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Liver Disease

CareOregon Pharmacy



Today's Agenda

Networking & Introduction 8:00 – 8:15

Liver disease overview 8:15 – 9:45

Break 9:45 – 10:00

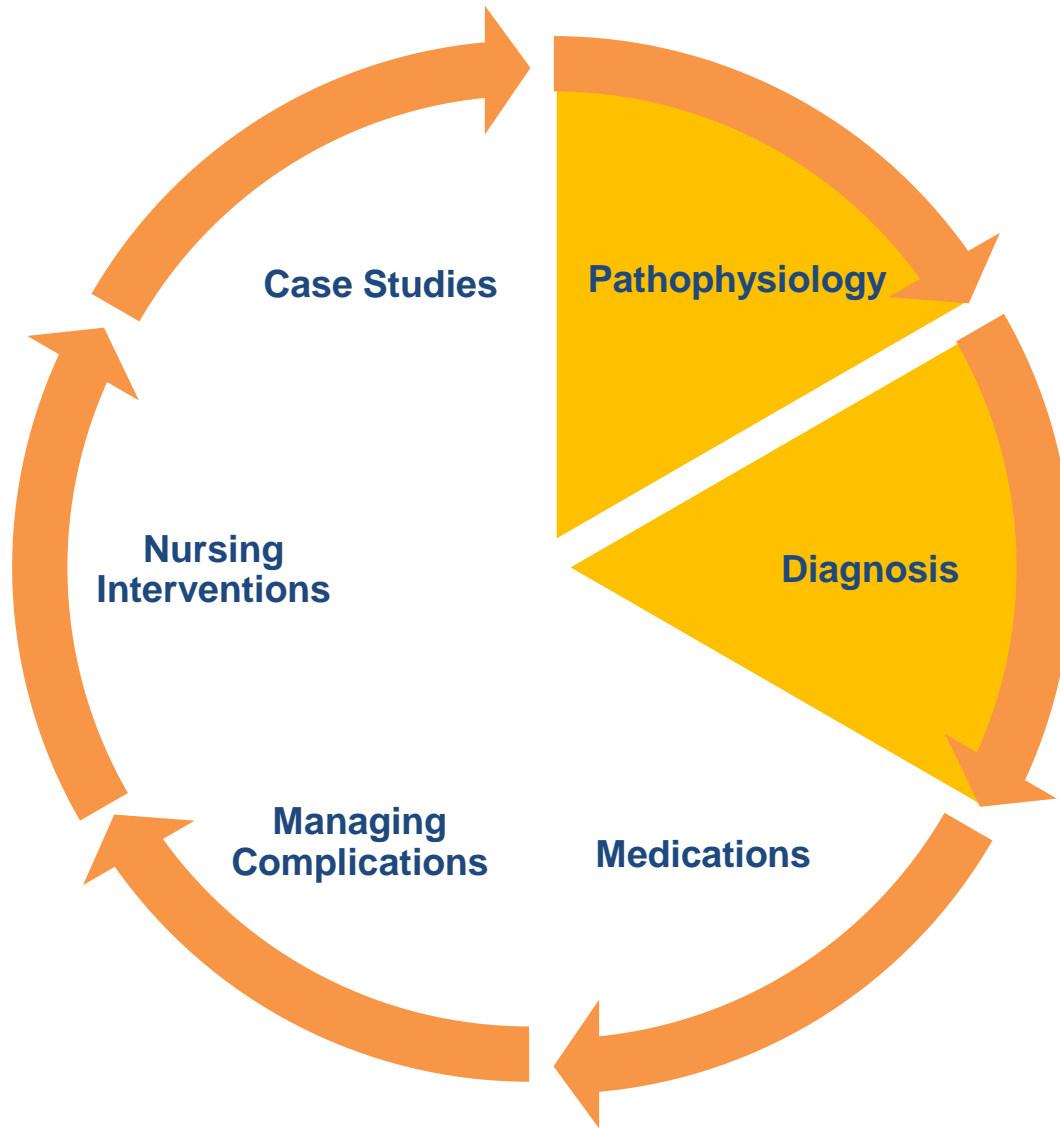
Medication review 10:00 – 11:00

Break 11:00 – 11:15

“A day in the life of a hepatology RN” 11:15 – 12:00

Questions 12:00 – 12:15

Networking & Closing 12:15 – 12:30



Objectives

- Identify the causes of chronic liver disease
- Understand the laboratory abnormalities seen in chronic liver disease
- Understand the methods to diagnose cirrhosis and identify the common complications of cirrhosis

Liver Disease

Atif Zaman, MD, MPH

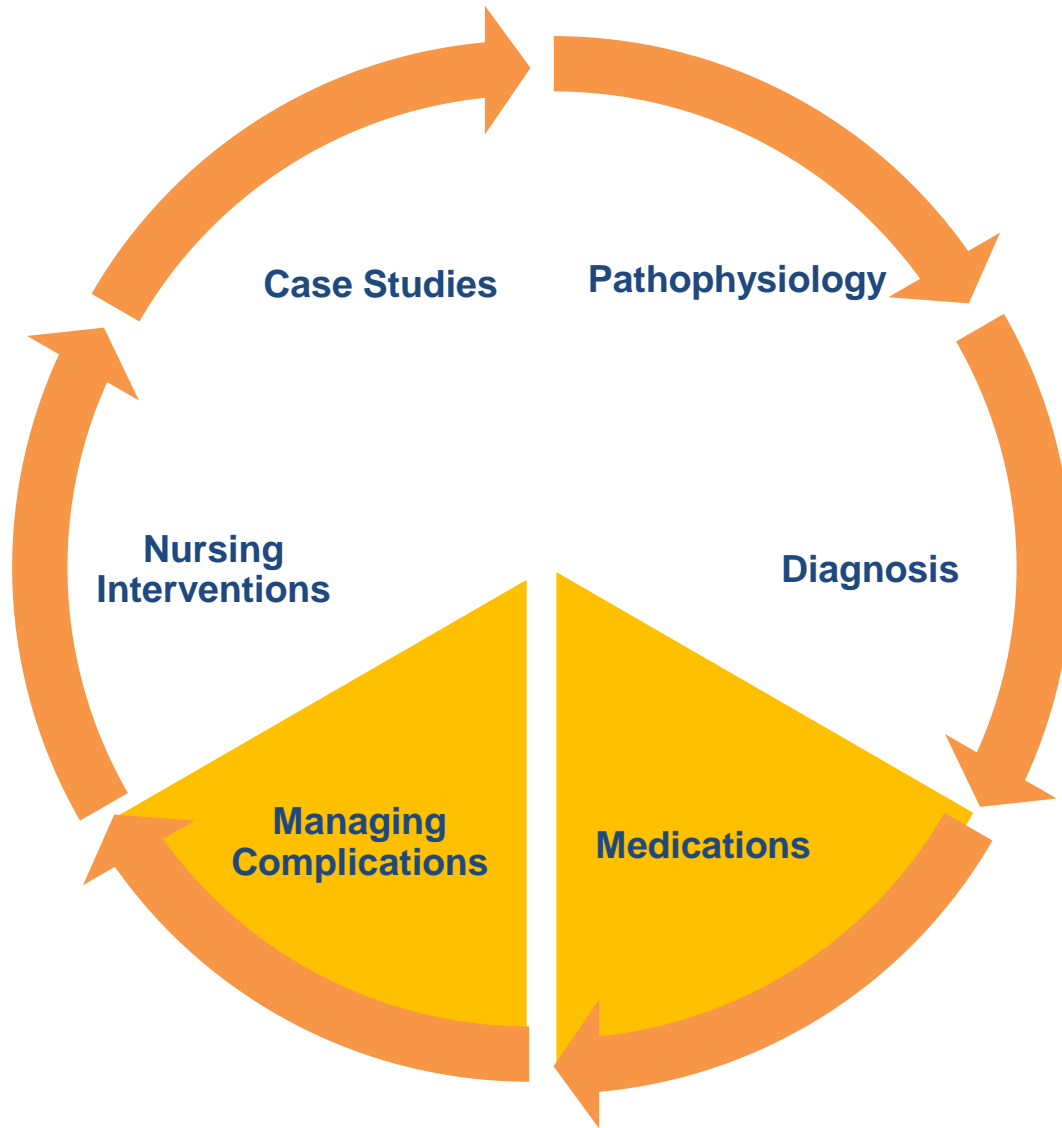
Professor of Medicine

Oregon Health & Science University





reak



Medications for Hepatitis C and Cirrhosis Complications

Maddie Fry, PharmD

Post-Graduate Year 2 Pharmacist Resident



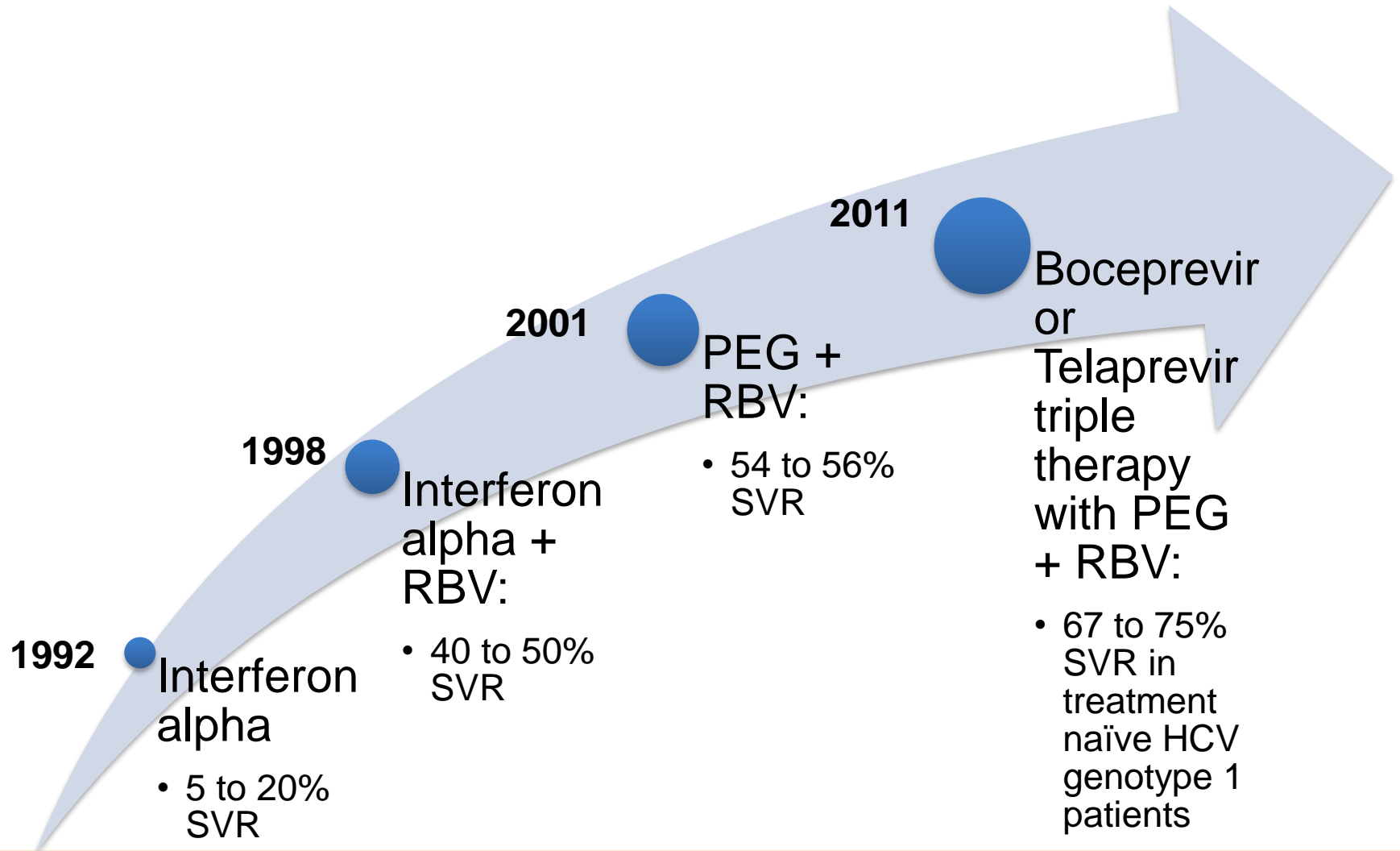
Learning Objectives

- Comprehend how rapidly Hep C treatment has changed in recent years
- Be able to identify medications to avoid in liver disease
- Identify and/or apply primary care patient education points for medications used in Hep C and cirrhosis complications

Drug Name Translator

Abbreviation or Generic Name	Brand Name
RBV	Ribavirin
Pegylated Interferon (PEG)	Peg-Intron
Simeprevir	Olysio
Sofosbuvir	Sovaldi
Ombitasvir-Paritaprevir- Ritonavir and Dasubravir	Viekira Pak
Ombitasvir-Paritaprevir- Ritonavir	Technivie
Daclatisvir	Daklinza
Ledipasvir-Sofosbuvir	Harvoni
Elbasvir-Grazoprevir	Zepatier

Treating HCV: A History



Treating HCV: NOW

- 2013
 - Nov: Simeprevir and Sofosbuvir. Both originally approved for combination therapy with peg-interferon alpha and RBV
- 2014
 - Oct: Ledipasvir-Sofosbuvir
 - Nov: Simeprevir and Sofosbuvir were approved for use together as an all-oral regimen without peg-interferon alpha
 - Dec: Ombitasvir-Paritaprevir-Ritonavir and Dasubravir
- 2015
 - Jul: Ombitasvir-Paritaprevir-Ritonavir
 - Jul: Daclatisvir
- 2016
 - Jan: Elbasvir-Grazoprevir

Spach DH., Kim HN. Medications to Treat HCV: Drug Studies, Clinical Studies, and Slide Decks. Accessed:
<http://www.hepatitisc.uw.edu/page/treatment/drugs/simeprevir-drug#drug-summary>

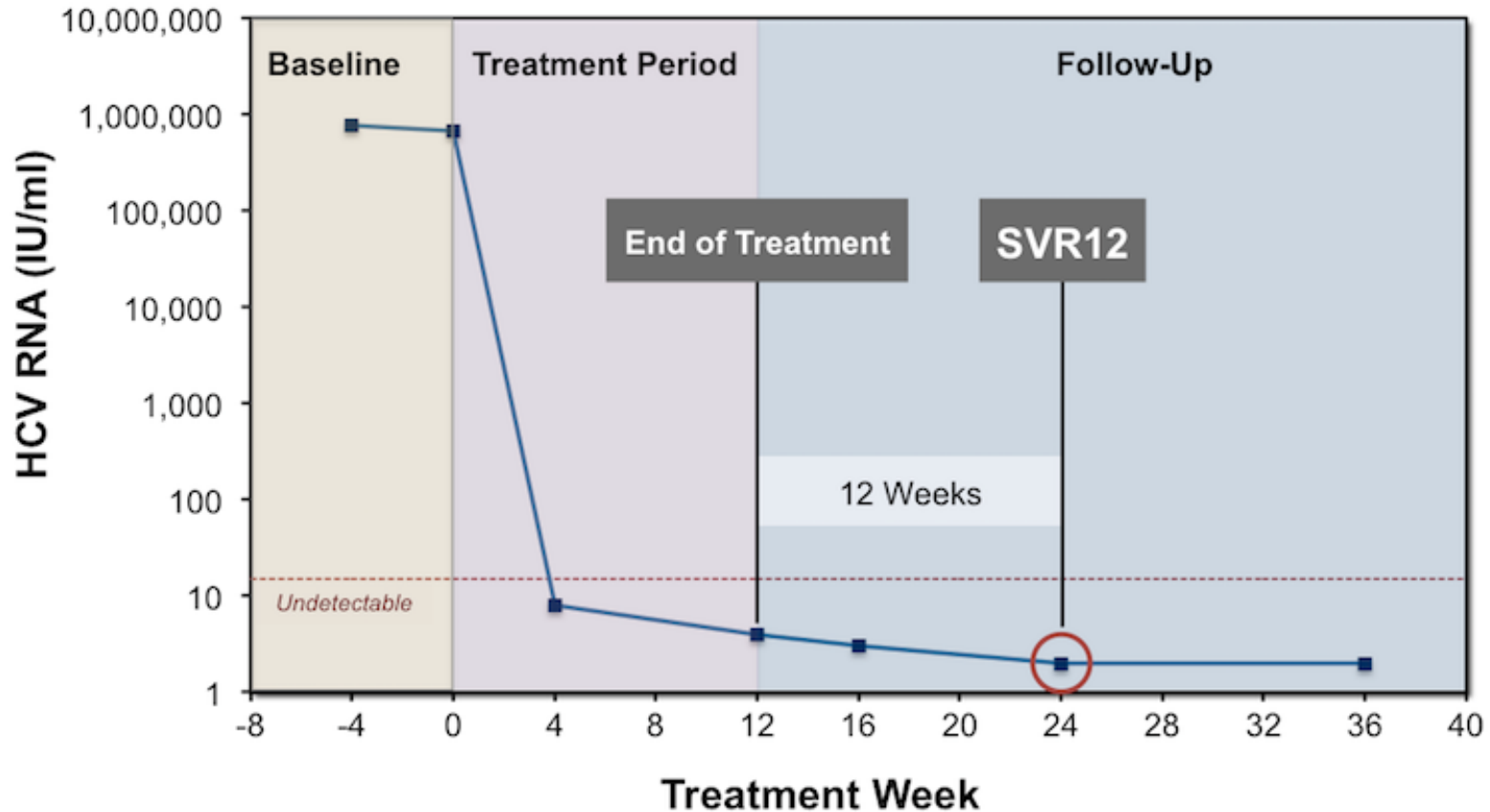
HCV Genotypes in the USA

- Genotype 1 = 70%
- Genotype 2 = 15-20%
- Genotype 3 = 10-12%
- Genotype 4 = 1%
- Genotype 5 and 6 = less than 1%

Thortan K. Natural History of Hepatitis C Infection. Accessed:
<http://www.hepatitisc.uw.edu/browse/all/core-concepts>

Goal of Therapy: SVR 12

Sustained Virologic Response 12 weeks after treatment completion



Scott, JD., Goals for Treatment and Predicting Response. Accessed:

<http://www.hepatitisc.uw.edu/go/evaluation-treatment/treatment-goals-predicting-response/core-concept/all#goals-rationale-treatment>

Assessing Readiness for Treatment

Checklist

- Good evidence of adherence and willing to comply with follow-up
- Adequate psychosocial support
- Psychiatrically stable
- Drug/alcohol use evaluated and addressed
- Potential drug-drug interactions addressed and plan in place to monitor

Scott, JD. Making a Decision on When to Initiate HCV Therapy. .

Assessed at <http://www.hepatitisc.uw.edu/go/evaluation-treatment/treatment-initiation-decision/core-concept/all>

Choosing a Treatment Regimen

Factors that influence treatment and duration of therapy:

- Genotype
- Prior treatment experience
- Fibrosis status

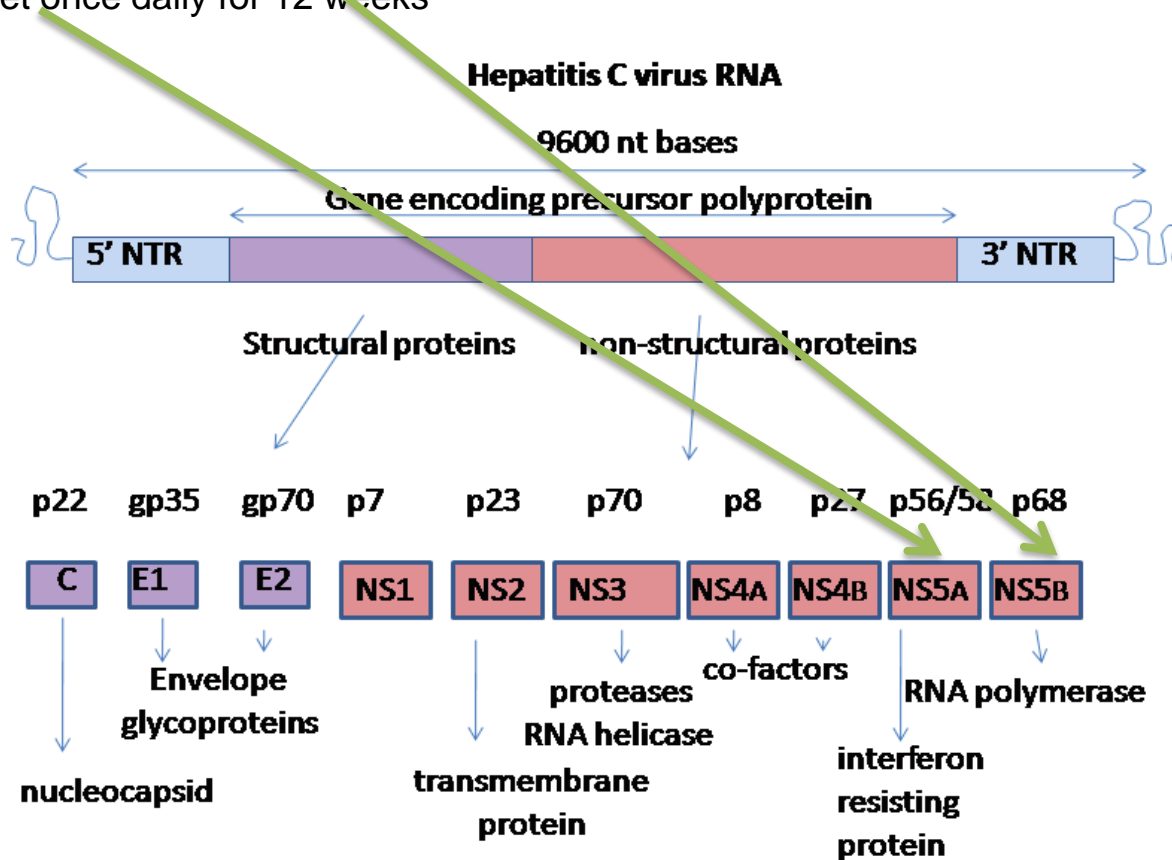
AASLD/IDSA Guideline Recommended Regimens for Genotype 1 Treatment Naïve Patients

****similar efficacy in general**

Harvoni Regimen

ledipasvir- sofosbuvir

One tablet once daily for 12 weeks



Ledipasvir-Sofosbuvir (Harvoni)

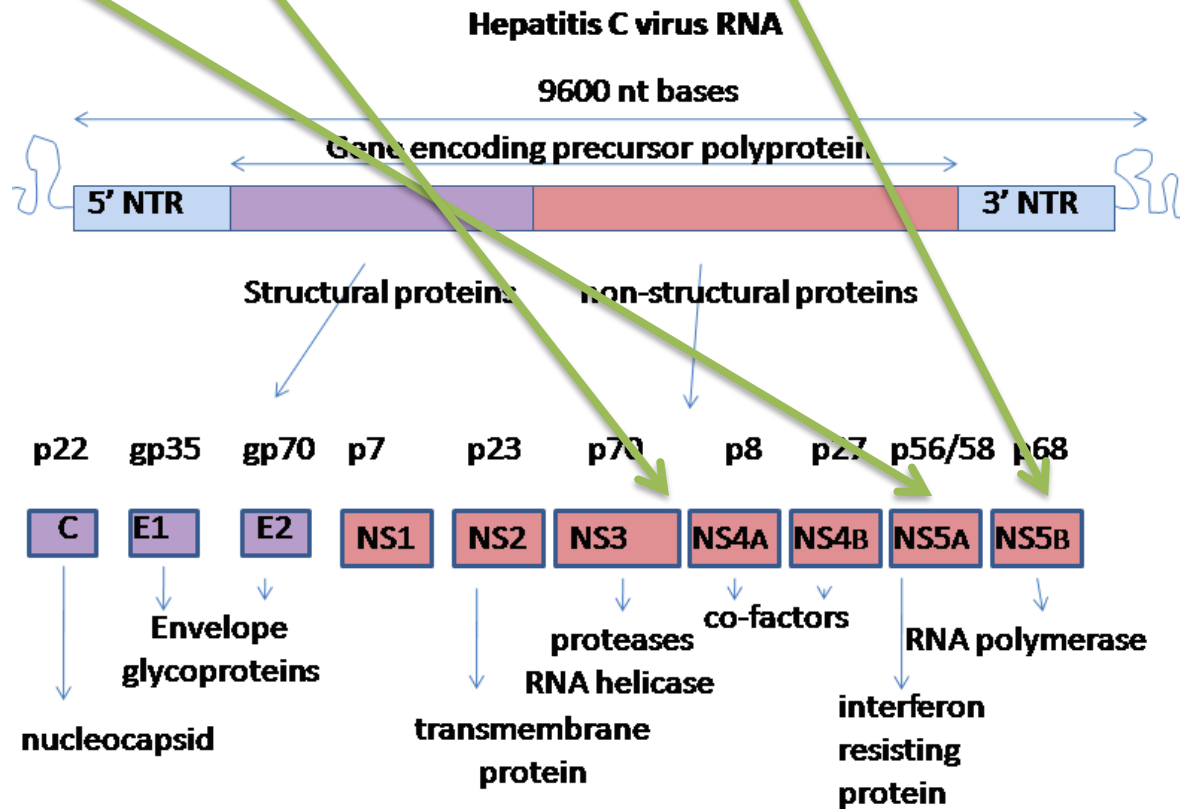
- Adverse effects
 - Very well-tolerated. Sometimes fatigue and headache
- Major Drug interactions
 - St. Johns Wort
 - Rifampin
- One pill once daily
 - + for compliance

Viekira Pak Regimen

ombitasvir-paritaprevir-ritonavir and dasabuvir

Fixed dose combo (two tablets once daily) + one tablet twice daily for 12 weeks (no cirrhosis) and 24 weeks (cirrhosis)

Pharmacologic booster



Ombitasvir-Paritaprevir-Ritonavir + Dasubravir (Viekira Pak)

- Adverse Effects

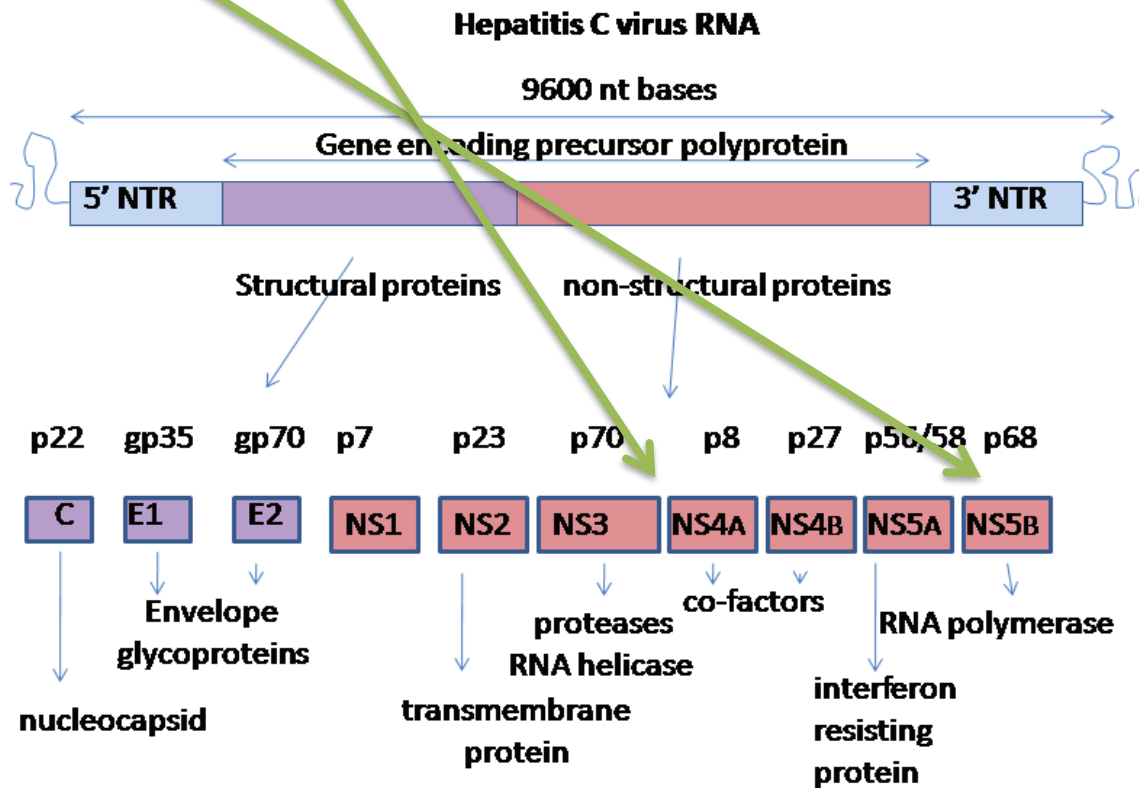
- Fatigue, nausea, pruritus, other skin reactions, insomnia
- October 2015: Drug Safety Warning
 - Can cause serious liver injury. Mostly in patients with advanced liver disease

- Major drug interactions

- Ritonavir (pharmacological booster)
- “boosts many other medications”

Sovaldi + Olysio Regimen

sofosbuvir + **simeprevir**
 400 mg once daily 12 weeks (non-cirrhosis) / 24 weeks (cirrhosis) + 150 mg once daily For 12 weeks (non-cirrhosis) vs. 24 weeks (cirrhosis)



Sofosbuvir (Sovaldi)

- Adverse effects
 - Generally well-tolerated
 - Fatigue and Headache when used with ribavirin
- Drug interactions
 - Anticonvulsants (depakote, valproate, phenytoin etc.)
 - Antimycobacterials (rifampin)
 - Herbal supplements (St. John's Wort)
 - HIV protease inhibitors (ritonavir, darunavir, etc.)

Simeprevir (Olysio)

- Only used in combination
- Adverse Effects
 - Photosensitivity rash (must use protection in the sun)

Daklinza Regimen

daclatasvir

60mg once daily for 12 weeks (no cirrhosis) vs. 24 weeks (cirrhosis)

+

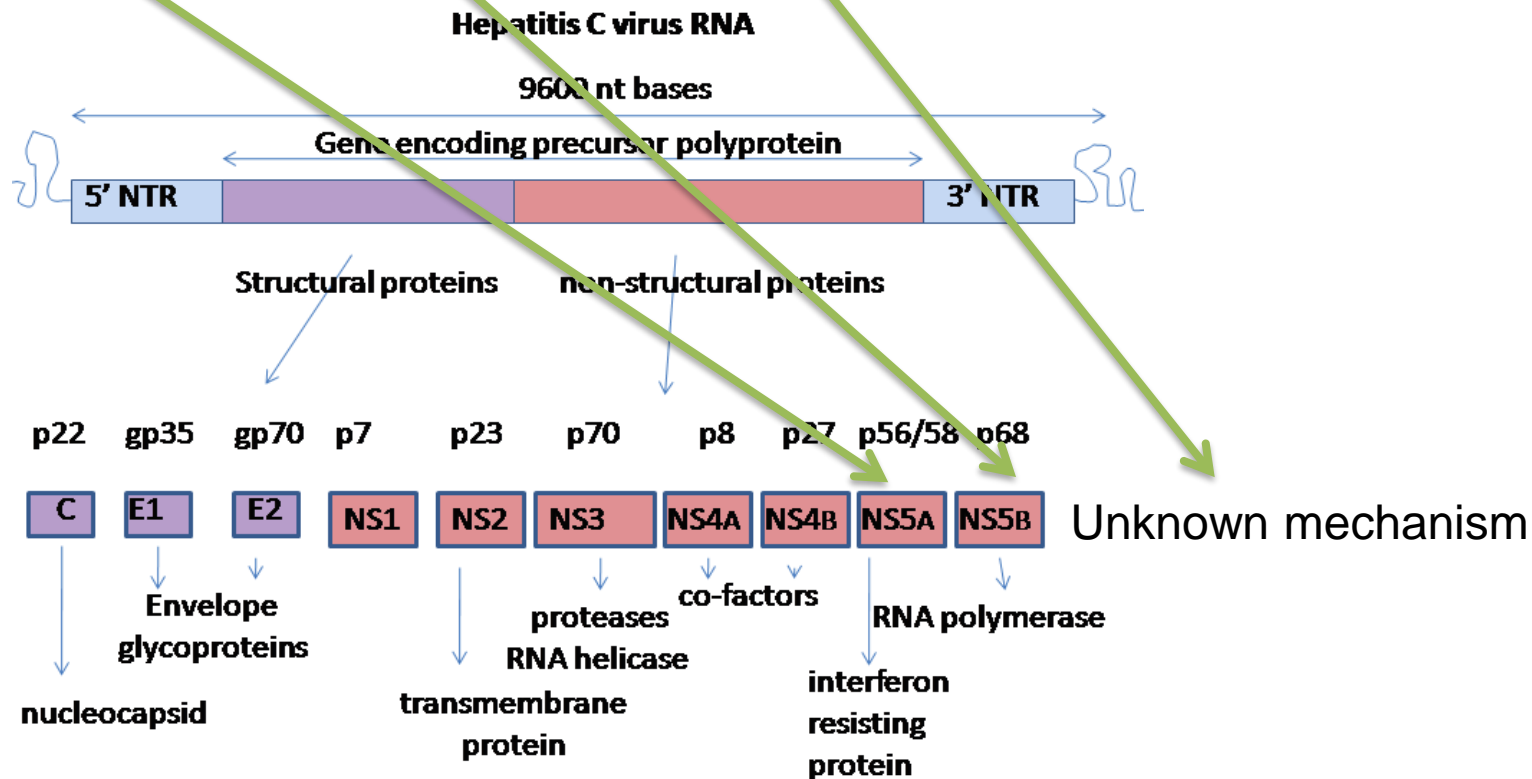
sofosbuvir

400mg once daily

+/-

ribavirin

Consider adding if cirrhosis. Dose depends on weight



Unknown mechanism

AASLD/IDSA. Initial treatment of HCV infection. Recommendations for testing, management, and treating hepatitis C.

Daclatasvir (Daklinza)

- Adverse Effects

- Fatigue (14%)
- Headache (14%)
- Nausea (8%)
- Diarrhea (5%)

- Drug Interactions

- Strong CYP3A4 inducers
 - Carbamazepine, phenytoin, rifampin, and St. John's Wort

Ribavirin

Adverse Effects (Black Box Warnings)

- Hemolytic anemia
 - Occurs suddenly usually in the first 1 to 2 weeks of therapy. Check hematocrit/hemoglobin prior to starting and at week 2 and 4.
 - Dose adjustment can be made.
- Birth Defects
 - Should not be used by women during pregnancy or by male partners of women who are pregnant. Pregnancy should be avoided for at least 6 months by both partners.

Adherence is Key to SVR

- Make a plan for missed doses (depends on the medication)
- Educate patients about the importance of adherence to regimen
- Some clinics will give out 1-2 weeks supply in the beginning to make sure patient can tolerate regimen

Drug interactions

- Hep C medications interact with many medications!
- Tool for assessing:
 - <http://hep-druginteractions.org/Interactions.aspx>
- New medications should be avoided while patient is undergoing treatment



Over-the-Counter Medications to Avoid with Hep C

- Current medication list should be solicited frequently
- Acetaminophen (Tylenol)
 - Up to two grams per day (chronic Hep C without cirrhosis)
 - Limited to 1 gram per day in those with cirrhosis
 - If alcohol intake avoid acetaminophen
 - Those taking acetaminophen should have lab monitoring for hepatotoxicity every 3 to 6 months
- NSAIDs (Aspirin, Ibuprofen, Naproxen)
 - Generally safe for those with Hep C at standard doses
 - Should be avoided in patients with cirrhosis

Over-the-Counter Medications to Avoid with Hep C (cont.)

- Iron
 - Should be avoided in chronic Hep C. These patients store excess iron in their liver
 - Multivitamin should not contain iron unless patient has diagnosed iron deficiency anemia
- Complementary or alternative medications (milk thistle, St. John's wort, ginseng, licorice root, etc.)
 - None have shown definite benefit for patients with hep C. Avoid with direct acting antivirals.

Medication Expense

Estimated Cost* for Treatment of Genotype 1 Chronic HCV	
Regimen^ and Duration of Therapy	Cost of Regimen*
Daclatasvir + Sofosbuvir x 12 weeks	\$147,000
Daclatasvir + Sofosbuvir x 24 weeks	\$294,000
Ledipasvir-Sofosbuvir x 8 weeks	\$63,000
Ledipasvir-Sofosbuvir x 12 weeks	\$94,500
Ledipasvir-Sofosbuvir x 24 weeks	\$189,000
Ombitasvir-Paritaprevir-Ritonavir + Dasabuvir x 12 weeks	\$84,000
Ombitasvir-Paritaprevir-Ritonavir + Dasabuvir x 24 weeks	\$168,000
Sofosbuvir + Simeprevir x 12 weeks	\$150,000
Sofosbuvir + Simeprevir x 24 weeks	\$300,000

*Cost estimates based on Wholesale Acquisition Cost (WAC)
 ^For regimens that include ribavirin add approximately \$500 for 12 weeks and \$1000 for 24 weeks

Woolston, SL. Cost and Access to Direct Acting Antiviral Agents.

Accessed from <http://www.hepatitisc.uw.edu/go/evaluation-treatment/cost-access-medications/core-concept/all>



RADIOLAB

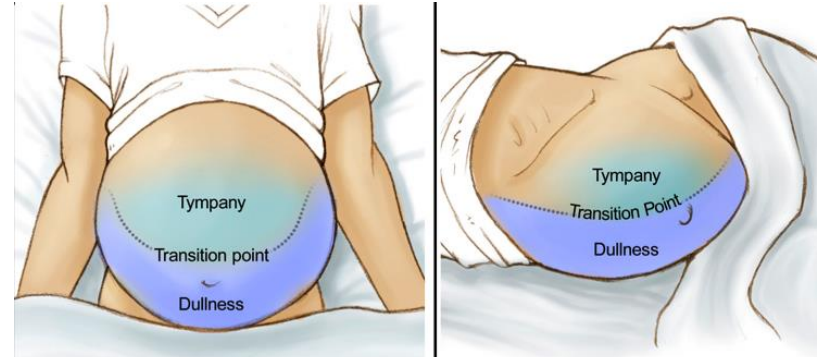
<http://www.radiolab.org/story/worth/>



Pharmacological Management of Cirrhosis-Related Complications

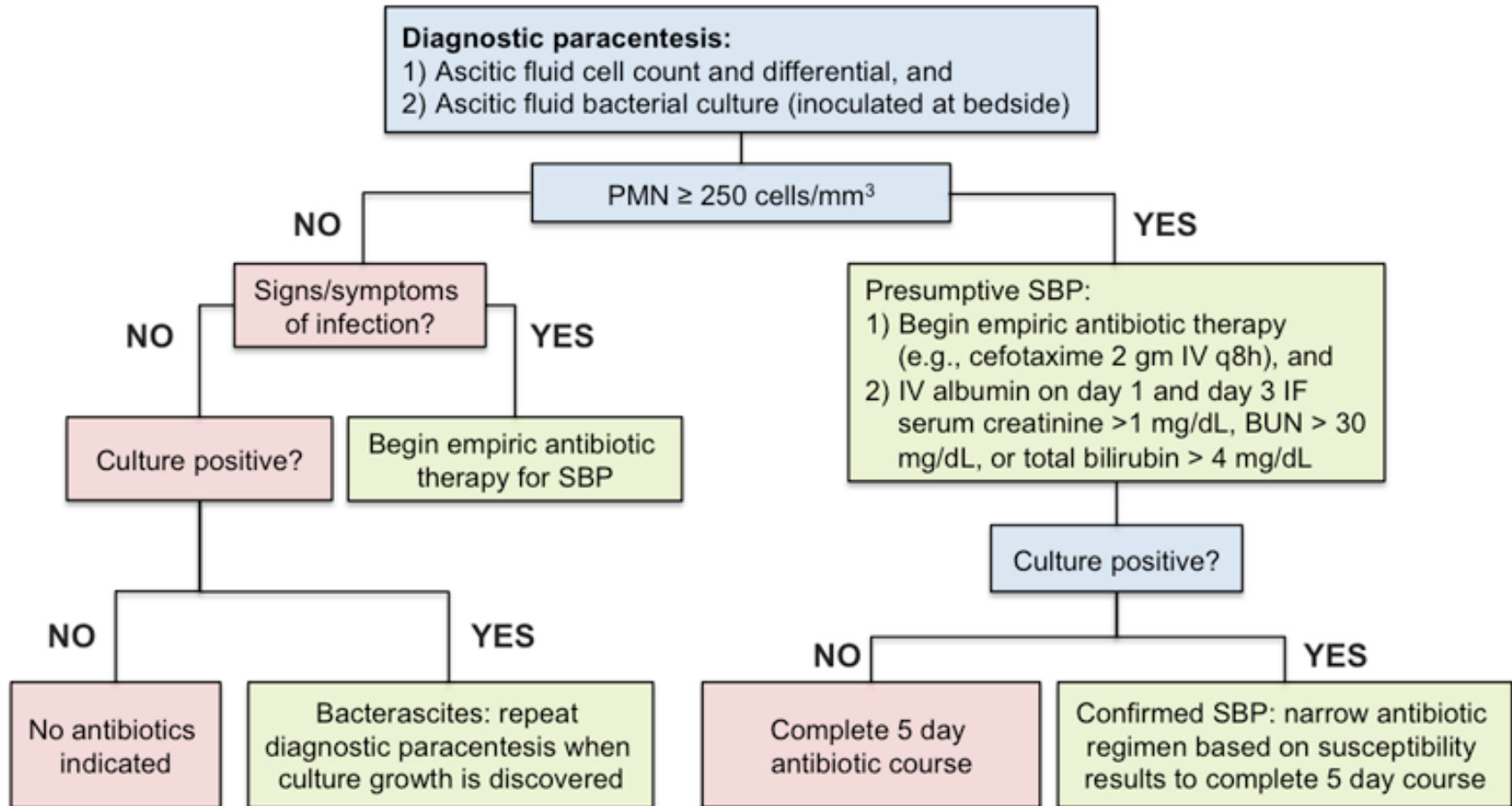
Ascites

- **Dietary Sodium Restriction**
 - No more than 2,000 mg daily
- **Fluid Restriction?**
 - Not as important as sodium restriction
 - Only necessary if serum sodium is less than 120 mmol/L
- **Diuretics**
 - Combination of furosemide and spironolactone (Gold standard)
 - Starting dose of 100mg spironolactone and 40mg furosemide
 - Spironolactone can be use alone but combination is good for rapid weight loss and decreases the risk of hyperkalemia
- **Weight Loss limit?**
 - No limit in patient with significant peripheral edema
 - Without weight loss limited to 0.5 kg maximum



Runyon BA. Management of adult patient with ascites due to cirrhosis: an update. Hepatology. 2009; 49: 2087-107

Spontaneous Bacterial Peritonitis



Runyon BA. Management of adult patient with ascites due to cirrhosis: an update. Hepatology. 2009; 49: 2087-107

Therapy considerations in SBP

Special Considerations	Preferred Antibiotic Therapy	Reasonable Alternative
Standard therapy	Cefotaxime 2 gm IV q8h x 5 days	Ceftriaxone 1 gm IV q12h or 2 gm IV q24h x 5 days
Uncomplicated SBP*	Ofloxacin 400 mg PO bid x 8 days is an option	Ciprofloxacin 500 mg PO bid <i>or</i> Levofloxacin 500 mg PO q24h
Nosocomial SBP	Extended spectrum antibiotics (carbapenems, piperacillin-tazobactam)	Depends on local resistance patterns
Patient receiving fluoroquinolone or trimethoprim-sulfamethoxazole SBP prophylaxis	Cefotaxime 2 gm IV q8h x 5 days	Ceftriaxone 1 gm IV q12h or 2 gm IV q24h x 5 days
Beta lactam hypersensitivity	Ciprofloxacin 400 mg IV q12h	Levofloxacin 750 mg IV q24h
Advanced liver or renal failure: serum creatinine greater than 1 mg/dL, blood urea nitrogen greater than 30 mg/dL, or total bilirubin greater than 4 md/dL	IV Cefotaxime 2 gm IV q8h x 5 days <i>plus</i> IV albumin 1.5 g/kg given on day 1 and 1.0 g/kg given on day 3	

Esophageal Varices

Recommended prophylaxis

Therapy	Dose and Frequency	Goal	Monitoring
Carvedilol	6.25mg once a day	Max tolerable or heart rate of 55 bpm, up to a dose of 12.5mg once a day	Assess heart rate at every visit
Nadolol	20 to 40mg once a day (adjust for renal insufficiency)	Max tolerance or HR of 55 bpm	Assess heart rate at every visit
Propranolol	20 mg twice daily	Max tolerance or HR 55 bpm	Assess heart rate at every visit

Garcia-Tsao G, Sanyal AJ, Grace ND, Carey W; Practice Guidelines Committee of the American Association for the Study of Liver Diseases; Practice Parameters Committee of the American College of Gastroenterology. Prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis. *Hepatology* 2007;46:922-38.

Hepatic Encephalopathy

- 1st line
 - Lactulose 10 to 30 g PO 2 to 4 times daily, titrated to 2 to 3 soft stools daily (non-absorbable disaccharide)
- 2nd line
 - Rifaximin (Xifaxin) 550mg twice daily (antibiotic)
 - Only 0.4% is systemically absorbed

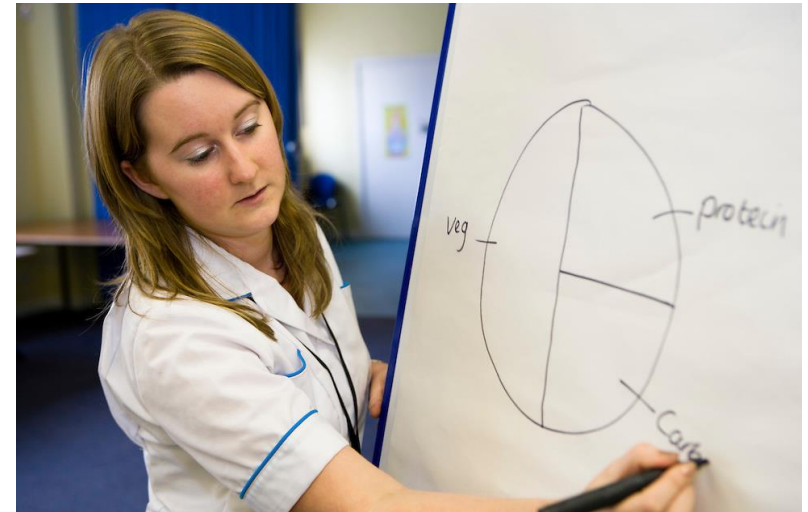
Khungar V, Poordad F. Hepatic encephalopathy. Clin Liver Dis. 2012;16;301-20

Resources

- Patient Education
 - <http://hcvadvocate.org/>
 - <http://www.hepatitis.va.gov/provider/hcv/index.asp>
- Drug interactions
 - <http://hep-druginteractions.org/Interactions.aspx>
- Nursing Education
 - Hepatitis C On-line (has nursing CE)
 - <http://www.hepatitisc.uw.edu/>

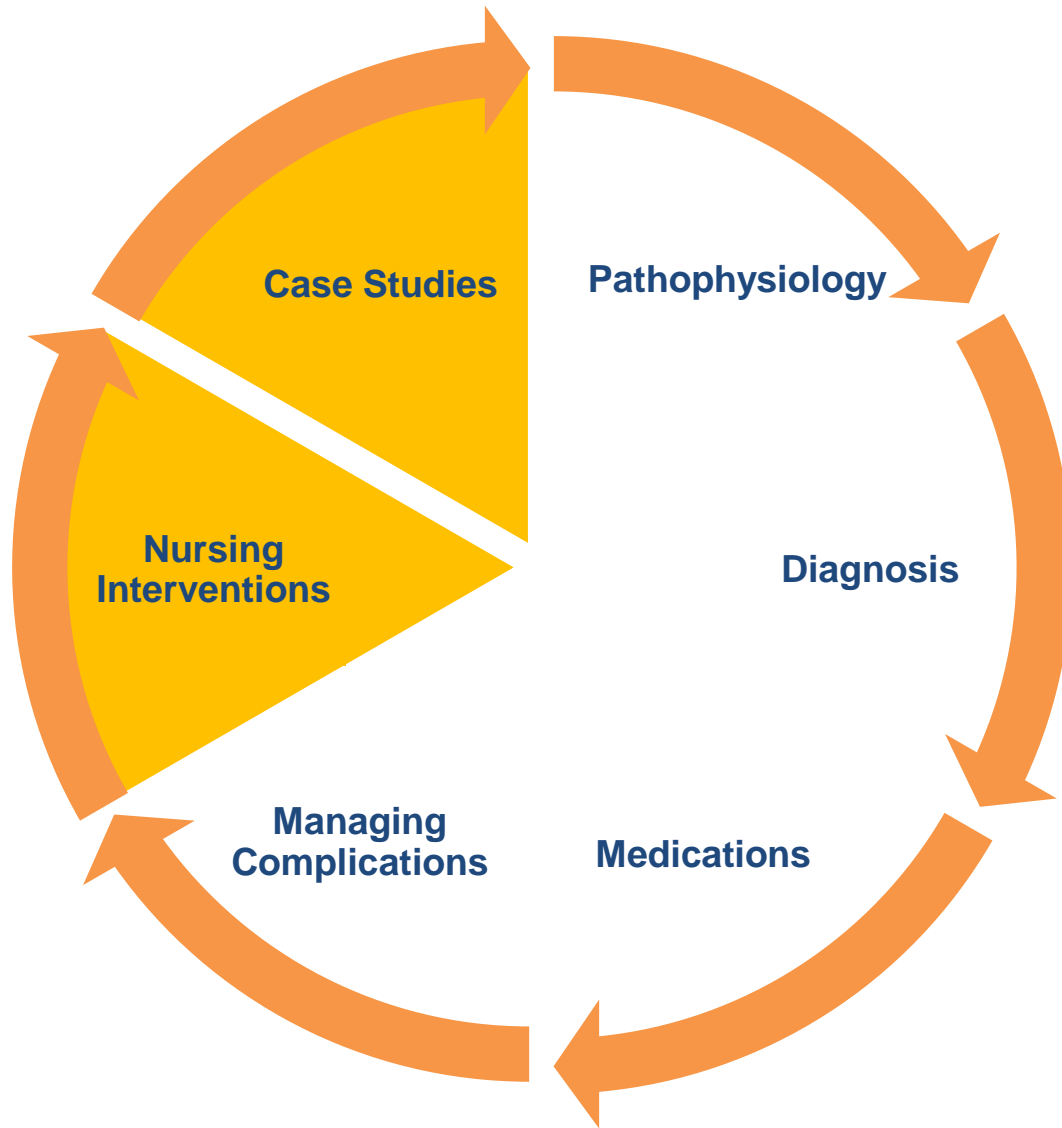
Now for an activity....

- Harvoni
- Viekira Pak
- Ribavirin
- Diuretics for ascites
- Beta Blockers for Esophageal Varices





Break



Hepatology: A Nurses Perspective

Karista Peabody RN, BS CMSRN

Hepatology Patient Care Coordinator

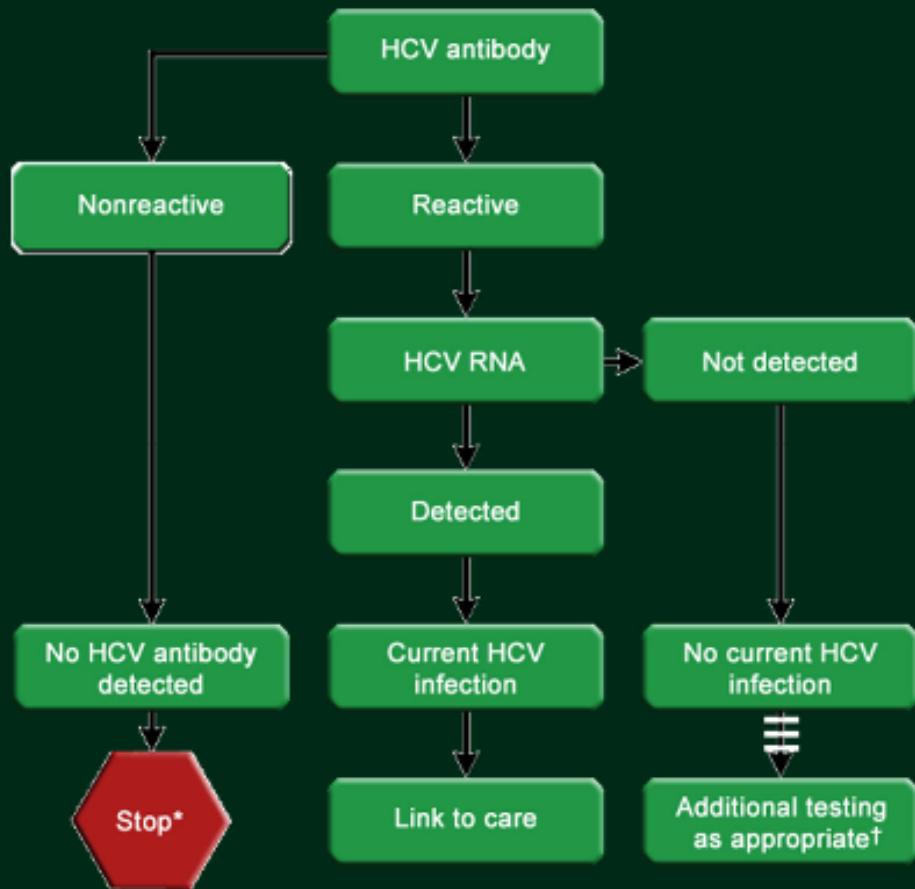
OHSU Hepatology



Points of Learning

- Hepatitis C
- Labs and monitoring
- Cirrhosis
- Case Studies
 - Hepatic Encephalopathy
 - Hepatitis C
 - Beta Blockers
 - Diet Tips
 - Liver Cancer Screening

HCV Testing and Linkage to Care







CDC Recommendation

Evaluation by a practitioner who is prepared to provide comprehensive management, including consideration of antiviral therapy, is recommended for all persons with current (active) HCV infection.

AASLD/IDSA Guidelines
www.hcv-guidelines.org

The Slow Burning Fire: Hepatitis C

PROGRESSION OF LIVER DAMAGE

HEALTHY LIVER	FIBROTIC LIVER	CIRRHOTIC LIVER	LIVER CANCER
			
<p>A healthy liver is able to perform its normal functions effectively, e.g. aiding digestion and breaking down harmful drugs and poisons.</p>	<p>Continuous inflammation of the liver caused by hepatitis C can lead to fibrosis – the formation of scar tissue within the liver.</p>	<p>Extensive scarring can block the flow of blood through the liver and cause liver function to deteriorate over time - this is called cirrhosis.</p>	<p>Hepatitis C is a leading cause of liver cancer – the formation of a malignant tumour in the liver.</p>

<http://uctclinic.com/liver-diseases-treatment>

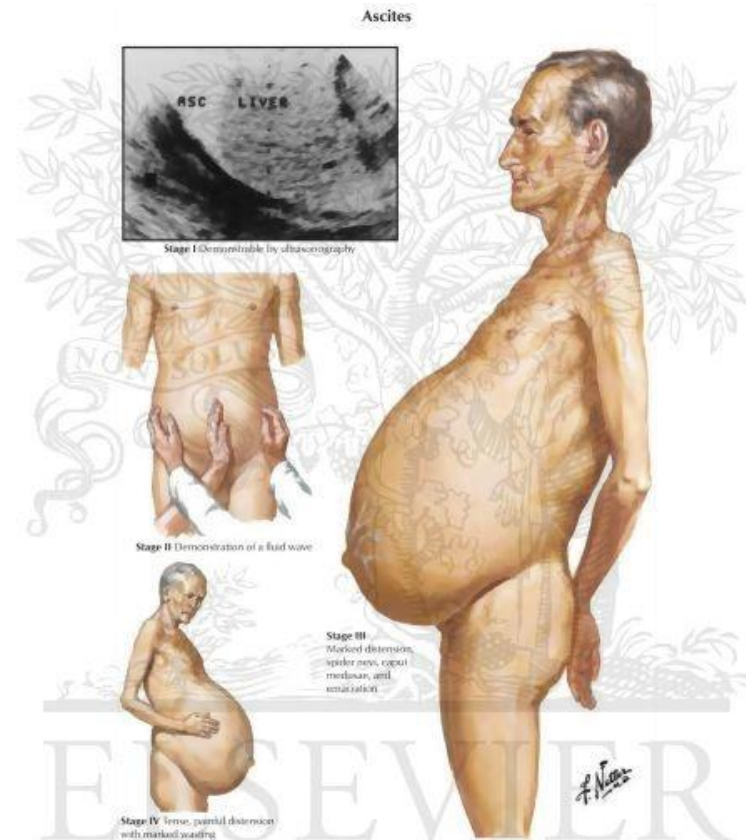
Fibroscan®

Examination with FibroScan®, also called transient elastography, is a technique used to assess liver stiffness (measured in kPa correlated to fibrosis) without invasive investigation. The result is immediate, and allows a biopsy free way to measure the degree of fibrosis. The FibroScan® examination is painless, quick, complication free and easy.



Cirrhosis Most Common Complications

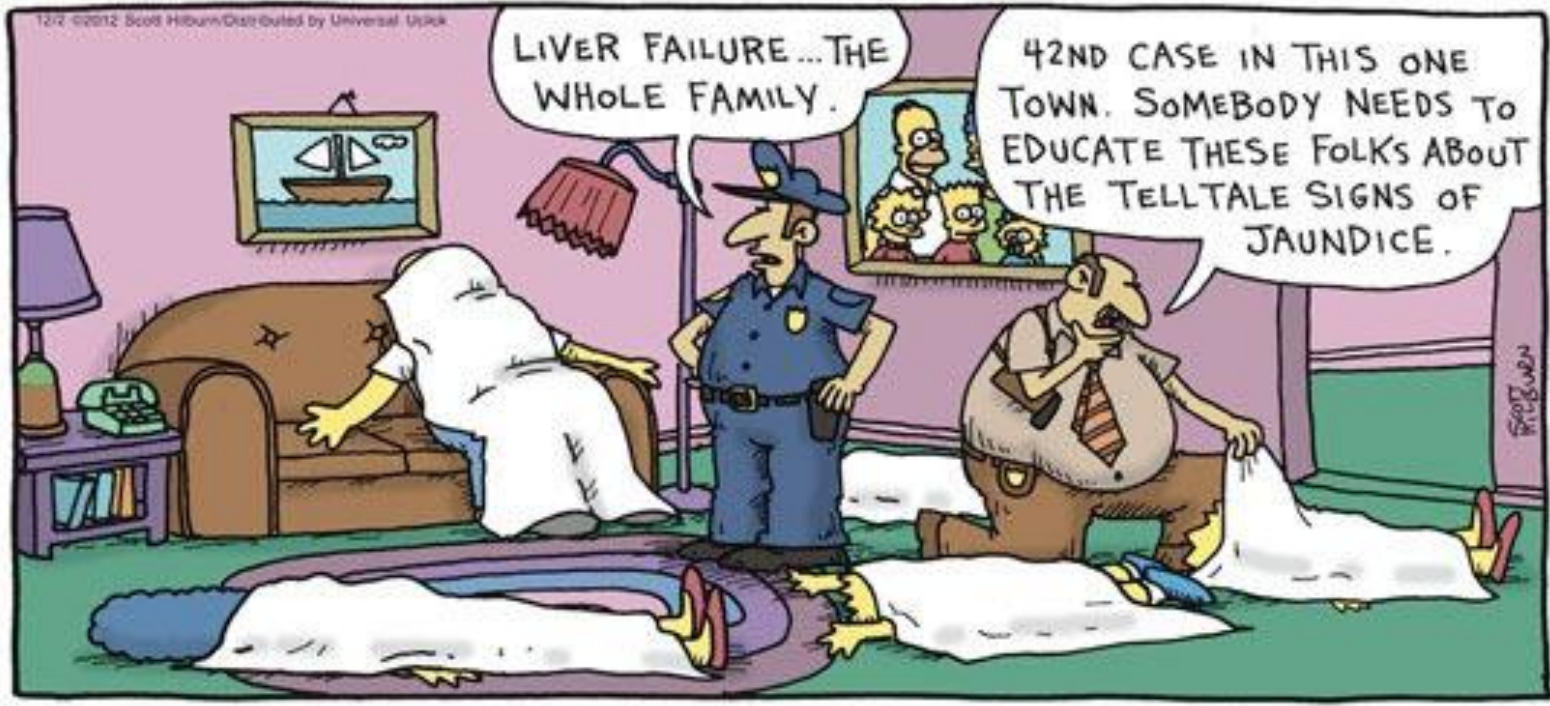
- Ascites
- Hepatic Encephalopathy
- Muscle Wasting
- Esophageal Varices
 - GI bleed
- Jaundice



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<http://old.netterimages.com/product/000000000000/37.5-4.htm>



more awesome pictures at THEMETAPICTURE.COM

Current Prioritization for Hepatitis C Treatment

- Advanced Fibrosis (Stage 3-4)
 - Stage 4=Cirrhosis
- Hepatocellular Carcinoma (treated)
- Co-infection with Hepatitis B/HIV
- Cryoglobulinemia
- Lymphoma
- Extra-hepatic Manifestations (including kidney diseases such as MPGN)

Treatment Monitoring Harvoni Monotherapy

- Harvoni monotherapy: Labs (CMP,CBC, INR if cirrhotic) weeks 4, End of treatment and 12 weeks post.
- Hep C PCR (Hepatitis C Viral Load) 4 weeks into treatment and 12 weeks post treatment (regardless of length or type of therapy).
 - Negative viral load 12 weeks post treatment is indicative of cure
- Ex: 12 week treatment

4 weeks	CMP,CBC,INR, Hep C Viral Load
12 weeks	CMP,CBC,INR
24 weeks	CMP,CBC,INR, Hep C Viral Load

Treatment Monitoring All Other Regimens (Viekira, Ribavirin, Zepatier, Daclatasvir)

- CBC, and CMP Q2 Weeks for first month and monthly thereafter
- INR to be drawn if patient is cirrhotic.
- Hepatitis C Viral Load, 4 weeks into treatment and 12 weeks post treatment (regardless of length or type of therapy).

Lab schedule:

12 week treatment

2 weeks	CMP,CBC,INR
4 weeks	CMP,CBC,INR, Hep C Viral Load
8 weeks	CMP,CBC,INR
12 weeks	CMP,CBC,INR
24 weeks	CMP,CBC,INR, Hep C Viral Load

24 week treatment

2 weeks	CMP,CBC,INR
4 weeks	CMP,CBC,INR, Hep C Viral Load
8 weeks	CMP,CBC,INR
12 weeks	CMP,CBC,INR
16 weeks	CMP,CBC,INR
20 weeks	CMP,CBC,INR
24 weeks	CMP,CBC,INR
36 weeks	CMP,CBC,INR, Hep C Viral Load

(Chemistry panel must have creatinine, total/direct bilirubin, uric acid, ALT, AST)

Case Study: Who has priority for hepatitis C treatment and why?

- a. 62 y.o. male, previous IV Drug user, HCV Ab positive, HBeag Positive, HCV viral load: 26,000,000 iu/ml. Ultrasound shows heterogeneous echotexture and splenomegaly. Platelets are 56.
- b. 28 y.o. female, HCV Ab positive, HCV viral load: weak positive. Ultrasound shows homogenous echotexture of liver. ALT 70.
- c. 52 y.o female, needlestick injury, HCV Ab positive, HCV viral load: 2,220,000iu/ml, cryoglobulin screen: positive, Liver biopsy shows S2F3.
- d. 48 y.o. male, HCV Viral load: 15,000. Patient has cirrhosis and treated Hepatocellular carcinoma.

(Would love the answer to be Everyone!)

Case Study

Frank a 56 y.o. man with fatty liver disease (NAFLD), and cirrhosis suffers from depression. His family has noticed over the last couple days that he is not getting out of bed and is increasingly somnolent. While triaging the call the patient is oriented to self and place but not time. Family also endorses that he hasn't taken any medications the last few days.

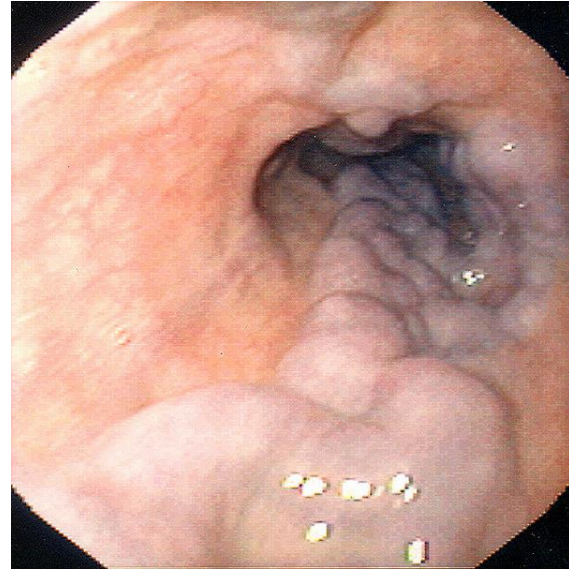
What do you do?



<http://www.healthadvice4life.com/wp-content/uploads/2012/09/Fatty-Liver-Disease.jpg>

Case Study: Esophageal Varices

Patient has an Endoscopy (EGD) showing small varices. No banding is done but the provider starts the patient on 20mg of nadolol. What are the next steps for nurses to advise patient?



Case Study: Esophageal Varices (Cont.)

The patient calls the following week and states his heart rate has been the following:

Date	Heart Rate
Monday	65
Tuesday	72
Wednesday	70
Thursday	75
Friday	62
Saturday	78
Sunday	67
Monday	66

What is the next step?

Case Study: Ascites

71 y.o. Female with NAFLD cirrhosis getting paracentesis q2 weeks. Creatinine 2.7, not on diuretics. Patient reports being on a low sodium diet. Upon further discussion “I don’t add any salt to anything but I love pickles, and canned soups are convenient.” What dietary tips would you advise?

Case Study: Cirrhosis

A patient has been cured of hepatitis C! They have cirrhosis based on labs and imaging. What is recommended for the patient?



Case Study: Cirrhosis (Cont.)

- Patient will need to continue getting labs and imaging every 6 months.
- Hepatitis C cure doesn't reverse cirrhosis
- Recommend Fibroscan one year after being cured to see if scarring has decreased at all.

Questions?



Next Session:

Transitions of Care



April 28th 2016

Summary

Charmian Casteel, RN

Primary Care Innovations Specialist

CareOregon



Thank you!