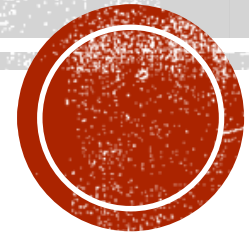


INTEGRATIVE MEDICINE IN CYSTIC FIBROSIS STRESS AND LUNG HEALTH



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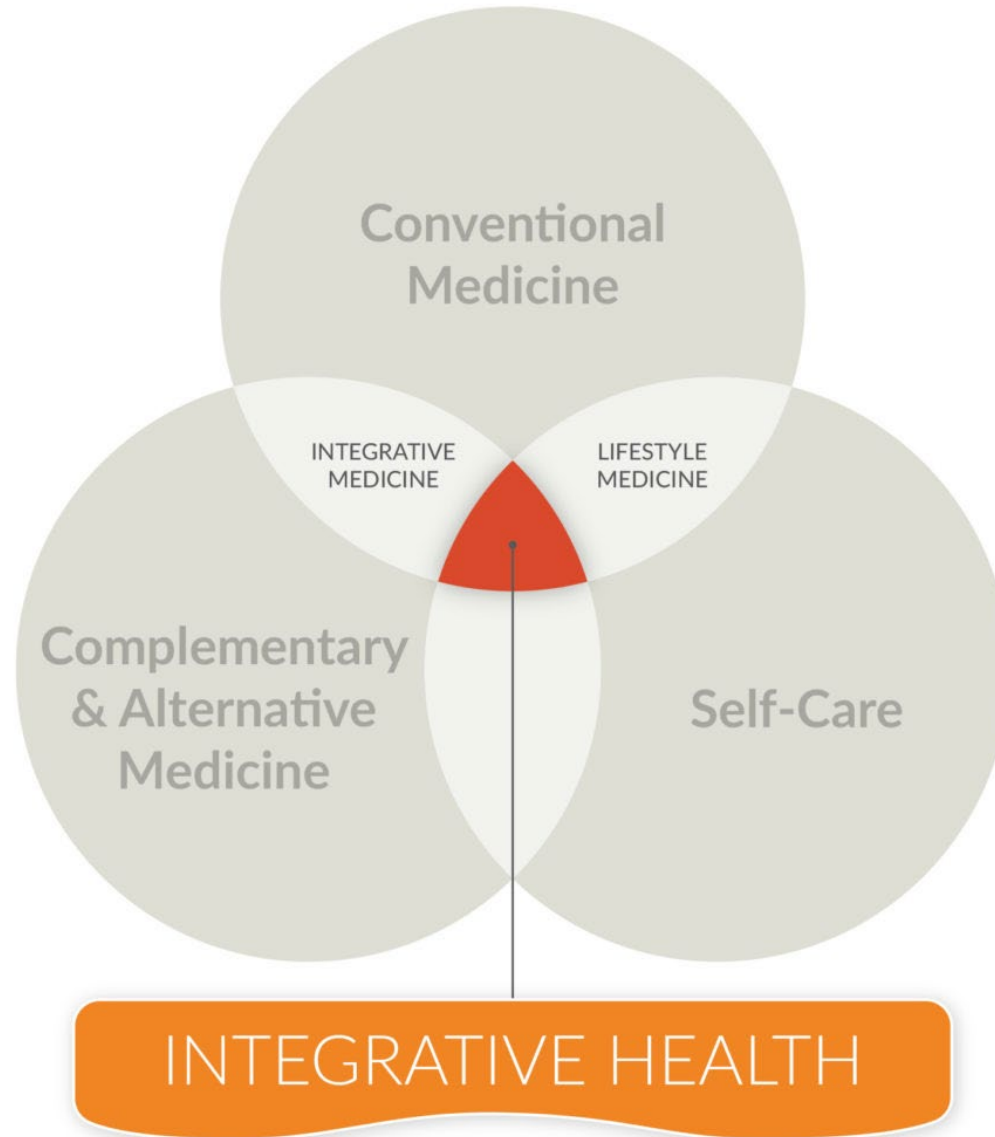
OBJECTIVES

To better understand how chronic stress and adverse childhood experiences (ACEs) may affect lung health

To better understand integrative medicine and the integrative or holistic approach to care to reduce stress

Understanding how an integrative medical approach to care of patient with cystic fibrosis may improve overall health.





CASE: 16 YEAR OLD SAMANTHA

Conventional therapies:

- ▶ Bronchodilator neb 2/day with VEST (30 minutes).
- ▶ 7% hypertonic saline nebs daily
- ▶ Dornase alfa (Pulmozyme) neb daily.
- ▶ Fluticasone/Salmeterol (Advair) 250/50 one click/day
- ▶ Tobramycin 300 mg neb 2/day
- ▶ Insulin glargine (Lantus), once a day
- ▶ Pancrelipase (Pancrecarb) MT-6- 8 tabs with meals, 3-4 with snacks
- ▶ Ursodiol (Actigall) 300 mg 2/day
- ▶ CFTR modulator (Trikafta)
- ▶ ADEK daily and Vit K 5 mg daily.
- ▶ Azithromycin 500 mg 3/wk (MWF)



CASE CONTINUED

Social/family

- Goes to “in person” school and makes “okay” grades
- Isn’t doing PE but would like to be more active
- Has some friends but rarely spends much time outside and often is on her phone or computer
- Lives in the Palo Alto area
- Even though she is feeling better on Trikafta, she has a chronic cough especially with activity
- Some nights will lie down and have some shortness of breath with coughing
- Multiple hospitalizations in the past but none for last 2 years



CASE 2: 6 YR OLD JOSE

Conventional therapies:

- Bronchodilator neb 2/day with VEST (30 minutes).
- 5% hypertonic saline nebs 2/day
- Pancrelipase (Pancrecarb) MT-2-3 tabs with meals
- CFTR modulator (Trikafta)
- ADEK daily.
- Azithromycin 500 mg 3/wk (MWF)
- Never hospitalized



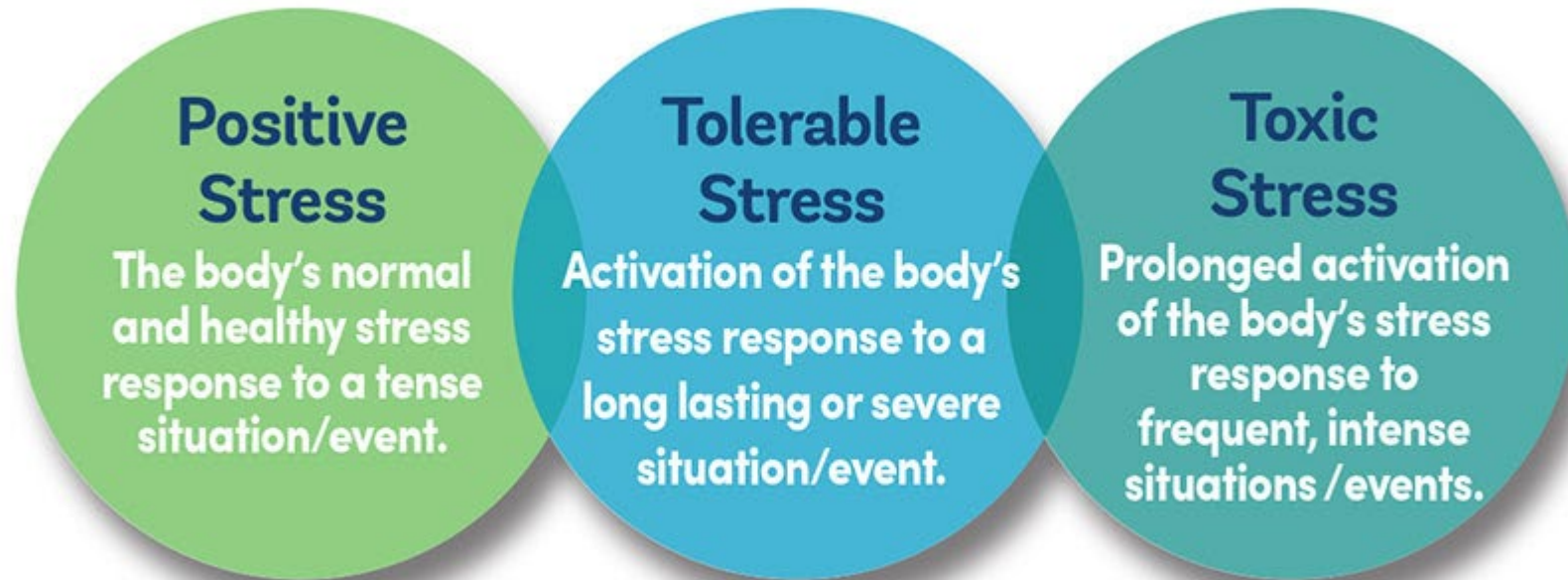
CASE 2 CONTINUED

Social/family

- Lives in two homes (parents divorced) but “gets along” with both mom (not remarried) and dad (has remarried, 3 children).
- Attends school in person, has several friends
- Is active- likes sports especially soccer
- Both parents live in the Salinas/Greenfield area (about 90 miles from CF Center)
- Sometimes doesn't do all of his daily therapies
- Good appetite but weight is at 20%tile
- Has three older step siblings (all boys) who live with his mother



Stressors?



The biology linking ACEs to risk of disease is postulated to be related to levels of stress hormones, referred to as toxic stress.



ADVERSE CHILDHOOD EVENTS (ACES)

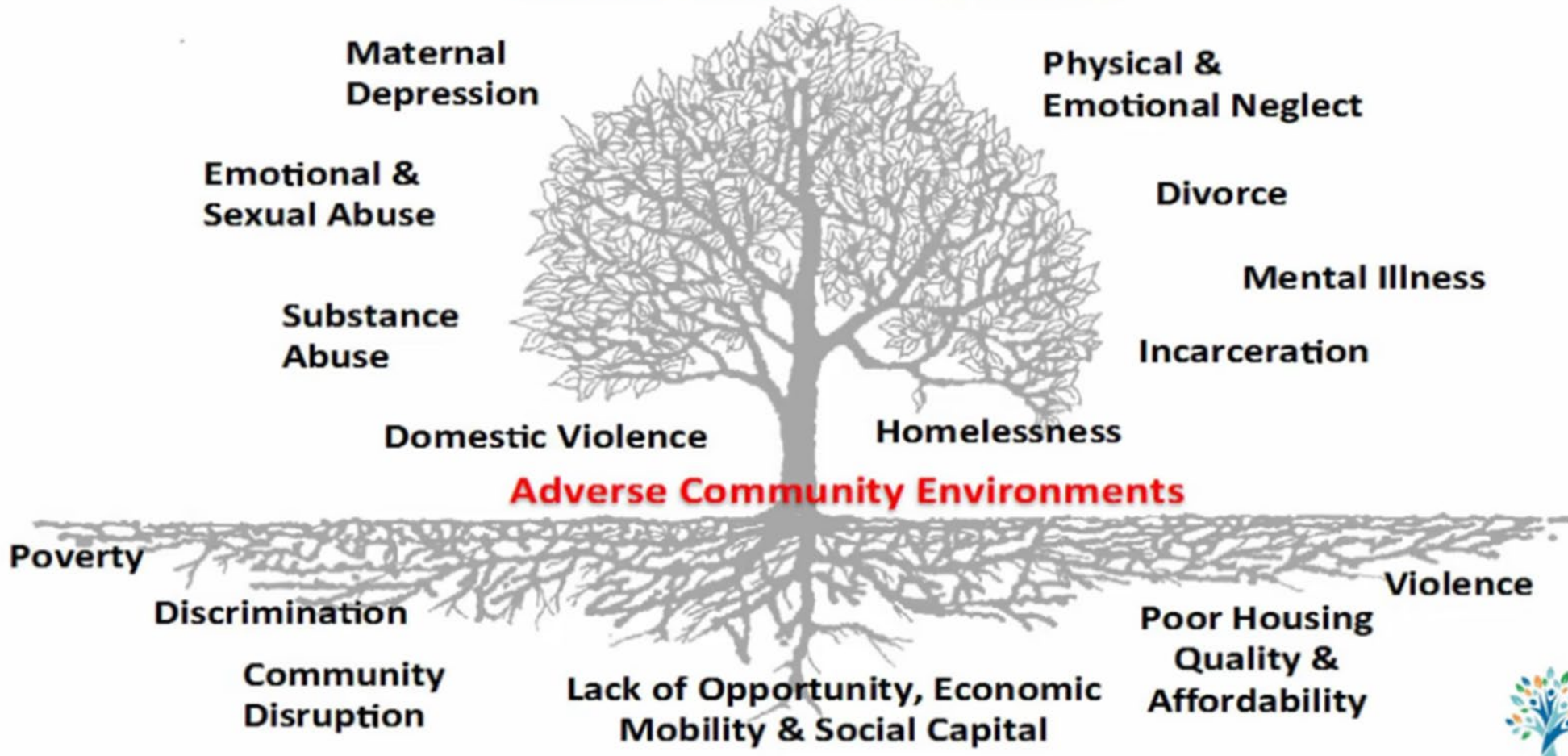
- ACEs are potentially traumatic events that cause stress and have lasting negative effects on physical and mental health
- Include abuse, maltreatment, neglect (including emotional), household dysfunction including divorce or separation, substance abuse and bullying victimization.
- Children who have experienced at least once ACE are at increased risk for chronic physical health problems during childhood including learning delays and behavioral problems.
- 67% of youth in a study of urban youth reported at least 1 ACE and 12% had 4 or more. Nationally, 46% (ages 0-17) have experienced 1 ACE and 40% (ages 12-17) have experienced 2 or more.
- It is estimated that 1/3 of pediatricians never inquire about ACEs. Screening has been challenging for those who try and screen for ACEs.



ADVERSE CHILDHOOD EVENTS (ACES)

The Pair of ACEs

Adverse Childhood Experiences



ACES IN CYSTIC FIBROSIS PATIENTS

- Very little published data and often children with CF may be protected against early adversity due to increase healthcare agencies involvement
- However, children with chronic illness/disability are more likely to be maltreated and even neglected
- Treatments are often complex and time-consuming and this may be perceived as “high-burden” which may result in strain to families and finances
- May have undergone (or going to undergo) frightening or painful procedures.
- This may impact trust in professionals and even adherence.
- These have been reported in CF patients as stressors: parental separation, emotional neglect, frightening hospitalizations/procedures, pain/discomfort and bullying by peers and family members
- Studies have shown that CF patients and parent are open to ACE screening but would rather report “number” of ACEs rather than specific ACEs.



Table I The Prevalence of Each Individual ACE in a CF Population, Compared with National Prevalence Data for the Whole Population

ACE		CF Sample %	National Prevalence (N = 1921)* %
Child maltreatment	Verbal abuse	31.3	22.1
	Physical abuse	18.8	17.0
	Sexual abuse	10.0	7.3
	Emotional neglect	8.8	7.8
	Physical neglect	2.5	4.6
Household dysfunction	Parental separation	32.5	27.8
	Mental illness	20.0	18.8
	Domestic violence	16.3	17.9
	Alcohol abuse	12.5	14.3
	Drug abuse	2.5	6.7
	Incarceration	3.8	4.5
Medical/Health Trauma	Frightening hospital admission	56.3	
	Painful/frightening procedure	65.0	
	Forced to have treatment	28.8	
	Severe pain/discomfort	48.8	
	Bullied by peers	46.3	

Note: *Comparative sample of 18–60 year olds drawn from representative general population survey in Wales.⁸

Study of 80 CF patients, ages 18-58

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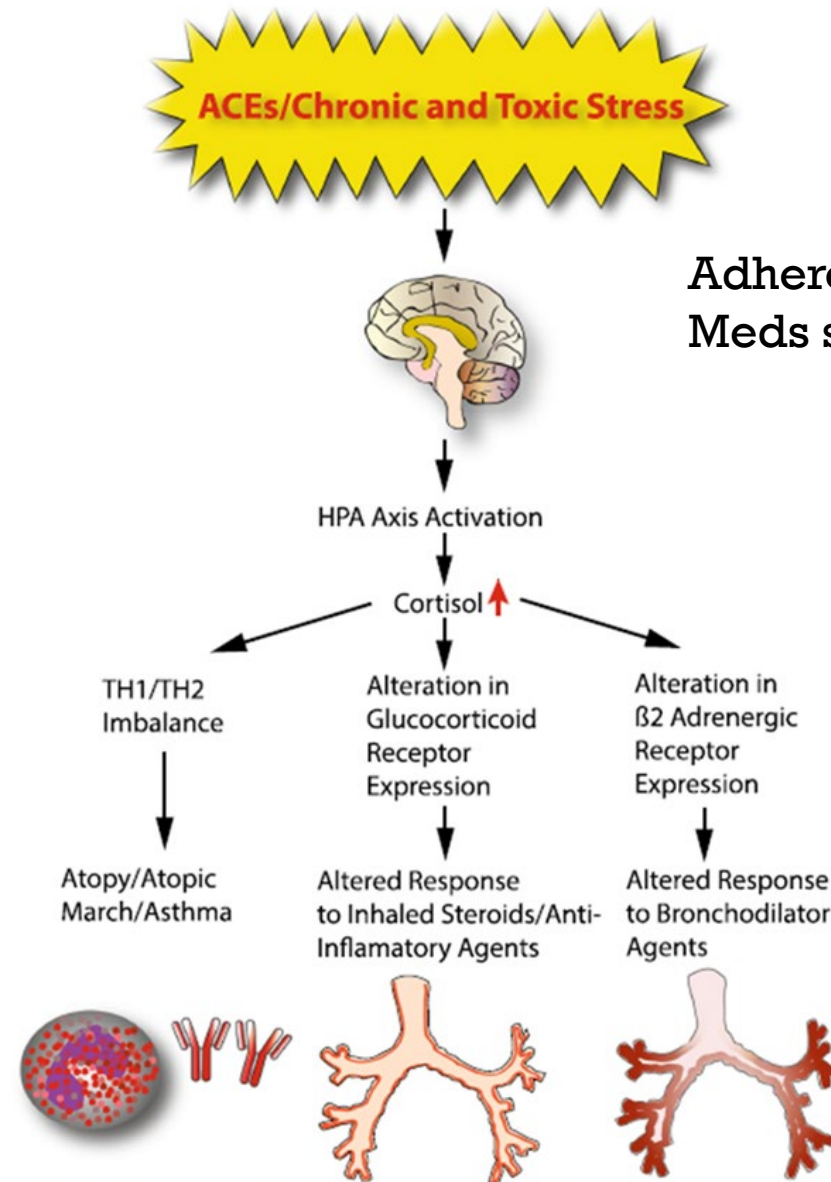


ACES AND TOXIC STRESS



- ACEs are more common than previously thought and may result in worse health outcomes. The biology linking ACEs to risk of disease is postulated to be related to levels of stress hormones.
- Toxic stress is a common response to ACEs is characterized by chronic dysregulation of the neuroendocrine and immune system via the hypothalamic-pituitary axis (HPA).
- The HPA axis stress response involved production and secretion of cortisol which alters tissue function to mobilized or store energy in order to meet metabolic demands.
- HPA axis is important to regulate metabolic, cardiovascular, immune and behavioral processes.
- The response to stress and resultant HPA stimulation may increase inflammation, decrease immune response, impact cardiovascular health and response to many commonly used pulmonary medications.
- This may lead to multi-systemic alterations and changes to the body's metabolic and even expressions of disorders and/or disease.





Adherence vs Decrease Effectiveness-
Meds such as albuterol, inhaled steroids?



Fig. 2 The effects of ACEs and chronic and toxic stress on the HPA axis, cortisol and described biological changes and postulated asthma pathophysiology/therapeutic response



CASE- 1



“Live life to the fullest and focus on the positive”

“I’m the one that’s gotta die when it’s my time; so let me live my life the way I want to.” Jimi Hendrik



CASE 2



Fighting/Getting along



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Feeling lonely/Having friends



Neighborhood crime



INTERVENTION

- Screening- being developed but may be as easy as 2-3 questions
- Biomarkers- currently being studied (like HbA1c for stress)

Anticipatory guidance:

- Healthy relationships
 - Incorporating family therapy into a more traditional asthma psychoeducation program led to significant decrease in airway inflammation as indicated by eNO levels
 - Resources and referrals for psychological interventions such as
 - psychotherapy for child/parent
 - focused cognitive behavioral therapy
 - biofeedback



SLEEP



- Sleep affects the immune system and healthy sleep allows for normal circadian rhythms of cortisol level and supports decreases in sympathetic nervous system output.
- Healthy sleep is associated with a reduced risk of infection and improved infection outcomes
- Alterations in sleep are associated with altered immune cell counts and dysregulation of inflammatory markers
- Decreased sleep duration has been associated with increase respiratory symptoms (asthma and CF)



NUTRITION



- Diet can directly affect the immune system
- “Fast foods” and overly processed foods are pro-inflammatory (omega 6 fatty acids or vegetable oils)
- Diets such as the Mediterranean diet which emphasize olive oil, fish, whole grains, fresh fruits and vegetables are associated with reduced inflammation and decrease risk for cardiovascular disease, diabetes and asthma
- Supplementation of omega 3 fatty acids (flax seed, fish oil etc) may lower norepinephrine, adrenocorticotrophic hormone and plasma cortisol



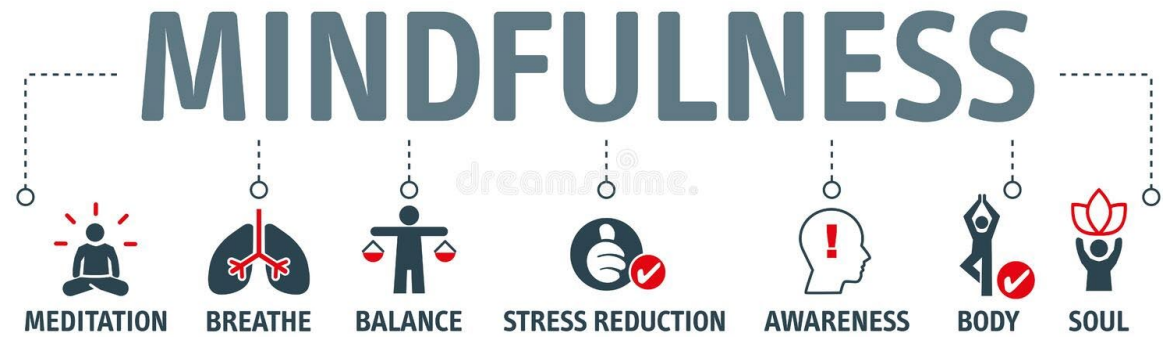
EXERCISE



- Physical activity has been associated with overall improved immune system function
- Regular exercise may lead to a general anti-inflammatory effect over time
- Moderate exercise has been associated with decreased upper respiratory tract infections
- Exercise especially regular aerobic like running/swimming/biking improves symptom management and mental health including self esteem



MINDFULNESS



- Mindfulness practices reduce stress related neuroendocrine, immune, and metabolic markers such as cortisol, C-reactive protein and tumor necrosis factor
- Mindfulness practice such as yoga, decreased sympathetic activation, lower blood pressure and increasing heart rate variability
- Children who practiced yoga regularly for twelve weeks had a significant increase in their vital capacity, FVC and peak expiratory flow rate compared to the control group
- Mindfulness-based interventions offer inexpensive, non-invasive approaches which may decrease stress and anxiety and improve lung function in children and adolescents.



IM APPROACH TO CF CARE



Integrative:

- Monitor for stress/ACEs
- Mind-Body therapies-relaxation, stress reduction
- Nutrition-fresh fruits, vegetables, healthy fats
- Breathing- Yoga, martial arts
- Exercise Program
- Cognitive therapies especially if family dysfunction
- Continue conventional therapies



Thanks!

