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It Takes a Team: A Case of Acquired Common Variable Immune Deficiency Syndrome

Moderator: Elizabeth Wall, MS, RDN-AP, CNSC

Panelists:
Valerie Reynolds, MS, RDN, CNSC, CSO
Scott Lozano, PharmD, BCNSP, BCPS
David Hakimian, MD
Crystal Dowell-Green, BSN, RN

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- Today's webinar is approved for 2.0 Continuing Education credit hours.

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It Takes a Team: A Case of Acquired Common Variable Immune Deficiency Syndrome

UChicago Medicine's Adult GI/Nutrition Support Team

David Hakimian, MD

Crystal Dowell-Green, RN

Scott Lozano, PharmD, BCNSP,

Valerie Reynolds, MS, RDN, CNSC, CSO

Elizabeth Wall, MS, RDN-AP, CNSC

Multidisciplinary Team Panel

Crystal Dowell-Green, RN

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David Hakimian, MD

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Disclosures

- Crystal Dowell-Green – none
- David Hakimian – none
- Scott Lozano – none
- Valerie Reynolds – none
- Elizabeth Wall – Baxter Advisory Board, Zealand Pharma Advisory Board

Learning Objectives

- At the conclusion of this webinar participants will
  - appreciate the benefits of a multidisciplinary team approach to patient care.
  - understand the intricacies and meticulous management required to nourish severely malnourished patients who require parenteral nutrition support.

Outline

- Brief description of each discipline's role
- Parenteral nutrition (PN) case
- Questions & answers

Current State

- Founded in 1980
- 2020 ASPEN Nutrition Support Team of Distinction
- 12 member team
- Patient services
- Education
- Academic involvement

UChicago GI/Nutrition Support Team 2022

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NST Clinicians

- Professional practice
- Discipline's role
- Patient care expertise

Physician: Inpatient Responsibilities

- Responsible for the consultation service for management of complex nutritional issues.
  - Team leader
  - Consults received from a variety of services throughout the hospital
- Assessment
  - Malnutrition and underlying etiology
  - Nutritional –macro and micronutrient needs
  - Medical evaluation as needed
- Collaborate with the primary team and other consultation disciplines

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Physician: Inpatient Responsibilities

- Design parenteral and enteral nutrition formulations based on each individual patient's nutritional demands, medical history and current disease.
- Understand the patient's clinical condition and make recommendations for additional nutrition-related examinations
  - Indirect calorimetry
  - Urinary studies - urea nitrogen, sodium, electrolytes
  - GI assessment – stool studies for fat, fecal elastase, etc.
- Round and discuss patients with the NST

Physician: Inpatient Responsibilities

- Manage parenteral and enteral complications
  - Central venous catheter (CVC) associated infections
  - Electrolytes abnormalities
  - Percutaneous enteral gastrostomy (PEG) site complications
    - Infection or leakage/skin integrity
- Order, schedule, and perform endoscopic procedures
  - Upper endoscopy
  - Colonoscopy
  - PEG placement
  - Nasojejunal tube placement
  - Double balloon endoscopy
- Determine the patient's discharge plan of care (with the NST)
  - Clinic appointments, procedures, nutrition support prescription

Physician: Outpatient Responsibilities

- Continuity of care clinic for patients with complex nutrition/feeding/small bowel issues
- Consult and discuss clinical updates with the NST
  - Enteral and parenteral support patients
- Manage complications of home PN patients
  - Catheter infections/malfunctions or organ dysfunction (liver, kidney)
- Attend and manage home PN patients in continuity with the NST
  - Trends in biochemical measurements
  - Readiness for transition to oral or enteral support

Pharmacist

- Inpatient
  - Coordinate systems between pharmacy operations and patient care with respect to PN ordering
  - Content expert for PN compounding and medication dosing
  - Medication ordering/ pharmacokinetic dosing
  - Education
- Outpatient
  - Coordination of home PN patient care
  - Point of contact for compounding pharmacies
  - Direct patient care

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Nurse

- Inpatient
  - •Direct, holistic GI/Nutrition patient care
  - •Initiate & adjust PN and/or enteral feedings
  - •Catheter care/troubleshooting
  - •Education
- Outpatient
  - •Ongoing Coordination of home PN patient care
  - •Coordination of GI/Nutrition Clinic
  - •Communicate w/ home health pharmacy and nursing agencies

Dietitian

- Inpatient
  - Assessment
  - Order MNT, EN, PN
  - Guide feeding transitions
  - Provide patient-focused diet educations & counseling
- Outpatient
  - Coordination of home PN, EN, malabsorption patient care
  - Contact for home health pharmacy and nursing agencies
  - Coordination of care with other providers

Parenteral Nutrition Case - Disease Course

- 62 yo male
- 2008 – diagnosed with marginal zone lymphoma of the parotid gland, treated with Rituximab
- 2013 - diarrhea with weight loss
- 30 kg weight loss
- 2020 - diagnosed with acquired Common Variable disease (CVID) based on low immunoglobulin levels
  - Admitted to outside hospital with severe malnutrition and frailty
  - Started on loop diuretics and parenteral nutrition (PN)
- Referred for UCMC GI/Nutrition Clinic with chronic diarrhea, severe weight loss and loss of functionality

Physical Examination

- Vitals –
  - Blood pressure 104/66
  - **pulse 116**
  - temperature 37.5 °C
- **Anthropometrics**
  - Height 188 cm ,weight **51.2 kg , BMI 14.5** kg/m^2
- **NFPE: Severe diffuse muscle wasting**
- Review of systems
  - CARDIAC: Rapid S1, S2.No murmurs, rubs or gallops.
  - PULMONARY: Clear bilaterally to auscultation and percussion.
  - ABDOMEN: Soft, non-tender, non-distended. Bowel sounds are present.
  - MUSCULOSKELETAL: No signs of arthritis
  - EXTREMITIES: Normal without edema.
  - SKIN: Without rash
  - NEUROLOGICAL: No Asterixis
- **PSYCH:** Oriented X 3**, apathetic mood**

Workup

Stool results

- C diff, PCR panel – all negative
- Stool Alpha 1-Antitrypsin: Normal
- Electrolytes: Sodium 20, K^+ 36 mmol/L Cl^- 16
- Osmolality: 327 mOsm/kg
- Stool fat - **High**

Blood results

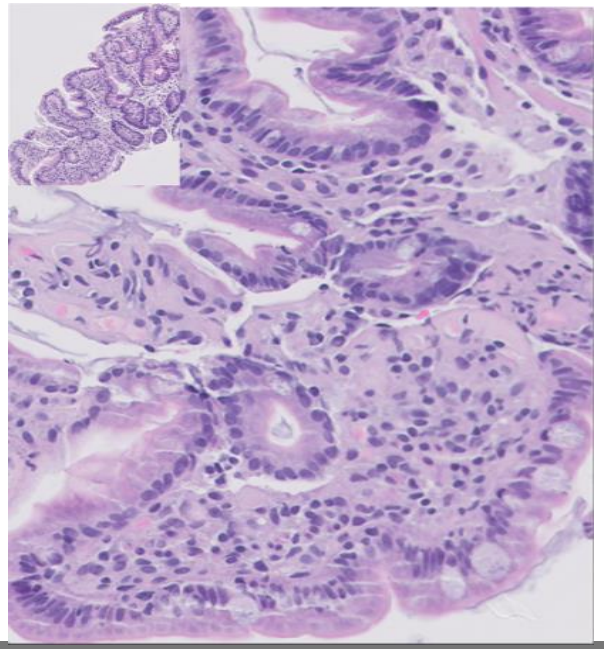
Albumin, Median gr/dL ⇩	**2.1 (3.5 - 5.0)**
Total protein, Median gr/dL ⇩	**4.5 (6.0 - 8.3)**
Pre Albumin, Median gr/dL ⇩	**16 (21 – 41)**
Creatinine mg/dl	0.5 (0.5-1.4)
Hemoglobin, Median gr/dL ⇩	**10.6 (13.5 - 17.5)**
Sodium mmol/L ⇩	**133(135-145)**
Potassium mmol/L	4.1(3.5-5)
Alkaline phosphatase u/L ⇧	**215(50-150)**
ALT u/L	30 (8-35)

Workup - Vitamins and Minerals

Copper ug/mL ⇩	**0.33 (0.75 - 1.45)**
25-Hydroxy Vitamin D ng/ml	56 (12 - 99)
Vitamin B12 pg/ml	576 (240 - 900)
FATTY ACIDS, ESSENTIAL Triene:Tetraene Ratio	0.023(0.010-0.038)
Free Retinol (Vit A) mg/L	9 (5.5 - 17.0)
Vitamin B1 nmol/L	265(70 – 180)
Vitamin B6 ug/L	6(5 – 50)
Zinc ug/mL ⇩	**0.43(0.66 - 1.10)**
Selenium ng/mL ⇩	**65 (70-150)**

GI - Workup

- Upper endoscopy with fissured and small bowel mucosal atrophy
  - Small bowel biopsies with villi atrophy and **low plasma cell** in the mucosa
- Video capsule showed small erosions in proximal jejunum
- CT lymphoma remission



Case Summary

- This is a 62 YO M with chronic malabsorptive diarrhea
- Past Lymphoma treated with Rituximab. In remission
- Diagnosed with CVID
- Upper endoscopy demonstrated villous atrophy and low plasma cells
- Referred due to Severe malnutrition with low vitamins and minerals

Your Thoughts -

1. Treatment recommendations?
   - *Admit Vs Outpatient*
   - *EN Vs PN*
2. Differential diagnosis?

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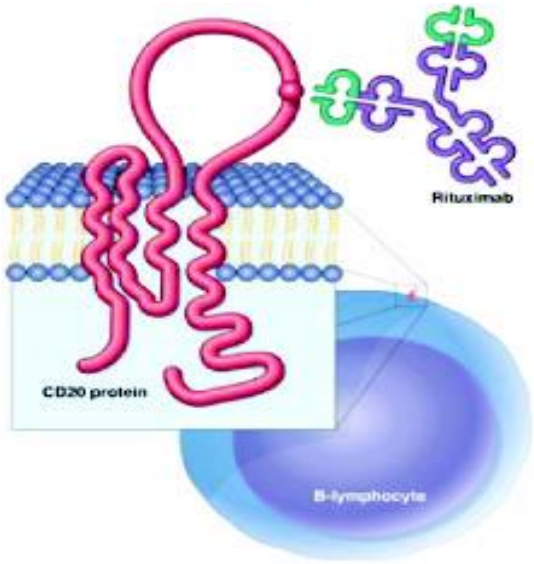
Rituximab

- Rituximab is a chimeric anti CD 20 highly effective monoclonal antibody
- Highly efficient treatment for lymphoma, cancer and some autoimmune disease
- Specific affinity for the B-lymphocyte transmembrane protein, CD20
- RTX causing cell death and depletion of B cells
- RTX reported cases of inflammatory bowel disease (IBD) related to RTX treatment



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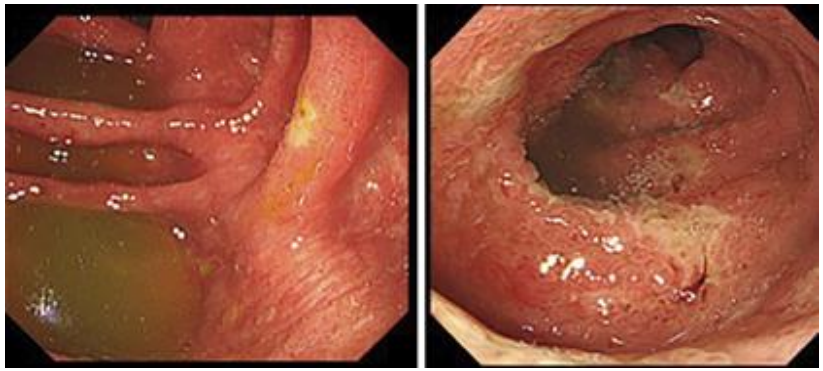
1.Tsuzuki, et al. Internal Medicine 2021; 60.5 : 731-738

Rituximab Gastrointestinal Adverse Events

- 35 reported cases of inflammatory bowel disease (IBD) like related to RTX treatment[1]
  - Crohn's, UC, microscopic colitis, ileocolitis
  - Occurred months to years from treatment

- Histology of colonic biopsies
  - **Inflammatory cell infiltration**
  - **Increased lymphocytes and plasma cells**
- B cell depletion causes activation of T cells



1.Tsuzuki, et al. Internal Medicine 2021; 60.5 : 731-738

2.Mallepally, et al. Am J Clin Oncol 2019;6: 539-545

Common Variable Immunodeficiency Disease (CVID)

- Usually a primary immunodeficiency
- Characterized by recurrent sinus/URI infections/Malabsorption
- Onset 20-50 years
- Diagnosis
  - Low antibody levels (IgG, IgM and IgA)
  - Loss of plasma cells in both bone marrow and intestinal mucosa
- IVIG therapy
  - Efficient in treating recurrent infections
  - Ineffective in treating gastrointestinal symptoms

Uzzan, et al. Current gastroenterology reports 2016; 18.4 : 1-12

CVID and the gastrointestinal system

- Diarrhea and weight loss most common clinical manifestation (20-60%)
- **Diarrhea may be due to :**
  - **Infectious** (Giardia, Campylobacter, Salmonella, norovirus).
  - **Inflammatory** (celiac-like, microscopic colitis ,Crohn's like)
  - **Malignant** (lymphoma)
- CVID enteropathy is characterized
  - Villous blunting, crypt distortion
  - Increased intraepithelial T lymphocytes, lymphoid aggregates
  - **Lack of plasma cells in the lamina propia**

Uzzan, et al. Current gastroenterology reports 2016; 18.4 : 1-12
Pikkarainen, et al *The Am. J. gastroenterology* 2019 ; 114.4 : 648.

Common variable immunodeficiency- like Enteropathy associated with rituximab B-cell depletion therapy

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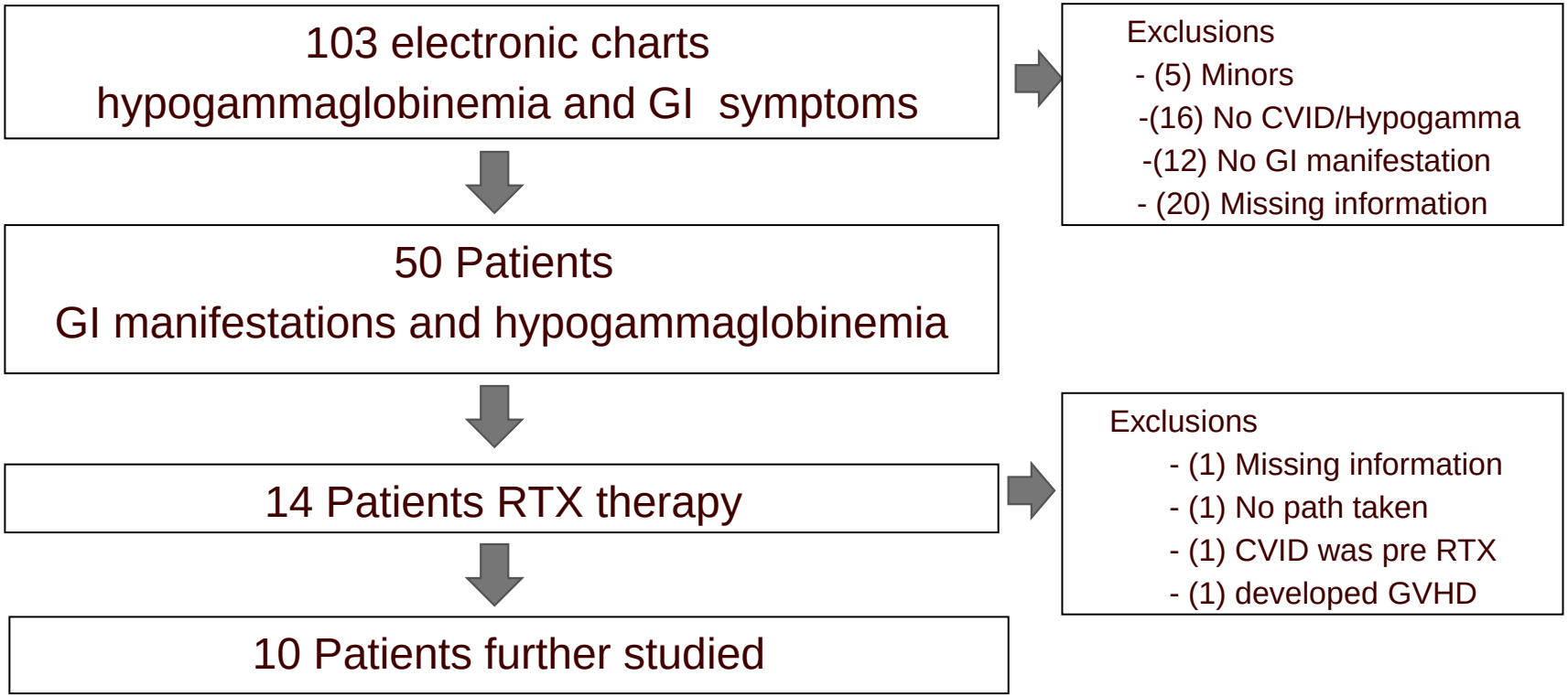
Methods

- Retrospective analysis of medical charts
  - Patients with enteropathy
  - UCMC gastroenterology clinics
  - 2008 -2021
- Identification codes
  - Common variable immunodeficiency disease (CVID)
  - Enteropathy
  - Malabsorption
  - Weight loss
  - Diarrhea
- Patients with Rituximab use were further studied
  - Clinical data
  - Laboratory values
  - Endoscopy
  - Pathology

Methods



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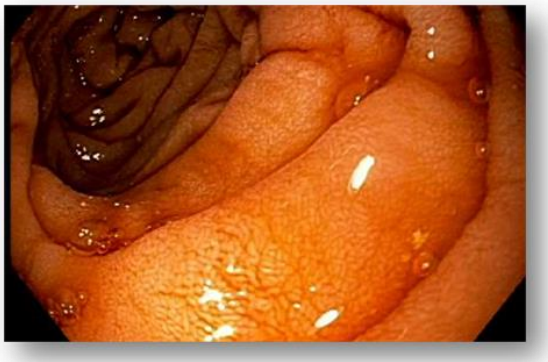
Results

Patients Characteristics	
Number of patients	10
Age, median	63
Male n(%)	5(50)
Rituximab indication	
Cancer n(%)	9(90)
Non Hodgkin's lymphoma	8 (88)
Gastrointestinal manifestations n(%)	
Diarrhea	10(100)
Severe abdominal pain	1(10)
Nutrition Status	
Weight loss n(%)	6(60)
Weight loss median, Kg	13.5
Severe malnutrition n(%)	7(70)



Results

Treatment	
Patients	10
IVIG therapy	(100) 10
Infusion frequency, Median, weeks	4
Symptomatic Improvement n(%)	2(20)
PN management n(%)	5(50)
Other therapies* n(%)	7
Prednisone	6(85)
Budesonide	2(28.5)
Vedolizumab	1(14)
Infliximab	2(28.5)
Adalimumab	1(14)
Xeljanz	1(14)
*All ineffective aside from partial response to Xeljanz	

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Results

- First case series describing severe RTX associated CVID-like enteropathy
- Patients presented with diarrhea, malabsorption and weight loss
  similar to primary CVID enteropathy
- Most had Low plasma cells in the intestinal mucosa
  Unknown mechanism
- IVIG, steroids and biologics therapy was not effective
- **All gained weight on parenteral nutrition**

Back to our patient - Admission

Admitted from clinic

- Single lumen tunneled catheter was placed
  - Tip in the SVC
- Parenteral nutrition

  1.5 L

  1.4 gr dextrose /kg

  1.3 gr protein/kg

  50 gr of intralipid

  Adult Multivitamins, minerals, trace minerals, and thiamine
- Observed for refeeding syndrome
- Muscle strength and weight improved on PN

PN Case – Hospital Course

- Started oral vitamins and minerals – including vitamin A
- Medications – Prednisone, Loperamide, Cholestyramine
- Calories increased during hospitalization to goal of 25 kcal/kg, 1.5 g pro/kg

Micronutrients	Result	Range
Vitamin A	**11.2**	32-78 ug/dL
Vitamin D	53	12-99 ng/mL
Vitamin E	**9**	5.5-17 mg/L
Vitamin B12	576	240 – 900 Pg/mL
Zinc	**0.43**	0.6-1.1 ug/mL
Copper	**0.43**	0.75-1.45 ug/mL
Prealbumin	**4**	21-41 mg/dL

Preparation for Discharge

- Education - PN management and line care
  - Patient and wife
  - Written, video, hands-on demonstration
  - Return demonstration
- Discharged to rehabilitation
  - Collaboration with the RDN/PharmD at the receiving facility

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Outpatient

- Discharged from rehabilitation to home
- Intake - Oral and PN
  - 33 kcal/Kg
  - Protein 2 g/kg, Dextrose 4 g/kg, Lipid 50 g/d
- Weight increased from 51 to 67 kg in 13 weeks
- Functionality improved with physiotherapy
- Complication – Central line infection and sepsis
- Current management - home PN managed by UCMC nutrition team and MNT
- Ongoing clinical follow-up - phone and clinic
- Micronutrients
  - Vitamin A 42 (32.5-78), zinc 0.79 (0.7-18)

PN Case – Key Practice Points

- Understand the underlying pathology of malabsorption/malnutrition
  - This will help to determine the appropriate mode of support
- Check all micronutrient levels prior to starting nutrition support
  - Insist on baseline vitamin/mineral levels
- Start slowly and advance as clinically appropriate
  - May need to replete electrolytes prior to starting support
  - Advise providers initiation and advancement will be slow and do not plan for rapid discharge
- Education/re-education
  - Home PN infusion is complex and will take multiple, repetitive sessions before the pt/caregiver becomes competent
- Ongoing Clinical monitoring is essential
  - Home PN support patient must have ongoing, in-person clinical encounters

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Summary

- Multidisciplinary teams are recommended when caring for patients with complex nutrition issues
- Working within a multidisciplinary team enables clinicians to expand patient care roles

THANK YOU

Questions?

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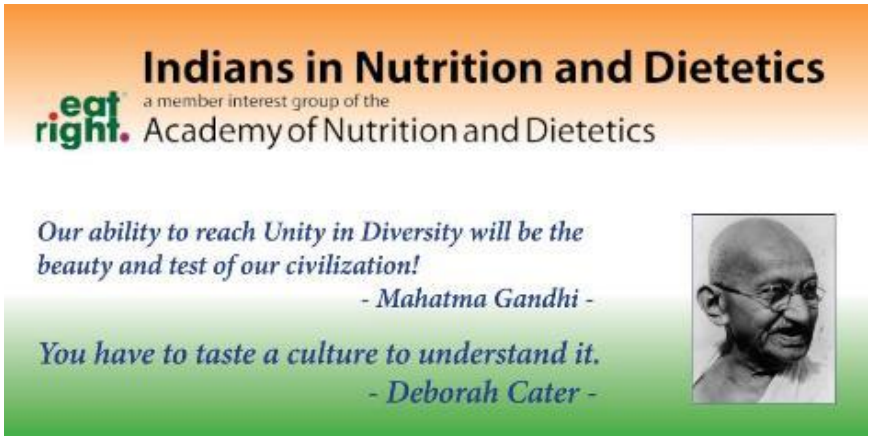

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Thank You!

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On behalf of the IND MIG ~ Thank you for joining us today! Be well and be safe!