NHS
Tayside

TAYSIDE HEPATITIS C VIRUS (HCV) MANAGED CLINICAL NETWORK

Clinical Guidelines

July 2008

SECTION 1 : AIMS

Remit of the Guidelines

This guideline provides evidence-based recommendations covering all stages of the patient care pathway; screening, testing, diagnosis, referral, treatment, care and follow up of patients with, or exposed to Hepatitis C Virus (HCV) infection.

Aims of Management Guidelines

- To improve communication between health care professionals caring for clients/patients with HCV
- To identify patients/clients who are infected with HCV
- To develop pathways of care to increase the offer of HCV testing in a range of clinical settings
- To standardise services provided in primary and secondary care
- To identify patients suitable for anti-viral treatment
- To monitor the progress of clients/patients diagnosed with HCV
- To ensure that local practice is in line with Scottish intercollegiate Guidelines Network (SIGN) Guidelines for the Management of hepatitis c http://www.sign.ac.uk/pdf/sign92.pdf
- To meet outcomes of Hepatitis C Action Plan

SECTION 2: HCV TESTING

National and international guidelines recommend that individuals who have an excess risk of being infected and might benefit from knowing their HCV status should be offered a test. This recommendation is based upon the need to diagnose an often silent infection, allowing the initiation of prompt antiviral treatment if appropriate (SIGN, 2006)

The following groups should be tested for HCV:

- Blood/tissue donors
- Patients on haemodialysis
- Healthcare workers who intend to pursue a career in a speciality that requires them to perform exposure prone procedures

The following groups should be offered an HCV test:

- Patients with an otherwise unexplained persistently elevated alanine aminotransferase
- People with a history of drug use
- People who are human immunodeficiency virus (HIV) positive
- Recipients of blood clotting factor components before September 1991 and organ/tissue transplants in the UK before 1992
- Children whose mother is known to be infected with HCV
- Healthcare workers following percutaneous or mucous membrane exposure to blood which is, or is suspected to be, infected with HCV
- People who have received medical or dental treatment in countries where HCV is common and infection control may be poor
- People who have had tattoos or body piercing in circumstances where infection control procedure is, or is suspected to be sub optimal
- People who have had a sexual partner/household contact who is HCV infected

Description of HCV Tests

Diagnostic tests for HCV first became available in 1989. Since then the newer generation tests have increased in sensitivity and specificity. The diagnosis of HCV is a two-stage process. Initial screening tests are available which detect the presence of HCV antibodies. The presence of HCV antibody reflects current or previous infection. Active virus infection is confirmed by testing plasma (from a purple EDTA vacutainer) using the Polymerase chain reaction (PCR) test. This detects the presence of HCV RNA and is required to determine if there is a chronic infection .

Testing for antibodies can be carried out by either taking venous blood tests or oral fluid testing kits. Blood tests are the gold standard and should be used in preference to oral tests as the sensitivity and specificity of oral tests are lower than blood tests

Recommendations for testing are:

- Diagnostic testing for HCV should be performed on serum or plasma where possible
- Following an isolated acute percutaneous exposure to blood infected, or strongly suspected of being infected, with HCV, healthcare workers will be offered HCV RNA testing at 6, and 12 weeks and HCV antibody testing and 12 and 24 weeks following established OHSAS protocols. (Note, NHSD Tayside BBV Infection control policy which is available in the infection control section of the intranet, includes guidance on minimising and managing exposures to blood).
- If acute HCV infection is suspected (for example a patient at risk of HCV presenting with jaundice) or if the patient is immuocomprimised then HCV RNA in addition to HCV antibody testing should be considered (SIGN 2006)

NAME	DESCRIPTION	RESULTS	LABORATORY
HCV Antibody test	Blood is tested for antibodies to the hepatitis C virus using enzyme-linked immunosorbent assay (ELISA). This test has a 99% specificity	Positive results are verified with supplemental tests (2nd Elisa and PCR) Positive results indicated current or past infection. Negative result – No further evaluation required, unless recent exposure is suspected, in which case retest 12 weeks post exposure	Send venous blood to Microbiology in yellow top container
HCV RNA	Polymerase chain reaction (PCR) test determines the presence of HCV RNA in the serum	PCR positive result in client who is antibody positive suggests active infection PCR negative results can indicate resolved infection	Send venous blood to Microbiology in purple top container (EDTA)

Health care professionals who will offer testing

Providing necessary training has been undertaken and there is a suitable environment, the health professionals who may offer this service include:

- General Practitioners
- Practice Nurses
- District Nurses
- Drug workers
- Prison Healthcare Workers
- Needle Exchange Workers
- Needle Exchange Pharmacists
- Secondary Care Medical and Nursing Staff

Criteria for testing by staff

Before testing is carried out the health care professional must ensure that:

- They have received the necessary education and training
- They have access to Health Professionals education material and patient information
- There is a room/space available where a confidential conversation can occur
- They have access to testing equipment
- They have received training in testing procedures
- A pre-test discussion has taken place which will include implications of positive and negative tests
- There is a mechanism in place to report back results to the patient/client
- There is a mechanism in place to organise referral to the specialist centre

SECTION 3: POST TEST ADVICE AND GUIDANCE

Prevention of secondary transmission

Secondary transmission is defined as the onward transmission of infection from individuals who are HCV infected. Observational studies indicate that there is a very small risk of people with diagnosed HCV infection transmitting infection to their family or close contacts and sexual partners. Cohort studies of couples discordant for HCV infection indicated an HCV incidence of 0-2 per 1,000 years of sexual contact (SIGN 2006)

Transmission through sexual and household contact

- After being advised of the low risk of HCV being transmitted sexually, individuals infected with HCV should consider using condoms for sexual intercourse
- Individuals co-infected with HIV/HCV should be advised to practice safe sex and use condoms
- Individuals infected with HCV should be advised to avoid activities which could result in percutaneous or mucous membrane exposure of their blood to others such as the sharing of razors or toothbrushes

Transmission through injecting drug use

- Injecting drug users known to be infected with HCV should be given advice on how they can prevent transmission of infection to other injecting drug users

Transmission between healthcare workers and patients

- Standard infection control precautions against blood borne virus transmission should be undertaken by all healthcare workers regardless of the patients known or suspected infective status

Any healthcare worker sustaining a needle stick injury should follow guidance from NHS Tayside occupational health department. Healthcare workers sustaining needle stick injuries from HCV infected sources should be advised that:

- The overall risk of transmission is probably less than 2% and may be much lower
- The risk is higher from deep injuries and from blood-filled needles, transmission from solid needles is very unlikely

Health care workers who are aware they are HCV RNA positive should not undertake exposure prone procedures

Diagnosis & management of antibody negative individuals

The individual should:

- Receive a post test discussion with healthcare professional regarding result and accuracy of testing.
- Be provided with harm reduction advice
- Be informed that they do not require a retest unless they continue with high risk practices (eg, sharing needles).
- Be informed that if recent exposure has occurred that they should be retested in 3 and 6 months
- Be vaccinated against HBV (without prior immunity)

Diagnosis & management of antibody positive individuals

The individual should:

- Receive a post test discussion with a healthcare professional regarding result and accuracy of testing..
- Be appropriately informed about the nature of the hepatitis C infection. Provided with an information sheet (download from hepcscotland.co.uk) and given contact number of support group Body Positive (01382 226860)
- Be advised to drink less than 2 units of alcohol per day
- Be vaccinated against HAV and HBV (without prior immunity).
- Be informed that supplementary blood tests should be carried out
- Have blood taken for HCV PCR, FBC, coagulation, U&Es, liver function tests and liver screen

Management of antibody positive PCR negative individuals

- If PCR negative on at least 2 occasions but remain antibody positive will be appropriately informed about hepatitis C, that it is very unlikely that they will develop significant liver disease and are not infectious.

Management of antibody positive, PCR positive individual

- Receive a discussion with a Health Care Professional regarding whether referral to specialist service for assessment and treatment is appropriate.

- If individual does not consider HCV to be a priority and does not wish regular follow up, information to be given on support services

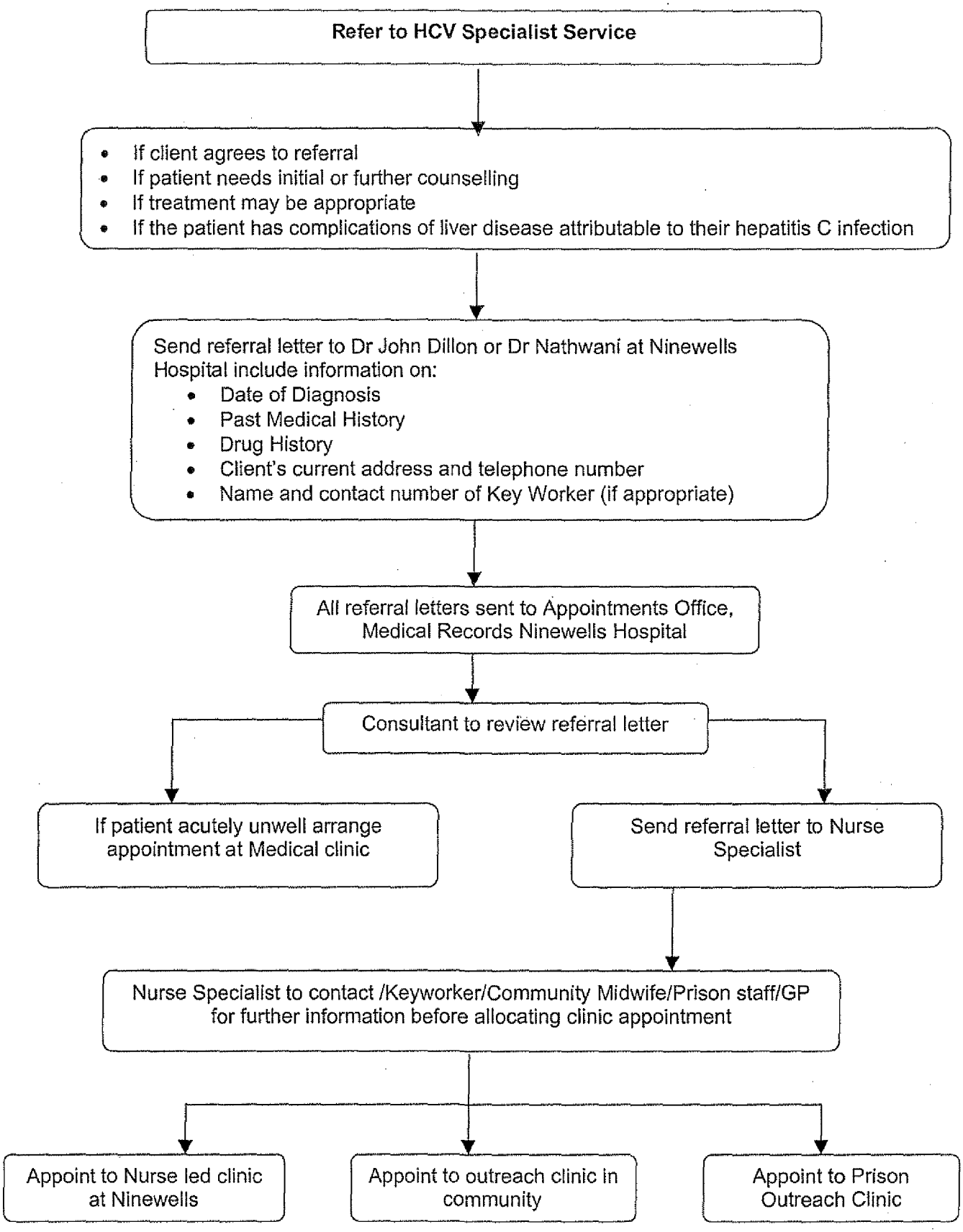
SECTION 4: REFERRAL TO SPECIALIST SERVICES

Referral to specialist care should be considered for all patients with active HCV infection and not restricted to potential candidates for antiviral therapy. Specialist clinics are often a source of information for patients and relatives, including health promotion and methods of avoiding secondary transmission of the virus (SIGN, 2006)

Categories of patients should be considered for referral to specialist services:

- Those patients for whom treatment of their hepatitis C may be appropriate
- Patients needing initial or further counselling that cannot be provided from the resources of the area in which they were diagnosed
- Patients with complications of liver disease attributable to their hepatitis C infection

A specialist Hepatitis C Clinic is coordinated from Ninewells Hospital. The Consultants in Charge of HCV Specialised Services are Dr John Dillon Consultant Physician in Hepatology and Gastroenterology and Professor Dilip Nathwani Consultant Physician in Infection Diseases
All referrals to be addressed to the Consultants at Ninewells Hospital and letter sent to Appointment Office, Medical Records, Ninewells Hospital.


Refer to HCV Specialist Service
If client agrees to referral
If patient needs initial or further counselling
If treatment may be appropriate
If the patient has complications of liver disease attributable to their hepatitis C infection
Send referral letter to Dr John Dillon or Dr Nathwani at Ninewells Hospital include information on:
Date of Diagnosis
Past Medical History
Drug History
Client's current address and telephone number
Name and contact number of Key Worker (if appropriate)
All referral letters sent to Appointments Office, Medical Records Ninewells Hospital
Consultant to review referral letter
If patient acutely unwell arrange appointment at Medical clinic
Send referral letter to Nurse Specialist
Nurse Specialist to contact /Keyworker/Community Midwife/Prison staff/GP for further information before allocating clinic appointment
Appoint to Nurse led clinic at Ninewells
Appoint to outreach clinic in community
Appoint to Prison Outreach Clinic

SECTION 5 :MANAGEMENT WITHIN SPECIALIST SERVICE

Assessment of new patients at first visit

New patients will be assessed by the Clinical Nurse Specialist in Gastroenterology at their first visit.. The information will then be entered into the Hepatitis C database.

The Nurse Specialist will review results and/or arrange blood tests (Table 3), will arrange Liver ultrasound and Medical Follow up for 3 months.

If patient requests or if liver complications are detected, Medical Staff will review the patient at the first visit Medical Staff (if available) or an urgent appointment for medical clinic will be arranged

Patient assessment will include:

- Previous and current health
- Drug and alcohol history
- Evidence for liver disease and other serious disorders
- Details of potential sources for HCV infection
- Natural History of the illness

The patient will be provided with additional information on:

- The nature of the infection, potential sources of infection and the natural history of the illness
- The investigations required, plan for follow up and possible treatment options
- Measures to prevent spread of the infection
- The benefits of reducing alcohol intake to less than 2 units of alcohol per day
- The benefits of healthy eating
- Contacting their GP to discuss vaccination against HAV and HBV as necessary.

Investigations carried out first visit

Department	Investigation
Haematology	Blood test for: Full blood count Coagulation screen
Biochemistry	Blood tests for Liver function tests including GGT Urea & Electrolytes Ferritin Alpha-1-antitrysin Alpha-fetoprotein Caeruloplasmin (if <aged 40years) Thyroid function tests
Virology	Blood tests for Hepatitis B antibodies (anti-HBs) if vaccinated and HbsAg if unvaccinated Qualitative PCR for HCV RNA HIV (if appropriate) HCV genotype (in patients being considered for treatment)
Immunology	Auto-antibodies Serum immunoglobulins
Radiology	Abdominal Liver ultrasound

Table 3: Investigations reviewed/carried out at first clinic attendance

Clinical Follow up within Specialist Service

Management of PCR negative individual

- If PCR negative on at least 2 occasions, but remain antibody positive will be appropriately informed about hepatitis C and informed that it is very unlikely that they will develop significant liver disease and are not infectious.
- If they have normal LFTS they will be discharged to the care of their GP
- If they have abnormal LFTs, these patients will be investigated further by specialist services.

Management of acute hepatitis C

Acute hepatitis C is usually asymptomatic. Laboratory diagnosis should start with testing for HCV antibodies but in early cases HCV RNA may be the only marker of infection. Spontaneous recovery occurs in 30-50% of patients with symptomatic infection, usually within three months of diagnosis. This is most common in females with an icteric illness.

- Patients with acute HCV infection require clinical and laboratory monitoring for the initial three to six months following diagnosis as they will often have a self limiting illness.
- Treatment should start six months after diagnosis of acute hepatitis C if the infection has not resolved spontaneously
- Patients should be treated with pegylated interferon alfa therapy for 24 weeks irrespective of genotype.

Management of HCV PCR positive patient

- The patient will be considered for combination treatment provided they fulfil the inclusion/exclusion criteria.
- The use of combination Interferon/Ribavirin will be managed according to the treatment Guidelines.
- If patient not suitable for treatment or decline treatment they will be placed on yearly follow up at the hepatitis C clinic.

Management of PCR positive patient with hepatic cirrhosis

- The patient will be individually assessed by a Hepatologist for consideration of treatment or hepatic transplantation.

- If neither is deemed suitable or necessary, they will be placed on 6 monthly follow up, and on the hepatoma-screening programme which includes the measurement of alpha fetoprotein and ultrasound examination should take place at six monthly intervals

Management of the patient post Interferon treatment

- If the patient remains HCV PCR positive or relapse after treatment, they will be followed up at yearly intervals

- If the patient is PCR negative on 1 occasion, greater than 6 months after the cessation of treatment, they will be discharged from the clinic.

- Contact information of the patient will be kept and the patient will be informed they will be contacted if needed pending the outcome of long term follow up studies

SECTION 6: HCV TREATMENT

Information on current treatment

The current recommended therapy for chronic HCV is a combination of Pegylated Alfa Interferon and Ribavirin. Response to therapy is judged by clearance of virus (PCR NEG). Sustained Viral Response (SVR) is measured by a negative HCV PCR six months after therapy is discontinued. SVRs can vary from 30% to 80%.

Response to treatment is affected by

- HCV genotype
- Viral load
- Sex and age of patient
- Degree of fibrosis
- Compliance to treatment

Table 4: Results from randomised controlled trial of therapy with combination pegylated interferon and ribavirin in naïve patients (Wong, 2005, in SIGN, 2006)

Study	Results	Genotype 1		Genotype 2/3	
		No. Treated	SVR	No. treated	SVR
Manns et al, 2001	Peg-IFN alfa-2b 1.5 (4 wk) □.5 ug/kg/wk (44 wk) + ribavirin (1000mg <75 kg, 1200 mg ≥75 kg) X 48 wk	349	34%	153	80%
	Peg-IFN alfa-2b 1.5 ug/kg/wk + ribavirin (800 mg/dly) X 48 wk	348	42%	147	82%
Fried et al, 2002	Peg-IFN alfa-2a 180 ug/wk + ribavirin (1000 mg <75 kg, 1200 mg ≥75 kg) X 48 wk	298	46%	140	76%
Hadziyannis et al, 2004	Peg-IFN alfa-2a 180 ug/wk + ribavirin (800 mg/dly) X 24 wk	101	29%	106	78%
	Peg-IFN alfa-2a 180 ug/wk + ribavirin (1000 mg <75 kg, 1200 mg ≥75 kg) X 24 wk	118	41%	162	78%
	Peg-IFN alfa-2a 180 ug/wk + ribavirin (800 mg/dly) X 48 wk	250	40%	111	73%
	Peg-IFN alfa-2a 180 ug/wk + ribavirin (1000 mg <75 kg, 1200 mg ≥kg) X 48 wk	271	51%	165	77%

Pegylated alfa interferons require subcutaneous injection once per week and twice daily oral Ribavirin tablets

Response to treatment

Response to treatment is measured at various points. Table 5 lists terms used when assessing response to treatment

Rapid Viral Response (RVR)	PCR negative 4 weeks after starting treatment
Early viral Reponses (EVR)	PCR negative 12 weeks after starting treatment
Partial response (PR)	PCR positive at 12 weeks, a reduction of viral load of more than 2 logs
Non-response (NR)	PCR positive at 12 or 24 weeks
End of Treatment Response (ETR)	PCR negative for HCV-RNA at the end of treatment
Relapse (R)	ETR, followed by HCV-RNA positive within six months
Sustained viral response (SVR)	HCV-RNA negative at least six months after end of treatment

Treatment duration

Genotype 1,4, 5 and 6

- Patients with genotype 1,4.5 and 6 infection should be treated with pegylated interferon and ribavirin for 48 weeks.
- Patients should be tested for HCV RNA at weeks 4 and 12
- If they remain positive or do not have a 2 log drop in viral load at 12 weeks then treatment will be discontinued
- Patients who have had a 2 log drop in viral load at 12 weeks should have HCV RNA rechecked at week 24. If they remain HCV RNA positive treatment will be discontinued
- There is ongoing research into duration of treatment for patients with genotype 1 infection and a low viral load, ≤600,000 IU/ml. Patients who have a rapid response (HCV RNA negative at 4 weeks) after discussion with patient treatment may be considered to be reduced to 24 weeks duration (Zeuzem, S. 2006)

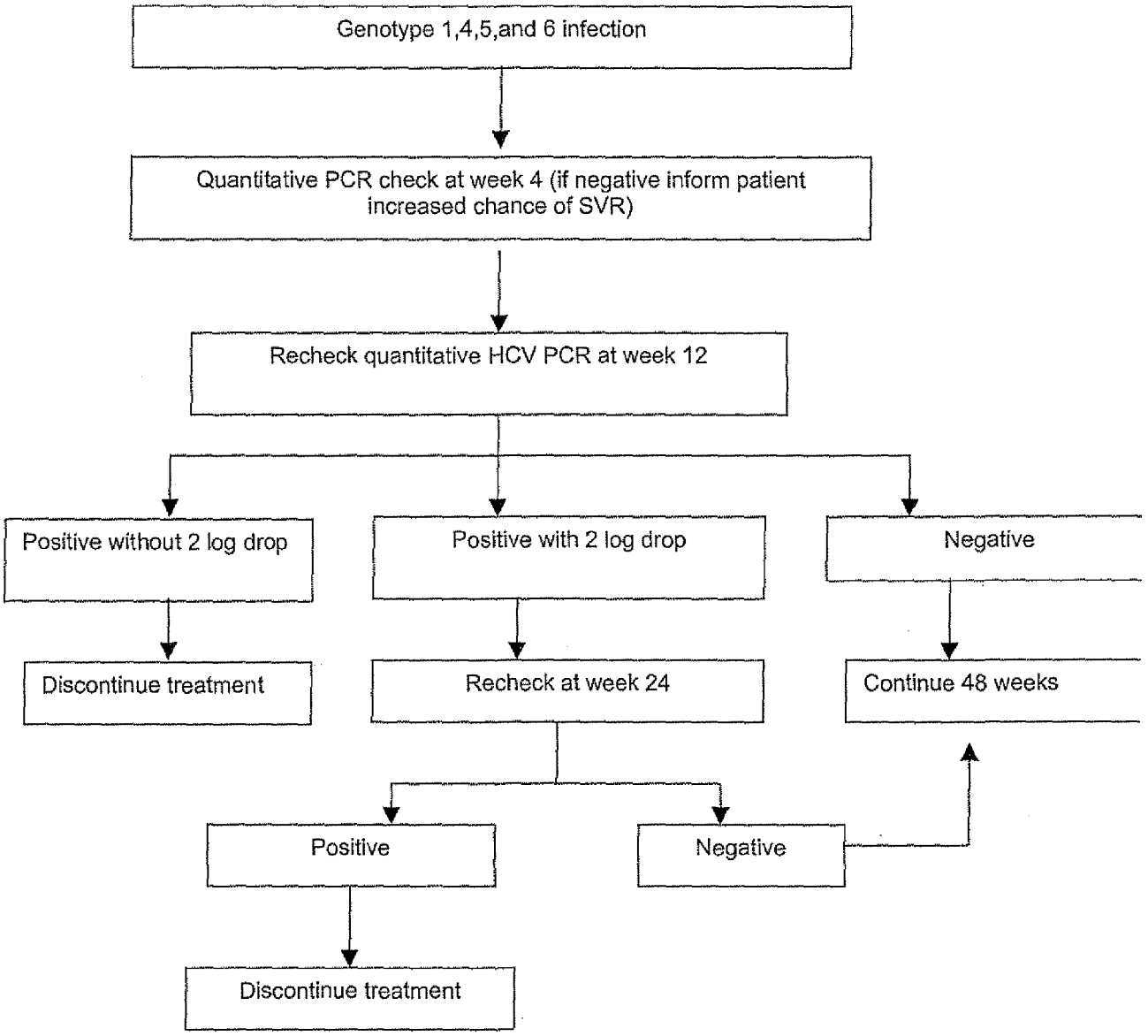
Genotype 2 or 3

- Patients with genotype 2 or 3 infection should be treated with pegylated interferon

and ribavirin for 24 weeks

- Patients should have an HCV RNA test performed at 4 weeks after commencing therapy.
- A negative PCR at week 4 increases chance of SVR
- There is ongoing research into duration of treatment for patients with genotype 2/3. Patients who have a rapid response (HCV RNA negative at 4 weeks) may be considered for a reduced duration of therapy of 12 or 16 weeks if they are having severe side effects of treatment

Genotype 1, 4.5 and 6



Selection of patients for treatment

Patients will be considered for treatment if they fulfil the inclusion criteria below, and if after a full explanation of side effects and success rate of treatment, elect to consider treatment

Inclusion criteria for treatment with combination therapy

- Hepatitis C RNA positive
- Adult male or female aged 18-70
- Compensated liver disease
- HIV status known
- Minimum haematology and biochemical criteria

  Hb 11 gram/dl, WBC 3,000/mm3
  Platelets 70,000/mm3
  Prothrombin time less than 3 seconds prolonged compared to control
  Bilirubin less than 20 microm/1
  Albumin within normal limits
  Serum creatinine not greater than 10% above upper limit of normal

Exclusion criteria:

- Patients with features of decompensentated liver failure (consider for transplantation).
- Evidence of primary hepatocellular carcinoma
- Pregnancy, breast feeding mother, or pre-menopausal female not using effective contraception
- Patients with contraindication to use of interferon or ribavirin such as congestive cardiac failure or known hypersensitivity to either product
- Patients thought unlikely to be able to co-operate with subcutaneous injections or follow-up at the clinic

Special Cautions

- Any cause for liver disease based on patient history and biopsy (where available) other than chronic hepatitis C. Haemochromatosis, Wilson's disease, autoimmune hepatitis, alcoholic liver disease, obesity induced liver disease, drug related liver disease.
- Patients with significant co-morbidity due to neoplasia or cardiac, respiratory and

renal disease

- Patient's with unstable mental health
- History of seizure disorder
- Poorly controlled diabetes
- Immunologically medicated disease (e.g. inflammatory bowel disease, systemic lupus erythematosus)
- Alcohol consumption greater than 40 grams per day

Patient Subgroups

HCV/HIV Co-Infected Patients

- As patients with higher CD4 counts appear to respond better to HCV therapy, so treating the HIV infection first to maintain a CD4 count that is as high as possible is a logical treatment strategy.

- Due to the potential hepatotoxicity of anti-retroviral therapies used to treat HIV infection it may be necessary in patients with severe liver disease to treat the HCV infection first so they can tolerate treatment for HIV infection.

- Patients should not be started on both treatments at the same time, but rather should be stabilised on one therapeutic regimen for at least one to two months before initiating any additional treatment so that any adverse events can be correctly attributed.

- Prior to starting HCV treatment HIV medication should be reviewed to ensure compatibility

- Patients should be given 48 weeks of treatment irrespective of genotype

Additional Inclusion Criteria

1. CD4 count sustained at >200
2. HIV RNA viral load <5000 (on treatment)
3. Try to avoid the use of Didanosine and Ritonavir in co-infected patients.

Patients with Renal Failure

Ribavirin causes a dose-dependent haemolytic anaemia and the degree of haemolysis is dependant on the severity of the renal failure (SIGN 2006)

- Patients with renal failure should be treated with pegylated interferon alfa 2a at 135 micrograms.
- Ribavirin commenced at 200mg per day then increased to 400mg per day if tolerated
- Patients should be supported with the use of erythropoetin

Patients with cirrhosis

Patients with cirrhosis are defined as having compensated or decompensated cirrhosis. Those with decompensation have deterioration with development of one or more of the following jaundice, ascites, variceal bleeding or encephalopathy. Studies have shown that antiviral therapy is less effective in this group of patients.

- Patients with compensated cirrhosis should be considered for therapy with pegylated interferon and ribavirin for 48 weeks irrespective of genotype.

Acute Hepatitis C

Most patients who spontaneously clear hepatitis C do so within 12 weeks of diagnosis. There are no data to suggest that delaying treatment from 3 to 6 months post-diagnosis compromises treatment response, whilst allowing for spontaneous clearance to occur. (SIGN 2006). The response rate for treatment with interferon monotherapy is 98%

Acute HCV infection is considered if patients have had a positive serum HCV-RNA by a reverse transcriptase-polymerase chain reaction assay, raised serum alanine aminotransferase (ALT) levels (normal range 1–40 U/L), and at least one of the following criteria

- documented seroconversion for HCV antibodies in the previous 6 months (enzyme-linked immunosorbent assay or at least one new band on immunoblotting);

- first episode at risk of blood-borne diseases in the previous 6 months (intravenous drug use, major surgery, needlestick exposure, sexual contact with HCV-positive person) with evidence of normal ALT during the year preceding the infection
- serum ALT levels at least 25 times higher than the upper limit of the normal range with evidence of normal levels during the year preceding the infection

Other causes of liver disease, such as toxic hepatitis autoimmune hepatitis or co-infection by other hepatitis viruses must be ruled out.

Patients with mental health problems

Patients with stable mental health problems should not be excluded from treatment. Patients should have their psychiatric symptoms monitored prior to and throughout interferon treatment. Formal psychiatric assessment should be considered if necessary.

Patients with hypertension and diabetes

Patients with hypertension or diabetes should have ophthalmic examination performed by a physician prior to commencing treatment, paying particular attention to cotton wool spots and retinal haemorrhage (SIGN 2006)

: Requirements for referral for treatment

- Approved by Consultant
- Discussion taken place including side effects and success rate of treatment with patient
- Full liver screen including hepatoma screen, thyroid antibodies, FBC carried out
- Genotype and viral load checked
- Refer to nurse specialists in gastroenterology

Pegylated interferon and ribavirin doses

Pegylated interferon alfa 2b (Viraferon PEG)

Pegylated interferon alfa 2b 1.5 micrograms/kg body weight subcutaneously once weekly plus oral ribavirin 800-1200 mgs daily (Shering Plough 2007)

Body weight (kg)	Viraferon Peg		Ribavirin capsules	
	Pen Strength Micrograms	(ml)	Total daily dose (mg)	Number of tabs (200mg)
<40	50	0.5	800	4
40-50	80	0.4	800	4
51-64	80	0.5	800	4
65-75	100	0.5	1,000	5
76-85	120	0.5	1,000	5
>85	150	0.5	1,200	6

Pegylated interferon alfa 2a (Pegasys)

The recommended dose of pegylated interferon 2a is 180 micrograms irrespective of genotype or weight, but reduce dose to 135 micrograms in patients with renal failure. The dose of ribavirin depends on viral genotype and the patients body weight (Roche 2007)

Table 3

	Weight	Ribavirin capsules	
		Total daily dose (mg)	Number of capsules (200 mgs)
Genotype 2/3		800 mgs	4
Genotype 1/4	<74 kgs	1,000mgs	5
Genotype 1/4	>75 kgs	1,200mgs	6

Assessment prior to treatment

The success and ability of the patient to complete treatment can be improved with careful planning. All patients will be reviewed by Nurse Specialist in Gastroenterology prior to commencing treatment

The objectives of the review will include:

- Discuss outcomes of treatment dependent on viral genotype
- Discuss treatment length
- Describe potential side effects, provide patient with information booklet on treatment
- Discuss measures taken to reduce or treat side effects
- Describe monitoring protocol with patient and ensure patient is able to commit to this
- Education on the safe storage and disposal of medications and equipment
- Discuss suitable start date taking into account any imminent family, house or employment commitments of the patient
- Demonstration of procedure for the administration of Interferon Injections
- Ensure all relevant prior treatment investigations has been completed
- Correspondence with GP and other services
- Discuss need for contraception to be used during treatment and for 6/7 months post treatment
- Discuss importance of abstaining from alcohol /illicit drugs

Monitoring Protocol for Interferon and Ribavirin Therapy

All patients receiving treatment will be reviewed regularly by the Nurse Specialists in Gastroenterology. Table 6 lists the routine investigations that will be carried out during treatment

Responsibilities of follow up review include

- Practical instruction re administration of Interferon Injections
- Monitoring blood tests as per protocol
- Monitoring the patient for adverse side effects
- Inform Consultant re dose modifications required
- Advising and discussing problems and side effects of treatment
- Co-ordinate supply of prescription with Pharmacist
- Record any missed doses or adverse affects of treatment

	Baseline	Weeks 1,2,4, then 4/52	At three months	At 6 months	At end of treatment	6 Months post treatment
Haematology	✓	✓	✓	✓	✓	✓
Biochemistry	✓	✓	✓	✓	✓	✓
Urinalysis	✓					
HbsAg and HIV status	✓					
Prothrombin time	✓					
TSH	✓			✓		
HCV genotype	✓					
HCV RNA	✓		✓			✓
Monitoring side effects		✓	✓	✓		
Dose Modifications		✓	✓	✓		

Table 3: Follow up during Combination therapy

Dose Modifications to Treatment

Management of adverse events is generally achieved by dose reduction, in the case of life threatening adverse effects therapy should be discontinued permanently. (Refer to table 6)
If severe adverse event persists despite use of lower dose, therapy should be stopped until resolution of adverse event. Treatment should be restarted at 50% of dose. If these doses are tolerated for at least two weeks the treatment dose can be doubled.
If adverse event recurs the patient can be maintained at reduced dose or can be withdrawn from the treatment.

DOSE REDUCTION

	Reduce only viraferon peg dose to one-half dose if:	Reduce only ribavirin dose to 600/400 mgs/day	Discontinue therapy
Haemoglobin Level		Less than 10g/dl	Less than 8.5 g/dl
	In patients with cardiac disease reduce ribavirin if more than 2g/l reduction in four week period		
White Blood Count	Less than 1.5 x 10^9/L		Less than 1.0 x 10^9/L
Neutrophils	Less than 0.75 x 10^9/L		Less than 0.5 x 10^9/L
Platelets	less 50 x 10^9/L		Less 25 x 10^9/L
Creatinine	N/A		> 2.0 mg/dl
ALT / AST	N/A		2 x baseline and 10 x ULN (400u/l)
Bilirubin	N/A		2.5 x upper limit normal

Table 4 Dose Modifications

Management of adverse effects of treatment

Side effects found in almost all patients include malaise, fever, shivering, and influenza-like symptoms within hours of the first few injections. (Table 5) They should be warned of this response and advised to take prophylactic paracetamol. Anorexia, fatigue and weight loss are occasionally seen with continuing therapy. Depression and autoimmune thyroid disease may occur. All patients show some degree of marrow suppressions. Side effects or toxicity may necessitate a reduction in dose or cessation of therapy at any stage.

Side effect	Management
Flu like symptoms	Be advised to use paracetamol within manufacturers guidelines. advised to maintain an adequate fluid intake throughout treatment. to coordinate their injection of pegylated interferon with periods of reduced activity, such as weekends.
Depression	Be monitored for signs of depression before, during and immediately post-treatment. Patients who experience depression should be considered for treatment with antidepressants and for referral to a specialist if

	necessary
Skin reactions	Be advised to avoid overexposure to the sun. Be advised to rotate injection sites The use of emollients and topical corticosteroids can be considered for non-specific rashes. The use of antihistamines can be considered for pruritus. Severe dermatological reactions or those that to not respond to first line treatment should be referred for dermatological opinion.
Thyroid dysfunction	Thyroid function should be monitored as baseline before interferon therapy and 12 weekly throughout treatment and at any time where there is a suspicion of thyroid dysfunction. Patients developing thyroid dysfunction should be referred to an endocrinologist.
Dyspnoea	Patients who report dyspnoea that is not related to anaemia should be urgently assessed for cardiopulmonary problems.
Retinopathy	Any patient reporting visual disturbance during treatment should be examined further by an ophthalmologist or optician. Interferon should be discontinued in any patient with visual disturbance until it has resolved or there is confirmation of no retinal injury.
Alopecia	Be advised that treatment related hair loss is reversible on cessation of treatment.
Weight loss	Patients should be weighed at each follow up visit Advice given about increasing nutritional intake If more than 10% of body weight occurs, refer for nutritional supplements (prescribed by GP) to a dietitian . If weight based treatment given consider reduction in dose

Table 5: Treatment side effects and management

Section 7: Post Treatment Care

PCR Positive at 12 weeks or viral load less than 2 log drop

- Treatment discontinued
- Explanation to patient why treatment stopped
- Reviewed by Medical Staff
- Appointment at Hepatitis C Outpatient clinic for 3 months

End of treatment

- End of treatment HCV PCR recorded
- Appointment Hepatitis C Outpatient clinic for 6 months

HCV PCR negative after 6months of cessation of therapy

- Patient informed of the result
- No regular follow up arranged
- Patient contact information entered onto database
- Patient informed they will be contacted if required pending the outcome of long term follow up studies

HCV PCR positive after 6 months of cessation of therapy

- Patient informed of the result
- Explanation given re effects of treatment and future treatment options
- Arrange follow up in 6 months

References:

Management of hepatitis c a national clinical guideline. Scottish intercollegiate Guidelines Network (SIGN) http://www.sign.ac.uk/pdf/sign92.pdf

Useful websites

Scottish Executive. Hepatitis C: proposed action plan in Scotland. Edinburgh: Scottish Executive; 2005. [cited 28 September 2006]. Available from: www.scotland.gov.uk/Resource/Doc/54357/0013088.pdf

Royal College of Physicians of Edinburgh (RCPE). Consensus conference on hepatitis C: final consensus statement. Edinburgh: The College; 2004. [cited 28 September 2006]. Available from: www.rcpe.ac.uk/education/standards/consensus/hep_c_04.php

Health Care Professional's Information

NHS Scotland http://www.hepcscotland.co.uk

National Hepatitis C Resource Centre Telephone 020 7735 6645 www.hep.centre.com

Patient leaflets

Download and print from hepcscotland.co.uk
http://www.hepcscotland.co.uk/patients-and-carers/information-about-hepatitis-c-for-patients-and-carers.html

Patient support Groups

Body Positive Tayside Telephone 01382 226860 www.bodypositive.org.uk

British Liver Trust Telephone 01473 276326 www.britishlivertrust.org.uk

Guidelines adapted from NHS Grampian Guidelines
February 2008 Pauline Dundas Clinical Nurse Specialist