS)
- ► Long COVID
- ► COVID Long Haulers

POST-ACUTE	SEQUELAE	OF	SARS-COV2
INFECTION			

- ▶ Described by WHO as persistence of symptoms or new symptoms more than 30 days post-SARS-CoV-2 infection
- ▶ CDC: 4 or more weeks after infection
- ▶ British NIH and Care Excellence (NICE): 12-weeks during or after infection; not explained by alternative diagnosis
- ► These longer effects of COVID-19 are actively being investigated and
- ▶ Clinical definition and understanding of underlying mechanisms of Long COVID are still in flux

POST-ACUTE SEQUELAE OF SARS-COV2 INFECTION

- ▶ Lingering symptoms may persist months and in some cases years after the acute infection
- ▶ ICD-10 CM code for "post COVID-19 condition, unspecified"=U09.9
- ▶ Deployment of an ICD-10-CM code in US took nearly 2 years after patients began describing their symptoms
- ► Countries around the world are all dealing with Post COVID in their populations

Pfaff ER, Madlock-Brown C, Baratta JM, et al. Coding Long COVID: Characterizing a new disease through an ICD-10 lens. Preprint. medRxiv. 2022;2022.04.18.22273968. Published 2022 Sep 2. doi:10.1101/2022.04.18.22273968

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POST-ACUTE SEQUELAE OF COVID: FACTS OVERVIEW

- Legacy of acute SARS-CoV-2 infection, affecting 10-69% of patients with different signs and symptoms across a wide range of organs and systems
- Most frequent manifestations of PASC, compromised lung functions, neurocognitive alterations; alterations of cardiovascular functions and increased risk of acute cardiac events; and fatigue.
- SARS-CoV-2 virus seeds and persists in different organs and tissues.
- Pathogenesis of PASC is multifactorial and includes:
- Virus seeding and persistence in different organs; activation and response to unrelated viruses (e.g., EBV); autoimmunity; uncontrolled inflammation
- ▶ Biomarkers of clinical PASC include levels of IgG, cytokines, chemokines, PTX3, and interferons.
- Mantovani, A., Morrone, M.C., Patrono, C. et al. Long Covid: where we stand and challenges ahead. Cell Death Differ 29, 1891–1900 (2022) 50 ½ Yuan D, Chen DG, et al. Multiple early factors anticipate post-acute COVID-19 sequelae. Cell. 2022;185(5):881-895.e20. doi:10.1016/jcr.2022.01.014

POTENTIAL CONTRIBUTORS TO PASC SYMPTOMS

The individualized nature of PASC symptoms suggests to

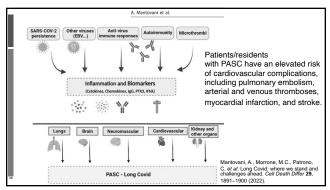
approaches may be required to

ge care for specific th the discussion

- ► Injury to one or multiple organs,
- ▶ Persistent reservoirs of SARS-CoV-2 in certain tissues,
- Re-activation of neurotrophic pathogens such as herpesviruses under conditions of COVID-19 immune dysregulation,
- SARS-CoV-2 interactions with host microbiome/virome communities,
- ► Clotting/coagulation issues,
- ▶ Dysfunctional brainstem/vagus nerve signaling,
- ▶ Ongoing activity of primed immune cells,
- ▶ Autoimmunity due to molecular mimicry between pathogen and host proteins.

Edward Galaid, MD, RSFH Medical Director of Occupational Medicine. Roper St. Francis Healthcare. Management of PostA Cute Seguelae of SARS CoV-Infections. https://www.youtube.com/watch?v=nw7Ag06GDLtg. YouTube Accessed 10/30/22

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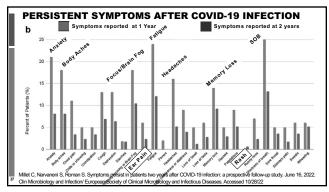


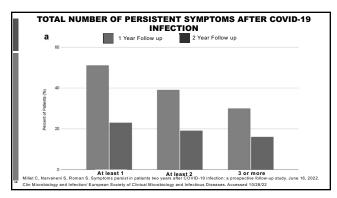
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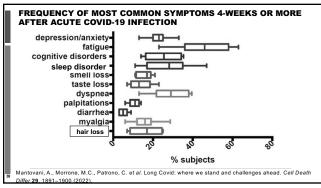
LONG COVID = POST-ACUTE SEQUELAE OF SARS-COV-2 (PASC)

- Research indicated an ongoing, sustained inflammatory response following mild, moderate, and severe SARS-CoV-2 infections
- "We can show that the macrophages from people with mild COVID-19 exhibit an altered inflammatory and metabolic expression for three to five months post-infection,"
- ➤ "Even though the majority of these people did not have any persistent symptoms, their immune system was more sensitive than that of their healthy counterparts."

Hetsouphanh, C., Darley, D.R., Wilson, D.B. et al. Immunological dysfunction persists for 8 months following initial mild-to-moderate SARS-CoV-2 infection. Nat Immunol 23, 210–216 (2022).







Multiple early sequelae	y factors a	inticipate post-acute COVID-19
Multiple early factors anticipat 19 sequelae Complete during the C	Article te post-acute COVID- Admir. Admir.	Omics = various disciplines in biology whose names end in omics; e.g., genomics, proteomics, transcriptomics Longitudinal multi-omics associate PASC with autoantibodies, viremia, and comorbidities Reactivation of latent viruses during initial infection may contribute to PASC Subclinical auto-antibodies negatively correlate with anti-SARS-CoV-2 antibodies Gastrointestinal PASC uniquely present with post-acute expansion of cytotoxic T cells

OTHER FACTORS THAT MAY CONTRIBUTE TO SYMPTOMS AND TREATMENT OF PASC

- Having COVID-19 can bring to light existing health problems that might not have been noticeable before or worsen the symptoms of a known health condition.
- People who require intensive care for any serious illness, including COVID-19, are more likely to develop weakness, brain and mental health disorders, and other long-term health issues after they leave the hospital.
- Social challenges related to COVID-19, such as isolation and limited access to regular health care, may also underlie some aspects of Long COVID.

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IT'S A QUANDARY

- Unclear why some people develop long-lasting symptoms after having COVID-19, while other people recover completely.
- ► Understanding the causes of Long COVID is critical for finding ways to prevent, detect, and treat its symptoms.

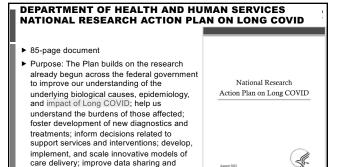
https://www.nia.nih.gov/health/what-do-we-know-about-long-covid

ISSUE FOR LTC RESEARCH AND PASC

- ▶ Long Covid associated with more than 200 symptoms and 50 health conditions
- ▶ What do we do with this issue in the LTC setting???
- ▶ In general, PASC research has excluded older adults, especially the older old
- ▶ Also excluded are those with:
 - Multiple complex comorbidities
 - Frailty
 - Disability
 - Dementia
 - Impaired immune function
- ▶ All of which are frequent characteristics of LTC residents



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Most Common Types of Long Covid Rehab

- ▶ Physical therapy
- ▶ Pulmonary rehab
- ► Cognitive rehab
- ► Mental health support
- ▶ Early evidence suggests that some complications, such as heart or lung damage, may improve with time, particularly if patients receive rehabilitative

transparency among researchers



A.

https://www.medicalnewstoday.com/articles/covid-19-rehabilitation#who-needs-it

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Effects of Exercise Rehabilitation in Patients With Long Coronavirus Disease

European Journal of Preventive Cardiology, May 2022

- Conclusion: Improvements in both cardiorespiratory function and muscular strength were seen in patients with long COVID with a combined aerobic and resistance exercise program. While no control group was compared to the intervention group, this study highlights the potential gains from exercise interventions for this population.
- Persistent Exertional Dyspnea and Perceived Exercise Intolerance After Mild COVID-19: A Critical Role for Breathing Dysregulation? Physical Therapy, July 2022
- Conclusion: Breathing dysregulation may help explain COVID-related dyspnea and perceived exercise intolerance after mild infection. The study authors propose that breathing relaxation strategies might be helpful for some individuals, while rebreathing therapy may be required for others.

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REHAB STUDIES

- Case Report: Overlap Between Long COVID and Functional Neurological Disorders Frontiers in Neurology, January 2022
- Conclusion: This case report highlights functional neurological disorder as a consideration for patients diagnosed with long COVID. The patient presented with persistent attention and memory difficulties as well as limb dysesthesia after COVID-19 infection. A neurological examination found no organic disorder, and the patient was treated for functional neurological disorder with psychotherapy and physical therapy. The patient's dysesthesia symptoms resolved, and cognition improved.
- Effect of pulmonary rehabilitation approaches on dyspnea, exercise capacity, fatique. lung functions. and quality of life in patients with covid-19: A systematic review and meta-analysis.

Archives of Physical Medicine and Rehabilitation, October 2022

Conclusion: Pulmonary rehabilitation (exercises, training, education and behavioral changes) were found to be significantly effective in improving dyspnea and exercise capacity in patients with acute and chronic COVID-19 with mild to severe symptoms. Fatigue and lung functions were significantly improved in acute COVID-19 patients with mild symptoms

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PASC REHABILITATION APPROPRIATE CONDITIONS

- Heart damage or inflammation, such as myocarditis or pericarditis
- Cognitive impairments that affect memory or concentration
- Lasting effects from complications:
- · Heart attacks,
- Stroke.
- · Pulmonary embolism
- Depression,
- Muscle/joint pain.
- Chronic fatigue

COVID LONG-HAULERS AND THE SKIN

- ▶ Persistent morbidity noted in all systems of the body including skin
- ▶ Urticarial and morbilliform eruptions short duration
- ▶ Papulosquamous eruptions, particularly pernio longer-lasting
- American Academy of Dermatology data revealed previously unreported subset of patients who experience long-hauler symptoms in dermatologydominant COVID-19
- ► Finding raises questions about persistent inflammation; even in patients who initially experienced relatively mild COVID-19
- ► More studies are needed to understand the long-hauler dermatologic manifestations

Caff is, Bernabel R, Land F, Gemelli Against C-P-ACSG Persistent symptoms in patients after acute COMD-19. JANA 2020, \$24: 693-105.

10, Puntoman NO, Carely M, Wileless J, et al. Outnoise of antiovacular magnetic resonance imaging in patients recently recovered from coronavirus disea.

2019 (COMD-19. JANA Cond of 2020; 5: 1265-73.

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LESSONS FROM PRACTICE-COVID SKIN MANIFESTATIONS

- ▶ Patients with COVID-19 may present with unusual skin manifestations, including urticarial rashes, vesicular lesions, and chilblains on fingers or toes
- ► These skin and mucous membrane manifestations may be the first sign of COVID-19 disease
- ▶ Most cutaneous manifestations of COVID-19 are self-resolving.
- Where treatment is appropriate, medium or high-potency topical corticosteroids, oral antihistamines, or systemic corticosteroids are usually sufficient for symptomatic relief
- Coinciding drug therapy reactions are a possible confounding factor for cutaneous manifestations of COVID-19

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OPEN QUESTIONS REGARDING PASC AND COVID SKIN MANIFESTATIONS

- ► Occurrence, mechanism, and significance of SARS-CoV-2 persistence in different organs?
- ► Mechanisms, targets, and significance of autoimmune reactions?
- ► Role of other viruses?
- ► Impact of host genetics and microbiome?
- Occurrence and severity of PASC after infection with future variants?
- ► Preventive and therapeutic approaches?
- ► Years and years of research to come for the regarding PASC

ISSUES WITH RESEARCH IN LTC RESIDENTS

- Research design and interpretation of long COVID outcomes for LTC residents require special consideration of their complex comorbidities and diverse physical, psychological, and social care needs
- ► Concerns regarding communication impairments that limit self-reporting of symptom
- How do providers and bedside clinical teams tease out long COVID symptoms that may be attributed to pre-existing conditions?

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FEW STUDIES IN THE U.S. FOR LTC RESIDENTS WITH PASC

- Research/studies needed asap to address the lack of guidelines for care and rehabilitation for Long COVID patients and residents in the LTC setting
- ▶ LTC is a unique care setting
- ▶ Long COVID needs to be addressed in LTC,
- ► This issue will probably continue considering the ongoing COVID-19 breakouts by continuously emerging variants
- ► This and many other immense challenges face the LTC sector related to COVID-19 disease
- ▶ We're doing the best we can
- https://www.nia.nih.gov/health/what-do-we-know-about-long-covid#funding

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QUESTIONS Comments



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SKIN AND	MUCOCUTANEOUS	MANIFESTATIONS
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