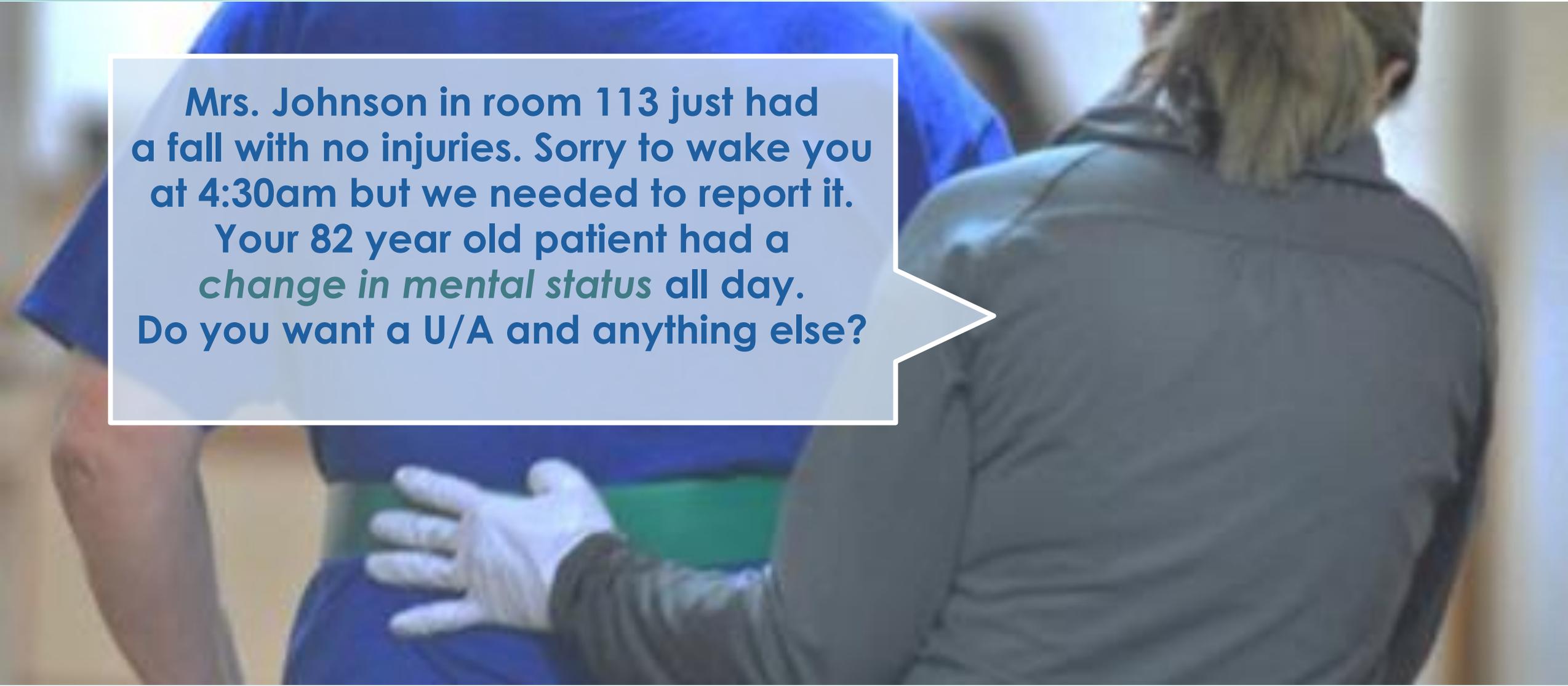




Change in *Mental Status* **Hepatic Encephalopathy (HE)**

Treatment & IDT Process



Mrs. Johnson in room 113 just had a fall with no injuries. Sorry to wake you at 4:30am but we needed to report it. Your 82 year old patient had a *change in mental status* all day. Do you want a U/A and anything else?

Causes of Altered Mental Status in Adults



- Fever or infection
- Poisoning or overdose
- Blood sugar/endocrine problems
- Head injury
- Inadequate oxygenation or ventilation
- Conditions leading to decreased blood flow or oxygen to the brain
- Cardiac or diabetic emergencies
- Shock
- Stroke
- Behavioral Illness
- Seizures

Chronic Liver Disease (CLD) affects over 5.5 million patients in the USA¹, of who more than 600,000 have cirrhosis.²



Hepatic Encephalopathy (HE)

HE is most commonly a syndrome observed in patients with **cirrhosis**.

Subtle signs of it are observed in nearly 70% of these patients. Given its extremely high prevalence, HE should be a condition that LTC providers are readily able to diagnosis and treat.³

However, due to its episodic nature, slow progression and symptoms which overlap those of other diseases, clinicians often miss this diagnosis.

Top cause of 30-day hospital readmissions⁴

LTC providers need to be both knowledgeable and vigilant regarding its prevalence, pathophysiology, diagnosis and treatment.

3. Elwir 2017

4. Tapper et al 2016

Diagnosis and Factors



Diagnosis of hepatic encephalopathy

- Elevated free arterial serum ammonia level. **BUT NOT ALWAYS...**
- EEG: shows non-specific high amplitude low frequency waves and tri-phasic waves.
- CT scan and MRI of the brain may be necessary in ruling out intracranial lesions. In acute encephalopathy brain edema may be seen.

Common precipitating factors:

Dehydration, ascites, changes in diet and alcohol use

Others include; Renal failure, GIT bleeding, infection, constipation, increased dietary protein intake. Opiates, benzodiazepines, anti-depressants and anti-psychotics may also worsen encephalopathy. Hypokalemia and alkalosis (due to vomiting or excessive use of K-losing diuretics) increase solubility of NH_3 thus increase its passage across the blood brain barrier.

Differential diagnosis of encephalopathy (other causes of coma):

Intracranial lesions (intracranial he, tumor, abscess), infections (meningitis, encephalitis), metabolic encephalopathy (hypoglycemia, uremia, electrolyte imbalance), alcoholic encephalopathy, post-seizure encephalopathy.



Treatments

Analysis

Life

Treat

Pharmacy

Disease

Symptom

Care

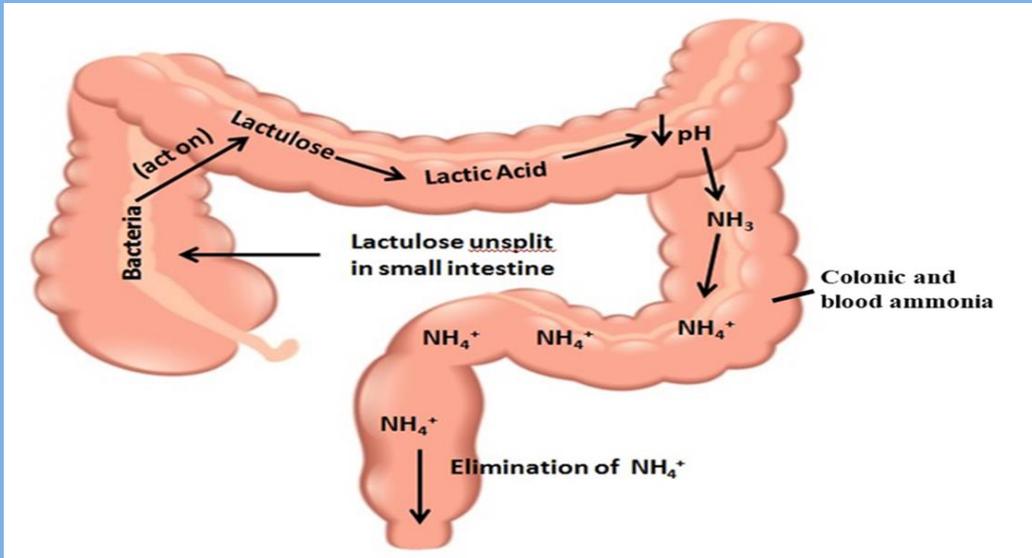
Anat

Pain

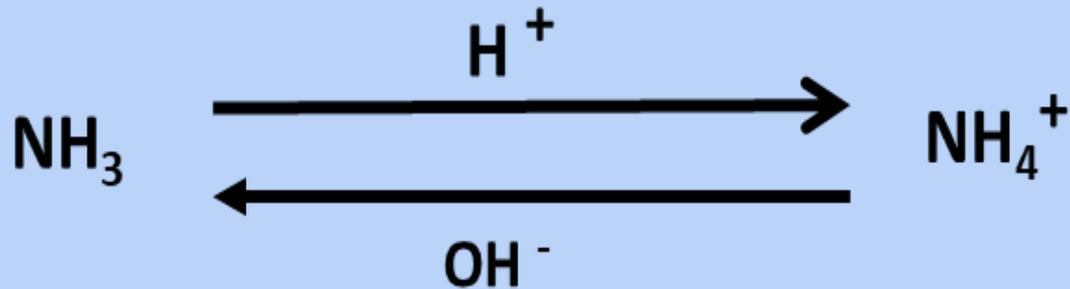
Health

X-Ray

Mechanism of Action of Lactulose for OHE



- A non-absorbable disaccharide
- It produces osmosis of water — Diarrhea^{5,6}
- It reduces pH of colonic content & thereby converts freely diffusible NH₄ into ammonium ions (NH₄⁺), which cannot be absorbed and are therefore excreted^{5,6}
- Lactulose reaches the colon unsplit. It is then converted by bacteria to organic acids and an acid stool results. This may also affect the ionization of ammonia in the colon and reduce its absorption.^{5,6}
- The current AASLD/EASL guideline (2014) recommends rifaximin as an add-on to lactulose for prevention of recurrent episodes of HE after the second episode.⁷



Rifaximin

RIFAXIMIN is a minimally absorbed oral antimicrobial agent that is concentrated in the gastrointestinal tract, has broad-spectrum activity against gram+ and gram- aerobic and anaerobic enteric bacteria, and has a low risk of inducing bacterial resistance.⁸

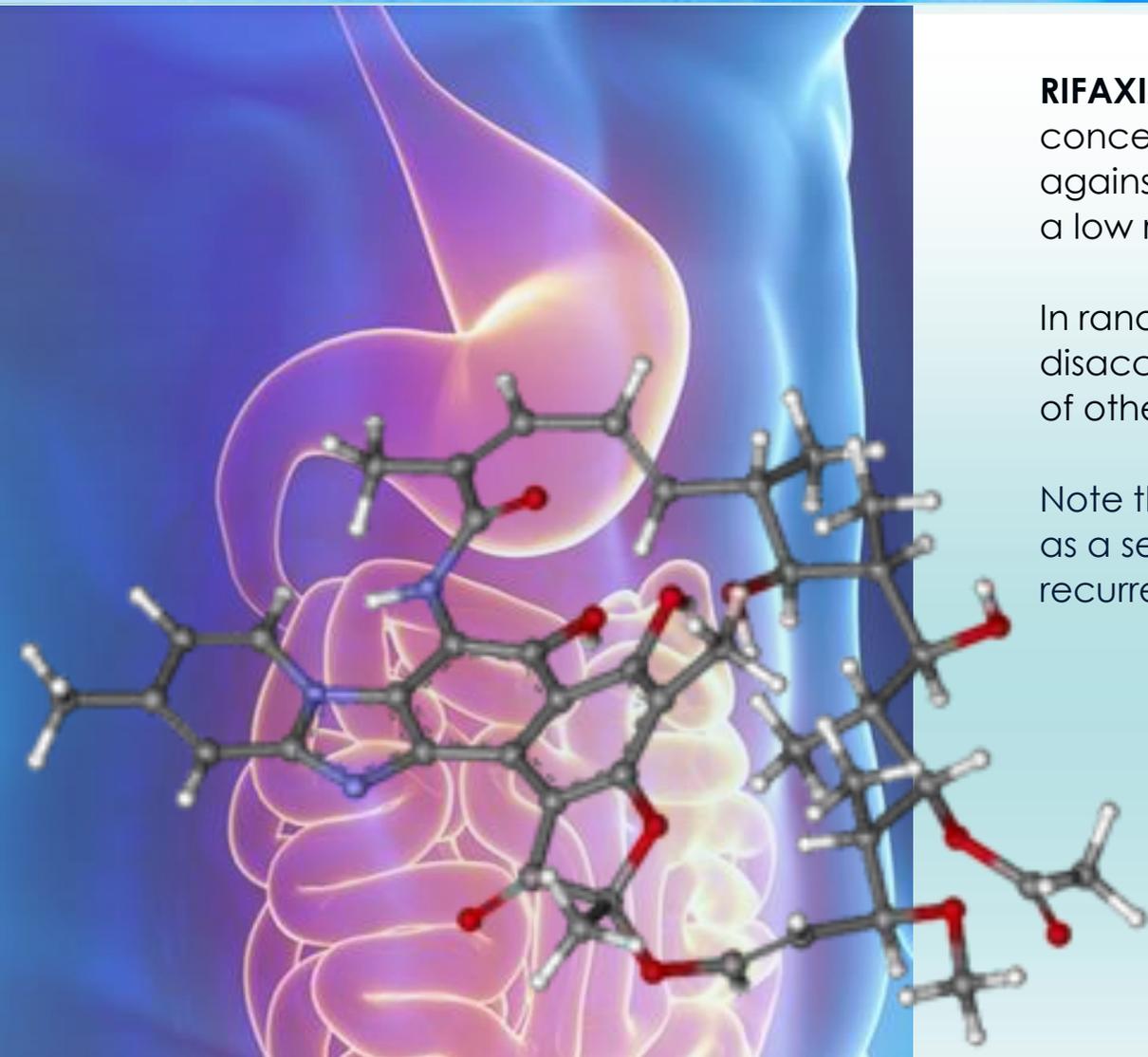
In randomized studies, **Rifaximin** was more effective than non-absorbable disaccharides and had efficacy that was equivalent to or greater than that of other antibiotics used in the treatment of acute HE.⁹

Note that rifaximin is not a treatment for OHE. It should rather be positioned as a secondary prophylaxis strategy for use with lactulose to prevent recurrence of HE and related hospitalizations.¹⁰

⁸ Debbie 2008

⁹ Paik 2005

¹⁰ Bass 2010



Usual Adult Dose for Hepatic Encephalopathy



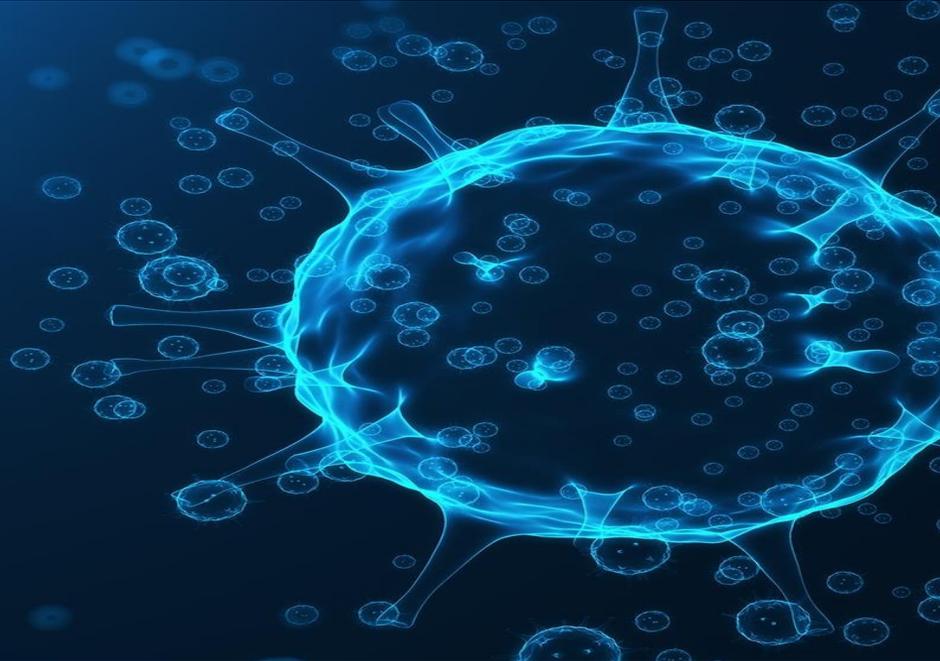
Lactulose **30 mL** orally 3 times a day or **300 mL** in **700 mL** water or normal saline as an enema retained for 30-60 minutes every 4 to 6 hours.

Maintenance dose:
30-45 mL orally 3x a day.



Rifaximin 550 mg orally twice a day

Probiotics, Nutrition and Exercise



Probiotics have been found to be effective for HE compared to placebo but not more so than lactulose.¹¹

Nutrition: Cirrhotic patients commonly have malnutrition, muscle wasting (sarcopenia) and reduced survival as a consequence. Research dating back decades has debunked ideas of reducing protein intake as a means of lowering nitrogen load and ammonia burden (see reference below). Indeed, the recommendations now encourage small frequent protein meals throughout the day with a night-time snack of complex carbohydrates. This is often optimized in conjunction with a nutritional support team.

Consensus recommendations of the International Society for Hepatic Encephalopathy and Nitrogen Metabolism include optimal daily caloric intake of 35-40 kcal/kg and protein intake of 1.2-1.5 g/kg ideal body weight and provision of night time supplementation.¹² Zinc is occasionally helpful where there is deficiency or confirmed losses.

Exercise: As with normal patients, exercise in patients with liver disease can improve functional capacity, lean body mass and risk of falls.^{13,14} Exercise has the potential as an adjunct to improve nutrition, to reduce the frailty of patients that predisposes them to higher ammonia levels and greater risk of falls. However, more studies are needed to clearly identify the parameters for which it can be safe and effective. One can generally expect long-term care residents with multiple co-morbidities to benefit from exercise, with significant improvements in depression and pain relief as a consequence of endorphin release.¹⁵



¹¹ Saab 2016
¹² Amodio 2013

¹³ El-Khoury 2013
¹⁴ Roman 2016
¹⁵ Balchin 2016

Branched Chain Amino Acids (BCAA) & L-Ornithine-L-Aspartate (LOLA)



(BCAA)

- A preparation of amino acids (valine, leucine, and isoleucine) normally given orally or by nasogastric tube, has been postulated to alter the balance of amino acids in the brain as well as to provide energy supplementation. A recent Cochrane review of 16 randomized clinical trials found high quality evidence of clinical benefit but no effect on mortality, quality of life, or nutrition parameters.¹⁶ Thus, for some patients who are intolerant to the recommended protein intake, BCAA supplements may be considered as a means of meeting this nutritional need without risking detrimental effects on the mental state.¹⁷

(LOLA)

- A combination containing the amino acids ornithine and aspartic acid given by intravenous infusion. A meta-analysis of 20 randomized controlled trials showed LOLA to be as effective as non-absorbable disaccharides, with a trend towards superiority, with few adverse effects.¹⁸



Liver Transplantation and Embolization of Portosystemic Shunts



Patients resistant to rifaximin and lactulose may be considered for embolization of portosystemic shunts.

Evidence from retrospective studies suggests that the procedure decreases hospital admissions and improves but adverse effects include gastro-esophageal varices, worsening ascites, and renal dysfunction due to contrast-induced nephropathy.¹⁹

Liver Transplantation: Overt HE improves significantly and reverses after liver transplantation, although for some of these patients signs of cognitive impairment persist.^{20,21} Moreover, the prospect of patients with HE receiving a liver transplant in a timely manner may be hindered by the MELD score (Model for End-Stage Liver Disease), which does not correlate well with this disease entity.²²

¹⁹ Laleman 2013

²⁰ Campagna 2014

²¹ Garcia-Martinez 2011

²² Yoo 2003

Ongoing Care for HE Patients

Symptom / need	Assessment	Intervention
Systolic hypertension	Blood pressure, signs of headaches	Monitor vital signs QD for patients with liver failure, potential for HE
Increased muscle tonicity (partial or generalized)	Assess increased muscle tone	Monitor for changes in muscle tonicity, difficulty in moving, turning or repositioning.
Myoclonus (decerebrate posturing)	Assess muscle tightness, extremity positioning changes; fall risk; balance scores	Physical Therapy Restorative nursing plan
Dysconjugate eye movements	Monitor eye movements tonicity	Eye tracking charting: convergence, divergence
Fluid and electrolyte imbalance; clotting disorder	Changes in symptoms	Laboratory draws for electrolytes, bilirubin, prothrombin and pre-albumin; family and patient education; dietary consultation; maintain schedule
Mental status changes	Track behaviors, consciousness, aggression, uncooperative behavior, ability to attend to directions and details, and West Haven Criteria	Plan interventions which reduce distress and allow person-centered EBP care; utilize facility behavior tracking sheets; plan activity interventions; incorporate family into 1:1 intervention as needed.
Mood changes	Mood scores, Depression evaluation, BIMS, Anxiety score, MMSE, Delirium	Person-centered daily care which accommodates needs of patients and family visits; testing and interventions supportive of EBP; meds per physician / NP orders
ADL changes	Monitor ADL scores; task segmentation; SOB during care; mobility deficits	Care needs to be individualized
Eating assistance with caloric management	Weights; Assistance with eating	Small, frequent protein meals; monitor changes in food and fluid intake, as needed; labs as above; weights
Family-patient updates by IDC team	Monitor for education deficits; Care questions	Team meetings; Rounds with SBAR or IPASS; Regular charting of involvement and updates during condition changes

Palliative Care



The very effectiveness of treatments for HE and other aspects of chronic liver disease has enabled elderly patients to survive longer with increasingly intensive care, often with substantial discomfort and suffering of the patients and considerable burden on families, caregivers and the healthcare system.²³ Despite this, data from the UK reports that referral to palliative care is low and over 2/3 of patients with liver disease die in the hospital after multiple inpatient hospital stays. The benefits of palliative care are numerous including improved quality of life and prolonged survival.^{24,25}

²³ The Lancet 2018

²⁴ Temel 2010

²⁵ Bakitas 2009

Roles & Responsibilities

LTC Interdisciplinary Team (IDT)

Analysis

Life

Treat

Pharmacy

Disease

Symptom

Care

Anat

Pain

Health

X-Ray

Director of Nursing / Nursing Staff



Dx

- Monitor signs and symptoms of cognitive changes, liver flap, HE, MDS assessment for changes, interim assessment, clinically complex resident with exacerbation of symptoms care planning
- Monitor disease trajectory

Tx

- Medication administration with comfort and polypharmacy
- Compliance of medication consumption
- Community health transitions of care support and follow-up
- Patient and Family Education on medications and compliance
- Provide palliative, progressive disease care and education, and end-of-life (EOL) Hospice Care

Attending Physician / APN / PA



Dx

- Clinical History and physical
- Order psychometric tests (PHES: "gold standard")

Tx

- Prescribe Lactulose and Rifaximin
- Coordinate with other specialists on diagnostics and treatment

Consultant Pharmacist



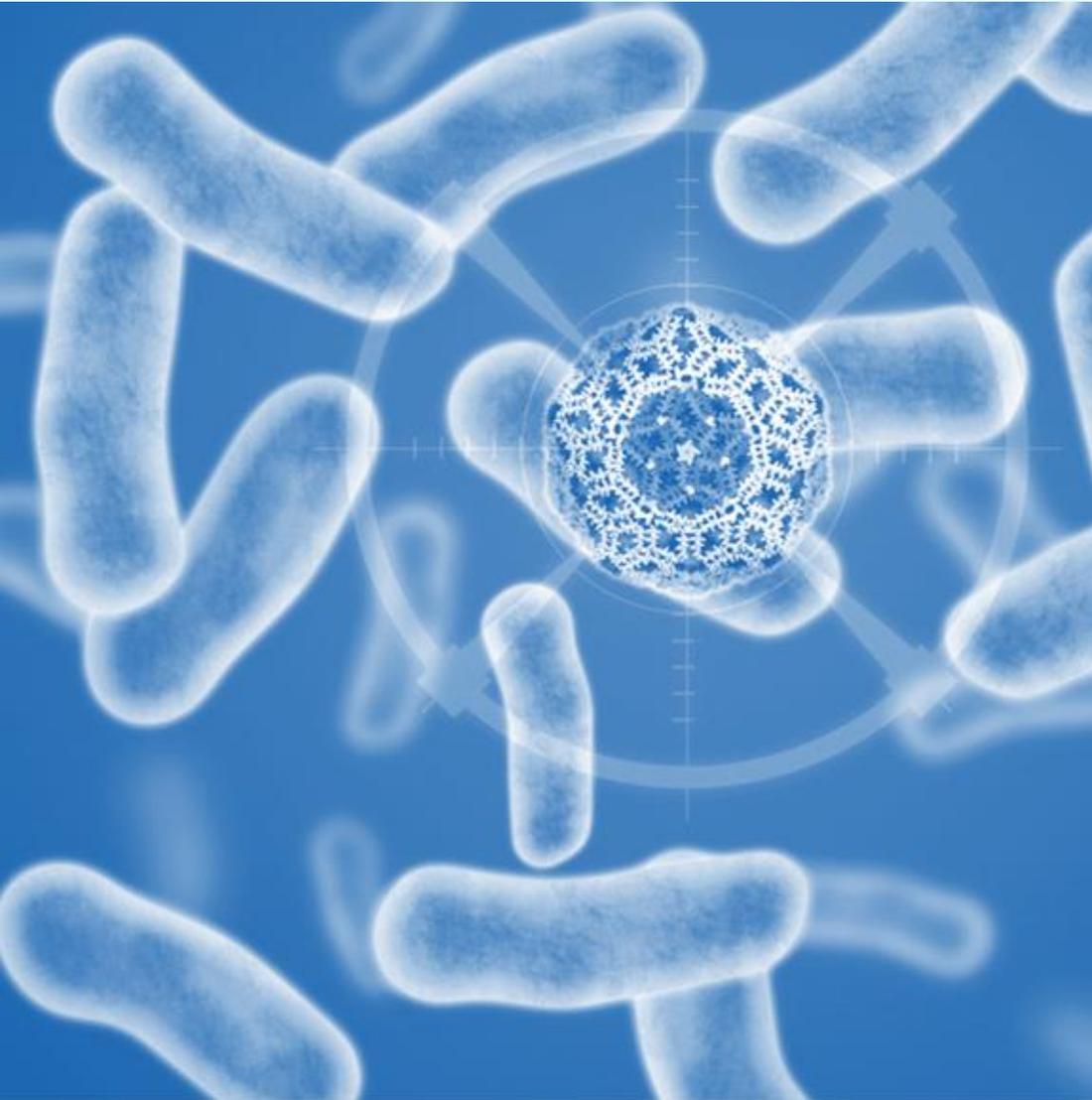
Dx

- Polypharmacy monitoring
- Drug-drug interactions
- Evidence-based pharmaceutical guides
- Disease-specific evaluation
- Therapeutic response

Tx

- Prescribe Lactulose and Rifaximin
- Coordinate with other specialists on diagnostics and treatment

Specialist



Dx

- Rule out or treat advanced renal disease and uremia or other conditions

Tx

- Treat renal disease
- Advise multidisciplinary team of implications for clearance of ammonia and other toxic substances

Diagnostic & Therapeutic Roles

LTC INTERDISCIPLINARY TEAM (IDT)

Discipline	Diagnostic	Therapeutic
Nursing Team	Monitor physical and cognitive signs and symptoms of HE, and food acceptance	Patient and family education on medications and compliance, disease trajectory; administer medications, provide behavioral, palliative care.
Pharmacist	Evaluate and monitor polypharmacy, drug-drug interactions, pharmaceutical guides and evidence based pharmaceutical guides.	Coordinate with other specialists on diagnostics and treatment Recommend lactulose and rifaximin (AASLD 1-A-1 Guideline)
Primary Care Provider	Obtain clinical history, conduct physical exam, and order psychometric tests (PHES: "gold standard")	Prescribe lactulose and rifaximin; coordinate with other specialists on diagnostics and treatment.
Neurologist	Evaluate electroencephalogram (spectral, versus visual EEG)	Treat and manage neurologic disease; manage patient's pain
Psychologist	Conduct Stroop text, smartphone application	Provide patient counseling.
Psychiatrist	Assess psychiatric symptoms, alcoholic liver disease, and withdrawal	Provide patient counseling, and management of anxiety, depression and pain.
Infectious Disease	Rule out, or treat infectious disease having symptoms similar to HE, or which might precipitate or exacerbate HE	Prescribe appropriate antibiotics
Endocrinologist	Identify severe hyperglycemia and poorly-controlled diabetes	Ensure that patient's glycemic levels are well-controlled.
Nephrologist	Rule out or treat advanced renal disease and uremia	Treat renal disease; advise interdisciplinary team of implications for clearance of ammonia and other toxic substances
Social Worker	Get feedback from patient and family on adherence to therapy; Provide support and person-centered counseling; monitor for cognitive changes	Coordinate with family and other caregivers to help ensure adherence to therapy; provide support system, and adequate housing.
Occupational Therapist	Evaluate safety of home and work environments, skill evaluations, driving, and other life skills and activities affected by HE	Advise patient, caregivers and interdisciplinary team of these risks and interventions to minimize them.
Dietitian	Evaluate adequacy of total caloric and protein intake	Adjust diet to mitigate frailty and sarcopenia

Analysis

Life

Treat

Pharmacy

KTAP

Disease

Key Take Away Points

Symptom

Care

Anat

Pain

Health

X-Ray

Key Take Away Points



1. Keep HE (Hepatic Encephalopathy) top of mind as one potential cause for 'Change in Mental Status.
2. Develop a process for your facility to efficiently and effectively diagnosis and treat HE.
3. The AASLD/EASL guideline recommendations are a helpful resource for the management of HE in the LTC environment.
4. Lactulose and rifaximin post an episode of OHE is a well studied combination and proven to reduce the risk of OHE recurrence and HE related hospitalizations
5. **Include all members of the IDT in this process with a continuous quality improvement (CQI) process to assure that appropriate outcomes are being met.**

Analysis

Life

Treat

Pharmacy

Q&A

Disease

Questions & Answers

Symptom

Care

Anat

Pain

Health

X-Ray

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