HEPATITIS C CLINICAL PATHWAY

Version 4.0
5/25/2003

Maurizio Bonacini, M.D.
California Pacific Medical Center
San Francisco, CA

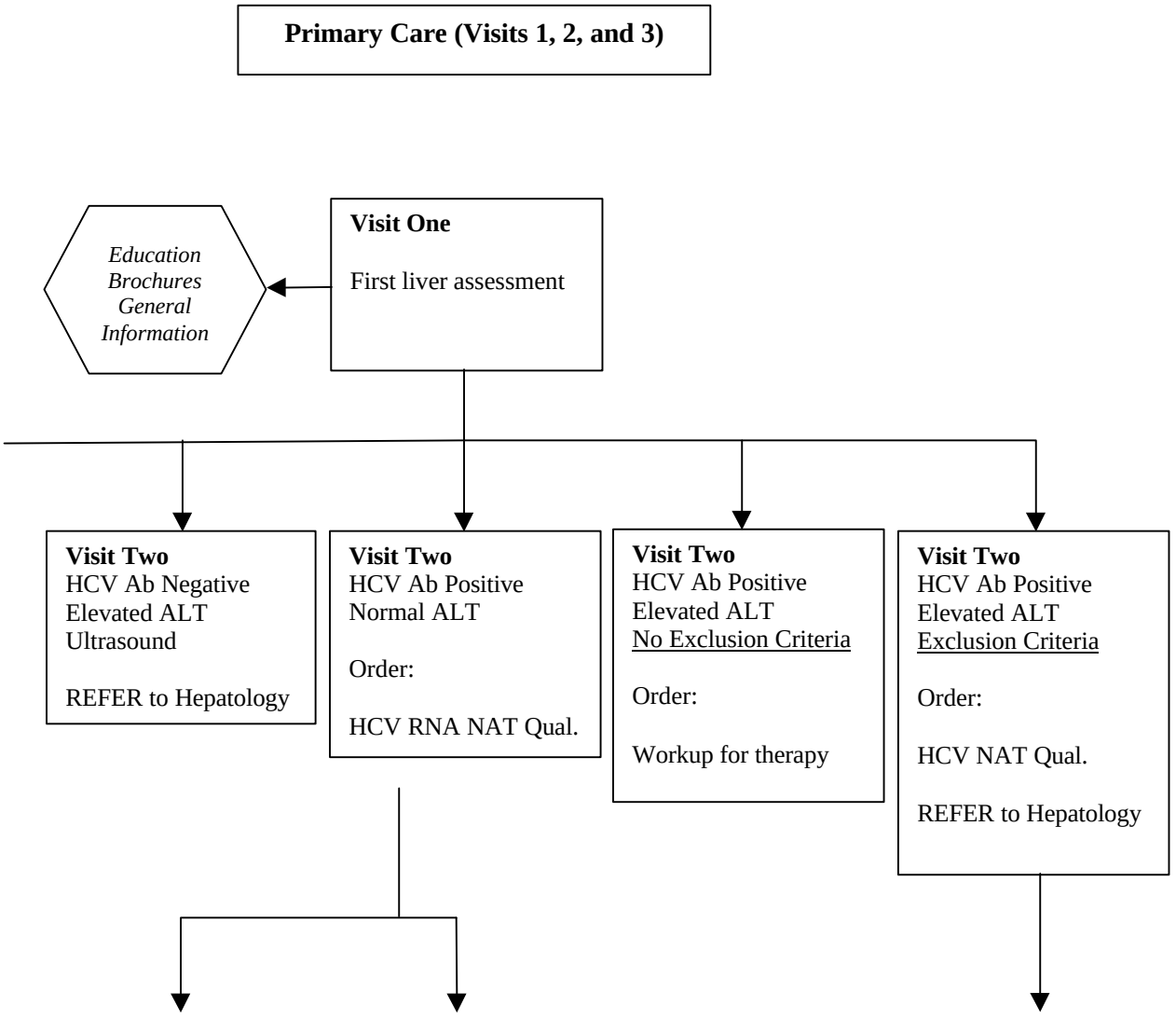
William Morris, M.D.
Physicians Medical Group,
Santa Cruz, CA

Vivek Huilgol, MD
Chief, Gastroenterology and Hepatology
Overton Brooks VA Medical Center,
Shreveport, Louisiana

Robert G. Gish, M.D
California Pacific Medical Center
San Francisco, CA

TABLE OF CONTENTS

Hepatitis C Clinical Pathway Overview



Positive	Negative	*Visit Three*
Further followup with ALT. If ALT abnormal, consider therapy	Repeat yearly X 2 years. If negative d/c followup No referral to Hepatology	*Hepatitis A and B vaccines, Pneumovax and Flu vaccines as appropriate*

Hepatitis C Clinical Pathway

Primary Care

Primary Care Visit One (h/o HCV or elevated Transaminases or Alkaline phosphatase)

1. Risk Criteria—Assess individuals for the presence or history of any of the following:

a. Transfusion of blood products prior to 1992. Y N

b. Injection illicit drug use: past or present, any number of injections, and subcutaneous or intravenous site. Y N

c. Unequivocal blood exposure on or through skin (or mucous membrane) for health care worker , combat casualty care, needle stick injury.

d. Sexual partner positive for HCV

e. Multiple sexual partners, past or present.

f. Hemodialysis.

g. Tattoo or body piercing.

h. Intranasal cocaine use, past or present.

2. Alcohol use:
   - -years daily (or nearly daily)
   - -average daily quantity
   - -last alcohol date:
   - -Binge drinking in the past: Y N

2. Past history of jaundice.
3. Ever tested positive for hepatitis B.
4. Ever tested positive for HIV.

To do:

1. Basic liver disease investigation:
   a. Anti-HCV antibody
   b. HBsAg

c. Anti-HBc
d. Anti-HBs
e. HAV Ab,
f. Globulin (TP – Alb) > 4 g/dL → ANA, SMA
g. Antinuclear antibody if female patient
h. Fe/TIBC, ferritin
i. Ceruloplasmin if younger than 50 years
j. Anti-mitochondrial antibody (AMA) if alkaline phosphatase > 1.5 ULN or if itching present
k. Cholesterol/Triglycerides
l. Abnormal fasting Glucose → Repeat FBS

2. Provide Hepatitis C education (See Hepatitis C Virus CPMC brochure).

Primary Care Visit Two

1. If the HCV antibody is **negative** with **elevated ALT** within 12 months, needs the work-up on page 4. If negative, obtain ultrasound and refer to Hepatology for possible biopsy (mainly to rule out liver steatosis/inflammation).

2. If the **HCV antibody is positive** with consistently **normal ALT**, order:

   (1) HCV NAT (nucleic acid testing; TMA, bDNA or PCR) qualitative [TMA or PCR] (i.e. result positive do quantitative test or negative: no need for quantitation),
   (2) If HCV RNA negative, Repeat yearly X 2 years by qualitative NAT. If still negative, consider HCV cure and d/c followup for HCV.
   (3) If HCV RNA positive, follow-up in Primary Care until: elevation or liver enzymes OR patient enters clinical study (CPMC research).

3. If the **HCV antibody is positive with elevated ALT**, assess CANDIDACY for therapy **(See Exclusion Criteria p.8)**. If appropriate treatment candidate, order the following:

   a. Liver biopsy
   b. HCV genotype
   c. HCV NAT quantitative
   d. CBC, Liver panel, Protime INR
   e. AFP
   f. HIV
   g. TSH
   h. Pregnancy Test in females
   i. Liver Ultrasound (UTZ) to: assess liver surface nodularity and r/o incidental mass> If UTZ positive for cirrhosis or nodule/mass, refer to hepatology

4. If HCV antibody is positive with elevated ALT but contraindications for treatment (**See Exclusion Criteria p.8)**, order:
    (1) HCV NAT quantitative
    (2) HIV Aby
    (3) Refer to Hepatology Clinic after consultation with appropriate specialists (p. 9).

Note: Some of the exclusions listed in p. 8 may still be considered for therapy but in the Specialist Clinic.

Primary Care Visit Three

1. If the HCV RNA by NAT is negative, Repeat yearly X 2 years. If still negative, consider HCV cure and d/c followup for HCV.

2. If the HCV NAT qualitative is positive, and the patient has exclusion criteria:

    a) -Referral to Local HCV Education and Support Group
    b) -Offer vaccination (Hep A, Hep B or Twinrix as appropriate according to serology) #
    c) -Note patients' questions/concerns after reading brochure from visit 1.
    d) -Refer to Hepatology

Vaccinate for hep A if Hep A antibody total is negative
Vaccinate for hep B if Hep B core antibody and hep B surface antibody are negative
If susceptible for both, vaccinate for both (Twinrix vaccine)

3. If the HCV NAT qualitative is positive, and the patient has no exclusion criteria, implement the following:

A. HCV Genotypes 1,4,6

a. Discuss risks and benefits of liver biopsy (Strongly recommended)
b. Liver biopsy by Radiology under Ultrasonographic guidance
c. Discuss therapy: - if Fibrosis score, F0 or F1, advocate expectant followup
    -If F2, F3, advocate therapy
    -If F4 (cirrhosis) advocate referral to Specialist Clinic

B. Genotypes 2,3

d. Discuss risks and benefits of liver biopsy (Optional)
e. If patient agrees, liver biopsy by Radiology under Ultrasonographic guidance
f. Discuss therapy: - if Fibrosis score, F0 or F1, advocate expectant followup
    -If F2, F3, advocate therapy
    -If F4 (cirrhosis) advocate referral to Specialist Clinic

4. Administer BDI-II (refer to psychiatry if Beck depression index > 14). (See page 8)

Clinical exclusion Criteria for HCV Treatment: *Document carefully*.

*** = May be treated in PC Clinic if improvement occurs**
**** = May be treated at Specialist level (GI/Hepatology/Infect. Dis.)**
***** = Absolute Contraindication to treatment**

1. Alcohol/drug use (6 months abstinence required for treatment). Stable methadone is OK. *

2. Severe depression (e.g. suicidal ideation), history of hospitalization for moderate to severe psychiatric disease or unstable psychiatric disease. BDI-II (Beck depression index > 20). (see page 8). *

3. Documented noncompliance with treatment (e.g. medications, clinic visits). *

4. Short life expectancy/severe comorbidity. ***

5. Age 65 years or older.**

6. Known advanced cirrhosis with clinical decompensation (e.g. any history of ascites, encephalopathy, variceal bleeding or SBP). ***

7. Pregnancy in females or Failure by male or female to use adequate birth control. ***

8. Any Anemias: work-up anemia prior to possible referral (examples of unsuitability for treatment include sickle cell disease or thalassemia). **

9. Inadequate social support, including inability to comply with parenteral medication. ***

10. Autoimmune disorder: **

    a. Non-organ specific, e.g. rheumatoid arthritis, SLE, Sjögren's syndrome, scleroderma, polymyositis, rheumatic fever.
    b. Organ specific, e.g. Myasthenia gravis, Grave's disease, thyroid disease, insulin-resistant diabetes, pernicious anemia, psoriasis, bullous pemphigoid, autoimmune hemolytic anemia, ITP, inflammatory bowel disease.

11. Moderate to Severe pulmonary disease (e.g. COPD, asthma). **

12. Mild to Moderate cardiac disease, further work-up is essential (e.g. Stress Test). **

13. Severe cardiac disease is an absolute contraindication. ***

Laboratory exclusion Criteria for HCV Treatment : **

1. Neutrophils < 1500 prior to therapy
2. Hb < 12 g% in men and <11 g% in females
3. Platelets < 100,000
4. Bilirubin >1.5 (except documented Gilbert's)
5. Positive autoimmune test: ANA, SMA, or AMA
6. Creatinine > ULN, Nephrology consult

Special clinical issues:

1. Mild to moderate **CARDIAC** disease, further work-up is essential (Cardiology clearance).

2. Moderate to Severe **PULMONARY** disease (Pulmonary clearance).

3. Mild to moderate depression (BDI score 14-20, 0 to 13 being normal), therapy at discretion of Primary care with monitoring. Other Psych disease and SEVERE depression, need further work-up and Psychiatry clearance.

4. **ANEMIA**: complete evaluation. Refer to Specialist Clinic for support with Procrit PRIOR to therapy.

5. ALL patients with **DIABETES** or **HTN** need ophthalmology exam to rule out retinopathy (interferon has been associated with retinopathy)

HCV treatment (HT) **Clinic**

HT Visit One

1. Review Liver biopsy (make sure no cirrhosis)

2. Review labs done in Primary Care Clinic and consider additional testing if appropriate (e.g. if liver biopsy indicates additional diagnosis), for exclusion of other liver diseases, such as:
   a. AAT deficiency, order Alpha-1 antitrypsin and phenotype.
   b. Autoimmune hepatitis or Overlap Syndrome, order ANA/AMA, Anti-smooth antibody (ASMA), {pANCA, anti-LKM-1 upon Hepatology consult].
   c. If Rheumatoid Factor positive, check cryoglobulins, U/A for protein.
   d. If Cryo positive, do panel to see if monoclonal: if monoclonal patient needs bone marrow biopsy with heme consult for lymphoma workup

3. Review Liver ultrasound (Refer to Hepatology is nodule/mass).

4. Ensure Hepatitis A and Hepatitis B vaccination have been started (see page 6).

5. Contraindications to treatment reviewed and documented (pages 7, 8).

6. Risks and benefits to treatment reviewed and discussed.

7. Document: ascites, encephalopathy, and classify as Child's A, B, or C.

Child-Turcotte-Pugh Classification

	1 point	2 points	3 points
Bilirubin (mg/dL)	<2	2-3	>3
Albumin (g/dL)	>3.5	2.8-3.5	<2.8
PT (sec prolonged)	1-3	4-6	>6
(INR)	<1.7	1.8-2.3	>2.3
Ascites	none	slight	moderate
Encephalopathy	none	1-2	3-4

Child-Turcotte-Pugh Class: A = 5-6 points
B = 7-9 points
C = 10-15 points

Note: No Primary Care PEG-Intron or PEGASYS treatment if score = 6 or above

HT Visit Two

(Baseline for Treatment Protocol)

a) Begin HCV combination therapy. Calculate by weight:

i. PEG-Intron 1.5 micrograms/Kg SQ injection WEEKLY
ii. Or PEGASYS 180 mcg per week

iii. Ribavirin 11 mg/Kg, round up to next multiple of 200 mg, orally DAILY

iv. Patients with genotype 2 and 3 may be treated for ONLY 24 weeks, and Ribavirin dosage may be 800 mg/day without weight-adjusted dosing.

b) Document baseline CBC-diff, CMP, TSH, HCV RNA viral load [quantitative NAT] **.

c) Obtain pregnancy test in females (Stat Urine HCG)

d) Schedule for Clinic in two weeks with CBC-diff, CMP.

= If cirrhosis by biopsy step-wise approach:
50 micrograms PEG-Intron/ week for 2 weeks (week 1 and 2)
or 90 mcg PEGASYS
100 micrograms PEG-Intron/ week for 2 weeks (week 3 and 4) if tolerated
or 120 PEGASYS
full dose (120-180 micrograms depending on weight) (week 1 and 2) if tolerated
180 mcg of PEGAYS

** do not repeat if done w/in 6 months

Treatment Protocol: HCV Clinic OR Primary Care Managers and Physicians

Week 2	Assess **Adverse Events (AE's**), CBC-diff, CMP.
Week 4	Assess AE's, CBC-diff, CMP, pregnancy test in females
Week 8	Assess AE's, CBC-diff, CMP, pregnancy test in females, BDI.
Week 12	Assess AE's, CBC-diff, CMP, TSH, pregnancy test in females, BDI. **If BDI score is increased by at least 2 points, add antidepressant (SSRI) therapy (Refer to Adjunct Therapy for the Clinician).** **HCV RNA: if positive, consider stopping therapy.**
Week 16	Assess AE's, CBC-diff, CMP, pregnancy test in females.
Week 20	Assess AE's, CBC-diff, CMP, pregnancy test in females.
Week 24	Assess AE's, CBC-diff, CMP, TSH, pregnancy test in females, HCV NAT qualitative, Alpha feto protein, liver ultrasound Determine functional status with BDI. *Patients with genotypes 2 and 3, stop therapy at 24 weeks AND schedule F/U Clinic visit in 6 months. *Patients with genotype 1 and positive HCV NAT qualitative, stop therapy at 24 weeks AND schedule F/U Clinic visit in 6 months. *Patients with genotype 1 and negative HCV NAT qualitative, continue therapy for a total of 48 weeks.
Week 28	Assess AE's, CBC-diff, CMP, pregnancy test in females.
Week 32	Assess AE's, CBC-diff, CMP, pregnancy test in females.
Week 36	Assess AE's, CBC-diff, CMP, pregnancy test in females.
Week 40	Assess AE's, CBC-diff, CMP, pregnancy test in females.
Week 44	Assess AE's, CBC-diff, CMP, pregnancy test in females.
Week 48	Assess AE's, CBC-diff, CMP, pregnancy test in females, HCV NAT qualitative, Alpha feto protein, liver ultrasound. Determine functional status with BDI. Schedule F/U Clinic visit in 6 months.

Treatment of Side Effects

First, see below BLACK BOX WARNINGS for Interferon (Intron) and Ribavirin (Rebetol). Similar read for PEGAYS and COPEGUS

CONTRAINDICATIONS AND WARNINGS

Combination REBETOL/INTRON A therapy is contraindicated in women who are pregnant and in the male partners of women who are pregnant. Extreme care must be taken to avoid pregnancy during therapy and for 6 months after completion of treatment in female patients, and in female partners of male patients who are taking combination REBETOL/INTRON A therapy. Women of childbearing potential and men must use two reliable forms of effective contraception during treatment and during the 6-month post treatment follow-up period. Significant teratogenic and/or embryocidal effects have been demonstrated for ribavirin in all animal species studied. See CONTRAINDICATIONS and WARNINGS. REBETOL monotherapy is not effective for the treatment of chronic hepatitis C and should not be used for this indication. See WARNINGS .

Follow-up Protocol

1. Pregnancy tests in females for 6 months post therapy.

2. Monthly assessment of adverse events (AEs).

DOSE REDUCTION AND/OR DISCONTINUATION

(See "Use of Growth Factors, p. 15 prior to dose reduction and/or discontinuation)

RIBAVIRIN (Component of Combination Therapy)

Patients with cardiac disease:

REDUCE dose if Hb decrease >2g/dL during any 4 week period.
DISCONTINUE if Hb <12g/dL after 4 weeks on reduced dose.

Patients without cardiac disease:

REDUCE dose if Hb <10g/dL.
DISCONTINUE if Hb <8.5g/dL.

INTERFERON (Monotherapy or part of Combination Therapy)
(All Patients)

WBC:

REDUCE dose if WBC <1.5.
DISCONTINUE if WBC <1.0.

Neutrophil Count:

REDUCE dose if Neutrophil Count <0.75.
DISCONTINUE dose if Neutrophil Count <0.5.

Platelet Count:

REDUCE dose if Platelet Count <50K.
DISCONTINUE dose if Platelet Count <30K.

USE OF GROWTH FACTORS IN THE TREATMENT OF HCV

OBJECTIVES:

1. Maintain patients on the therapeutic doses of interferon and ribavirin.
2. Avoid dose reductions or discontinuation.
3. Improve side effects, e.g. fatigue.
4. Endpoint: Increase sustained virologic response (SVR).

GUIDELINES FOR USE:

1. Epogen® Procrit®: If Hb <11.5 g/dL or Hb decrease >2.5 g/dL from base line.
2. Neupogen®: If WBC <2.5 or ANC <1.0 or WBC decrease >50% and/or ANC decrease >50% from base line.

LABS TO FOLLOW:

- Once growth factor therapy is initiated, then CBC should be obtained weekly until achieving maintenance dosing.
- Once anemia is noted, the physiopathology needs to be identified: Bone marrow suppression (low reticulocyte count) vs. hemolysis (elevated LDH, decreased haptoglobin) or both.
- Labs ordered: Haptoglobin, LDH, and Reticulocyte count.
- In patients with baseline anemia or low MCV, Hemoglobin electrophoresis may be ordered.
- In patients with gross evidence of hemolysis, dose reduction for ribavirin may be considered more appropriate than if no hemolysis parameters are noted.

MEDICATIONS USED:

1. Procrit® or Epogen®: Epoetin Alfa recombinant.
   - Dose Regimen A:
     - 40,000 units SQ once a week.
     - Dose is then adjusted once therapeutic response is achieved.
     - Dose is reduced by 25% weekly until reaching maintenance dose required to maintain Hb >10 g/dL.
   - Dose Regimen B:
     - 10,000 units three times per week (100-150 units/kg)
     - Dose is reduced gradually once therapeutic response is noted.
2. Neupogen®: Filgrastim (G-CSF)
   - Dose:
     - 300 mcg SQ three times per week (5mcg/kg)
     - Dose can be increased to 300 mcg/day.
     - Once therapeutic response is noted, then does can be reduced to achieve maintenance dose and maintain WBC >1.5 and ANC > 0.75.

Note: Growth factors can still be used in combination with dose reduction guidelines for interferon and ribavirin.

ADJUNCT THERAPY FOR THE CLINICIAN

Condition	Therapy Options
Myalgia and flu-like symptoms (common with initial Interferon)	Tylenol (acetaminophen) 325-650 mg one hour before **first** injection, 325-650 mg one hour before **second** injection, 325-650 mg one hour before therapy for each subsequent dose for the **first four weeks, then as needed only.** Vioxx or Celebrex can also be useful
Headache	Same as above If not relieved, Tylenol #3, If still not relieved, Neurontin (gabapentin) (very effective) start at 100 mg qhs up to 1200 mg qd (Consider neurologist consult if high dose needed)
Fever	Tylenol (acetaminophen) 325-650 mg q6-8h prn – no more than 2.5 grams per day.
Anemia	Consider Epogen (epoetin alfa) and/or Neupogen (filgrastim) for anemia/leukopenia in consult with hematologist. See Dose Reduction (page 14).
Fatigue (HCV or therapy induced)	Ritalin (methylphenidate) 5 mg am and 5 mg noon; can use up to 10 mg am and 10 mg noon (Caution: substance abuse relapse) [Schedule II]. **Check CBC and/or TSH.
Alopecia	Nioxin shampoo (Must be started BEFORE initiating combination therapy if patient is concerned about possible hair loss).
Insomnia	Trazodone 50 mg qhs or Ambien (zolpidem) 5-10mg at bedtime.
Irritability/anxiety, Confusion, and/or MILD depression	Zoloft (sertraline)/Paxil (paroxetine)/Prozac (fluoxetine) or Wellbutrin (bupropion). Start low dose a month BEFORE initiating anti-HCV therapy and confirm efficacy via spouse or partner [Effects seen usually after two weeks of therapy]. **Note:** Confusion may be a manifestation of occult infection and/or hepatic encephalopathy and therefore need further urgent management.

MODERATE psychiatric Disease (with Psychiatrist)	Buspar (buspirone) or Celexa (citalopram) for anxious depression. Effexor XR (venlafaxine) for flat depression. Elavil (amitriptyline), Desyrel (trazodone) for sleep. Wellbutrin (bupropion) is especially flat depression (take in a.m., stimulatory).
Impotence	Discuss with physician.
Diarrhea	Kaopectate (attapulgite) 15-30 ml after each loose stool or every 2 hours (up to 8 times a day); Imodium (loperamide) 2 mg capsules – 4 mg initially, then one after each loose stool (up to 16 mg per day); Lomotil (atropine/diphenoxylate) 1-2 tablets after each loose stool (up to 8 per day).
Nausea/vomiting	Compazine (prochlorperazine) 25 mg supp. 1 per rectum q12h prn; Phenergan (promethazine) inj. 12.5-25 mg IM/IV q4-6h prn or 25 mg tab 1-2 tabs po q4h.

SIDE EFFECTS MODULE FOR THE CLINICIAN

A number of side effects are associated with the treatment of HCV. This module is intended to inform the clinician about these side effects and possible causes. **Refer to Dose Reduction, p.13 and Adjunct Therapy, p. 15-16 for treatment of side effects.** This module is a guide to possible causes of symptoms and does not contain every side effect. All clinicians are encouraged to consult the medical literature and/or consult the hepatologist.

Common Side Effects of Alpha Interferon

Influenza-like	Fatigue, fever, myalgia, malaise, poor appetite, tachycardia, chills, headache, and arthralgias.
Neuropsychiatric	Apathy, irritability, mood changes, insomnia, cognitive changes.
Miscellaneous	Diarrhea, nausea, abdominal pain, back pain, pruritus. Weight loss (up to 10%) is common. Anything >10% needs investigation.
Laboratory	Decrease in granulocytes, platelet counts, and red blood cell counts, increase in serum triglyceride concentrations, proteinuria, increase in serum alanine and aspartate aminotransferase.

Serious Adverse Events Reported with Alpha Interferon Therapy (Prompt assessment and intervention may be required)

Neuropsychiatric	Psychosis, depression/suicide, delirium, confusion, extrapyramidal-ataxia, paresthesia, seizures, substance abuse relapses.
Immune disorders	Autoimmune thyroid disease, autoimmune hepatitis, systemic lupus erythematosis, primary biliary cirrhosis, septicemia, graft rejection.
Skin	Psoriasis, erythema multiforme.
Systemic	Hepatic decompensation, bleeding, cardiac arrhythmias, sudden death, dilated cardiomyopathy, hypotension, acute renal failure.
Other	Retinopathy, hearing loss, pulmonary interstitial fibrosis.
Laboratory	Severe Granulocytopenia, thrombocytopenia, anemia, hyperthyroidism, hypothyroidism.

Common Side Effects of Ribavirin Therapy

-Cough, dyspnea, rash, pruritis, nausea, insomnia, dyspepsia, anorexia and alopecia.

- Hemolytic anemia (leads to dose reduction in 7-10% of patient) The hemoglobin (Hb) decrease from pretreatment levels was 2 to 3 gm/dl, and usually occurs within the first 4 weeks of treatment.

Teratogenic: DO NOT administer to pregnant women, women of conceiving age and their male partners unless TWO contraceptive methods.
Emphasize to men that their partner's fetus could have birth defects if conceived while he is on therapy or 6 month post-therapy.

McHutchinson, J, Poynard, T. Combination Therapy with Interferon Plus Ribavirin for Initial Treatment of Chronic Hepatitis C. Seminars in Liver Disease 1999;19:57-65

*Dusheiko, G., Side Effects of Alpha Interferon in Chronic Hepatitis C, Hepatology 1997; 26(Suppl 1):112S-121S

SIDE EFFECTS MODULE FOR THE PATIENT

Common Side Effects	Things to do
Flu-like symptoms muscle aches, fever, chills, headache	Take pain relievers as prescribed by your doctor. Drink a lot of clear fluids each day. Keep extra blankets and clothes near bed to manage the chills. Give your Interferon injections at bedtime to sleep through symptoms.

You may take Tylenol 325 mg 1-2 tabs every 4-6 hours (do not take more than 8 tabs a day) for the first one to two weeks of Interferon therapy only.

Tylenol 325-650 mg one hour before **first** injection,
Tylenol 325-650 mg one hour before **second** injection,
Tylenol 325-650 mg one hour before each subsequent dose for the **first two weeks only.**

You may take Tylenol Extra-strength (500mg tab) 1-2 tabs for headache. Talk with your doctor if headaches continue.

NSAIDS (nonsteroidal anti-inflammatory drugs) can also be useful. **Examples include** aspirin (or aspirin-containing medicines), naproxen (Aleve, Anaprox, Naprosyn, Naprelan), ibuprofen (Advil, Motrin), indomethacin (Indocin), ketoprofen (Orudis).

Tiredness/fatigue	Rest as much as possible. Drink plenty of water and other nutritional fluids (10-16 glasses a day). Get light exercise (walking and stretching). Change work schedule, if possible. Get plenty of rest. You may take Diphenhydramine (Benadryl) 25-50 mg. at bedtime for sleep.
Irritability, depression, anxiety	Seek help from support groups. Try relaxation techniques. Find ways to laugh. Call your Doctor for feelings of depression that last longer than 1-2 days.
Loss of appetite/ weight loss	Eat small frequent meals even if you have no appetite. Treat food as medicine you must take to get healthy. In addition to water, drink clear juices.

	Brush teeth often to help eliminate metallic taste in your mouth. You may take Ensure or Boost as a food supplement. Inform your doctor if you have lost >10% body weight.
Nausea and diarrhea	Take over-the-counter medication for nausea/diarrhea. Avoid trigger foods and odors. Keep water and crackers near bedside for nausea and dry mouth. Try popsicles, dry toast or crackers. Eat small frequent meals. You may take Kaopectate 1-2 tablespoons after each loose stool or every 2 hours (up to 8 times a day).
Mild hair loss	Style hair in a fashion to make it fuller (hair will grow back after therapy finishes). Use scarves; wear hats and/or hair extensions. Do not over-wash or over-dry hair. Avoid sun exposure and hair dye. You may use Nioxin shampoo before you start the injections if hair loss is a potential concern for you.
Dizziness	Stand up slowly. Drink plenty of water every day.
Skin problems, **injection site reactions**, **rash, itching and dry skin**	Use lotions immediately after bathing. Rotate injection sites. Apply ice pack to injection site for a few minutes prior to injection. Use sunscreen lotion. Drink 10 or more glasses of water a day.

Call your doctor immediately if you have any of these side effects:

Very slow or fast heartbeat	Chest pain
Shortness of breath	Blue fingernails or lips
Sore throat	Fever
Depression	Urinary tract infection

Blurred vision, loss of vision, eye pain, or light sensitivity
Numbness or tingling in the hands or feet
Weight loss >10%