

Long COVID & Post-Viral Syndromes: Pediatric & Young Adults



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Patient cases are shared in this session for educational purposes. In some cases, the information does not relate to an individual, and instead represents a compilation of disease presentation.

In cases involving individual patient information, the patients have authorized the discussion of their case in this setting.

Objective

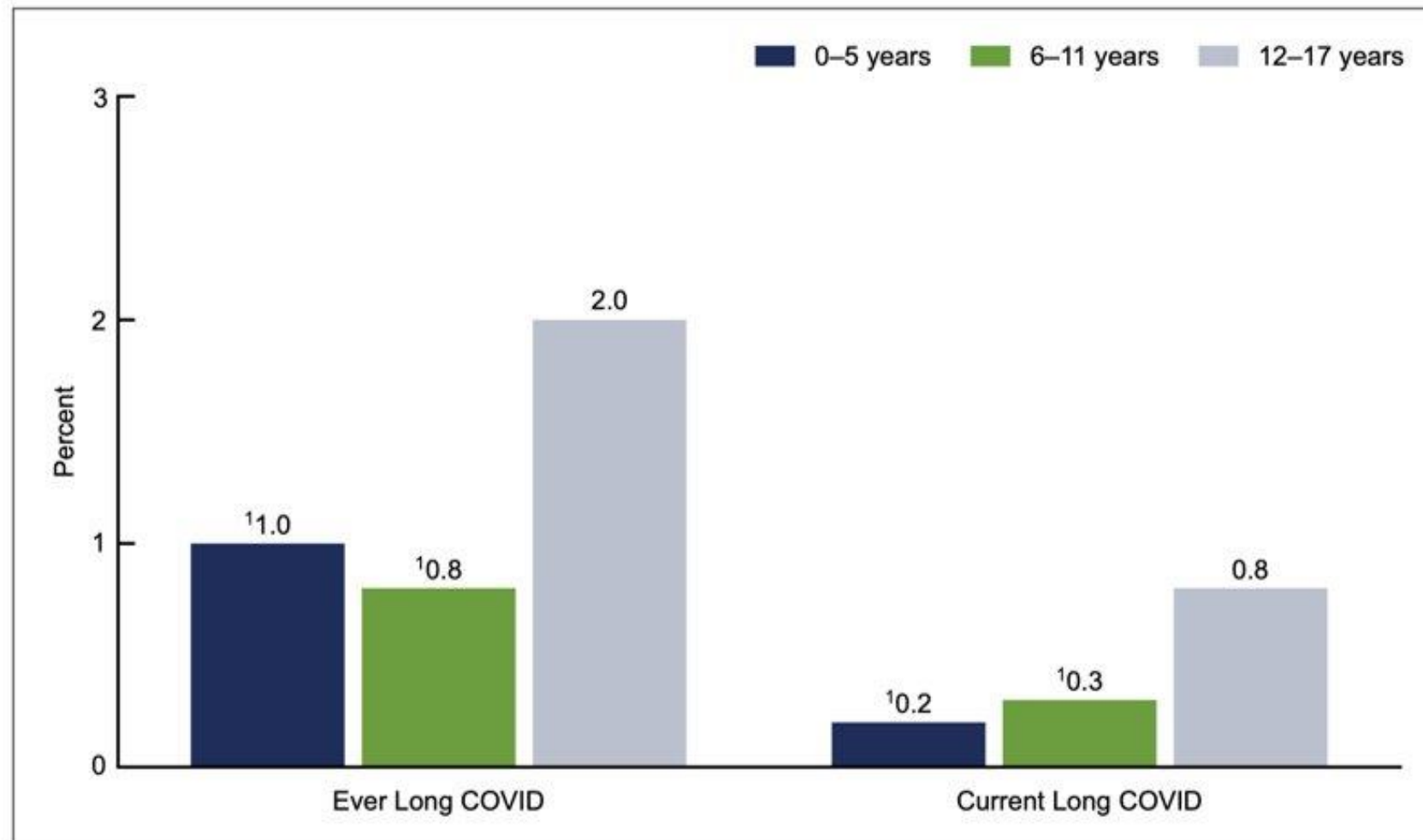
- Review the most recent epidemiological data on Long COVID in the young adult population
- Describe the proposed pathophysiologic mechanism involved in Long COVID
- Special considerations for assessment and management of LC in AYA
- Case discussion longitudinal care of young adult Long COVID patient

Terminology

- **LONG COVID:** Patient defined term, inclusive, new symptoms after COVID
- **POST COVID CONDITION (WHO):** Defined as new symptoms that start 3 months from the onset of COVID-19 that last for at least 2 months and cannot be explained by an alternative diagnosis.
- Other terms: **Post acute sequelae of SARS CoV-2 infection (PASC), long-haul COVID**

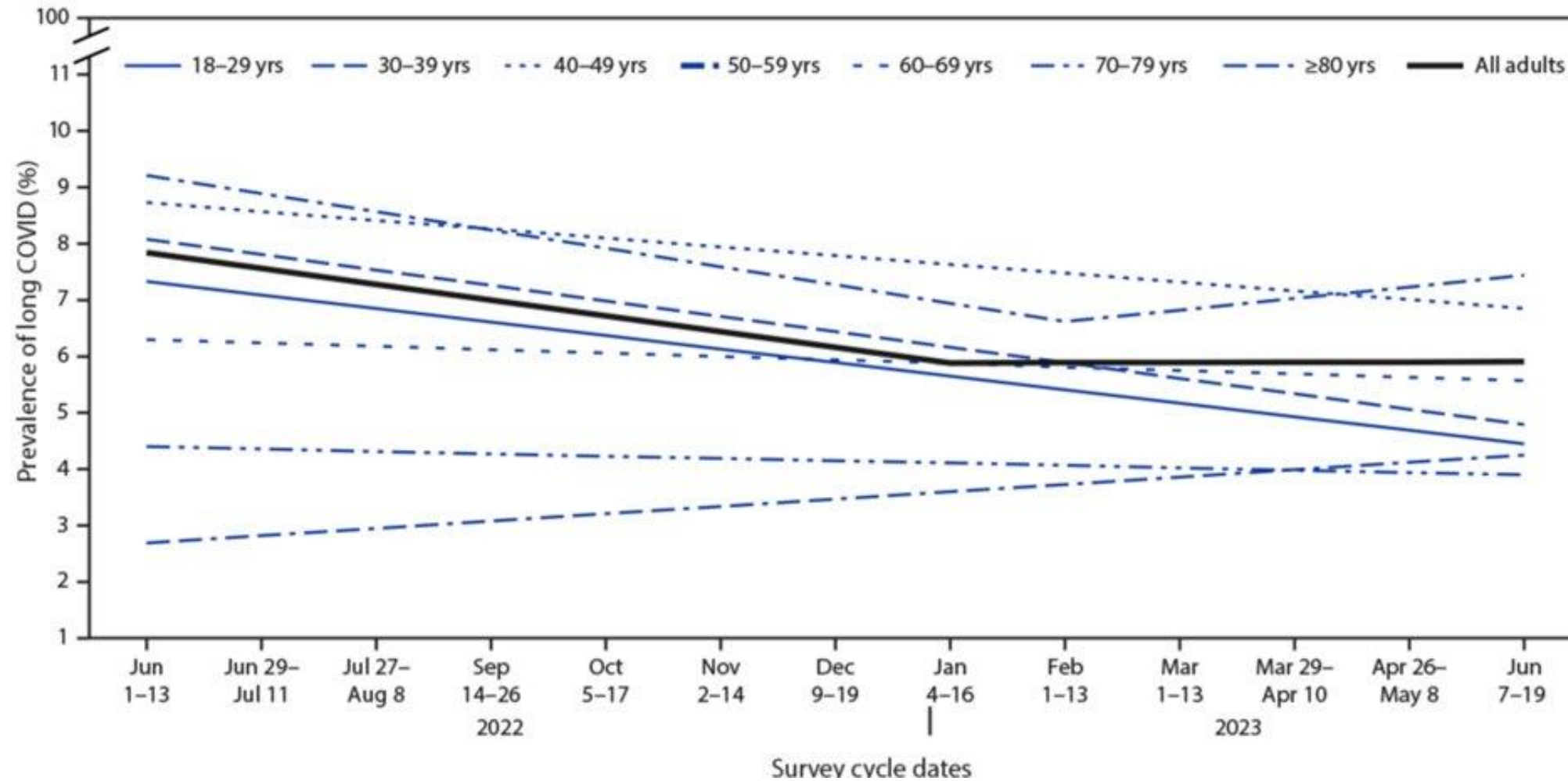
Long COVID in Children: United States, 2022

Anjel Vahratian, Ph.D., M.P.H., Dzifa Adjaye-Gbewonyo, Ph.D., M.P.H.,
Jin-Mann S. Lin, Ph.D., and Sharon Saydah, Ph.D.



Prevalence of Long COVID in Young adults

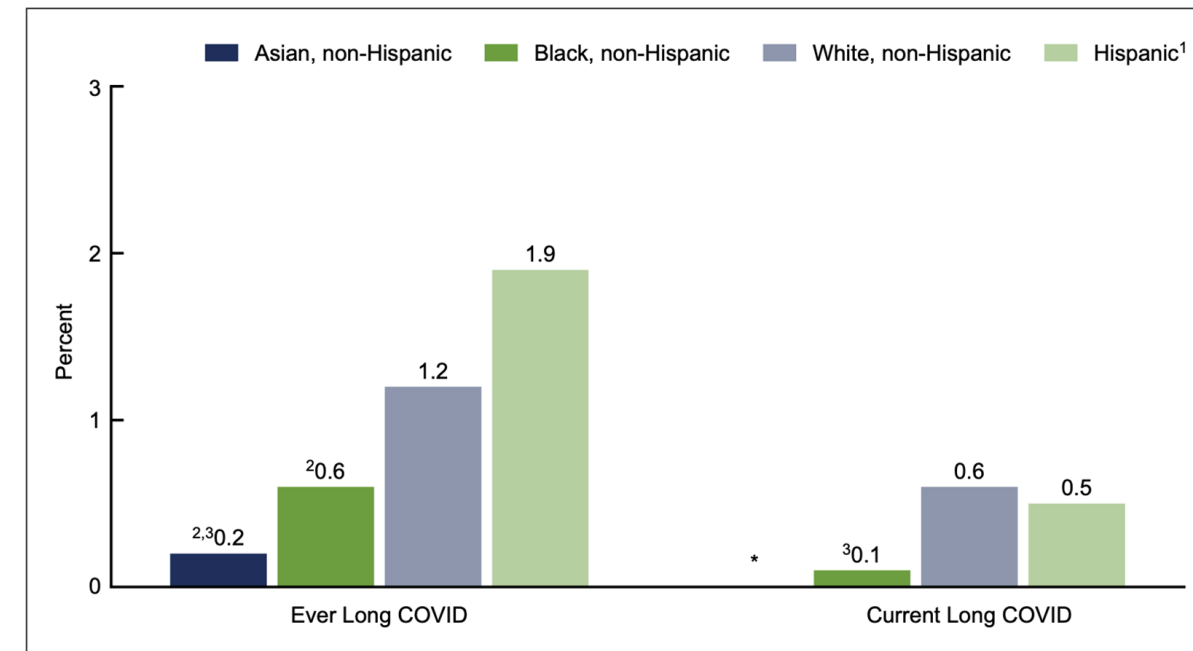
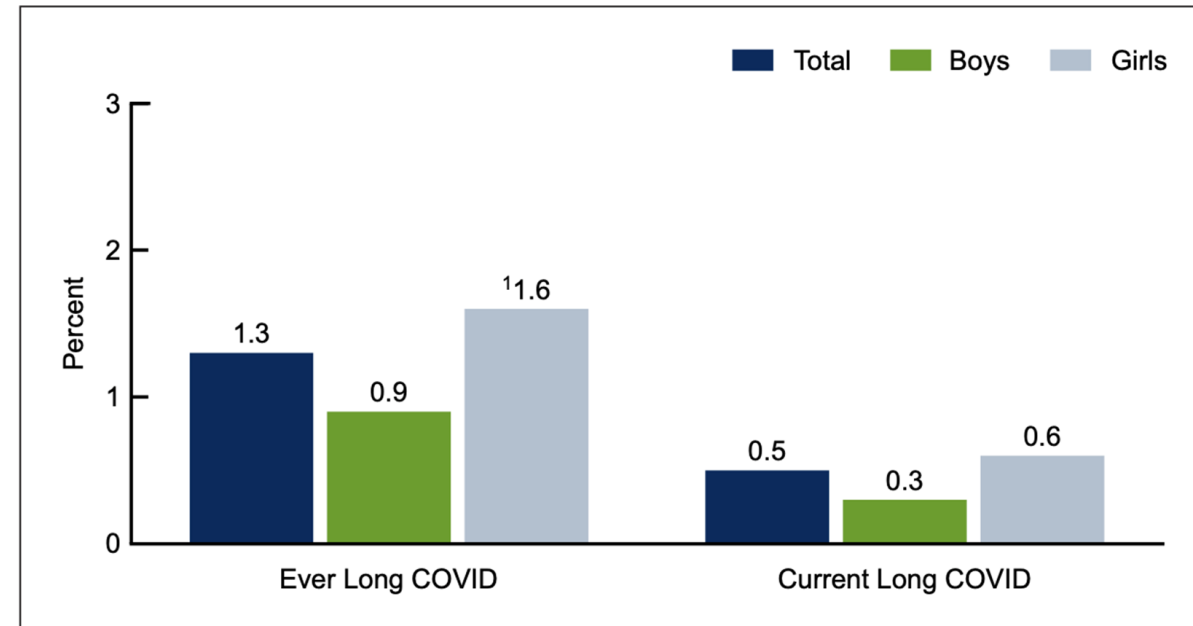
6/2022 to 6/2023



Ford ND, Slaughter D, Edwards D, et al. Long COVID and Significant Activity Limitation Among Adults, by Age — United States, June 1–13, 2022, to June 7–19, 2023. MMWR Morb Mortal Wkly Rep 2023;72:866–870. DOI: <http://dx.doi.org/10.15585/mmwr.mm7232a3>

Risk Factors

- Female sex at birth
- >10 years
- Hispanic
- Acute COVID 19 severity
- Co-morbid conditions
 - Allergic disease
 - Asthma
 - Obesity
 - Anxiety
 - Heart disease
 - Neurologic diseases.
- Reinfection with COVID-19 appears to be associated with an increased risk for PASC (adult data)



Vahratian, A., Adjaye-Gbewonyo, D., Lin, J. M. S., & Saydah, S. (2023). Long COVID in Children: United States, 2022. *NCHS Data Brief*, (479), 1-6.

AYA Consideration on Assessment & Management

- Assess the functional impact of PASC symptoms on activities of daily living, schooling, vocational and extracurricular/preferred activities.
- Symptoms might be triaged based on:
 - Most debilitating symptoms
 - Most treatable symptoms
 - Need to subspecialty referral
 - Patient-driven

Accommodations for AYA's

- A later start to the day as mornings can be more difficult symptom wise.
- Flexibility in assignment due dates and scheduling of testing dates
- Extended time for test-taking or ability to take breaks during tests.
- Flexibility with make-up work assignments and absences
- Ability to access fluids for increased fluid intake for help with OI.

Supporting AYA's

- Ensuring that patients feel validated and safe to disclose their symptoms
- Assist with navigating the health care system
- Referrals for psychotherapy focused on coping with the new physical and mental impairments from their chronic illness
- Loss of function and decreased quality of life contributes to development of new onset depression and anxiety symptoms or exacerbation of preexisting mental health conditions

Case 1

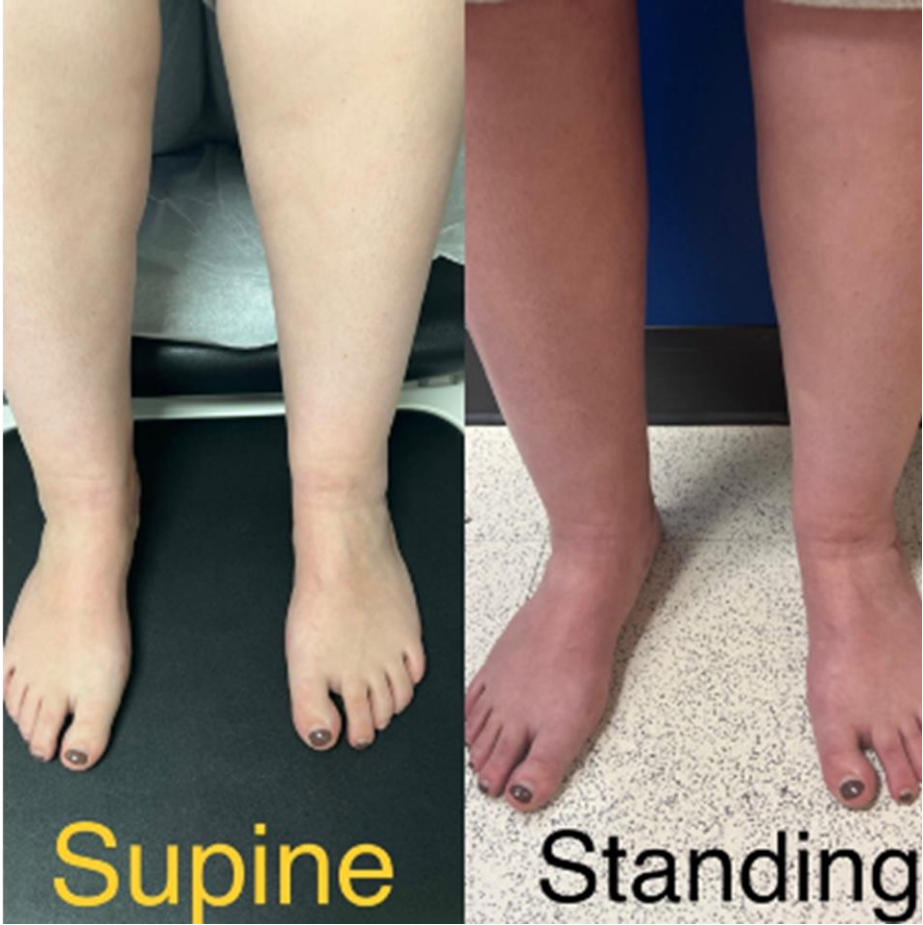
- 23-year-old female nurse practitioner with PMHx of Hashimoto's thyroiditis, celiac disease, anxiety (on sertraline) and Asthma, presenting with lingering symptoms after SAR CoV2 infection.
- First COVID sx on December 5, 2020 (positive NP test)
- Fever, myalgias, headaches, nausea, anosmia, ageusia and generalized malaise for 5 to 6 days.
- Day 7 felt well enough to start working
- Noted significant Brain Fog, decided to hold off from going back to work
- 17 Days after initial of symptoms was feeling 75% from baseline and decided to shovel snow in the driveway

Case 1

- After shoveling the driveway experienced severe SOB, CP, and fatigue. She was in bed for several days.
- Fluctuating course of symptoms since January 2021
 - 30% to 50% from her functional baseline
- Sx triggered by previously tolerated physical activity (ADLS) SOB, light headedness, dizziness, palpitations (HR140), chest tightness
- Sweating, cold/heat intolerance, flushing, altered vision (dark spots?)
- Diarrhea, Bloating, nausea
- Tingling in face and extremities
- Eczema flare and pruritus

Physical Exam

	Heart Rate (bpm)	Systolic (mmHg)	Diastolic (mmHg)
Sitting	83	114	75
Stand 1 min	105	132	69
Notes	Did not tolerate standing longer	Dizziness, nausea, chest pain, clammy skin, described tingling in bilateral hands	
After sitting for 5 min	88	110	60
Notes		Symptoms resolving, recovered after 7-10 min	

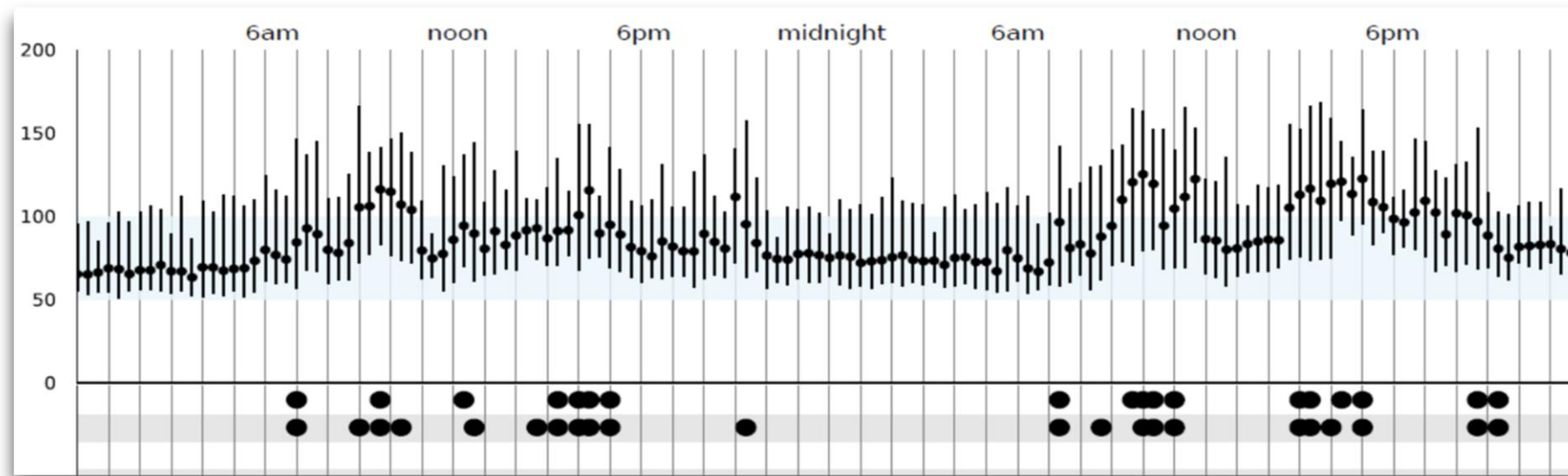


Acrocyanosis on Stand Test



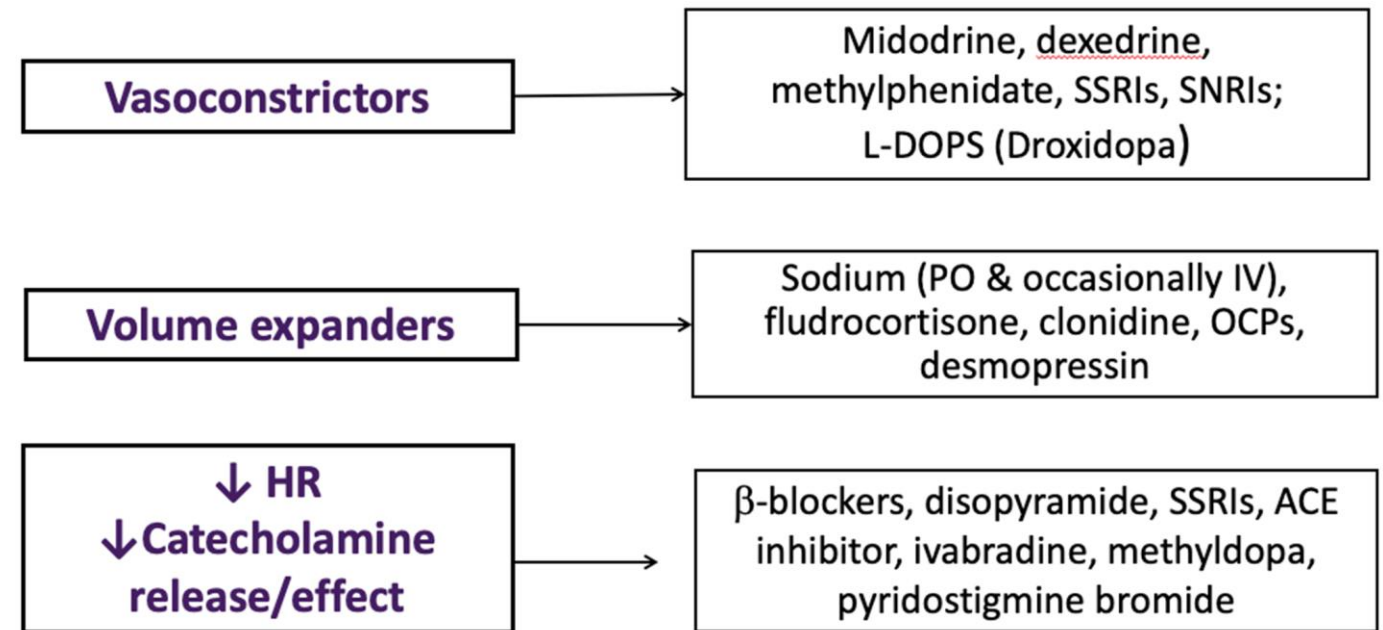
Initial Work Up

- Blood tests:
- CBC, CMP, TFT, vitamin B12, ferritin, morning cortisol, ANA, ESR, CRP
- Mast Cell activation labs: Elevated Histamine, normal tryptase
- EKG, Holter monitor, cardiac echo
- Tilt table + POTS
- Cutaneous nerve biopsy-negative for SFN and sudomotor denervation



OI interventions

- Fluids: Minimally 2 L per day
- Drink at least every 2 hours
- Avoid sleeping > 12 hrs/day
- Salt: 4-6 gm Sodium
- Supplement with salt tablets
- Elevate the Head of Bed
- Cooling garments in hot weather
- Autonomic rehabilitation
- For most impaired, start slowly, increase gradually
- Recumbent exercise may help at outset
- Beware rigid advancement of graded exercise
- Exercise might not be tolerated before orthostatic intolerance is treated



Plan

- Started nonpharmacologic POTS interventions and Midodrine
 - Improvement noted regarding standing and activity tolerance
- Scheduled to start Autonomic Rehabilitation (PT) 2 months after initial evaluation.
- Patient experiencing debilitating PEM for 2-3 days after therapy sessions. (Push Crash cycle)
- Overall functional decline, tolerating short household distances and requiring assistance for ADLS.

Plan

#POTS

- Goal of 3 L of fluid per day (oral)
- Increase intake of sodium to 10 gm/day per day
- Continue compression garments including stockings and abdominal binder when out of bed
- Continue midodrine to 7.5-10mg twice a day
- Did not tolerate beta blocker due to hypotension
- Ivabradine 7.5 twice daily
- Did not tolerate Florinef (mood SE) or Mestinon (GI SE and Bronchospasm)
- 1 L NS IVF two to three times per week

#MCAS

- Montelukast 10 mg daily
- Xyzal 10 mg q pm
- Quercetin 500 mg BID

Reinfection November 2021

- Treated with monoclonal antibodies in November 12, 2021
- Exacerbation of POTS symptoms
 - IVF increased to daily
- Exacerbation of brain fog
 - Trial of modafinil and methylphenidate, did not tolerated due to elevated HR
 - Started on LDN
- Exacerbation of MCAS
 - Gluten-free diet
 - Gastrocrom 400 mg 4 times daily
 - Twice daily H1 and H2 blockers
 - Nasocrom as needed
- Functional decline, required wheelchair for household ambulation

The Washington Post
Democracy Dies in Darkness



Mallory Stanislawczyk sits with her daughter Olivia, 3, while receiving a saline infusion at her Walkersville, Md., home. (Matt Roth for The Washington Post)

Anaphylaxis episode

- Admitted to Frederick Health Hospital for anaphylaxis on 9/5/2023
 - Possible trigger was Halibut
- Patient had 3 rounds of epinephrine, Decadron and Benadryl at the ER, was monitored over night and discharged the following day.
- For the following weeks she experienced severe PEM and was bed bound.

Young Adults with Long COVID: Clinical Care Points

- Suspect a diagnosis of PASC for adolescents and young adults (AYAs) presenting for care with multisystem symptoms after COVID-19 infection.
- Providers should evaluate for orthostatic intolerance using the 10-minute passive standing test
- Primary care providers can triage a symptom inventory, assess level of functioning, screen for orthostatic intolerance and post-exertional malaise, initiate treatment, and facilitate subspecialty referrals for AYAs presenting with PASC symptoms.

Pediatric Long Covid

Melanie Hoppers, MD
Internal Medicine/Pediatrics

Healthy 14-year-old

- 14-year-old female
- PMH significant for seasonal allergies
- Prior to illness she was in college prep honors classes and had several extra curricular activities
- Her health is described as generally very good before covid infection

First Covid Infection

- August 2020 (Delta Variant – associated with increased risk of long covid)
- Mild URI symptoms
- Recovered and returned to normal activities

Long Covid Symptoms

- Fatigue - school absences (once every couple of weeks), naps after school, slept until early afternoon on the weekends
- Headaches 5 days per week
- Brain fog – memory and attention affected
- Sleep disturbance – insomnia at night, difficulty awakening in the morning, frequent naps
- Describes post-exertional malaise (PEM) with crashing on weekend after school week – worsening of all symptoms, felt flu like at times, very fatigued

Second Covid Infection

- January 2021
- URI symptoms, fever, myalgias, chills, and rash
- Rash described as “red bumps that were small and itched and burned”
- After 1 week, patient was able to return to school and had improved from the acute symptoms

Long Covid Symptoms 2.0

- Fatigue – increased school absences (once a week) sometimes leaving early or starting late, less activities on the weekend and after school
- Brain fog – memory and attention problems, difficulty completing assignments.
- Post-Exertional Malaise (PEM)
- Headaches
- GI issues – worsening constipation/bloating/diarrhea
- Sympathetic overdrive – easily irritated, light and sound sensitivity, easily overwhelmed at school
- Rash – Intermittent lasting 1-3 days, burns and itches, sometimes associated with lip swelling, unable to determine triggers, dermatologist prescribed epi-pen
- Orthostatic Intolerance – dizzy when standing/taking showers, feels better supine

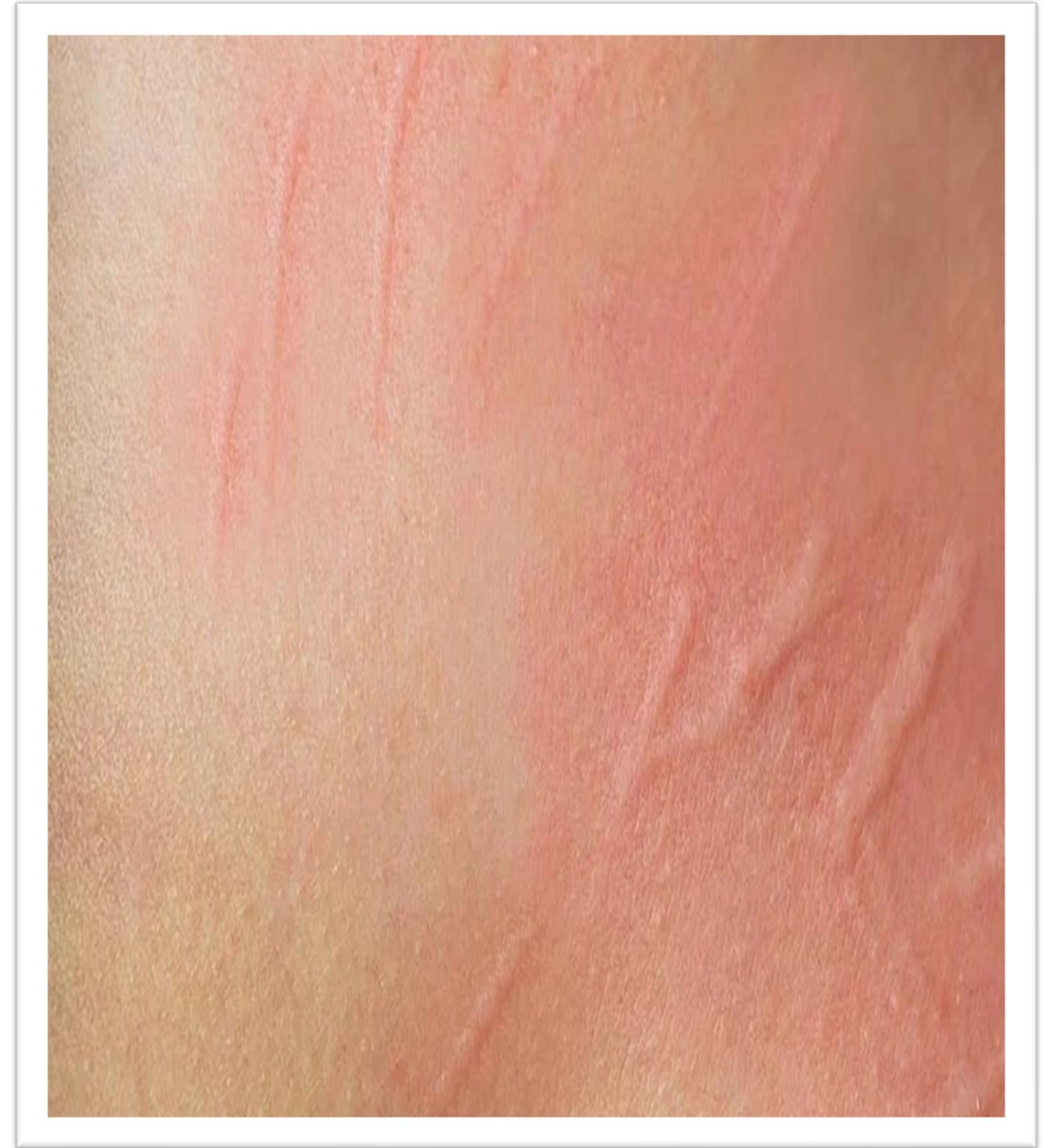
PHYSICAL EXAM FINDINGS

Dermatographia

Flushing of face and neck

Capillary refill – 4 seconds

Beighton Score - 5



DIAGNOSTIC STUDIES

- CBC, thyroid profile, AM cortisol, ACTH, thyroid profile, iron studies, serum tryptase and chromogranin, plasma histamine, chilled plasma PGD2, chilled urine for PGD2 and methylhistamine, quantitative immunoglobulins, iron studies, Vitamin B12, B6, folate, Vit D, and tissue transglutaminase IgA and IgG
- Echo and Event Monitor – normal
- Holter only placed for 1 day due to urticaria from the electrodes



<https://onlinelibrary.wiley.com/doi/10.1002/pmrj.12894>

Multi-disciplinary collaborative consensus guidance statement on the assessment and treatment of autonomic dysfunction in patients with post-acute sequelae of SARS-CoV-2 infection (PASC)



<https://batemanhornecenter.org/wp-content/uploads/2016/09/NASA-Lean-Test-Instructions-1.pdf>

Nasa Lean Test Instructions
Bateman Horne Center



Bateman Horne Center
RESEARCH | CLINICAL CARE | EDUCATION

Orthostatic Vital Signs/The NASA 10-minute Lean Test

	Blood Pressure (BP)		Pulse	Comments	PP
	Systolic	Diastolic			
Supine 1 minute	108	66	73		42
Supine 2 minute	106	66	69		40
Standing 0 minute	118	78	99	Very dizzy	40
Standing 1 minute	113	74	101		39
Standing 2 minute					
Standing 3 minute	115	78	107	Chest heavy	37
Standing 4 minute	120	76	110	Dizzy	44
Standing 5 minute	110	74	130	"I am going to pass out"	36
Standing 6 minute					
Standing 7 minute					
Standing 8 minute					
Standing 9 minute					
Standing 10 minute					

*The NASA 10-minute Lean Test is a variant of a test used by NASA researchers to test for orthostatic intolerance¹; it reduces muscular influences on venous return, a major cause of variability in orthostatic testing. Passive stand testing has been validated as an equivalent or superior measure of orthostatic intolerance as compared to head-up Tilt Table tests^{2,3}.

[1] Bungo, M. W., Charles, J. B., & Johnson Jr, P. C. (1985). Cardiovascular deconditioning during space flight and the use of saline as a countermeasure to orthostatic intolerance. *Aviation, space, and environmental medicine*, 56(10), 985-990.

[2] Shvartz, E., Meroz, A., Magazanik, A., Shoenfeld, Y., & Shapiro, Y. (1977). Exercise and heat orthostatism and the effect of heat acclimation and physical fitness. *Aviation, Space, and Environmental Medicine*, 48(9), 836-842.

[3] Hyatt, K. H., Jacobson, L. B., & Schneider, V. S. (1975). Comparison of 70 degrees tilt, LBNP, and passive standing as measures of orthostatic tolerance. *Aviation, Space, and Environmental Medicine*, 46(6), 801-808.



Autonomic Dysfunction

POTS

- Sustained Increase in HR \geq to 40 bpm or HR $>$ 120 on standing or with tilt table test
- Absence of Orthostatic Hypotension
- Absence of other causes of postural tachycardia such as dehydration
- Pt increased 61 bpm
- No drop in bp
- Became symptomatic
- Present for $>$ 6 mo

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MCAS

- H/O Allergies
- Intermittent rashes/lip swelling
- Urticaria with EKG electrodes
- H/O GI distress within minutes of eating
- EXAM-
Flushing/dermatographism



Proposed Diagnostic Criteria for ME/CFS

Diagnosis requires that the patient have the following three symptoms:

1. A substantial reduction or impairment in the ability to engage in pre-illness levels of occupational, educational, social, or personal activities, that persists for more than 6 months and is accompanied by fatigue, which is often profound, is of new or definite onset (not lifelong), is not the result of ongoing excessive exertion, and is not substantially alleviated by rest, and
2. Post-exertional malaise,* and
3. Unrefreshing sleep*

At least one of the two following manifestations is also required:

1. Cognitive impairment* or
2. Orthostatic intolerance

* Frequency and severity of symptoms should be assessed. The diagnosis of ME/CFS should be questioned if patients do not have these symptoms at least half of the time with moderate, substantial, or severe intensity.

For more information, visit www.iom.edu/MECFS



Advising the nation • Improving health

Long Covid and ME/CFS

Education

Pacing

School accommodations letter

MCAS

Claritin

Pepcid

Diary – identify
precipitating factors

POTS

Conservative measures

Midodrine 2.5 mg TID

Fluids – 2-3 liters/3-4 gm of salt
per day that can be given with
electrolyte drinks and salt tabs

Results of Interventions

- At return visit, patient reports much improvement of headaches, resolution of abdominal bloating/constipation/diarrhea.
- Occasional episodes of tachycardia but this is much better.
- No rash for past 6 weeks
- Anxiety resolved

Tools for the Practitioner

Myalgic Encephalomyelitis/Chronic Fatigue Syndrome
Diagnosis and Management in Young People: A Primer

<https://www.frontiersin.org/articles/10.3389/fped.2017.00121/full>



Tools for the Practitioner

International Consensus Primer for Medical Practitioners
– Letter to School

[https://www.massmecfs.org/images/pdf/pediatric/International Consensus Primer Letter to Educators.pdf](https://www.massmecfs.org/images/pdf/pediatric/International%20Consensus%20Primer%20Letter%20to%20Educators.pdf)



Special Considerations for the Pediatric Patient



Special Considerations for the Pediatric Patient

- EDUCATE, EDUCATE, EDUCATE
- Post exertional malaise/pacing needs to be taught early (consider OT/PT familiar with ME/CFS)
- Cultivate resources that can assist with education especially PEM

Special Considerations for the Pediatric Patient

- Early on, schedule visits 1-2 months
- Try to make visits the least energy consuming as possible – schedule later in day, avoid wait times, if possible don't have patient wait in the waiting room (make use of beeper or cell phone)
- Consider early counseling to provide patient someone other than parent they can communicate with. It is important that the counselor is familiar with ME/CFS

Long Covid and MCAS

- 17 yr. old with h/o covid in May of 2023. PMH includes seasonal allergies, eczema, dysmenorrhea, and depressive disorder
- She developed sx of syncope and associated tonic-clonic movements 1 month after covid infection.
- She had episodes most days up to 20 times a day.
- She had received evaluations at 2 Pediatric hospitals and had been diagnosed with POTS and Psychogenic Non-Epileptic Seizures
- She also had sx of fatigue, headaches, insomnia, constipation/diarrhea, urinary urgency, large swings in blood pressure and heart rate, and worsening of eczema



Interventions

- Claritin and Pepcid for MCAS
- Propranolol 5 mg TID for POTS

Results

- Syncopal episodes and non epileptiform
- Episodes were not improved
- Eczema much improved
- GI symptoms resolved

Interventions

- Added Fludrocortisone for POTS
- Added Gastrocrom for MCAS
- Ordered IVF 3x a week for 3 weeks

Results

- POTS – minimal improvement
- Non epileptic episodes stopped about 1 week after initiation of Gastrocrom
- No one able to get IV access as outpatient, patient struggling to get oral fluids/salt.
- Ordered PICC line

PICC LINE

- Day after PICC line was placed she began having episodes again
- Developed hematuria and urinary symptoms – UA revealed sterile urine
- Rash in area of the dressing of the PICC line
- GI symptoms re-appeared
- Recommended removal of PICC line



MCAS

- Removed PICC line
- Added Benadryl
- Episodes decreased in frequency after a couple of days and by one week had stopped completely for a month

Tools for the Practitioner

PRESENTATION, DIAGNOSIS, AND MANAGEMENT OF MAST CELL
ACTIVATION SYNDROME

-Lawrence B. Afrin

<https://edswellness.org/wp-content/uploads/2016/05/Dr-Afrin-2013-Management-of-MCAS-printable.pdf>

