This is Part 1 of our 2 part series on Changes in Mental Status – Hepatic Encephalopathy. This part covers the Management Overview from a review of problem, diagnosis and treatment. Part 2 goes into detail on the treatments for HE as well as the roles and responsibilities for each member of the Interdisciplinary Team.
Facilitator Notes:

How often does this scenario happen ...in most SNFs this is a weekly occurrence at least, if not more often.
And how often are we missing the real issue?

Let’s take the next few minutes to review one possible explanation for a change in mental status...Hepatic Encephalopathy.
Facilitator Notes:

An infection e.g. UTI, is only one of the possible causes of changes in mental status, but there are of course many others to consider.

One of the causes of changes in mental status is the buildup of toxic levels of serum ammonia in patients with chronic liver failure, which underlies hepatic encephalopathy (HE).
Facilitator Notes:

The behavior and personality changes that can occur with HE include more than a ‘change in mental status’. They can include any of the following 20 signs and symptoms highlighted on this slide.

These observations by nursing staff are much more beneficial to early recognition of HE than an early morning phone call to a provider of a ‘change in mental status’.
Facilitator Notes:

The more specific we can be regarding ‘change in mental status’, with more descriptions when we deliver our SBAR – Situation, Background, Assessment and Recommendation or Request, the better will be the prospect of hitting the mark on the true cause.

As such, recognizing the level of consciousness and awareness is important. This could be done through the use of one of the standard criteria or definitions such as Glasgow or Westhaven. The more detail the better.
Facilitator Notes:

So how big a problem is HE that we should keep this on our radars? – Let’s take a quick look at the numbers to appreciate why we should care about HE for our LTC patients.
Facilitator Notes:

Hepatic Encephalopathy is a term that means brain disease, damage, or malfunction that comes from issues with one’s Liver.

This comes from chronic liver disease which is especially prevalent in the US, including the serious progression of this disease to cirrhosis.

**Cirrhosis** is a late-stage of scarring (fibrosis) of the liver caused by many forms of liver diseases and conditions, such as hepatitis and chronic alcoholism.

With so many affected, many of these patients end up in our nursing homes.
Facilitator Notes:

A couple key points to remember about HE are as follows;

- HE is most commonly a syndrome observed in patients with cirrhosis.
- Subtle signs of it are observed in nearly 70% of these patients
- Due to its episodic nature, slow progression and symptoms which overlap those of other diseases, clinicians often miss this diagnosis
- Largest driver of 30-day hospital readmissions for cirrhosis patients
  Tapper EB et al. Clinical Gastro Hepatol 2016;14:1181-1188
- LTC providers need to be both knowledgeable and vigilant when they observe cirrhosis patients exhibiting symptoms like a change in mental status
Facilitator Notes:

An appreciate for these details can help lead our providers to the right diagnosis and ultimately right management of HE.
Facilitator Notes:

HE is a disease of the liver which causes the accumulation of ammonia – which is the toxin responsible for the change in mental status in addition to many other problems such as brain inflammation and reduced immune function leading to infections.

Because of this pathophysiology, the major treatments target the gut and liver. Let’s take just a moment to review this illustration to appreciate the roles that the liver and gut play on the neurological and immune systems.
Facilitator Notes:
So, once you suspect that a patient with cirrhosis may be suffering from HE, how does one confirm the diagnosis?

As cited on the slide and listed below here are some tests that can be utilized:

- Blood test that shows elevated ammonia levels
- EEG that shows brain wave activity
- Scan of the brain that rules out others causes and may show brain swelling

Regarding ammonia levels it is important to keep in mind that the diagnosis of HE is a clinical one, once other causes for confusion or coma have been excluded; **no test fully diagnoses or excludes it**. Serum ammonia levels are elevated in the majority of people, but not all hyperammonaemia (high ammonia levels in the blood) is associated with encephalopathy.

The American Association for the Study of Liver Diseases / European Association for the Study of the Liver (AASLD / EASL) Guideline (2014) provides guidance on testing for ammonia levels some of which are highlighted below:

- A normal value calls for diagnostic reevaluation.
- High blood-ammonia levels alone do not add any diagnostic, staging, or prognostic value in HE patients with chronic liver disease. However, in case an ammonia level is checked in a patient with OHE and it is normal, the diagnosis of HE is in question. For ammonia-lowering drugs, repeated measurements of ammonia may be helpful to test the efficacy.
- There may be logistic challenges to accurately measure blood ammonia, which should be taken into consideration. Ammonia is reported either in venous, arterial blood, or plasma ammonia, so the relevant normal should be used.
- Multiple methods are available, but measurements should only be employed when laboratory standards allow for reliable analyses.

While diagnostic tests, of course, require a provider’s order, it is beneficial for nursing staff and others to appreciate the process as a whole.

- EEG that shows brain wave activity
- Scan of the brain that rules out other causes and may show brain swelling

Common precipitating factors are dehydration, ascites, changes in diet, alcohol use, and others listed.

The AASLD/EASL Guidelines are a very credible source to build out a guide for your facility.
Facilitator Notes:

One of the key signs in HE is asterixis – which is a tremor of the hands when the arms are extended and the hands are bent upward. This is a neurological manifestation of the same systemic toxins (namely ammonia) responsible for encephalopathy and is an important early symptom nursing staff may recognize and bring to the attention of other healthcare professionals treating the patient.

Let’s spend a moment bending our own hands upward with our arms extended to see what this position looks like. Obviously, for us, we are not seeing our hands tremor, but it is important to appreciate how easy it would be to routinely utilize this test in our patients as an early indicator of HE.
Facilitator Notes:

There are several treatment options for Hepatic Encephalopathy which can prevent mental status changes.
Facilitator Notes:

Since the mental status change is due to toxins – getting them out of the body is critical. In this regard, a mainstay of the treatment for acute Overt HE is lactulose, which works by getting the gut flora to acidify the colon, leading to conversion of freely diffusible ammonia (NH$_3$) into ammonium ions (NH$_4^+$) which are not absorbable by the gut and are therefore excreted. This excretion is enhanced by the laxative effect of lactulose, due to its lowering of osmotic pressure of the gut contents, thereby drawing water into it and inducing diarrhea.

To help prevent the recurrence of OHE it should be noted that the current (AASLD/EASL) guideline recommends combined lactulose plus rifaximin for prevention of HE after the second episode.$^7$
Facilitator Notes:

**Rifaximin** works as a poorly absorbed antimicrobial agent that is thought to reduce ammonia production by eliminating ammonia-producing colonic bacteria.

Because of this mechanism of action, Rifaximin has been shown to be beneficial in combination with lactulose.

Remember rifaximin is not a treatment for acute OHE it should be positioned as a secondary prophylaxis strategy with lactulose to prevent recurrence HE and related hospitalizations.\(^\text{13}\)
Facilitator Notes:

The benefit of using Rifaximin with Lactulose has been demonstrated in several clinical studies. Here is a study that illustrated that benefit through a randomized double-blinded controlled trial.

In this type of trial, neither the investigator nor the participant are aware of which drug or placebo is administered and thus the observed drug effects are free from investigator or subject bias. Moreover, the randomization helps to ensure that findings are likewise not attributable to differences in the comparison groups prior to the study.

In this randomized, double-blind, controlled trial:

• XIFAXAN reduced the risk of OHE recurrence by 58% and HE Related hospitalizations by 50% versus Placebo.

• 91% of patients in both arms of the trial were on lactulose which means this data reflects benefits of rifaximin over and above those which previous studies have shown are due to lactulose alone.

This is important in weighing the value of managing patients with a regimen of lactulose alone, as compared to one with a combination of lactulose and rifaximin.
Facilitator Notes:

This illustrates a typical treatment regimen for patients with HE – one with which nurses should be familiar, both from an administration standpoint as well as from the standpoint of educating patients on the importance of these medications together.

One of the major reasons for patient non-adherence to treatments is their lack of appreciation for their benefits. This understanding can go a long way toward maintaining treatment adherence.
As we have discussed you can see in the AASLD/EASL guidelines #19 and #20 that Lactulose and Rifaximin are part of the standardized treatment of HE.

Specifically, the current AASLD/EASL guidelines recommend combined lactulose plus rifaximin for prevention of HE after the second episode.  

Rifaximin has excellent characteristics, including a slow rate of systemic absorption, a broad spectrum of antibiotic activity, and a low frequency of side effects.

This particular guideline on combination therapy is given the highest recommendation (Grade 1, A, 1) based on scientific merit and cost-effectiveness.
Facilitator Notes:

Now let's take a moment to review our key takeaway points that we can put into action to improve the care of our patients.
Facilitator Notes:

Four key points to take away include the following:

1. Keep HE (Hepatic Encephalopathy) top of mind as one potential cause for ‘Change in Mental Status’.
   • It’s often said that we don’t know what we don’t know, so if we didn’t know about HE before this discussion we would never consider it as a possible reason for a change in mental status – Now that we know, it is up to us to keep it top of mind as to one of the possibilities

2. Develop a process for your facility to efficiently and effectively diagnosis and treat HE.
   • Knowing is one thing but for things to happen consistently they require a process, so let’s not have it end here. Rather, work as a team to develop a process for the appropriate management of our patients with mental status changes that includes the consideration of HE.

3. The AASLD guideline recommendations are a helpful resource for the management of HE in the LTC environment.

4. Lactulose and rifaximin post an episode of OHE has been well studied, and proven to reduce the risk of OHE recurrence and HE related hospitalizations.
Facilitator Notes:

Now let’s take a few moments to address any questions or thoughts on the process we should implement to best manage our patients with HE.
References: