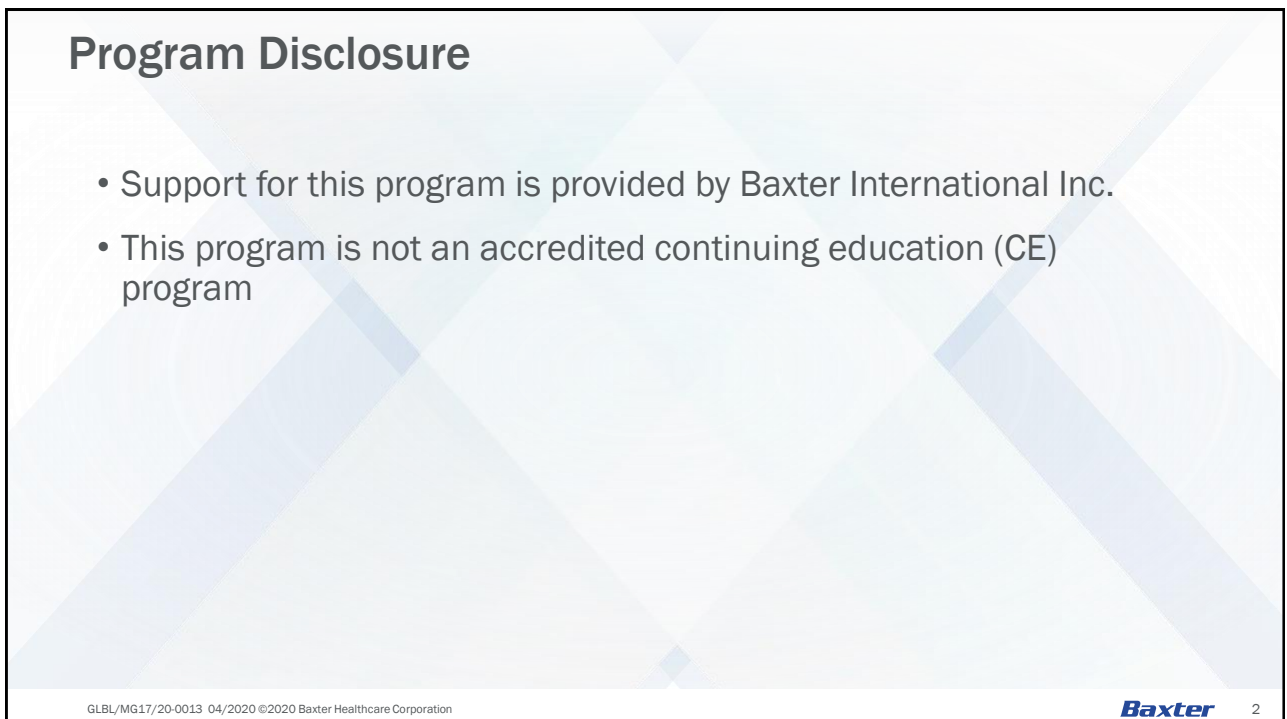




1



2

Faculty



Robert Martindale, MD, PhD

Professor of Surgery
Medical Director Hospital Nutritional Services
Oregon Health and Sciences University
Portland, Oregon USA



Jayshil Patel, MD

Associate Professor Pulmonary
Medicine Froedtert Hospital
Milwaukee, WI, USA

GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

Baxter

3

3

Disclosures



Robert Martindale, MD, PhD

Nestle: Educational Advisor

Fresenius-Kabi: Advisory Group

Baxter: Advisory panel
Educational development



Jayshil Patel, MD

Nestle: Consultant

Baxter: Advisory panel

GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

Baxter

4

4

Objectives

- Discuss the role of delivering and monitoring nutrition support in the COVID-19 ICU patient
- Describe best practices experienced in treating COVID-19 patients
- Identify characteristics and nutritional requirements of the patient with Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)
- Outline recommendations for SARS-CoV-2 patients to meet the nutritional requires using enteral and or parenteral
- Identify instances where managing the SARS-Co-2 deviates from the current nutrition guidelines for enteral and parenteral nutrition in the ICU patient
- Discuss potential novel nutrient recommendations for the SARS-CoV-2 patient

GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

5

5

Consider This Case...

- 53-year-old woman with breast cancer undergoing chemotherapy presents with 2 days of progressively worsening shortness of breath, fever, and malaise.
- In the emergency department, she is found tachypnic and hypoxemic with oxygen saturation 80% despite 6 liters high-flow nasal cannula. She is intubated and shortly afterwards, is hypotensive. She receives 2 liters crystalloid and is started on a norepinephrine infusion.
- CT chest shows dense bilateral lower lobe opacities.
- She is transferred to the medical ICU under strict isolation, remains febrile to 101°F and remains on norepinephrine at 0.04 mcg/kg/min.

GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

6

6

Nutrition Is an Integral Component of Any Supportive Care in the ICU

Critical illness exists in phases – early acute → late acute → post-acute

During the acute phase, hyper-catabolism is the general rule, which leads to energy debt and loss of lean body mass

Amino acids are mobilized from predominantly muscle, which leads to negative nitrogen balance and acquired sarcopenia

Critical illness induces gut dysfunction and dysbiosis, which propagates and accentuates the inflammatory response leading to cellular dysfunction with end result being multiple organ failure

GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

7

7

Consider This Case...

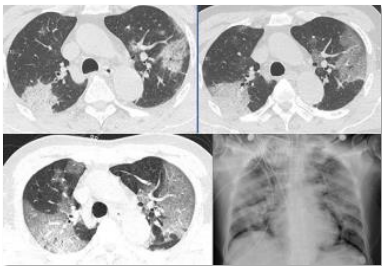
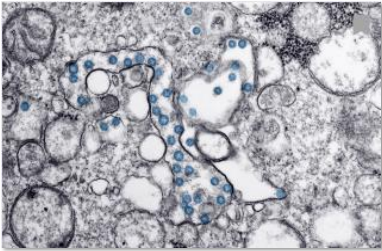
- 53-year-old woman with a past medical history of asthma presents with 2 days of progressively worsening shortness of breath, fever, and malaise.
- In the emergency department, she is found tachypnic and hypoxemic with oxygen saturation 80% despite 6 liters high-flow nasal cannula. She is intubated and short afterwards, is hypotensive. She receives 2 liters crystalloid and is started on a norepinephrine infusion.
- CT chest shows dense bilateral lower lobe opacities.
- She is transferred to the medical ICU under strict isolation, remains febrile to 101°F and remains on norepinephrine at 0.04 mcg/kg/min.
- **Testing for COVID-19 returns positive**

GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

8

8

Guidance and Recommendations for Nutritional Support for Critically Ill Patients with COVID-19



GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

Worldwide Cases: Thursday 4-9-20 12:00 pm

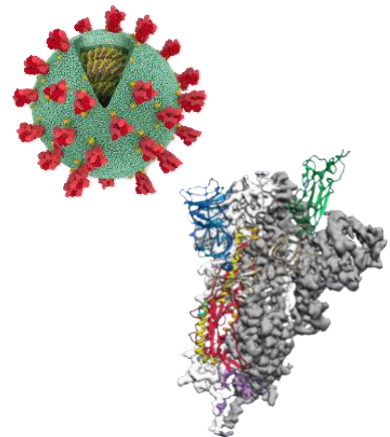
Location	Confirmed	Recovered	Deaths
 Worldwide	1,576,496	348,188	93,575
 United States	454,615	24,562	16,074
 Italy	143,626	28,470	18,279
 Spain	152,446	52,165	15,238
 China	81,865	77,370	3,335

9

9

What Is It About This Virus That Is Different from the Hundreds of Other Viruses Our Bodies Deal With Daily?

- Coronaviruses are a large family of viruses, including those that cause the common cold.
 - Coronaviruses are found throughout the world and account for up to 30 percent of upper respiratory tract infections in adults
 - Virus family is found in many different species of animals, including camels, cattle, and bats.
 - COVID-19 is single stranded positive-sense RNA
 - The virus rarely jumps species.
 - Several recent out breaks SARS-CoV 2002, MERS-CoV 2012
- Longer latency (incubation) period, up to two weeks
 - Shedding virus without symptoms
- COVID-19 is good at taking over host cells metabolic machinery
 - Binds human cells tighter than other SARS
 - Virus has 29 proteins encoded on its gene
 - Only 30,000 bases vs human genome with over 3 billion
- Encouraging news
 - Promising target protein found by NIH funded teams
 - Spike protein – good target for vaccine development
 - Spike protein allows entry into host cells



GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

10

10

Characteristics of and Important Lessons from the Corona Virus Disease 2019 (COVID-19) Outbreak in China

Summary of a Report of 72,314 Cases from the Chinese Center for Disease Control and Prevention

Age distribution (N = 44,672)

- ≥80 years: 3% (1408 cases)
- 30-79 years: 87% (38,680 cases)
- 20-29 years: 8% (3619 cases)
- 10-19 years: 1% (549 cases)
- <10 years: 1% (416 cases)

Spectrum of disease (N = 44,415)

- Mild: 81% (36,160 cases)
- Severe: 14% (6168 cases)
- Critical: 5% (2087 cases)

Case-fatality rate

- 2.3% (1023 of 44 672 confirmed cases)
- 14.8% in patients aged ≥80 years (208 of 1408)
- 8.0% in patients aged 70-79 years (312 of 3918)
- 49.0% in critical cases (1023 of 2087)

Health care personnel infected

- 3.8% (1716 of 44,672)
- 63% in Wuhan (1080 of 1716)
- 14.8% cases classified as severe or critical (247 of 1668)
- 5 deaths



Wu Z. JAMA. 2020;323(13):1239-1242

GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

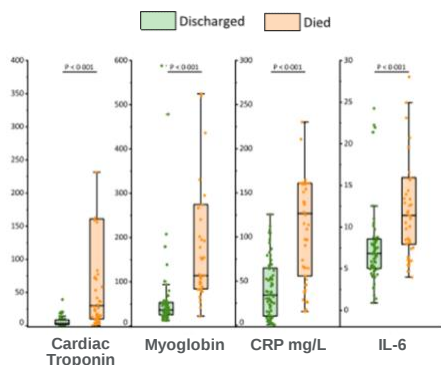
11

11

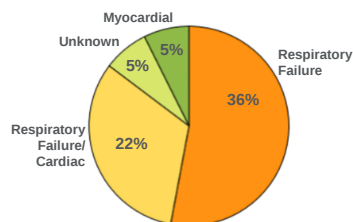
Clinical Predictors of Mortality Due to COVID-19 Based on an Analysis of Data of 150 Patients from Wuhan, China

Qiurong Ruan, Kun Yang, Wenxia Wang, Lingyu Jiang, and Jianxin Song JAMA 2020

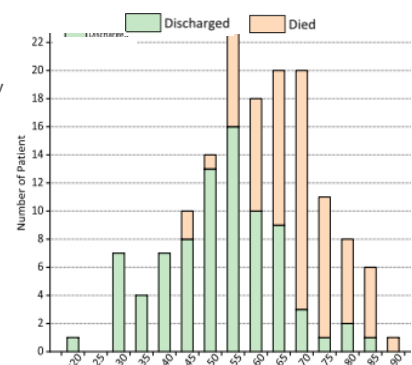
Intensive Care Medicine 2020



Cause of Death



Age (Years)



GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

12

12



The NEW ENGLAND
JOURNAL of MEDICINE

March 30, 2020

Covid-19 in Critically Ill Patients in the Seattle Region — Case Series

Pavan K. Bhatraju, M.D., Bijan J. Ghassemieh, M.D., Michelle Nichols, M.D., Richard Kim, M.D., Keith R. Jerome, M.D., Arun K. Nalla, Ph.D., Alexander L. Greninger, M.D., Sudhakar Pipavath, M.D., Mark M. Wurfel, M.D., Ph.D., Laura Evans, M.D., Patricia A. Kritek, M.D., T. Eoin West, M.D., M.P.H., Andrew Luks, M.D., Anthony Gerbino, M.D., Chris R. Dale, M.D., Jason D. Goldman, M.D., Shane O'Mahony, M.D., and Carmen Mikacenic, M.D.

Report of first 24 critically ill with Severe Acute Respiratory Syndrome COronaVirus-2 (SARS-CoV-2) from 9 hospitals in Seattle

- Mean age 64, 63%male
- Symptoms began 7 days before admission
 - Dry cough, SOB most common. 50% had fever. 58% DM
- Admitting diagnosis: hypoxemic respiratory failure 24/24
 - 18 needed mechanical ventilation (75%), 17/18 needed vasopressors for hypotension
- 12 patients (50%) died between day 1 and day 18
 - 4 patients had DNR on admission
- Of 12 surviving patients
 - At time of publication 5 discharged, 4 still in hospital out of ICU, 3 still on mechanical ventilation

GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

13

13

Characteristics of COVID-19 Patients Being Admitted: Global Observations

MOST PATIENTS:

Severe Inflammation-elevated CRP
Anorexia
Hypoxemia
Increase WOB
Fatigue

MANY PATIENTS:

NL or Low WBC
Decreased Lymphocytes
Elevated LFTs
AKI
GI Intolerance

GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

14

14

Basic Principles to Consider with COVID-19 in the ICU

- Infection control
- Duration of disease
- Support and resources required
 - Space
 - Staff
 - Supplies



GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

15

15

What Inferences Can We Draw About Critically Ill Patients with COVID-19?

Attribute	Potential Implications For Nutrition
Older patients	Pre-existing malnutrition, sarcopenia
More comorbidities	Pre-existing malnutrition, refeeding
Severe acute respiratory distress syndrome	Safety of feeding in prone positioning and ECMO
Circulatory failure	Safety and tolerance of feeding
Multiple organ failure	Role of EN in mitigating gut-derived inflammation
Cytokine release syndrome	Monitoring triglycerides in PN and propofol

Young BE, et al. *JAMA* published online March 3, 2020;
 Bhatraju PK, et al. *NEJM* published March 30, 2020;

Zhou F, et al. *Lancet* published online March 9 2020;
 Grasselli G, et al. *JAMA* published online April 6, 2020

GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

16

16

Guiding Principles RELEVANT to COVID-19

- “Cluster care” meaning all attempts are made to bundle care to limit exposure
- Adhere to Centers for Disease Control (CDC) and World Health Organization (WHO) recommendations to minimize exposures with COVID positive patients
- Preserve use of personal protective equipment (PPE)

GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

17

17

Recommendation #1

Estimated Needs:

- 15-20 kcal/kg actual body weight (ABW)/day (70-80% of needs)
- 1.2-2.0 gm protein/kg ABW/day

Rationale:

- The above guidelines should be followed for patients receiving either enteral nutrition (EN) or parenteral nutrition (PN). Critically ill patients with severe COVID-19 disease tend to be older with multiple co-morbidities.

1. Taylor B, McClave S, et al. *CCM* 2016;44:390; Arabi YM, et al. *NEJM* 2015;372:2398-2408

GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

18

18

Recommendation #1a

If refeeding syndrome risk is present^{1,2}

- Suspect if energy/calorie intake has been limited >7 days
- Restore circulatory volume
- Start at 25% of caloric goal with slow increase (4-7days)
- Frequent monitoring of serum phosphate, magnesium and potassium levels
- Monitor fluid balance

Rationale:

- If extremely limited or no energy/caloric intake for at least 5-7 days such patients are often at-risk of refeeding syndrome.

2. Doig G, et al. *Lancet Respir Med*. 2015;3:943-52; 1.da Silva JSV, et al. *NCP* 2020;35:178-195

GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

19

19

Recommendation #2

Initiate enteral nutrition (EN) early

- Within 24-36 h of ICU admission
- Within 12 h of intubation

Rationale:

- Provision of early EN in ICU pts has shown improved mortality and reduced infections when compared to delayed EN or withholding EN.^{1,2} Meta-analysis from 2000–2013 still demonstrated less infectious risk with EN when compared to PN use in ICU patients.¹ EN can be safely provided in patients with sepsis and shock in the absence of escalating vasopressors and symptoms of gastric ileus.³

1. Taylor B, McClave S, et al. *CCM* 2016;44:390; 2. Singer P, et al. *Clin Nutr* 2019;38;48; 3. Patel J, et al. *JPEN* Feb 2020.

GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

20

20

Recommendation #3

EN preferred over PN (parenteral nutrition)

- If patient can be successfully fed via gastric route through a nasogastric or orogastric tube placed at time of intubation
- If unable to feed into stomach have **low** threshold to convert to PN

Rationale:

- Placing nasojejunal tubes in COVID 19 patients in most cases *dramatically increases the risk of exposure to the health care providers.*
 - Limiting # of people and equipment in rooms, i.e. x-ray to confirm placement. Large bore nasogastric tubes do not normally require radiographic confirmation
 - If attempting to place nasojejunal tubes recommend N95 mask and PPE consistent with upper airway management protective equipment (see Surviving sepsis Guidelines-CCM)
- Considerations of “timing” on converting to PN
 - Distention, worsening hemodynamics, gastric contents noted in suctioning

GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

21

21

Recommendation #4

Start a standard EN isotonic (1.5 kcal/ml) high protein formula

- Start slowly 10-20 ml/h advancing to 80% of goal by the end of the first week with medical stability.¹
- Maintain trophic rate with questionable hemodynamics²
- If unable to progress by 5 to 7 days with EN consider supplemental PN
- If patient was malnourished pre-ICU admission and unsuccessful at EN start PN earlier

Rationale:

- Escalating vasopressors with a MAP <65 mmHg, rising lactate levels or when high pressure respiratory support is required (NIV, CPAP or PEEP). Many centers are not using NIPPV on COVID patients because of aerosolization risk. Placing NG or FT increases risk and breaks seal.
- If patient is at increase risk of ischemic bowel and potential for aspiration.¹

1. McClave S, et al. *JPEN*. 2016;40:159-211;2. Arabi YM, et al. *CCM* 2020;40:119-121.

GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

22

22

Recommendation #5

Do not check gastric residual volumes (GRVs)²

Rationale:

- GRVs are not reliable in ICU patients¹ and checking several times per day will significantly increase risk of virus exposure and transmission

1. Reignier J, et al. *JAMA*. 2013;309:249-56;

2. Taylor B, et al. *CCM* 2016;44:390-438.

GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

23

23

Recommendation #6

EN – Continuous *gastric* feeding preferred over post-pyloric

- With gastric feeding- minimal expertise if placement needed
- Allows use of existing NGT/OGT placed at time of intubation
- Continuous over bolus feeding – less diarrhea¹, optimizes BG control, less staff interaction needed

Rationale:

- There is less risk of tube occlusion with larger bore tubes. Continuous feeding requires less patient interactions and thus limits exposure.
- Newer studies confirm little metabolic difference in conserving muscle mass between bolus and continuous feeding in ICU patients

1. Singer P, et al. *Clin Nutr* 2019;38;48;

2. McNelly AS, et al. *Chest* 2020 (In press).

GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

24

24

Recommendation #7

Switch to PN when EN via gastric feeding is not an option^{1,2}

- Consider pro-motility agents and semi-elemental diet to improve tolerance
- If signs of ileus persists – change to PN¹
- If escalating vasopressor requirement – change to PN

Rationale:

- The threshold for switching to PN or supplementing with PN for the patient with COVID-19 may need to be lower, especially in sepsis or shock and EN is not safe.
- These patients will likely require a prolonged ICU stay and without adequate feeding will realize a large calorie and protein deficit. As the patient's condition improves, gastric EN should be reattempted.

NOTE: This is different than statements in Guidelines 2016

1. McClave S, et al. *JPEN*. 2016;40:159-211;

2. Singer P, et al. *Clin Nutr*. 2019;38;48.

What Do Guidelines Say About Exclusive PN?

Guideline	Year	Recommendation for Exclusive PN
SCCM/ASPEN	2016	(1) We suggest that, in the patient at <u>low nutrition risk</u> (e.g., NRS 2002 ≤ 3 or NUTRIC score ≤ 5), exclusive PN be withheld over the first 7 days following ICU admission if the patient cannot maintain volitional intake and if early EN is not feasible. (2) Based on expert consensus, in the patient determined to be at <u>high nutrition risk</u> (e.g., NRS 2002 ≥ 5 or NUTRIC score ≥ 5) or severely malnourished, when EN is not feasible, we suggest initiating exclusive PN as soon as possible following ICU admission.
ESPEN	2018	In patients who do not tolerate EN during the first week of critical illness, the safety and benefits of initiating PN should be weighted on a case-by-case basis

Safety of Exclusive PN Informed by RCTs

Trial of the Route of Early Nutritional Support in Critically Ill Adults

Sheila E. Harvey, Ph.D., Francesca Parrott, M.Sci., David A. Harrison, Ph.D., Danielle E. Bear, M.Res., Ella Segaran, M.Sc., Richard Beale, M.B., B.S., Geoff Bellingan, M.D., Richard Leonard, M.B., B.Chir., Michael G. Mythen, M.D., and Kathryn M. Rowan, Ph.D., for the CALORIES Trial Investigators*

Enteral versus parenteral early nutrition in ventilated adults with shock: a randomised, controlled, multicentre, open-label, parallel-group study (NUTRIREA-2)

Jean Reignier, Julie Boisramé-Helms, Laurent Brisard, Jean-Baptiste Lascarrou, Ali Ait Hssain, Nadia Anguel, Laurent Argaud, Karim Asehnoune, Pierre Asfar, Frédéric Bellec, Vlad Botoc, Anne Bretagnol, Hoang-Nam Bui, Emmanuel Canet, Daniel Da Silva, Michael Darmon, Vincent Das, Jérôme Devaquet, Michel Djibre, Frédérique Ganster, Maité Garrouste-Orgeas, Stéphane Gaudry, Olivier Gontier, Claude Guérin, Bertrand Guidet, Christophe Guitton, Jean-Etienne Herbrecht, Jean-Claude Lacherade, Philippe Letocart, Frédéric Martino, Virginie Maxime, Emmanuelle Mercier, Jean-Paul Mira, Saad Nseir, Gael Piton, Jean-Pierre Quenot, Jack Richecœur, Jean-Philippe Rigaud, René Robert, Nathalie Rolin, Carole Schwebel, Michel Sirodot, François Tinturier, Didier Thévenin, Bruno Giraudeau, Amélie Le Gouge, for the NUTRIREA-2 Trial Investigators and the Clinical Research in Intensive Care and Sepsis (CRICS) group

Harvey SE, et al. *NEJM* 2014;371:1673-1684;

Reignier J, et al. *The Lancet* 2018;391:133-143.

GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

27

27



Enteral versus parenteral early nutrition in ventilated adults with shock: a randomised, controlled, multicentre, open-label, parallel-group study (NUTRIREA-2)

The Lancet 2018;391:133-143

Jean Reignier, MD; Julie Boisramé-Helms, MD; Laurent Brisard, MD; Jean-Baptiste Lascarrou, MD; Ali Ait Hssain, MD; Nadia Anguel, MD; Prof Laurent Argaud, MD; Prof Karim Asehnoune, MD; Prof Pierre Asfar, MD; Frédéric Bellec, MD; Vlad Botoc, MD; Anne Bretagnol, MD; Hoang-Nam Bui, MD; Emmanuel Canet, MD; Daniel Da Silva, MD; Prof Michael Darmon, MD; Vincent Das, MD; Jérôme Devaquet, MD; Michel Djibre, MD; Frédérique Ganster, MD; Maité Garrouste-Orgeas, MD; Stéphane Gaudry, MD; Olivier Gontier, MD; Prof Claude Guérin, MD; Prof Bertrand Guidet, MD; Christophe Guitton, MD; Jean-Etienne Herbrecht, MD; Jean-Claude Lacherade, MD; Philippe Letocart, MD; Frédéric Martino, MD; Virginie Maxime, MD; Emmanuelle Mercier, MD; Prof Jean-Paul Mira, MD; Prof Saad Nseir, MD; Gael Piton, MD; Prof Jean-Pierre Quenot, MD; Jack Richecœur, MD; Jean-Philippe Rigaud, MD; Prof René Robert, MD; Nathalie Rolin, MD; Prof Carole Schwebel, MD; Michel Sirodot, MD; François Tinturier, MD; Didier Thévenin, MD; Bruno Giraudeau, PhD; Amélie Le Gouge, MSc for the NUTRIREA-2 Trial Investigators and the Clinical Research in Intensive Care and Sepsis (CRICS) group.

- PRCT EN vs PN in ventilated patients with shock (n=2410)
 - Mixed etiology of shock: 20% cardiac, 60% septic, 20% other
 - Pts met strict criteria for shock, feeding 10kcal/kg/d w/in 15 h of intubation
- Data collected:
 - Similar calories to both groups
 - Protein gm/kg/d 0.7 EN vs 0.8 PN
- No difference in major outcomes
 - Enteral group:
 - Ischemia 19 EN v 5 PN (p<0.007)
 - EN had increase in vomiting, diarrhea, colonic pseudo-obstruction (all significant)

GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

28

28

Recommendation #8

Protein dose in renal failure needing dialysis

- Provide 2.0-2.5 g/kg ABW/day in critically ill with renal failure undergoing renal replacement therapy(RRT)

Rationale:

- Patients with renal failure requiring dialysis lose as much as 10 grams amino acids in the dialysate. Observational data has demonstrated up to 2.5 g/kg/day protein is tolerated and associated with conversion to positive nitrogen balance.¹⁻²
- Micronutrients in critically ill with severe AKI
 - >30% of CRRT and non-CRRT had plasma level lower than normal³

1. McClave S, et al. *JPEN*. 2016;40:159-211; 2. Patel JJ et al. *Nutr Clin Pract*. 2017 Apr;32(1_suppl):101S-111S. Ostermann M et al *Scientific Reports* 2020;10:1505
GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

29

29

QUESTIONS FOR DISCUSSION: Appropriate PN Choices

1. Are there any indications for peripheral PN?
2. When should supplemental PN be used?
3. Are there any indications to start with PN?
4. When is PN contraindicated?

GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

30

30

Recommendation #9

Limit pure soybean lipid emulsions the first week^{1,2}

- Use alternative lipids or limit/withhold soybean lipids the first week
 - Alternate lipid emulsions available in USA:
 - Olive oil : Soy oil (80% Olive Oil : 20% soy)
 - Soy, MCT, Olive, Fish oil (30% soy: 30% MCT: 25% Olive oil: 15% Fish Oil)
- Monitor triglyceride levels early in the PN course
 - Early anecdotal reports are seeing rapid elevations in serum lipids with emulsions in those who have rapid progression of disease (from NYC, New Orleans and Milan, Italy)
 - Remember: Propofol in USA is in 10% soy solution

1. McClave S, et al. *JPEN*. 2016;40:159-211; 2. GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

Singer P, et al. *Clin Nutr*. 2019;38;48.

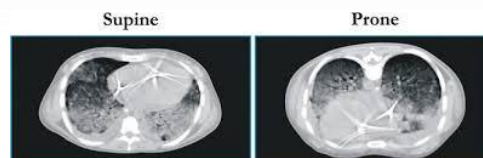
31

31

Recommendation #10

Prone Position – Use EN over PN

- Isotonic high protein formula starting at 10-20 ml/hr
- Keep HOB elevated (reverse Trendelenburg) to at least 10 to 25 degrees with gastric feeding



Rationale:

- No increased risk of GI or pulmonary complications in prone position has been noted.^{1,3}
- Increasing HOB will decrease the risk of aspiration of gastric contents, facial edema, and intra-abdominal hypertension.²

1. Saez de la Fuente I, et al. *JPEN* 2016 Feb;40(2):250-255; 2. Kallett RH, et al. *Resp Care* 2015;60:1660-1687; 3. Reigler J, et al. *Clin Nutrition* 2010;29:210-216. GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

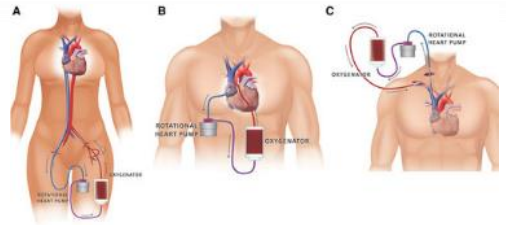
32

32

Recommendation #11

ECMO – Attempt EN via gastric feeding

- Start early, low dose EN
- Slow advancement to goal over the first week
- If septic, increasing vasopressor requirements – hold and consider PN



Rationale:

- In the largest observational study of EN during veno-arterial (VA) ECMO, early EN, as compared to delayed EN, was associated with improvement in 28-day mortality and zero incidence of bowel ischemia.¹
- Increased EN calories/protein delivered were associated with decreased risk of 90-day mortality.²
- Anecdotal discussions with ECMO centers find very poor outcome with SARS-CoV-2

1. Ohbe H, et al. *Intensive Care Med.* 2018;44:1258-1265;

2. Park J, et al. *Clin Nutr.* 2019 Nov 30 ahead of print.

Recommendation #12

Feeding patients in circulatory shock

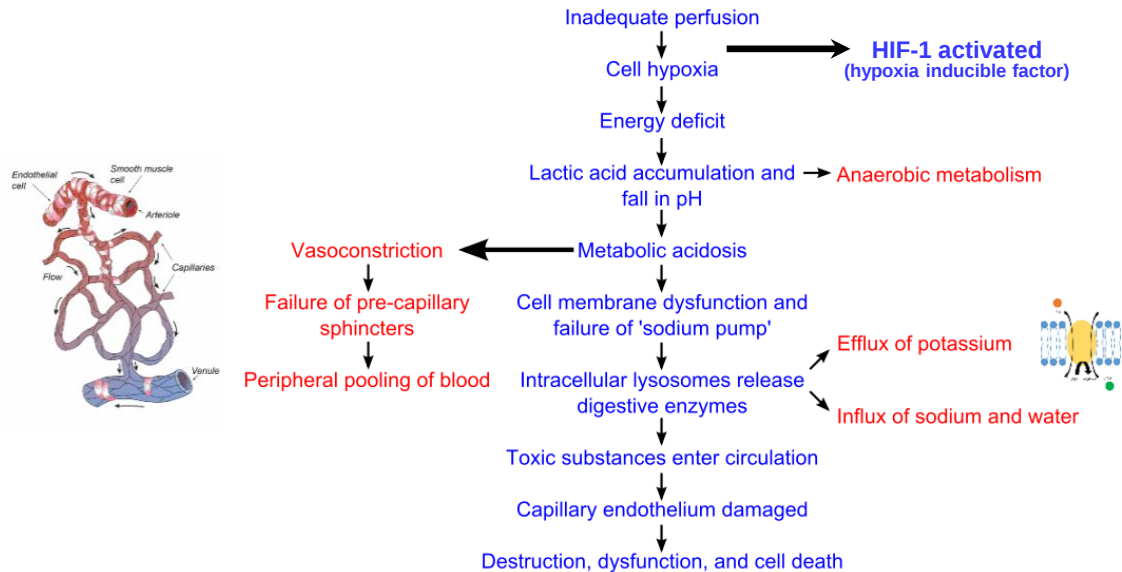
- Manage as any other shock patient
- If EN unsuccessful (e.g., EN intolerance), transition to PN early
 - Caution with both EN or PN in hemodynamically unstable pts

Rationale:

- No reason to alter standard guideline recommendation for therapy with the exception of minimizing exposure of health care workers.¹⁻³
- Overall, risk for NOBN is rare. 0.3% across observational and RCT level data.⁴

1. McClave S, et al. *JPEN.* 2016;40:159-211; 2. Singer P, et al. *Clin Nutr.* 2019;38;48; 3. Puthucherry ZA. *Thorax* 2018;73:926-935; 4. Patel JJ, et al. *JPEN* 2020.

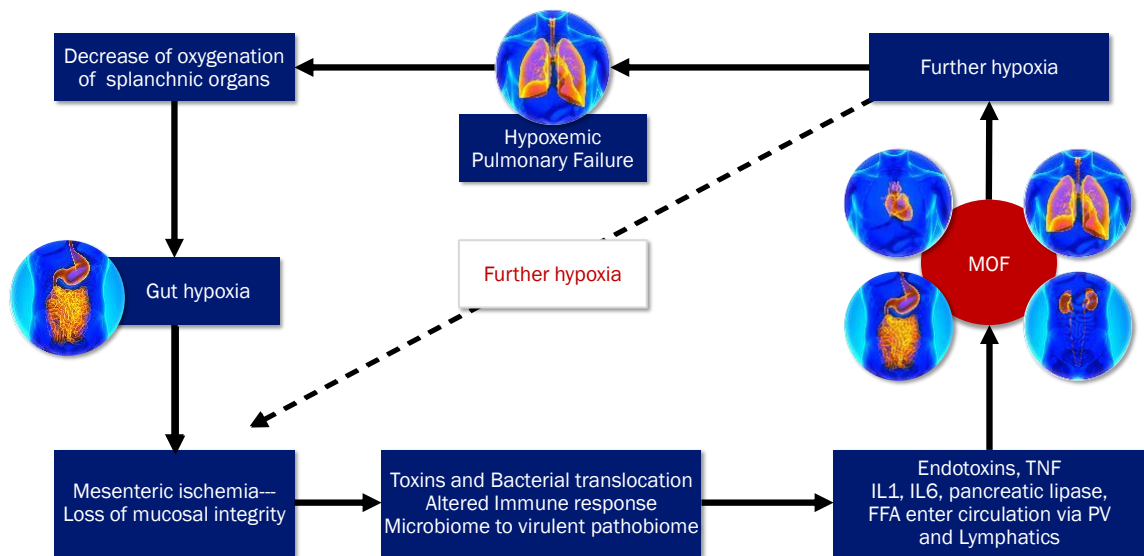
Shock: Events at the Cellular Level; O₂ Demand > O₂ Supply



35

35

Sequence of Events at the Organ Level



36

36

Disclaimer Statements

- Being fully transparent when delivering medical information is always the optimal plan.
- The worst thing we can do as health care professionals is give false hope.
- If no studies are available, clinicians need to provide scientific information which is rooted in rationale hypothesis
- In situations like the SARS-CoV-2 the key is “knowing what we know and more importantly is knowing what we don’t know”
- Care for our patients cannot be driven by fear and misinformation which often supersedes the scientific evidence.

GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

37

37

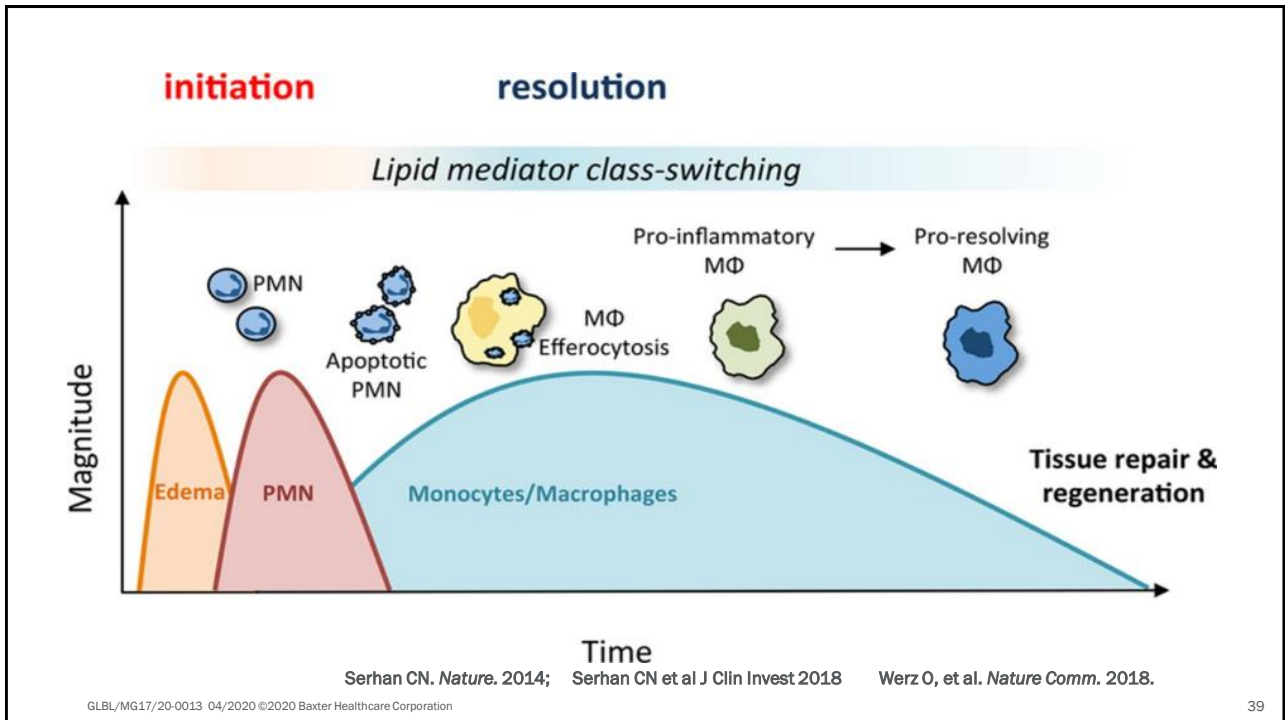
Potential Nutritional Approaches: Theory, Extrapolations, Anecdotes – NO COVID Specific Data Yet

- Inflammation control
- Fish oil
 - SPM and viral clearance
- Probiotics
 - Data from other Coronavirus family studies
- Vitamin supplements
- Mineral supplements

GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

38

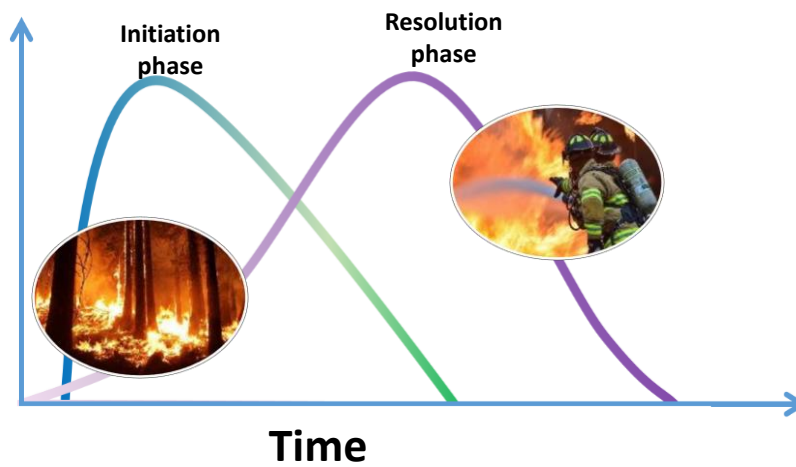
38



39

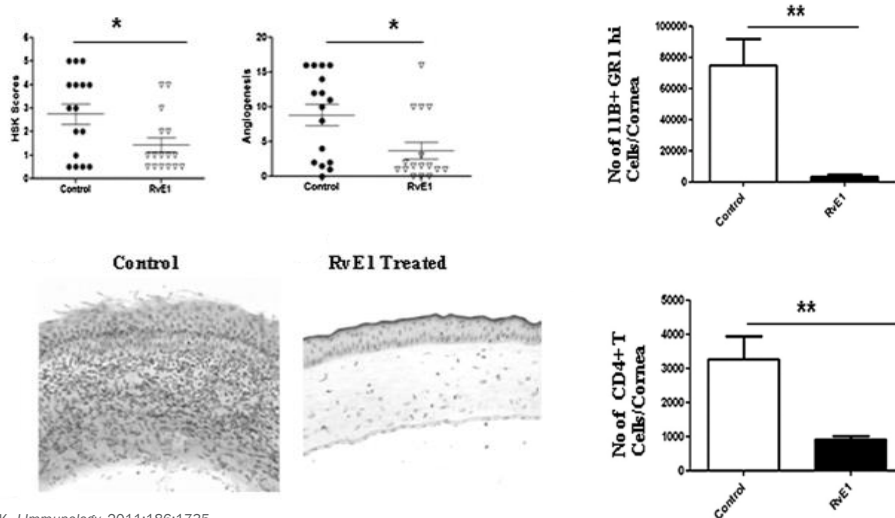
39

Inflammation has two phases: Initiation and Resolution

Modified from Serhan CN *JCI* 2018

40

Controlling Herpes Virus Simplex Virus-Induced Ocular Inflammatory Lesions with the Lipid-Derived Mediator Resolvin E1

Rajasagi NK. *J Immunology*. 2011;186:1735.

GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

41

41

The NEW ENGLAND
JOURNAL of MEDICINEClinical Implications
of Basic Research

Influenza — Time to Target the Host?

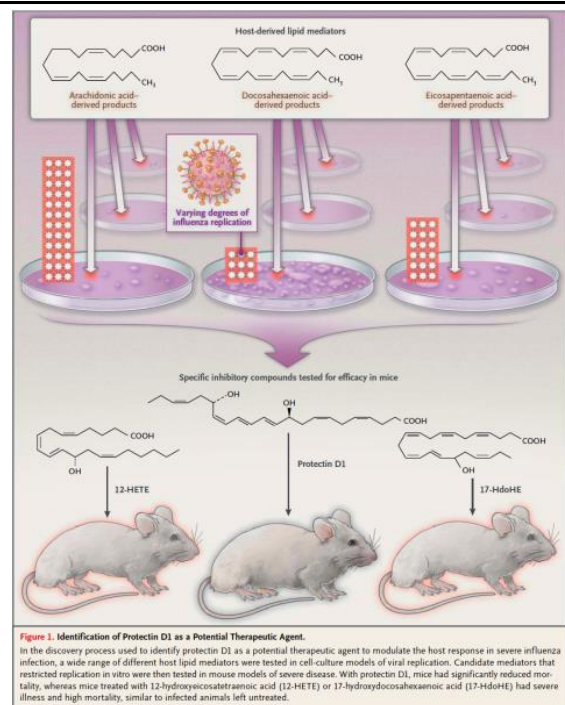
J. Kenneth Baillie, M.D., Ph.D., and Paul Digard, Ph.D.

Several SPMs Lower Mortality in Viral Illness

Protectin D1 - Inhibits Viral Replication

Baillie JK, et al. *NEJM* 2013.

GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation



42

42

Infection regulates pro-resolving mediators that lower antibiotic requirements

Nature 2012

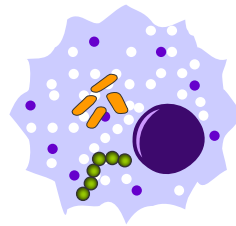
Nan Chiang¹, Gabrielle Fredman¹, Fredrik Bäckhed², Sungwhan F. Oh¹, Thad Vickery¹, Birgitta A. Schmidt¹ & Charles N. Serhan¹

Antibiotics

SPM's
Resolvins



Decrease antibiotic requirements



M₁



M₂



Host response to bacteria

Increase in:
Phagocytosis
Bacterial Containment
Bacterial Killing
Clearance of Bacteria

(*E. coli*, *S. aureus* skin)

SPM's accelerate resolution of infections, reduce inflammation
Treating the host with SPM **lowers** the required antibiotic doses

43

Critical Care
Medicine®
2017

Human Sepsis Eicosanoid and Pro-resolving Lipid Mediator Temporal Profiles: Correlations With Survival and Clinical Outcomes

Jesmond Dalli, PhD; Romain A. Colas, PhD; Carolina Quintana, MD; Diana Barragan-Bradford, MD; Shelley Hurwitz, PhD; Bruce D. Levy, MD; Augustine M. Choi, MD; Charles N. Serhan, PhD; and Rebecca M. Baron, MD

- Associated outcome with resolution mediators
- N=22 septic patients
 - Followed pro-inflammatory and pro-resolution mediators
 - Lipid mediator profiling - >30 bioactive mediators followed
 - AA, EPA, DHA metabolome
 - Serum lipid profiles w/in 48h admission then at 3 and 7 days
- Conclusion:
 - Resolution Lipid mediators associated with better survival and decrease **ARDS**

Caution: Association does not indicate causation!

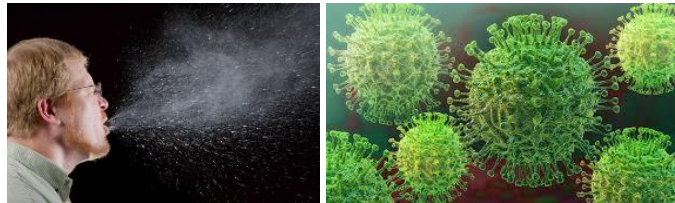
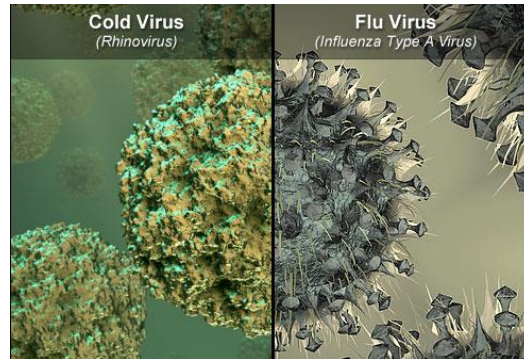
44

Probiotics and Prevention of Upper Respiratory Viral Infections



Rhinovirus is member of the Coronavirus family

GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation



45

45

Probiotics for Preventing Acute Upper Respiratory Tract Infections (Review)



- To assess the effectiveness and safety of probiotics (any specified strain or dose), compared with placebo, in the prevention of acute URTIs in people of all ages
- 12 Studies included in the analysis (71 studies available)
 - 3720 Participants (Children + Adults)
 - Placebo versus Probiotics
- Probiotics were better than placebo in number of acute URI
 - OR 0.53 95% CI 0.36-0.76 $p < 0.001$
- Probiotics were better than placebo in reducing the mean duration of URI
 - OR -1.89 days 95% CI -2.03 to -1.75 $p < 0.001$

Hao Q; Dong BR, et al. *Cochrane* Feb 3, 2015.

GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

46

46

Vitamin Supplementation

Animal data or theoretical – **NO COVID-19 specific data**

Vitamin B₁,B₂,B₃ (nicotinamide),B₆

- Multiple reports - results all over the map¹
 - Suspected benefits from immune function

Vitamin D

- If deficient helpful in viral infections (animal models)
- Recent ICU trials in Vit D deficient patients: **NO BENEFIT**^{2,3}

1) Zhang L et al J Med Virology 2020 2) NHLBI PETAL Clinical Trials Network: NEJM 2019 3) Amrein K et al JAMA 2014

GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

47

47

Vitamins (**NO COVID-19 specific data**)

Vitamin A

- Animal model (chickens) on low vitamin A diets show increased risk of coronavirus¹

Vitamin C

- SARS Coronavirus (increased resistance to avian coronavirus in broiler chickens)
J Antimicrobial Chemotherapy 2003²
- Vit C reported to decrease mechanical ventilation³
- Vit C study in sepsis and ARDS. 96h infusion vit C vs placebo: **NO Benefit**⁴

Vitamin E

- Data in animals (murine,bovine)
- Coxsackie virus B₃ a RNA virus

1. Zhang L, et al. J Med Virology, 2020.; 2. Hemila H, et al. J Antimicrob Chemother. 2003; 3. Hemila H, et al. J Int Care Med. 2020. 4. Fowler AA et al JAMA 2020.

GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

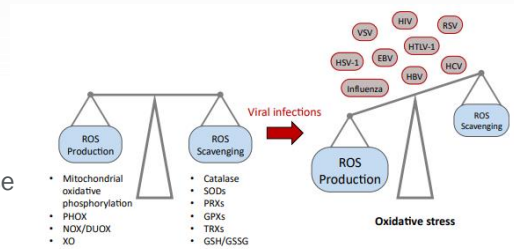
48

48

Trace Minerals

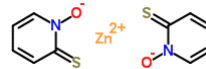
Selenium

- Oxidative stress associated with viral infections
 - Se associated with many anti-oxidant enzymes (selenoproteins) GPX, SOD, Thioredoxin reductase
 - Suspected to alter viral replication, protect cell from viral induced oxidative stress
- Speculation; Lots of questions regarding dose, timing, +/- deficiency



Zinc

- Key to development and function of immune system both innate and humoral
- Impairs viral replication (in-vitro)
 - Works in a variety of RNA viruses
 - Shown in SARS-CoV with pyrithione inhibits replication
- Clearly beneficial in viral infections **if deficient**
 - Supplements given to zinc deficient children with measles decreases mortality
- Zn acetate lozenges ?



Fani M, et al. *Biol Trace Min Res.* 2020;

Guillin OM, et al. *Nutrients* 2019;

Zhang L, et al. *J Med Virology* 2020.

GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

49

49

Bottom Line

1. Insufficient data to recommend any additional specific supplement over standard requirements **UNLESS** vitamin or mineral deficiency is suspected upon admission
2. No data for “antioxidant” cocktails, megadoses of supplements, etc.



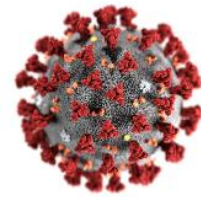
GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

50

50

Conclusions

- The delivery of nutritional therapy to the patient with SARS-CoV-2 should follow the basic principles of critical care nutrition as recommended by European and North American societal guidelines.
- Early use of continuous gastric feeds, not checking gastric residual volume (GRVs), early use of PN in patients intolerant to gastric feeds to avoid endoscopic/fluoroscopic placed post-pyloric tube are strategies which:
 1. Promote clustered care
 2. Reduce the frequency with which healthcare providers interact with COVID positive patients
 3. Minimize contamination of additional equipment while promoting optimal nutrition therapy for these patients.



GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

51

51

Case Resolution

- 53-year-old woman with breast cancer undergoing chemotherapy presents with 2 days of progressively worsening shortness of breath found to have COVID-19 pneumonia with acute respiratory failure → prone.
- Does the patient have pre-existing malnutrition or risk of refeeding?
- Taking guiding principles into consideration...
 - Start trophic dose EN but preserve protein dose at 1.2 g/kg/day
 - Feed into the stomach
 - Monitor for enteral feeding intolerance and refeeding
 - If intolerant despite prokinetic → low threshold to start PN
 - Slow ramp-up over the first week of critical illness
 - Special considerations (e.g., dialysis, triglyceride levels)

GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

52

52

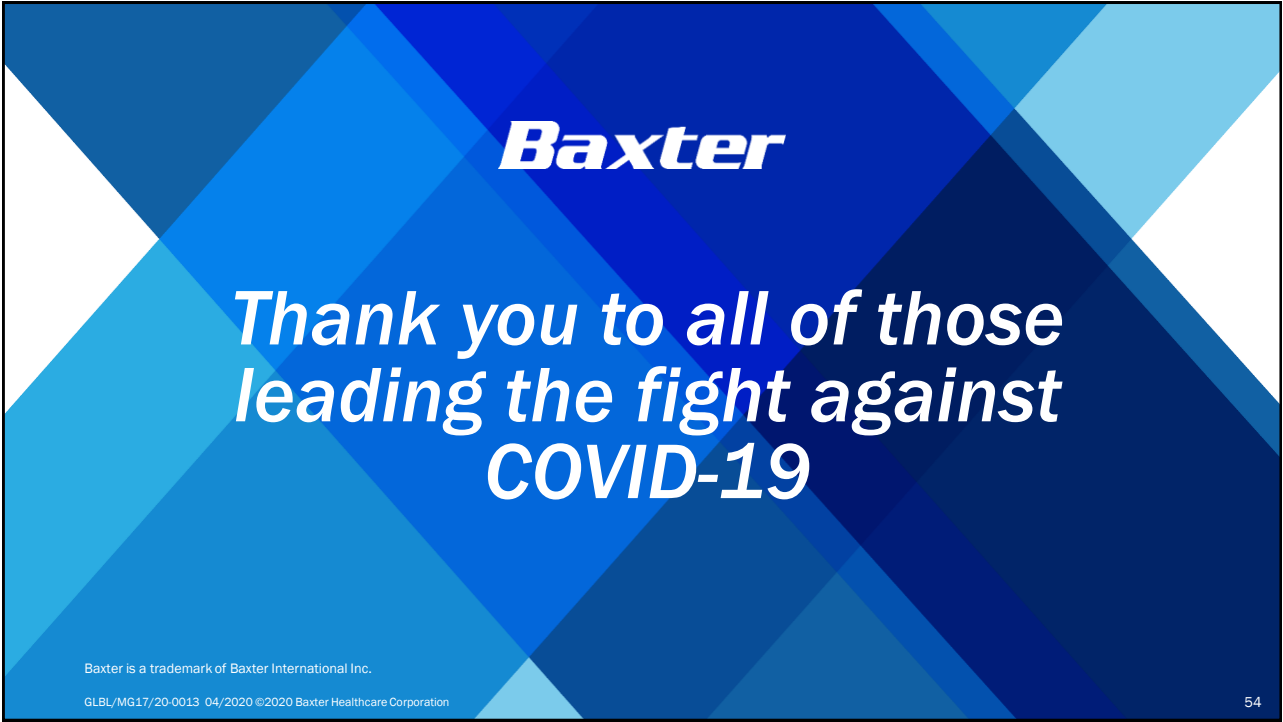


QUESTIONS?

GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

53

53



Baxter

***Thank you to all of those
leading the fight against
COVID-19***

Baxter is a trademark of Baxter International Inc.

GLBL/MG17/20-0013 04/2020 ©2020 Baxter Healthcare Corporation

54

54

PLEASE REGISTER TODAY:

https://www.baxterglobal.com/nutrition_hero_series

**PART 2: RESTRUCTURING NUTRITION SUPPORT SERVICES
TO FACILITATE CARE FOR COVID-19 PATIENTS**

Thursday, April 16, 2020 at 10:00 PST/13:00 EST/18:00 BST/19:00 CEST

OBJECTIVES

- To discuss the practical challenges of delivering nutrition support in the COVID-19 pandemic
- To understand the nutritional requirements and contribution of IV medications and renal replacement therapy
- To discuss the role of supplemental parenteral nutrition when enteral is not possible

FEATURING SPEAKER:

Ella Terblanche, RD

Critical Care Dietitian at St Georges Hospital
University Hospitals NHS Foundation Trust, London
Chair of BDA Critical Care Specialist Group London,
UK

**PART 3: EARLY NUTRITIONAL SUPPLEMENTATION IN NON-ICU
HOSPITALIZED COVID-19 PATIENTS**

Thursday, April 23, 2020 at 08:00 PST/11:00 EST/16:00 BST/17:00 CEST

OBJECTIVES

- Address the nutritional requirements of COVID-19 patients
- Discuss the role of delivery and monitoring of nutrition support in the COVID-19 ICU patient
- Review of best practices experienced in treating COVID-19 patients

FEATURING SPEAKERS:

Alessandro Laviano, MD

Associate Professor of Internal Medicine Department
of Clinical Medicine Sapienza University
Rome, Italy



Riccardo Caccialanza, MD

Director of UOC Dietetics and
Clinical Nutrition Fondazione IRCCS
Policlinico San Matteo Pavia, Italy