IN THE UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF OHIO
EASTERN DIVISION

JEFFREY D. MANN,
Grafton Corr. Inst.
2500 S. Avon-Belden Rd.
Grafton, Ohio 44044,

and

JOHN T. BRAGG,
Grafton Corr. Inst.
2500 S. Avon-Belden Rd.
Grafton, Ohio 44044,

and

ERIC PASTRANO,
Grafton Corr. Inst.
2500 S. Avon-Belden Rd.
Grafton, Ohio 44044

Plaintiffs,

-vs-

OHIO DEPT. OF REHAB. & CORR.
770 W. Broad St.
Columbus, Ohio 43222,

and

DR. ANDREW EDDY,
ODRC Collegial Rev. Committee
770 W. Broad St.
Columbus, Ohio 43222

and

MONA PARKS,
ODRC Medical Officer
770 W. Broad St.
Columbus, Ohio 43222

and

GARY MOHR,
Director, ODRC
770 W. Broad St.
Columbus, Ohio 43222,

and

2 18CV1565

Case No.

Judge: Judge Smith

Magistrat MAGISTRATE JUDGE DEAVERS

Civil Action under 42 USC §1983 and the Eighth Amendment to the United States Constitution
Declaratory and Injunctive relief and Money Damages Sought

Jury Demand Endorsed Herein

DAVID HANNAH,
Health Care Administrator,
Grafton Corr. Inst.
2500 S. Avon-Belden Rd.
Grafton, Ohio 44044,

and

DR. JANICE DOUGLAS,
Chief Medical Officer,
Grafton Corr. Inst.
2500 S. Avon-belden Rd.
Grafton, Ohio 44044,

and

VARIOUS UNKNOWN DOCTORS, NURSES AND OTHER HEALTH CARE PROVIDERS RESPONSIBLE TO PROVIDE HEALTH CARE FOR OHIO PRISONERS,

and

VARIOUS UNKNOWN STATE OFFICERS RESPONSIBLE FOR PROMULGATION OF ODRC MEDICAL POLICIES,

Defendants.

COMPLAINT

JURISDICTION AND VENUE

1. This Court has original jurisdiction over the instant justiciable controversy by virtue of Article III of the United States Constitution and pursuant to the relevant provisions of the Civil Rights Act of 1965, 42 U.S.C. §1983;

2. The acts and conduct upon which this action is based occurred primarily in the City of Columbus, County of Franklin, Ohio, wherein the majority of the defendants maintain their principal offices, and which is within the territorial jurisdiction of this Court, thus establishing this Court as the appropriate venue for this Action pursuant to F. R. Civ. P. 3.

PARTIES

3. Plaintiff Jeffrey D. Mann (hereinafter 'Mann') is a United States citizen who is currently under the custody and control of the Ohio Department of Rehabilitation and Corrections ('ODRC') serving an indefinite term of incarceration of fifteen (15) years to life stemming from Cuyahoga County, Ohio Case No. 92-CR-295500 and has been continually incarcerated since 1993, and who has been diagnosed with the Hepatitis-C virus ("HCV");

4. Plaintiff John T. Bragg ('Bragg') is a Canadian citizen who is currently under the custody and control of the ODRC serving an indefinite term of incarceration of forty-three (43) years to life stemming from Cuyahoga County, Ohio Case No. 89-CR-237718, and has been continually incarcerated since 1989, and who has been diagnosed with HCV;

5. Plaintiff Eric Pastrano ('Pastrano') is a United States citizen who is currently under the custody and control of the ODRC serving a definite term of incarceration of thirteen (13) years stemming from Maricopa County, Arizona Case No. CR2011100341, having been transferred under Interstate Transfer Protocols to serve his sentence under the custody and control of the ODRC, and has been continually incarcerated since 2011, and who has been diagnosed with HCV;

6. The Defendant ODRC is a State Agency, promulgated and operated under Section 5120 of the Ohio Revised and Administrative Codes and which is charged with the safety and security of all prisoners under its custody and control and to provide them with adequate food,clothing, bedding, shelter, a clean and healthy environment and adequate medical care, as well as to preserve their civil rights and obey the laws and Constitution;

7. Defendant Dr. Andrew Eddy is the Director of the ODRC "Collegial Review Committee" which operates to review recommended and prescribed medical care for Ohio prisoners to determine whether to authorize such prescribed medical care for the prisoners and who participates in the promulgation, interpretation and application of all ODRC Policies and Procedures related to providing medical care to Ohio prisoners, including, but not limited to each plaintiff and all others similarly situated thereto;

8. Defendant Mona Parks is the Chief Medical Officer for the ODRC who, inter alia, supervises all of the various doctors and other medical personnel in all Ohio prisons, including the Grafton Correctional Institution ('GCI') At which the Plaintiffs and others similarly situated are confined, and who participates in the promulgation, interpretation and application of all ODRC Policies and Protocols relating to providing medical care to Ohio prisoners, including, but not limited to, each plaintiff and all others similarly situated thereto;

9. Defendant Gary Mohr is the duly appointed Director of the ODRC, charged with overseeing the operation of all aspects of the ODRC pursuant to and in accordance with the Ohio Revised and Administrative Codes including, but not limited to participation in the promulgation, interpretation and application of all ODRC Policies and Protocols relating to the provision of medical care to all ODRC prisoners including, but not limited to, each plaintiff and all others similarly situated thereto, and for ensuring that the ODRC and all agents, actors, employees, officers, representatives, contractors and/or any others acting in any way on behalf of the ODRC are in compliance with state and federal laws and the U.S. Constitution;

10. Defendant David Hannah is the Health Care Administrator (HCA) at GCI, charged with oversight and implementation of health care for all prisoners at GCI including, but not limited to, each plaintiff and others similarly situated;

11. Dr. Janice Douglas is the Chief Medical Officer at GCI,charged with providing adequate medical care to all prisoners at GCI, including, but not limited to, each plaintiff and others similarly situated, and who is restricted in her ability to prescribe and practice medicine by the restrictions set forth in the ODRC Policies and Protocols relating to medical care;

12. The descriptors of defendants as "Various unknown doctors, nurses and other health care providers" relates to the doctors and nurses whose names are unknown at this time, but will be obtained and revealed through discovery, at all Ohio prisons, who are responsible for the provision of health care to all Ohio prisoners, including but not limited to each plaintiff and all others similarly situated, and who have refused to provide adequate health care as alleged further in this Complaint;

13. The descriptors of defendants as "Various unknown state officers responsible for promulgation of ODRC medical Policies" references any and all participants in the process of drafting, writing, promulgating and enacting any and all Policies and/or Protocols relating in any way to the medical treatment of Ohio Prisoners, including, but not limited to those policies relating to the provision of treatment and care for Chronic Liver Disease and/or Hepatitis C as applied to all prisoners under the custody and control of the ODRC including, but not limited to, each plaintiff and all others similarly situated, which defendants names are unknown at this time but will be obtained and revealed through discovery;

FACTUAL BACKGROUND

14. Hepatitis C is a viral invection that affects the liver in humans, causing cirrhosis, fibrosis, fatty liver, liver cancer and other dysfunctions of the liver; (Exhibit B, C & D)

15. Hepatitis C Virus (HCV) is the tenth leading cause of death in the United States with 10% of all deaths in the U.S. being linked to it; (Exhibit J, CDC Report)

16. Twenty thousand (20,000) people died of HCV in 2015, but the number could, in fact, be five times higher; (Exhibit E, CDC Report)

17. The pravalence of chronic HCV infections among prisoners in the U.S. is between 12 and 35 percent (12-35%), compared to about 1.3% in the general popluation, and the prevalance of end stage liver disease caused by HCV is estimated to be three times higher in prisoners than in those in the general population; (Worman, Howard J. "Diagnosis and Treatment of Chronic Hepatitis C in incarcerated Patients", The AMA Journal of Ethics. Feb. 2008)

18. HCV causes, inter alia, cirrhosis, which leads to fibrosis and interferes with liver function, (Exhibit A), fibrosis,which obliterates the architecture and function of the underlying organ or tissue, (Exhibit B), fatty liver, caused by the disruption of fat metabolism caused by HCV and depositing excessive amounts of fat on the liver, interfering with liver function and leading to liver cancer, caused by fatty liver and genotype 3 HCV, and hepatocyte ballooning, which is necrosis (or dying off) of liver tissue as an inflammatory response to fatty liver and the effects of untreated HCV; (Exhibit C&D)

19. In general,treatment of HCV will reverse the process of fatty liver if implemented at an early stage; (Exhibit C)

20. Treatment for HCV infection is indicated if the virus is present for six months; (Exhibits E and F)

21. Ninety percent (90%) of HCV infections can be cured with 8-12 weeks of therapy, (Exhibits E and F) and treatment is recommended at the earliest posible stage for maximum efficacy, (Exhibits G and I); and the only treatment is medications, (id);

22. The indicators for severity of infection are reflected as the "APRI" [ACT Serum to Platelet Ratio Index] which measures the viral load, in combination with determining the extent of fibrisis, if any; (Exhibit H)

23. The use of a biopsy for assessment of the existence and extent of fibrosis has been established to be inaccurate, and is disfavored in favor of vibration-controlled transient liver elastography which measures the stiffness of the liver and any resultant cirrhosis or fibrosis;

24. Treatment is recommended for all patients with chronic HCV infection; (Exhibit I); (cf. Exhibit K)

25. Hepatitis has been established to constitute a serious medical need sufficient to satisfy the objective component of an Eighth Amendment Claim by the Sixth Circuit. **Owens v Hutchinson** (CA 6, 2003) 79 Fed. App'x. 159, 161;

26. The current prison population in Ohio is approximately 53,000 prisoners;

27. The low end estimate of 12% of prisoners with HCV calculated for Ohio's prison population equals six thousand, three hundred-sixty (6,360) prisoners with HCV, while the higher end estimate of 35% yields a figure of eighteen thousand, five hundred-fifty (18,550) prisoners with HCV in Ohio prisons;

28. The defendants herein are aware of the prevalence and seriousness of HCV infections among the prisoners in their collective charge, as shown not only by the fact that the defendants distribute informational pamphlets to prisoners freely at the medical departments, (see, e.g. Exhibits N, O, P and Q; provided in an open display for taking at the GCI medical department on October 20, 2018) but also by the promulgation of policies and protocols addressing testing, diagnosis and treatment for HCV in prisoners; (see, e.g. Exhibits L and M);

PLAINTIFF JEFFREY D. MANN

29. Plaintiff Jeffrey D. Mann, born May 31, 1957, is a 61 year old man who has been continually incarcerated since 1993, and who was diagnosed with HCV in 2001, and who sought treatment therefor beginning in 2001 and, in 2007, was provided with the then-prevailing treatment (only 50% success rate) of Interferon and Ribovirin for 46 weeks after he grieved the issue, and the treatment was not completely successful;

30. Following partial remission, the HCV viral load returned and he has awaited treatment ever since; repeatedly seeking and requesting treatment, to no avail;

31. In May, 2018, after being seen by a "chronic care" nurse practitioner at GCI medical for review, Mann was advised that his APRI was .36, and that, until the APRI reached 1.5, he would not be eligible for treatment, even though it was acknowledged that an APRI of over 1.5 indicated the later stages of the diseaase, with irreversible damage to the liver and its functions; (Exhibit R) with the stated reason for the delay being the costs;

32. Despite repeated requests and exhaustion of the grievance process, the defendants herein refuse to provide adequate and necessary medical care to Mann, on the basis of expressed reliance upon "ODRC Policy 68-MED-04 and Protocol C-5", as well as ODRC Policies 68-MED-01 and -14; (Exhibit R)

33. At no time have the defendants acceded to Mann's request for an ultrasound or vibration-controlled transient liver elastography to properly assess the degree of liver damage he has suffered due to untreated HCV infection;

34. Plaintiff is representative of a class of Ohio prisoners who have undergone unsuccessful Interferon/Ribovirin treatment for HCV, at various different stages of the disease, and who

continue to be denied medically accepted diagnostics and re-treatment with evolved drugs with 90% efficacy, and who are serving indefinite terms of incarceration of such duration that they have no ability to seek treatment after their incarceration in sufficient time as to forestall permanent liver damage resulting from lack of treatment.

PLAINTIFF JOHN T. BRAGG

35. Plaintiff John T. Bragg, born October 1, 1959, is a fifty-nine year old man who has been continually incarcerated since 1989, and who was diagnosed with HCV in approximately 1999, and who sought treatment therefor beginning in 2004 and, in 2007, was provided with the then-prevailing treatment (only 50% success rate) of Interferon and Ribovirin for 46 weeks after his grievances about the issue, and the treatment was only partially successful;

36. Following partial remission, the HCV viral load returned and he has awaited treatment ever since, repeatedly seeking and requesting treatment, to no avail;

37. In June of 2018, following yet another request for treatment, Bragg was denied with the accompanying advisement that he could not be eligible for treatment under the relevant Policies and Protocols unless his APRI exceeds 1.5, despite the acknowedgement that this number reflects end stages of liver disease with irreversible liver damage, based solely upon reliance on ODRC Policy 68-MED-01 and -14, and Protocol C-5, (Exhibit S);

38. At no time have the defendants acceded to Bragg's request for an ultrasound or vibration-controlled transient liver elastography to properly assess the degree of liver damage suffered due to untreated HCV infection;

39. As a Canadian citizen, the only criteria to qualify for treatment with the evolved and 90% effective drugs available is HCV positive RNA test, or the presence of the virus;

40. Bragg's repeated attempts to access the International Treaty for Prisoner Exchange with Canada to the ODRC defendant herein have been to no avail, as Ohio's enabling Legislation for the Treaty compliance contains requirements that are the direct opposite of the requirements set forth in the Treaty, thus rendering it inaccessible to Ohio prisoners, and thus acting to further deny Bragg access to readily available modern and effective treatment for HCV, from his own country, and to avoid any additional permanent liver damage;

41. Plaintiff Bragg is representative of a Class of Ohio prisoners who have undergone unsuccessful Interferon/Ribovirin treatment for HCV at various different stages of the disease, and who continue to be denied medically accepted diagnostics and re-treatment with evolved drugs with 90% efficacy, and who are

serving indefinite terms of such duration that they have no ability to seek treatment after their incarceration in sufficient time as to forestall permanent liver damage resulting from lack of treatment, and who have readily available treatment options that are being denied due to their incarceration in Ohio, based solely and completely upon Ohio's policies.

PLAINTIFF ERIC PASTRANO

42. Plaintiff Eric Pastrano, born March 15, 1970, is a 48 year old man who has been continually incarcerated since 2011 and who was diagnosed with HCV in 2006, and who sought treatment therefor beginning in 2011 and has been continually completely denied both treatment and appropriate medically accepted diagnostics, including an ultrasound or vibration-controlled transient liver elastography and who is even being denied the periodic blood testing required by Ohio policies and protocols, despite repeated requests therefor as well as exhaustion of the available grievance process, by the defendants herein; (Exhibit T)

43. Plaintiff Pastrano is representative of a class of Ohio prisoners serving stated prison terms who continue to be refused access to generally accepted medical care for a known and acknowledged serious medical need by the defendants herein, based solely and completely upon Ohio's Policies, where such policies were promulgated, interpreted and applied in such a way as to intentionally deny access to necessary medical care, which will result in permanent liver damage, where the readily available medical treatment has a 90% efficacy when administered at earlier stages of the disease.

ALL PLAINTIFFS

44. All plaintiffs herein have been diagnosed with HCV infections, have suffered from a variety of symptoms, including, but not limited to, fatigue, jaundice, pain and reduced liver function, as well as continuing and ongoing progressive and irreversible liver damage;

45. All plaintiffs have repeatedly sought proper and medically accepted diagnostics, including, but not limited to, ultrasound and vibration-controlled transient liver elastography, and have protested the insistence to deny or delay treatment unless and until they are in the later stages of disease progression, where such denial is based solely and completely upon the promulgation, interpretation and application of Ohio Policies and Protocol which are designed to prohibit or delay access to readily available and effective medical care and treatment based solely upon cost;

46. All plaintiffs herein exemplify and represent the 6,360 to 18,550 Ohio prisoners who have been diagnosed with HCV and are being refused readily available and medically acceptible diagnostics and treatment based solely and completely upon Ohio Policies and Protocols, which are designed to prohibit or delay

access to readily available and effective medical care and treatment, based solely upon costs, and despite having full knowledge of the progressive and irreversible nature of the damage caused by HCV.

DEFENDANTS

47. The ODRC defendant is responsible for any and all acts and conduct of its agents and employees and is, thus, responsible for all acts and conduct upon which this action is based, and the damages caused thereby;

48. Defendant Dr. Andrew Eddy, as the Chair of the ODRC "Collegial Review Committee" has a direct role in interpreting and applying ODRC Medical Policies and Protocols, including those cited herein, and is directly and proximately responsible for the denial of adequate and timely readily available prescribed health care for Ohio Prisoners, including treatment for HCV for the Plaintiffs and all others similarly situated; moreover, this defendant has an established pattern of denying necessary medical care, in violation of the Eighth Amendment to the Constitution and in violation of the civil rights of the prisoners, thus establishing that the acts and conduct relating to the instant action are part of an ongoing pattern of conduct and are being committed deliberately, purposefully and with the intent to deprive prisoners of necessary health care and to violate their rights as set forth herein;

49. Defendant Mona Parks, as the Chief Medical Officer for the ODRC (and unqualified for the position, as she is only an RN, not a doctor of any kind), has a direct role in the promulgation, interpretation and application of ODRC medical Policies and Protocols, including those cited herein, and is directly and proximately responsible for the denial of adequate and timely readily available prescribed health care for Ohio prisoners, including treatment for HCV for the Plaintiffs and all other similarly situated;

50. Defendant Gary Mohr, as the Director of the ODRC, is responsible and liable for any and all actions taken by any employee or agent of the ODRC under his supervision and has a direct role in the promulgation of ODRC Policies, including those cited herein, and is thus directly and proximately responsible for the denial of adequate and timely readily available prescribed health care for Ohio prisoners, including treatment for HCV for the Plaintiffs and all others similarly situated;

51. Defendant David Hannah, as the Health Care Administrator for GCI, is charged with the supervision and oversight of all medical personnel and care at GCI for all GCI prisoners and is responsible and liable for any and/or all acts and conduct of said personnel and is directly and proximately responsible for the denial of adequate and timely readily available prescribed health care for GCI prisoners, including treatment for HCV for the Plaintiffs and others similarly situated at GCI;

52. Defendant Janice Douglas is the Chief Medical Officer at GCI, responsible for the provision of health care for all prisoners at GCI and is directly and proximately responsible and liable for the denial of adequate and timely readily available prescribed health care for GCI prisoners, including treatment for HCV for the Plaintiffs and others similarly situated at GCI;

53. The various unknown health care and medical personnel referenced and described in Paragraph 12 of this Complaint are those responsible for the provision of health care to all Ohio Prisoners, and are directly and proximately responsible and liable for the denial of adequate and timely readily available prescribed health care for all Ohio Prisoners, including provision of treatment for HCV for the Plaintiffs and all others similarly situated;

54. The various and unknown state officers referenced and described in Paragraph 13 of this Complaint are those responsible for writing, drafting, submitting and approving for implementation any and/or all ODRC medical Policies and Protocols that work to deny necessary, adequate, timely and readily available health care to Ohio Prisoners, including the provision of treatment for HCV to Plaintiffs and all others similarly situated;

55. The acts and conduct of the defendants aforesaid, together and/or severally, acting alone or in concert with one or more other defendants or persons not named as defendants herein, in promulgating, interpreting and applying Ohio's Policies and Protocols related to the provision of medical care, serve to delay and/or deny access to medical care, including treatment for HCV, to the Plaintiffs and all other Ohio Prisoners similarly situated, based solely upon the stated reason of the cost of providing the necessary care;

56. The acts and conduct of the defendants aforesaid, together and/or severally, acting alone or in concert with one or more other defendants or persons not named as defendants herein, were committed purposely and/or knowingly, and with the intent to delay and/or deny access to medical care, including treatment for HCV, to the Plaintiffs and all other Ohio Prisoners similarly situated, and with the intent to cause the damages to the Plaintiffs and all others similarly situated, set forth below;

57. The acts and conduct of the defendants aforesaid, together and/or severally, acting alone or in concert with one or more other defendants or persons not named as defendants herein, have caused damages to the plaintiffs herein, and to all others similarly situated, including, but not limited to, the incurrence of irreversible liver damage and reduced function that would not have occurred in the absence of the acts and conduct of the defendants aforesaid, as well as pain and suffering and an increased risk of death, as well as physical, psychological and emotional stress and trauma, and the loss of the ability to enjoy life as thoroughly and completely as in the absence of the acts and conduct of the defendants aforesaid.

CLAIMS FOR RELIEF

FIRST CLAIM

58. Plaintiffs hereby incorporate the allegations set forth in Paragraphs One through Fifty-seven (1-57) of this Complaint as if fully rewritten herein;

59. The acts and conduct of the defendants aforesaid constitute deliberate indifference to the serious medical needs of the plaintiffs herein and of all others similarly situated, which constitutes a violation of the Eighth Amendment to the United States Constitution; and have caused the damages set forth in Paragraph Fifty-seven (57) of this Complaint;

SECOND CLAIM

60. Plaintiffs hereby incorporate the allegations set forth in Paragraphs One through Fifty-nine (1-59) of this Complaint as if fully rewritten herein;

61. The acts and conduct of the defendants aforesaid constitute a violation of the Civil Rights of the Plaintiffs and all others similarly situated, and have caused the damages set forth in Paragraph Fifty-seven (57) of this Complaint.

DEMAND FOR RELIEF

Wherefore, Plaintiffs demand relief as follows:

A. Declaratory relief in the form of a declaration that the Policies and Protocols of the ODRC related to the provision of medical care for Hepatitis C and Chronic Liver Disease do not conform to the standards of care generally accepted in the medical community and serve to deny adequate necessary medical care to the Plaintiffs and to all others similarly situated;

B. Injunctive relief requiring the defendants herein to immediately begin adequate, timely, effective and appropriate diagnostics and treatment generally accepted in the medical community for HCV for the Plaintiffs and all others similarly situated;

C. Compensatory damages in an amount determined by a jury, but no less than a total of fifty milion dollars ($50,000,000.00) to be apportioned between the Plaintiffs and all others similarly situated, and to include those who have died as a direct and/or proximate result of the acts and conduct of the defendants herein;

D. Reasonable attorney fees;

E. The recovery of the costs and expenses of the Plaintiffs in bringing this Action;

F. Any other and/or further relief to which the Plaintiffs and all others similarly situated may be entitled and which this Court deems just and equitable.

EXHAUSTION

Pursuant to the PLRA, each named Plaintiff herein certifies that he has fully and completely exhausted all available administrative remedies under Ohio Adiminstrative Code §5120-9-31, (Exhibits R, S and T).

JURY DEMAND

Plaintiffs hereby demand a trial by jury of all issues so triable herein.

VERITY

We, the undersigned, do hereby swear and affirm, under penalty of perjury, that the statements set forth in this Complaint are true and correct, to the best of our knowledge and belief.

Respectfully submitted,

Nov. 23 2018
Date:

Jeffrey D. Mann, #A283-016
Grafton Corr. Inst.
2500 S. Avon-Belden Rd.
Grafton, Ohio 44044
Plaintiff, in pro se

Nov 23, 2018
Date:

John T. Bragg, #A215-337
Grafton Corr. Inst.
2500 S. Avon-Belden Rd.
Grafton, Ohio 44044
Plaintiff, in pro se

Nov. 23, 2018
Date:

Eric Pastrano, #A655-761
Grafton Corr. Inst.
2500 S. Avon-Belden Rd.
Grafton, Ohio 44044
Plaintiff, in pro se

APPENDIX; LIST OF EXHIBITS

A: Diagram of Normal and Diseased Liver (printout, 03/14/18) (1p)

B. "Fibrosis", Wikipedia, (w/diagram) 03/13/18 (4 pp)

C. "Fatty Liver", Wikipedia (w/ 2 diagrams) 03/13/18 (10 pp)

D. "Grade 1, Stage 1 Hepatitis C" Reference.com, 04/02/18 (2 pp)

E. "Hepatitis C FAQ's for Health Professionals, CDC, 03/26/18 (12 pp)

F. "Viral Hepatitis, Hepatitis C medications: a review and update for patients" Veteran's Affairs", 03/26/18 (5 pp)

G. "HCV Testing and Linkage to Care" American Assoc. for the Study of Liver Disease, 04/05/18 (10 pp)

H. "AST to Platelet Ratio Index (APRI) Calculator", Hepatitis C Online, 04/05/18 (3 pp)

I. "When and in Whom to Initiate HCV Therapy/HCV Guidance", Amer. Assoc. for Study of Liver Disease. 04/05/18 (9 pp)

J. "Recommendations for Prevention and COntrol of HCV..." CDC, 05/20/18 (23 pp)

K. "Hepatitis C Primary Care Practice Guideline", New York State Division of Corrections, 08/12/16 (37 pp)

L. "Testing and Treatment Guidelines for Chronic Hepatitis C", Protocol C-5, ODRC Bureau of Med. Svcs. 08/09/16 (11 pp)

M. "Liver Disease Chronic Care Clinic", Protocol A-6, ODRC Bureau of Med. Svcs. 03/04/13 (8 pp)

N. Pamphlet: "Know the Facts", Gilead Sciences, 2016 (14 pp)

O. Pamphlet: "Why Get Tested", Gilead Sciences, 2016 (14 pp)

P. Pamphlet: "Understanding Your Diagnosis", Gilead, 2016 (18 pp)

Q. Pamphlet: "Planning for Treatment", Gilead, 2016 (18 pp)

R. Exhaustion of Admin. Remedies, Plaintiff Jeffrey D. Mann (printout of electronic grievance process results)(1 p)

S. Exhaustion of Admin. Remedies, Plaintiff John T. Bragg (Printout of electronic grievance process results) (1 p)

T. Exhaustion of Admin. Remedies, Plaintiff Eric Pastrano (Printout of electronic grievance process results) (2 pp)

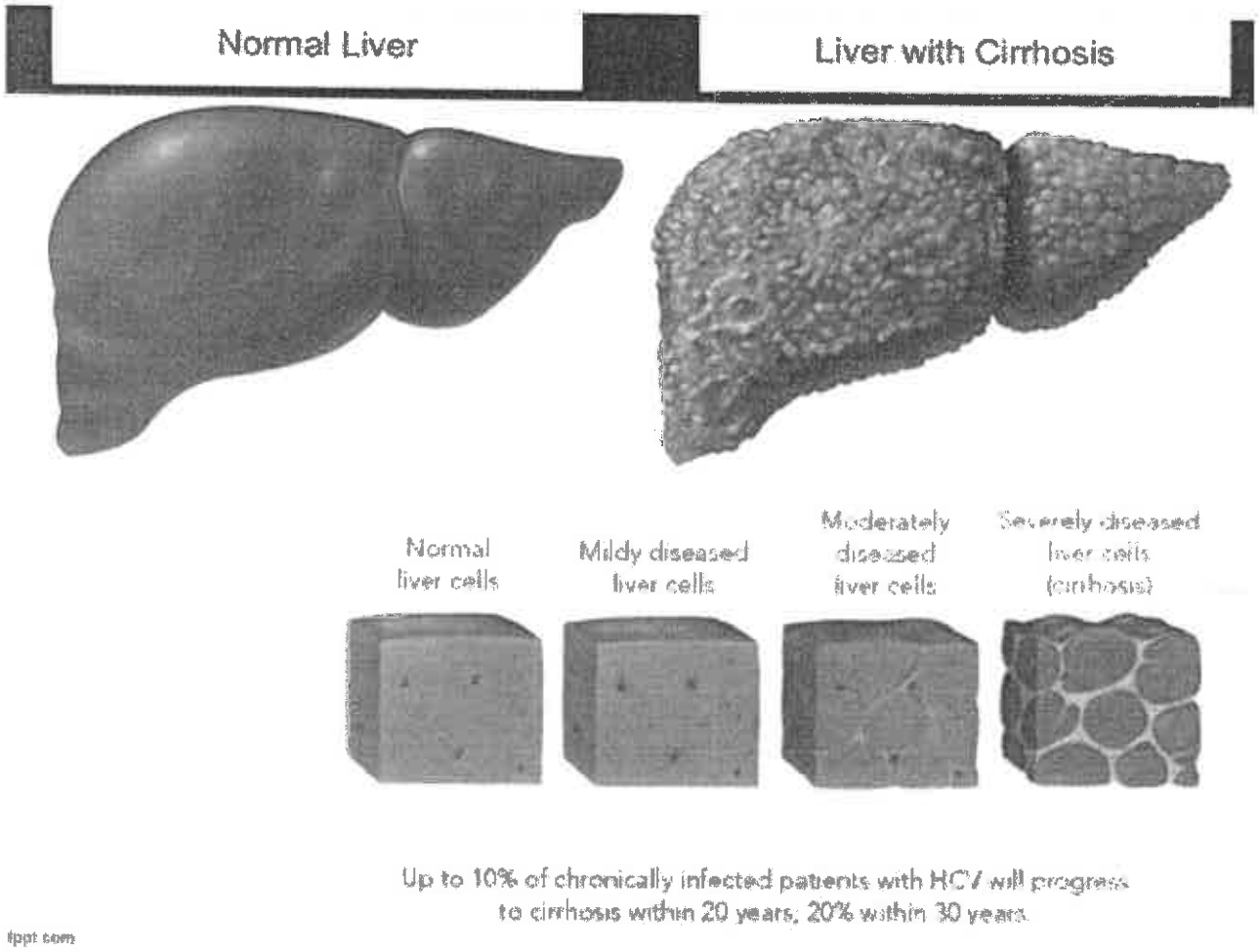


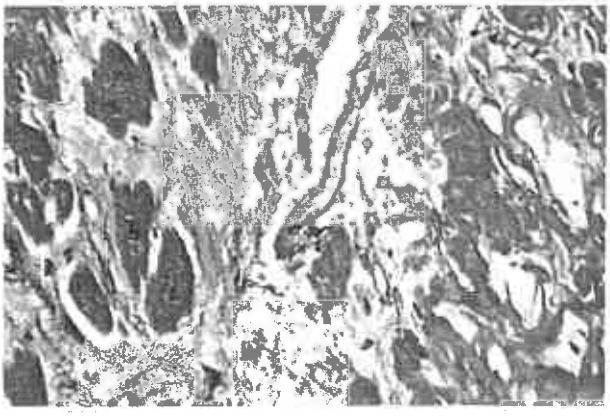
Exhibit A

WIKIPEDIA

Fibrosis

Fibrosis is the formation of excess fibrous connective tissue in an organ or tissue in a reparative or reactive process.[1] This can be a reactive, benign, or pathological state. In response to injury, this is called scarring, and if fibrosis arises from a single cell line, this is called a fibroma. Physiologically, fibrosis acts to deposit connective tissue, which can obliterate the architecture and function of the underlying organ or tissue. Fibrosis can be used to describe the pathological state of excess deposition of fibrous tissue, as well as the process of connective tissue deposition in healing.[2] Defined by the pathological accumulation of extracellular matrix (ECM) proteins, fibrosis results in scarring and thickening of the affected tissue, it is in essence an exaggerated wound healing response which interferes with normal organ function.[3]

Fibrosis



Micrograph of a heart showing fibrosis (yellow - left of image) and amyloid deposition (brown - right of image). Movat's stain.

Classification and external resources

Specialty	Pathology
MeSH	D005355 (https://www.nlm.nih.gov/cgi/mesh/2018/MB_cgi?field=uid&term=D005355)

Contents

Physiology

Fibrosis is similar to the process of scarring, in that both involve stimulated fibroblasts laying down connective tissue, including collagen and glycosaminoglycans. The process is initiated when immune cells such as macrophages release soluble factors that stimulate fibroblasts. The most well characterized pro-fibrotic

Exhibit B

mediator is TGF beta, which is released by macrophages as well as any damaged tissue between surfaces called interstitium. Other soluble mediators of fibrosis include CTGF, platelet-derived growth factor (PDGF), and Interleukin 4 (IL-4). These initiate signal transduction pathways such as the AKT/mTOR[4] and SMAD[5] pathways that ultimately lead to the proliferation and activation of fibroblasts, which deposit extracellular matrix into the surrounding connective tissue. This process of tissue repair is a complex one, with tight regulation of ECM synthesis and degradation ensuring maintenance of normal tissue architecture. However, the entire process, although necessary, can lead to a progressive irreversible fibrotic response if tissue injury is severe or repetitive, or if the wound healing response itself becomes deregulated.[3]{

Examples of fibrosis

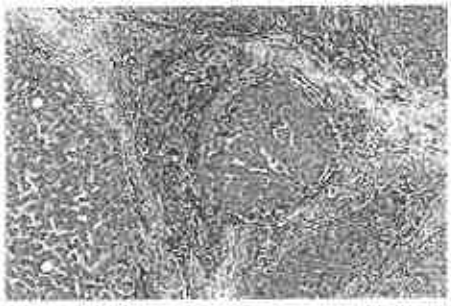
Fibrosis can occur in many tissues within the body, typically as a result of inflammation or damage, and examples include:

Lungs

- Pulmonary fibrosis
  - Cystic fibrosis
  - Idiopathic pulmonary fibrosis (idiopathic meaning the cause is unknown)
- Radiation-induced lung injury following treatment for cancer

Liver

- Cirrhosis
- Biliary atresia



Micrograph showing cirrhosis of the liver. The tissue in this example is stained with a trichrome stain, in which fibrosis is colored blue. The red areas are the nodular liver tissue

Heart

- Atrial Fibrosis
- Endomyocardial fibrosis
- Old myocardial infarction

Brain

- glial scar

Other

- Arterial stiffness
- Arthrofibrosis (knee, shoulder, other joints)
- Crohn's Disease (intestine)
- Dupuytren's contracture (hands,fingers)
- Keloid (skin)
- Mediastinal fibrosis (soft tissue of the mediastinum)
- Myelofibrosis (bone marrow)
- Peyronie's disease (penis)
- Nephrogenic systemic fibrosis (skin)
- Progressive massive fibrosis (lungs); a complication of coal workers' pneumoconiosis

- Retroperitoneal fibrosis (soft tissue of the retroperitoneum)
- Scleroderma/systemic sclerosis (skin, lungs)
- Some forms of adhesive capsulitis (shoulder)

References

1. Birbrair, Alexander; Zhang, Tan; Files, Daniel C.; Mannava, Sandeep; Smith, Thomas; Wang, Zhong-Min; Messi, Maria L.; Mintz, Akiva; Delbono, Osvaldo (2014-11-06). "Type-1 pericytes accumulate after tissue injury and produce collagen in an organ-dependent manner" (http://stemcellres.com/content/5/6/122/abstract). *Stem Cell Research & Therapy.* **5** (6): 122. doi:10.1186/scrt512 (https://doi.org/10.1186%2Fscrt512). ISSN 1757-6512 (https://www.worldcat.org/issn/1757-6512). PMC 4445991 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4445991). PMID 25376879 (https://www.ncbi.nlm.nih.gov/pubmed/25376879).
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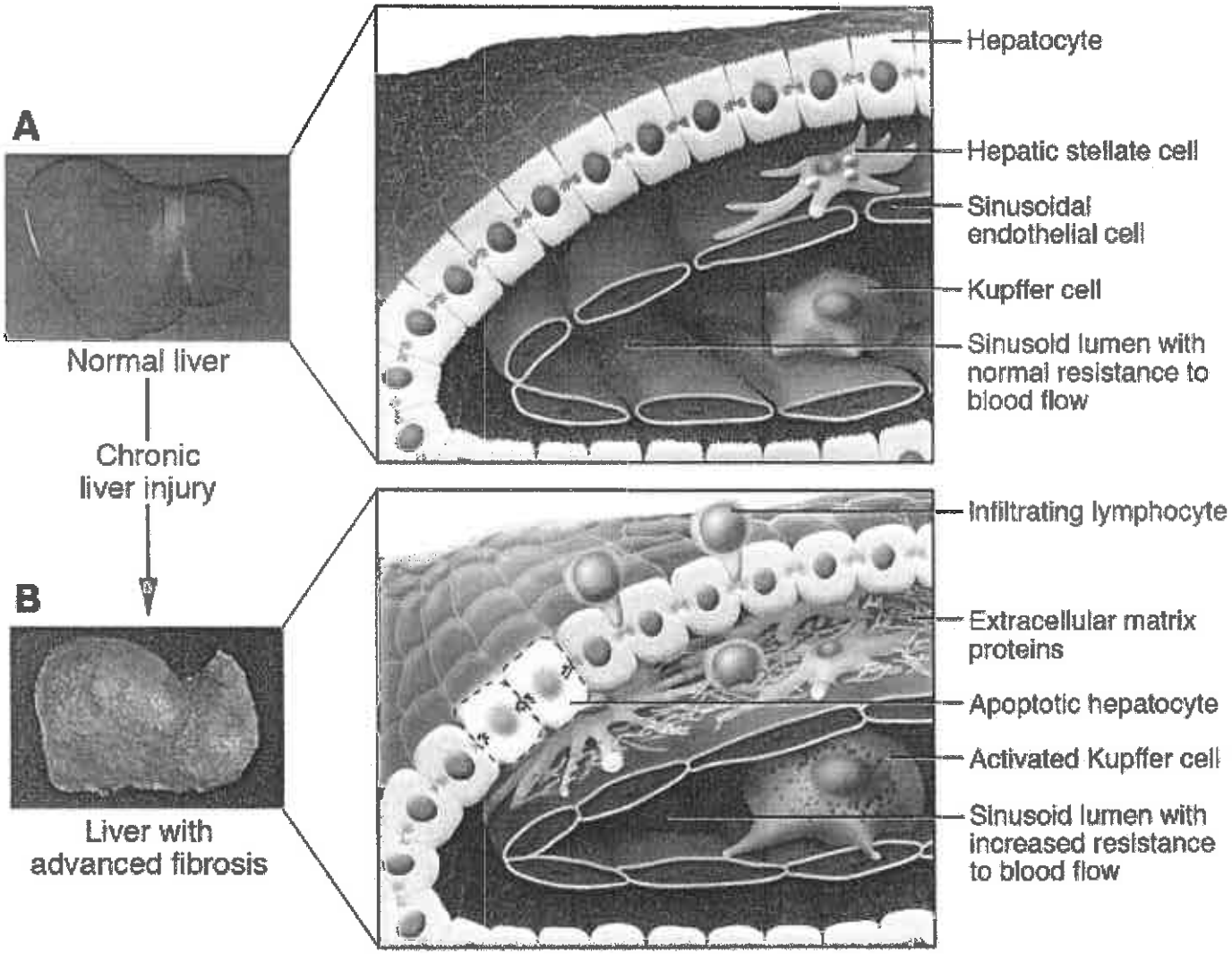
External links

- International Scar Meeting in Tokyo 2010 (http://www.gerd-gauglitz.de/international-scar-meeting-in-tokyo-2010/) International Scar Meeting



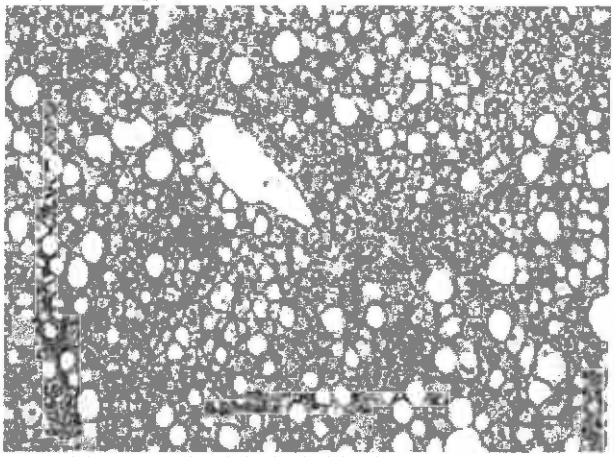
WIKIPEDIA

Fatty liver

Fatty liver is a reversible condition wherein large vacuoles of triglyceride fat accumulate in liver cells via the process of steatosis (i.e., abnormal retention of lipids within a cell). Despite having multiple causes, fatty liver can be considered a single disease that occurs worldwide in those with excessive alcohol intake and the obese (with or without effects of insulin resistance). The condition is also associated with other diseases that influence fat metabolism.[1] When this process of fat metabolism is disrupted, the fat can accumulate in the liver in excessive amounts, thus resulting in a fatty liver.[2] It is difficult to distinguish alcoholic FLD, which is part of alcoholic liver disease, from nonalcoholic FLD (NAFLD), and both show microvesicular and macrovesicular fatty changes at different stages.

Fatty liver

Synonyms Fatty liver disease (FLD), hepatic steatosis



Micrograph showing a fatty liver (macrovesicular steatosis), as seen in non-alcoholic fatty liver disease. Trichrome stain.

Specialty Gastroenterology

The accumulation of fat in alcoholic or non-alcoholic steatosis may also be accompanied by a progressive inflammation of the liver (hepatitis), called steatohepatitis. This more severe condition may be termed either alcoholic steatohepatitis or non-alcoholic steatohepatitis (NASH).

Exhibit C

Contents

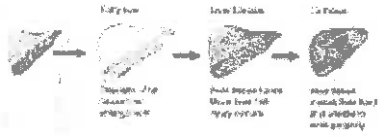
Signs and symptoms

Complications

Up to 10% of people with cirrhotic alcoholic FLD will develop hepatocellular carcinoma. The overall incidence of liver cancer in nonalcoholic FLD has not yet been quantified, but the association is well-established.[3]

Causes

Fatty liver (FL) is commonly associated with alcohol or metabolic syndrome (diabetes, hypertension, obesity, and dyslipidemia), but can also be due to any one of many causes:[4][5]



Different stages of liver damage

Metabolic
abetalipoproteinemia, glycogen storage diseases, Weber–Christian disease, acute fatty liver of pregnancy, lipodystrophy

Nutritional
malnutrition, total parenteral nutrition, severe weight loss, refeeding syndrome, jejunoileal bypass, gastric bypass, jejunal diverticulosis with bacterial overgrowth

Drugs and toxins
amiodarone, methotrexate, diltiazem, expired tetracycline, highly active antiretroviral therapy, glucocorticoids, tamoxifen,[6] environmental hepatotoxins (e.g., phosphorus, mushroom poisoning)

Alcohol

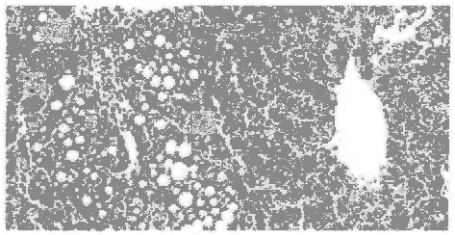
Alcoholism is one of the major causes of fatty liver due to production of toxic metabolites like aldehydes during metabolism of alcohol in the liver. This phenomenon most commonly occurs with chronic alcoholism.

Other

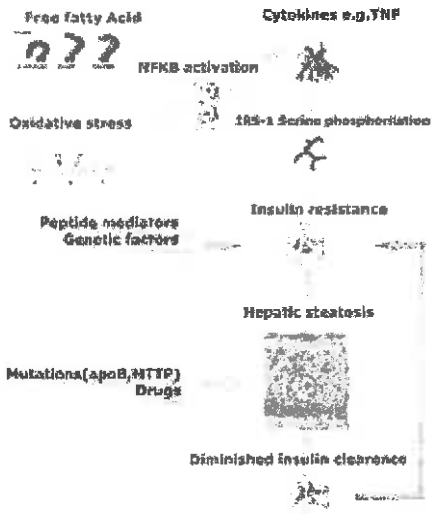
celiac disease,[7] inflammatory bowel disease, HIV, hepatitis C (especially genotype 3), and alpha 1-antitrypsin deficiency[8]

Pathology

Fatty change represents the intracytoplasmatic accumulation of triglycerides (neutral fats). At the beginning, the hepatocytes present small fat vacuoles (liposomes) around the nucleus (microvesicular fatty change). In this stage, liver cells are filled with multiple fat droplets that do not displace the centrally located nucleus. In the late stages, the size of the vacuoles increases, pushing the nucleus to the periphery of the cell, giving characteristic signet ring appearance (macrovesicular fatty change). These vesicles are well-delineated and optically "empty" because fats dissolve during tissue processing. Large vacuoles may coalesce and produce fatty cysts, which are irreversible lesions. Macrovesicular steatosis is the most common form and is typically associated with alcohol, diabetes, obesity, and corticosteroids. Acute fatty liver of pregnancy and Reye's syndrome are examples of severe liver disease caused by microvesicular fatty change.[9] The diagnosis of steatosis is made when fat in the liver exceeds 5–10% by weight.[1][10][11]



Micrograph of periportal hepatic steatosis, as may be seen due to steroid use, trichrome stain

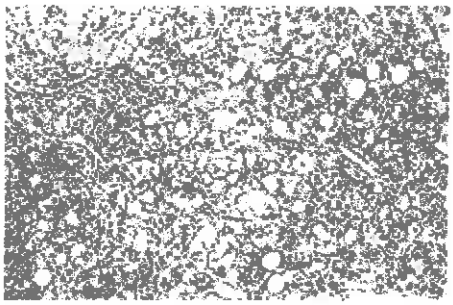


Mechanism leading to hepatic steatosis

Defects in fatty acid metabolism are responsible for pathogenesis of FLD, which may be due to imbalance in energy consumption and its combustion, resulting in lipid storage, or can be a consequence of peripheral resistance to insulin, whereby the transport of fatty acids from adipose tissue to the liver is increased.[1][12] Impairment or inhibition of receptor molecules (PPAR-α, PPAR-γ and SREBP1) that control the enzymes responsible for the oxidation and synthesis of fatty acids appears to contribute to fat accumulation. In addition, alcoholism is known to damage mitochondria and other cellular structures, further impairing cellular energy mechanism. On the other hand, non-alcoholic FLD may begin as excess of unmetabolised energy in liver cells. Hepatic steatosis is considered reversible and to some extent nonprogressive if the underlying cause is reduced or removed.

Severe fatty liver is sometimes accompanied by inflammation, a situation referred to as steatohepatitis. Progression to alcoholic steatohepatitis (ASH) or non-alcoholic steatohepatitis (NASH) depends on the persistence or severity of the

inciting cause. Pathological lesions in both conditions are similar. However, the extent of inflammatory response varies widely and does not always correlate with degree of fat accumulation. Steatosis (retention of lipid) and onset of steatohepatitis may represent successive stages in FLD progression.[13]

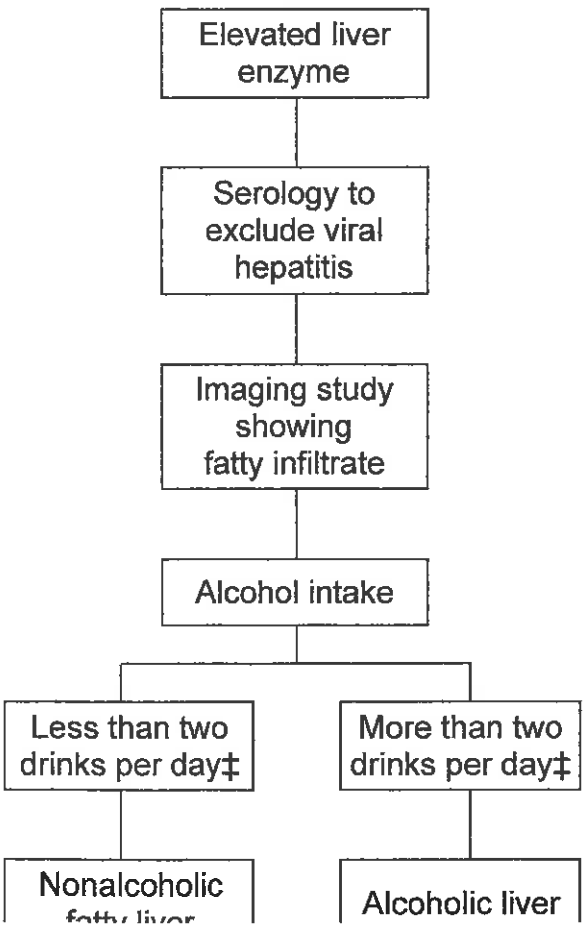

Micrograph of inflamed fatty liver (steatohepatitis)

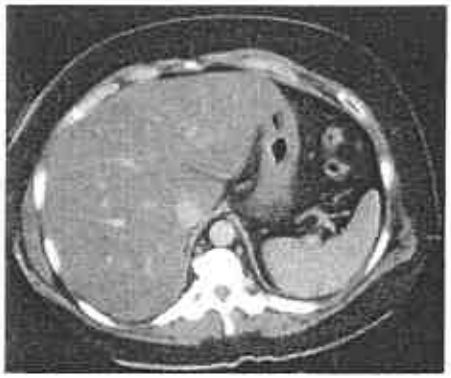
Liver disease with extensive inflammation and a high degree of steatosis often progresses to more severe forms of the disease.[14] Hepatocyte ballooning and necrosis of varying degrees are often present at this stage. Liver cell death and inflammatory responses lead to the activation of hepatic stellate cells, which play a pivotal role in hepatic fibrosis. The extent of fibrosis varies widely. Perisinusoidal fibrosis is most common, especially in adults, and predominates in zone 3 around the terminal hepatic veins.[15]

The progression to cirrhosis may be influenced by the amount of fat and degree of steatohepatitis and by a variety of other sensitizing factors. In alcoholic FLD, the transition to cirrhosis related to continued alcohol consumption is well-documented, but the process involved in non-alcoholic FLD is less clear.

Diagnosis

Flow chart for diagnosis, modified from[5]




Liver steatosis (fatty liver disease) as seen on CT

‡ Criteria for nonalcoholic fatty liver disease: consumption of ethanol less than 20 g/day for women and 30 g/day for men[16]

Ultrasound showing diffuse increased echogenicity of the liver.

Most individuals are asymptomatic and are usually discovered incidentally because of abnormal liver function tests or hepatomegaly noted in unrelated medical conditions. Elevated liver biochemistry is found in 50% of patients with simple steatosis.[17] The serum alanine transaminase level usually is greater than the aspartate transaminase level in the nonalcoholic variant and the opposite in alcoholic FLD (AST:ALT more than 2:1).

Imaging studies are often obtained during the evaluation process. Ultrasonography reveals a "bright" liver with increased echogenicity. Medical imaging can aid in diagnosis of fatty liver; fatty livers have lower density than spleens on computed tomography (CT), and fat appears bright in T1-weighted magnetic resonance images (MRIs). No medical imagery, however, is able to distinguish simple steatosis from advanced NASH. Histological diagnosis by liver biopsy is sought when assessment of severity is indicated.

Treatment

The treatment of fatty liver depends on its cause, and, in general, treating the underlying cause will reverse the process of steatosis if implemented at an early stage. Two known causes of fatty liver disease are an excess consumption of alcohol and a prolonged diet containing foods with a high proportion of calories coming from lipids.[18] For people with non-alcoholic fatty liver disease with pure steatosis and no evidence of inflammation, a gradual weight loss is often the only recommendation.[4] In more serious cases, medications that decrease insulin resistance, hyperlipidemia, and those that induce weight loss have been shown to improve liver function.[5]

For advanced cases of non-alcoholic steatohepatitis (NASH), there are no currently available therapies.

Bariatric surgery, while not currently recommended as a treatment for fatty liver disease (FLD) alone, has been shown to revert FLD and advanced steatohepatitis in over 90% of people who have undergone this surgery for the treatment of obesity.[19]

A number of dietary changes may be recommended, evidence to support them is limited as of 2017.[20]

Epidemiology

The prevalence of FLD in the general population ranges from 10% to 24% in various countries.[4] However, the condition is observed in up to 75% of obese people, 35% of whom progress to NAFLD,[21] despite no evidence of excessive alcohol consumption. FLD is the most common cause of abnormal liver function tests in the United States.[4] "Fatty livers occur in 33% of European-Americans, 45% of Hispanic-Americans, and 24% of African-Americans."[22]

See also

- Steatosis
- Steatohepatitis
- Alcoholic liver disease
- Non-alcoholic fatty liver disease
- Metabolic syndrome
- Cirrhosis
- Focal fatty liver
- Acute fatty liver of pregnancy
- Feline hepatic lipidosis

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External links

Classification	V · T · D

	ICD-10: K70 (http://apps.who.int/classifications/icd10/browse/2016/en#/K70), K76.0 (http://apps.who.int/classifications/icd10/browse/2016/en#/K76.0) · **ICD-9-CM**: 571.0 (http://www.icd9data.com/getICD9Code.ashx?icd9=571.0), 571.8 (http://www.icd9data.com/getICD9Code.ashx?icd9=571.8) · **DiseasesDB**: 18844 (http://www.diseasesdatabase.com/ddb18844.htm)
External resources	**eMedicine**: med/775 (http://www.emedicine.com/med/topic775.htm) article/170409 (https://emedicine.medscape.com/article/170409-overview)

- American Association for the Study of Liver Diseases (http://www.aasld.org)
- American Liver Foundation (http://www.liverfoundation.org)
- Fatty Liver Disease (http://www.liver.ca/liver-disease/types/fatty-liver.aspx), Canadian Liver Foundation
- *00474 (http://chorus.rad.mcw.edu/doc/00474.html)* at CHORUS
- Photo at Atlas of Pathology (http://www.pathologyatlas.ro/fatty-change-liver-steatosis-pathology.php)
- Healthdirect (http://www.healthdirect.gov.au/fatty-liver)

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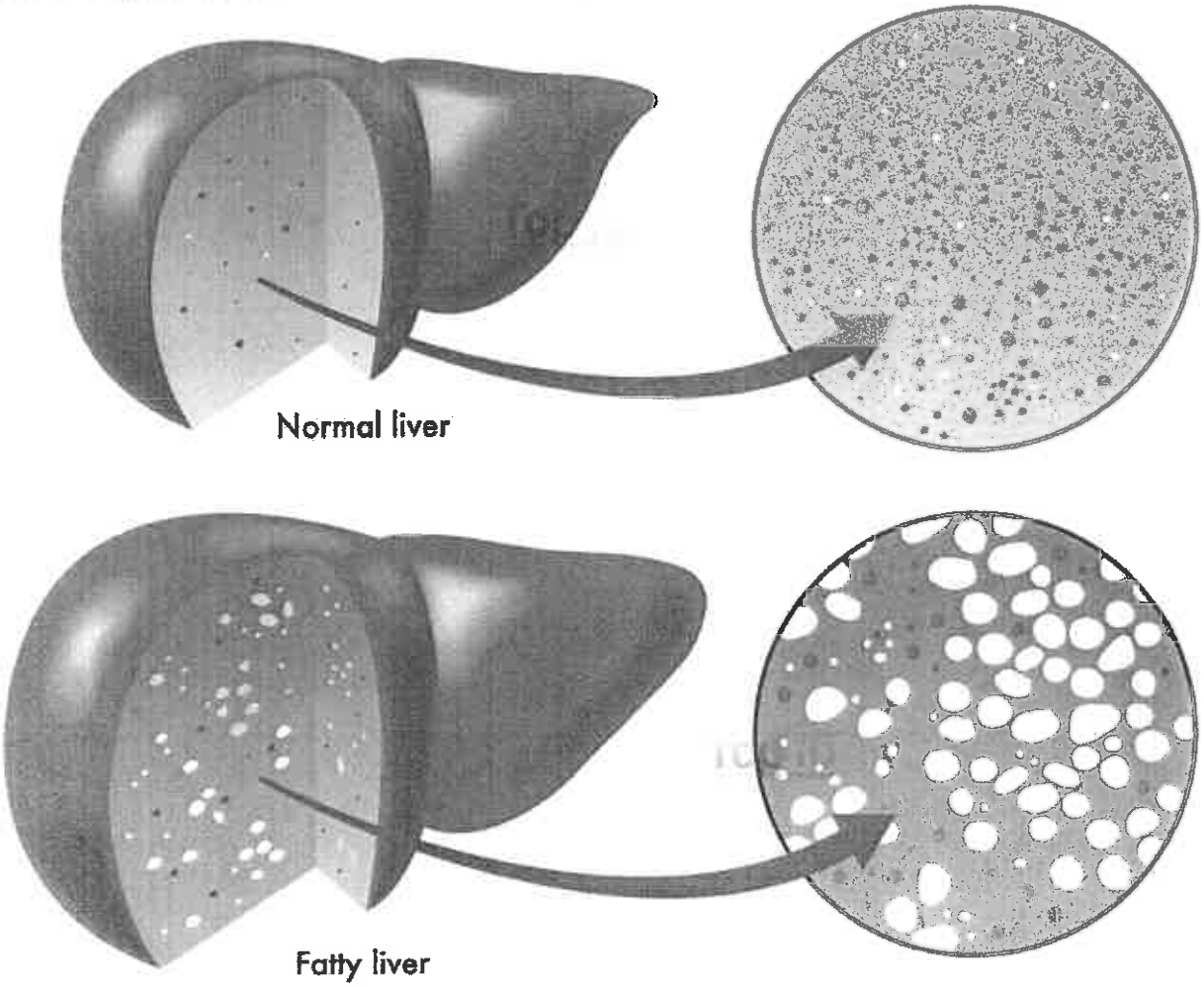
This page was last edited on 22 February 2018, at 06:47.

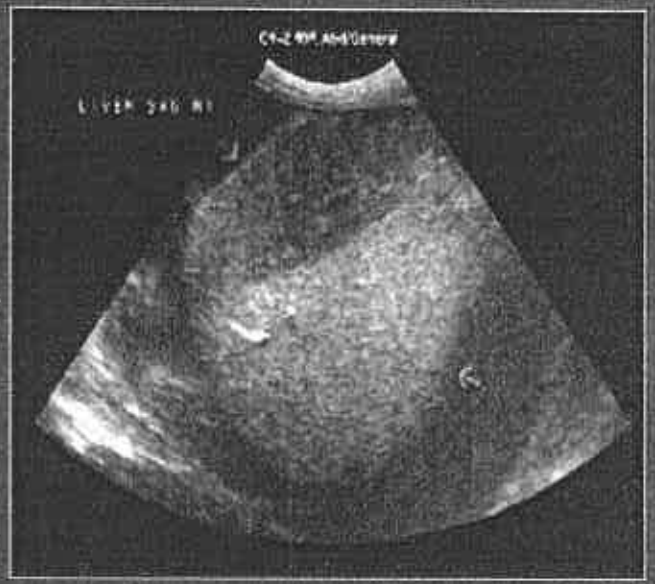
Top 10 Home Remedies

Hepatic Steatosis
(Fatty liver)



Focal fatty infiltration

- usually affects large areas of the liver with a geographical or wedge-shaped outline and a subcapsular distribution.
- Areas of focal fatty infiltration commonly interdigitate with areas of normal hepatic parenchyma.
- Normal vessels may be seen coursing through these areas indicating preservation of hepatic architecture.



Q: What is grade 1, stage 1 in hepatitis C cases?

A:

QUICK ANSWER

A grade 1, stage 1 hepatitis C case has minimal inflammation with only portal fibrosis, according to Mayo Clinic. An individual at this point is only minimally affected by the disease. CONTINUE READING

KEEP LEARNING

What is hepatitis C?

What are the usual stages of progression for hepatitis C?

What's the difference between hepatitis B and C?

RELATED VIDEOS

Atopic Dermatitus

Exhibit D

FULL ANSWER

Doctors score cases of the hepatitis C virus, or HCV, by the grade of necroinflammation, or the rate of death and inflammation of the liver cells, and the stage of fibrosis, or the rate of the scarring of the liver tissues, explains Mayo Clinic. Grades go from A0 to A3, and stages range from F0 to F4. The most severe cases of HCV are grade A3, stage F4. At this point, patients experience severe necroinflammation activity and cirrhosis of the liver. Grade A1, stage F1 has very little scarring and inflammation. Those with grade A0, stage F0 have no symptoms of HCV.

Hepatitis C is a virus that attacks the liver and can lead to cirrhosis and liver cancer, explains WebMD. HCV is a sexually transmitted disease that can also spread through infected needles and bodily fluids. A person can get HCV through blood transfusions or organ transplants already infected with the virus. However, if doctors catch the disease early enough, certain drugs can cure or treat it.

LEARN MORE ABOUT CONDITIONS & DISEASES

Sources: mayomedicallaboratories.com [illegible]

RELATED QUESTIONS

Q: What happens in stage 4 of hepatitis C?

A: Stage 4, also known as the end stage, of hepatitis C means that the liver has been severely damaged and the patient is suffering from liver failure, accord... FULL ANSWER >

FILED UNDER: CONDITIONS & DISEASES

Q: What is the typical course of treatment for encephalitis?

A: The typical treatment course for mild cases of encephalitis includes bed rest, plenty of fluids and over-the-counter pain relievers that reduce inflammatio... FULL ANSWER >

FILED UNDER: CONDITIONS & DISEASES

Q: How easily is hepatitis C contracted?

A: Hepatitis C is fairly difficult to transmit unless a well person contacts the blood of a person suffering from the disease, notes WebMD. The most frequent ... FULL ANSWER >

FILED UNDER: CONDITIONS & DISEASES

Q: Is hepatitis C contagious?

A: Hepatitis C is a contagious liver disease that is spread through contact with blood infected with the hepatitis C virus, according to the Centers for Disea... FULL ANSWER >

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YOU MAY ALSO LIKE

- **Q:** What is the treatment for hammertoe?
- **Q:** Can a hematoma with unbroken skin in the lower leg cause septicemia?
- **Q:** What are the main causes of diabetes?
- **Q:** How do you heal hemorrhoids?
- **Q:** What is the treatment for a floating kneecap?
- **Q:** Which foods help with arthritis?

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Hepatitis C FAQs for Health Professionals

Index of Questions

Overview and Statistics

What are the case definitions for reportable hepatitis C virus (HCV) infections?

- The specific viral cause of illness cannot be determined based solely on signs, symptoms, history, or current risk factors, but must be verified by specific serologic testing. Case definitions have been developed by CDC, in collaboration with the Council of State and Territorial Epidemiologists, to provide uniform clinical and laboratory-testing criteria for the identification and reporting of nationally notifiable infectious diseases. The case definitions for acute and chronic hepatitis C are available at the following links:
  - Acute hepatitis C (https://wwwn.cdc.gov/nndss/conditions/hepatitis-c-acute/)
  - Chronic hepatitis C (https://wwwn.cdc.gov/nndss/conditions/hepatitis-c-chronic/)

  Additional guidance on viral hepatitis surveillance and case management is available.

How many new HCV infections occur annually in the United States?

In 2015, 2,436 cases of acute hepatitis C were reported from 40 states to CDC. The overall incidence rate for 2015 was 0.8 cases per 100,000 population, an increase from 2011–2012. After adjusting for under-ascertainment and under-reporting, an estimated 33,900 acute hepatitis C cases occurred in 2015. More information on hepatitis C surveillance is available: Surveillance for Viral Hepatitis—United States, 2015.

What is the prevalence of chronic HCV infection in the United States?

An estimated 3.5 million people in the United States have chronic hepatitis C (1).

Who is at risk for HCV infection?

The following people are at increased risk for HCV infection:

- Current or former injection drug users, including those who injected only once many years ago
- Recipients of clotting factor concentrates made before 1987, when less advanced methods for manufacturing those products were used
- Recipients of blood transfusions or solid organ transplants prior to July 1992, before better testing of blood donors became available
- Chronic hemodialysis patients
- People with known exposures to HCV, such as
  - health care workers after needle sticks involving HCV-positive blood
  - recipients of blood or organs from a donor who tested HCV-positive
- People with HIV infection
- Children born to HCV-positive mothers

Is it possible for someone to become infected with HCV and then spontaneously clear the infection?

Yes. Approximately 15%–25% of people clear the virus from their bodies without treatment and do not develop chronic infection; the reasons for this are not well known. Predictors of spontaneous clearance include jaundice, elevated ALT level, hepatitis B virus surface antigen (HBsAg) positivity, female sex, younger age, HCV genotype 1, and host genetic polymorphisms, most notably those near the IL28B gene (2, 3).

How likely is HCV infection to become chronic?

HCV infection becomes chronic in approximately 75%–85% of cases (2, 3).

Why do most persons remain chronically infected with HCV?

A person infected with HCV mounts an immune response to the virus, but replication of the virus during infection can result in changes that evade the immune response. This may explain how the virus establishes and maintains chronic infection (3).

What are the chances of someone developing chronic HCV infection, cirrhosis, or liver cancer or dying because of hepatitis C?

Of every 100 people infected with HCV, approximately:

- 75-85 will go on to develop chronic infection
- 10-20 will go on to develop cirrhosis over a period of 20-30 years

Among patients with cirrhosis, there is:

- 1-5% annual risk of hepatocellular carcinoma
- 3-6% annual risk of hepatic decompensation, for which the risk of death in the following year is 15-20%

Rates of progression to cirrhosis are increased in the presence of a variety of factors: males > females, age >50 years, alcohol, nonalcoholic fatty liver disease, HBV or HIV coinfection, immunosuppressive therapy (2–4).

Can people become infected with a different strain of HCV after they have cleared the initial infection?

Yes. Prior infection with HCV does not protect against later infection with the same or different genotypes of the virus. This is because people infected with HCV typically have an ineffective immune response due to changes in the virus during infection. For the same reason, no effective pre- or post-exposure prophylaxis (i.e., immune globulin) is available.

Is hepatitis C a common cause for liver transplantation?

Yes. Chronic HCV infection is a common reason for liver transplants in the United States (5, 6).

How many deaths can be attributed to chronic HCV infection?

In 2015, 19,629 U.S. death certificates had HCV recorded as an underlying or contributing cause of death (7). However, this is a conservative estimate. Evidence derived from a cohort of patients with known HCV infection who received care at four large health care organizations in the United States found that only 19% of decedents had HCV infection listed on their death certificates. More than 70% of these decedents had evidence of moderate to severe underlying liver disease (according to the electronic health record, liver biopsy, or FIB-4 score) and the average age at death was 59 years (8).

Is there a hepatitis C vaccine?

No vaccine for hepatitis C is available. Research into the development of a vaccine is under way.

Transmission and Symptoms

How is HCV transmitted?

HCV is transmitted primarily through parenteral exposures to infectious blood or body fluids that contain blood. Possible exposures include

- Injection drug use (currently the most common means of HCV transmission in the United States) (7)
- Receipt of donated blood, blood products, and organs (once a common means of transmission but now rare in the United States since blood screening became available in 1992)
- Needlestick injuries in health care settings
- Birth to an HCV-infected mother

Although infrequent, HCV can also be spread through:

- Sex with an HCV-infected person (an inefficient means of transmission, although HIV-infected men who have sex with men [MSM] have increased risk of sexual transmission)
- Sharing personal items contaminated with infectious blood, such as razors or toothbrushes (also inefficient vectors of transmission)
- Other health care procedures that involve invasive procedures, such as injections (usually recognized in the context of outbreaks)
- Unregulated tattooing

What is the prevalence of HCV infection among injection drug users (IDUs)?

There are no nationwide seroprevalence surveys targeting PWID in the United States; estimates based on smaller surveys in regional and metropolitan areas vary considerably. A multi-state systematic review of global HCV infection prevalence among PWID published in 2017 provided a point estimate of 53.1% in the United States, with a range of 38.1% to 68.0% (9).

Is cocaine use associated with HCV transmission?

There are limited epidemiologic data to suggest an additional risk from non-injection (snorted or smoked) cocaine use, but this risk is difficult to differentiate from associated injection drug use and sex with HCV-infected partners.

What is the risk of acquiring HCV infection from transfused blood or blood products in the United States?

Now that more advanced screening tests for HCV are used in blood banks, the risk is considered to be less than 1 chance per 2 million units transfused. Before 1992, when blood screening for HCV became available, blood transfusion was a leading means of HCV transmission (10, 11)

Can HCV be spread during medical or dental procedures?

As long as Standard Precautions and other infection control practices are used consistently, medical and dental procedures performed in the United States generally do not pose a risk for the spread of HCV. However, HCV is spread in health care settings when injection equipment, such as syringes, is shared between patients or when injectable medications or intravenous solutions are mishandled and become contaminated with blood. Health care personnel should understand and adhere to Standard Precautions, which includes Injection Safety practices aimed at reducing bloodborne pathogen risks for patients and health care personnel. If health care-associated HCV infection is suspected, this should be reported to state and local public health authorities.

Can HCV be spread within a household?

Yes, but this does not occur very often. If HCV is spread within a household, it is most likely a result of direct, –parenteral or percutaneous– exposure to the blood of an infected household member.

What are the signs and symptoms of acute HCV infection?

People with newly acquired HCV infection usually are asymptomatic or have mild symptoms that are unlikely to prompt a visit to a health care professional. When symptoms do occur, they can include:

- Fever
- Fatigue
- Dark urine
- Clay-colored stool
- Abdominal pain
- Loss of appetite
- Nausea
- Vomiting
- Joint pain
- Jaundice

What percentage of persons infected with HCV develop symptoms of acute illness?

Approximately 20%–30% of those newly infected with HCV experience fatigue, abdominal pain, poor appetite, or jaundice (12).

How soon after exposure to HCV do symptoms appear?

In those people who do develop symptoms, the average period from exposure to symptom onset is 2–12 weeks (range: 2–26 weeks) (13, 14).

What are the signs and symptoms of chronic HCV infection?

Most people with chronic HCV infection are asymptomatic or have non-specific symptoms such as chronic fatigue and depression. Many eventually develop chronic liver disease, which can range from mild to severe, including cirrhosis and liver cancer. Chronic liver disease in HCV-infected people is usually insidious, progressing slowly without any signs or symptoms for several decades. In fact, HCV infection is often not recognized until asymptomatic people are identified as HCV-positive when screened for blood donation or when elevated alanine aminotransferase (ALT, a liver enzyme) levels are detected during routine examinations.

Testing and Diagnosis

Who should be tested for HCV infection?

CDC recommends HCV testing for:

- Current or former injection drug users, including those who injected only once many years ago
- Everyone born from 1945 through 1965 (15)
- Recipients of clotting factor concentrates made before 1987, when less advanced methods for manufacturing those products were used
- Recipients of blood transfusions or solid organ transplants prior to July 1992, before better testing of blood donations became available
- Chronic hemodialysis patients
- People with known exposures to HCV, such as
  - health care workers after needle sticks involving HCV-positive blood
  - recipients of blood or organs from a donor who tested HCV-positive
- People with HIV infection
- Children born to HCV-positive mothers

U.S. Preventive Services Task Force (USPSTF) also recommends HCV testing (https://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/hepatitis-c-screening) for:

- Incarcerated persons
- People who use intranasal drugs,
- People who get an unregulated tattoo

What blood tests are used to detect HCV infection?

Several blood tests are performed to test for HCV infection, including:

- Screening tests for antibody to HCV (anti-HCV)
  - enzyme immunoassay (EIA)
  - enhanced chemiluminescence immunoassay (CIA)
- Qualitative tests to detect presence or absence of virus (HCV RNA polymerase chain reaction [PCR])
- Quantitative tests to detect amount (titer) of virus (HCV RNA PCR)

How do I interpret the different tests for HCV infection?

A table on the interpretation of results of tests for hepatitis C virus (HCV) infection and further actions is available at https://www.cdc.gov/hepatitis/HCV/PDFs/hcv_graph.pdf [PDF – 1 page].

Is an algorithm for HCV diagnosis available?

A flow chart that outlines the serologic testing process beginning with anti-HCV testing is available at https://www.cdc.gov/hepatitis/HCV/PDFs/hcv_flow.pdf [PDF – 541 KB].

How soon after exposure to HCV can anti-HCV be detected?

HCV infection can be detected by anti-HCV screening tests (enzyme immunoassay) 4–10 weeks after infection. Anti-HCV can be detected in >97% of people by 6 months after exposure (12, 16–19).

How soon after exposure to HCV can HCV RNA be detected by PCR?

HCV RNA appears in blood and can be detected as early as 2–3 weeks after infection (12, 16–19).

Under what circumstances is a false-positive anti-HCV test result likely?

False-positive anti-HCV tests appear more often when people at low risk for HCV infection (e.g., blood donors) are tested. Therefore, it is important to follow-up all positive anti-HCV tests with an RNA test to establish current infection.

Under what circumstances might a false-negative anti-HCV test result occur?

People with early HCV infection might not yet have developed antibody levels high enough that the test can measure. In addition, some people might lack the (immune) response necessary for the test to work well. In these people, further testing such as PCR for HCV RNA may be considered.

Can a patient have a normal liver enzyme (e.g., ALT) level and still have chronic hepatitis C?

Yes. It is common for patients with chronic hepatitis C to have liver enzyme levels that go up and down, with periodic returns to normal or near normal levels. Liver enzyme levels can remain normal for over a year despite chronic liver disease (17).

Where can I learn more about hepatitis C serology?

CDC offers an online training that covers the serology of acute and chronic hepatitis C and other types of viral hepatitis, available at https://www.cdc.gov/hepatitis/resources/professionals/training/serology/training.htm.

Management and Treatment

What should be done for a patient with confirmed HCV infection?

HCV-positive patients should be evaluated (by referral or consultation, if appropriate) for presence of chronic liver disease, including assessment of liver function tests, evaluation for severity of liver disease and recommended HCV treatment, and determination of the need for hepatitis A and hepatitis B vaccination. More information on recommendations for testing, management, and treating hepatitis C are available at: http://www.hcvguidelines.org (http://www.hcvguidelines.org)

When might a specialist be consulted in the management of HCV-infected persons?

Any clinician who manages a person with hepatitis C should be knowledgeable and current on all aspects of the care of a person with hepatitis C; this can include some internal medicine and family practice physicians, nurse practitioners, physician assistants, pharmacists, as well as specialists such as infectious disease physicians, gastroenterologists, or hepatologists.

What is the treatment for acute hepatitis C?

New treatment guidelines recommend no treatment of acute hepatitis C. Patients with acute HCV infection should be followed and only considered for treatment if HCV RNA persists after 6 months. For more information see http://www.hcvguidelnes.org (http://www.hcvguidelnes.org)

What is the treatment for chronic hepatitis C?

The treatment for hepatitis C virus (HCV) infection has evolved substantially since the introduction of highly effective HCV protease inhibitor therapies in 2011. Since that time new drugs with different mechanisms of action have become and continue to become available. Currently available therapies can achieve sustained virologic response (SVR) defined as the absence of detectable virus 12 weeks after completion of treatment; an SVR is indicative of a cure of HCV infection. Over 90% of HCV infected persons can be cured of HCV infection regardless of HCV genotype, with 8-12 weeks of oral therapy (20). For a complete list of currently approved FDA therapies to treat hepatitis C, please visit http://www.hepatitisc.uw.edu/page/treatment/drugs (http://www.hepatitisc.uw.edu/page/treatment/drugs) .

To provide health care professionals with timely guidance as new therapies are available and integrated into HCV regimens, the Infectious Diseases Society of America (IDSA) and American Association for the Study of Liver Diseases (AASLD), in collaboration with the International Antiviral Society–USA (IAS–USA), developed evidence-based, expert-developed recommendations for hepatitis C management: http://www.hcvguidelines.org (http://www.hcvguidelines.org/) .

How many different genotypes of HCV exist?

Seven distinct HCV genotypes and more than 67 subtypes have been identified (21). Genotype 1 is the most common HCV genotype in the United States (22, 23).

Is it necessary to do viral genotyping when managing a person with chronic hepatitis C?

Yes. Because there are seven distinct genotypes and more than 67 subtypes of HCV, genotype information is helpful in defining the epidemiology of hepatitis C and in making recommendations regarding appropriate treatment regimen. In the United States, HCV genotype 1 is most common, accounting for approximately 70% of prevalent cases. Once the genotype is identified, it need not be tested again; genotypes do not change during the course of infection (22, 23).

Can superinfection with more than one genotype of HCV occur?

Superinfection is possible if risk behaviors (e.g., injection drug use) for HCV infection continue; however, superinfection does not appear to complicate decisions regarding treatment, and new HCV antivirals with pangenotypic activity are available.

Does chronic hepatitis C affect only the liver?

A small percentage of people with chronic HCV infection develop medical conditions due to hepatitis C that are not limited to the liver. Such conditions can include:

- Fatigue
- Diabetes mellitus
- Glomerulonephritis
- Essential mixed cryoglobulinemia
- Porphyria cutanea tarda
- Non-Hodgkin's lymphoma

Counseling Patients

What topics should be discussed with patients who have HCV infection?

- First and foremost, patients should be informed about the effectiveness and benefits of new direct acting antivirals (DAAs) and referred for prompt assessment and treatment, if indicated.
- Patients should be informed about the low but present risk for transmission with sex partners.
- Sharing personal items that might have blood on them, such as toothbrushes or razors, can pose a risk to others.
- Cuts and sores on the skin should be covered to keep from spreading infectious blood or secretions.
- Donating blood, organs, tissue, or semen can spread HCV to others.
- HCV is not spread by sneezing, hugging, holding hands, coughing, sharing eating utensils or drinking glasses, or through food or water.

What should HCV-infected persons be advised to do to protect their livers from further harm?

- Patients should be informed about the effectiveness and benefits of new direct acting antivirals (DAAs) and referred for prompt assessment and treatment, if indicated.
- HCV-positive patients should be advised to avoid alcohol because it can accelerate cirrhosis and end-stage liver disease.
- Viral hepatitis patients should also check with a health professional before taking any new prescription pills, over-the counter drugs (such as non-aspirin pain relievers), or supplements, as these can potentially damage the liver.
- Clinicians may wish to consider vaccinating HCV-positive patients against hepatitis A and hepatitis B even in the absence of liver disease.

Should HCV-infected persons be restricted from working in certain occupations or settings?

CDC's recommendations for prevention and control of HCV infection specify that people should not be excluded from work, school, play, child care, or other settings on the basis of their HCV infection status. There is no evidence of HCV transmission from food handlers, teachers, or other service providers in the absence of blood-to-blood contact.

Hepatitis C and Health Care Personnel

What is the risk for HCV infection from a needlestick exposure to HCV-contaminated blood?

After a needlestick or sharps exposure to HCV-positive blood, the risk of HCV infection is 0.1% (24).

Other than needlesticks, do other exposures, such as splashes to the eye, pose a risk to health care personnel for HCV transmission?

Although a few cases of HCV transmission via blood splash to the eye have been reported, the risk for such transmission is expected to be very low. Avoiding occupational exposure to blood is the primary way to prevent transmission of bloodborne illnesses among health care personnel. All health care personnel should adhere to Standard Precautions. Depending on the medical procedure involved, Standard Precautions may include the appropriate use of personal protective equipment (e.g., gloves, masks, and protective eyewear).

Should HCV-infected health care personnel be restricted in their work?

There are no CDC recommendations to restrict a health care worker who is infected with HCV. The risk of transmission from an infected health care worker to a patient appears to be very low. All health care personnel, including those who are HCV positive, should follow a strict aseptic technique and Standard Precautions, including appropriate hand hygiene, use of protective barriers, and safe injection practices.

What is the recommended management of a health care worker with occupational exposure to HCV?

Postexposure prophylaxis (PEP) for hepatitis C is not recommended, as outlined in the 2001 MMWR on management of health-care personnel (HCP) who have occupational exposure to blood and other body fluids. Test the source for HCV RNA. If the source is HCV RNA positive, or if HCV infection status is unknown, follow this testing algorithm [PDF – 2 pages] (update to 2001 guidance).

After a needlestick or sharps exposure to HCV-positive blood, the risk of HCV infection is 0.1% (24). If the health care worker does become infected, follow AASLD/IDSA guidelines for management and treatment of hepatitis C (http://hcvguidelines.org/) .

Pregnancy and HCV Infection

Should pregnant women be routinely tested for anti-HCV?

At this time, pregnant women should be tested for anti-HCV if they have or are suspected to have risk factors for HCV infection (https://www.cdc.gov/hepatitis/hcv/hcvfaq.htm#a6) (20, 25. 26). CDC is in the process of reviewing the evidence to determine if additional HCV screening recommendations, specific to pregnant women, are warranted.

What is the risk that an HCV-infected mother will spread HCV to her infant during birth?

The overall risk of an HCV-infected mother transmitting infection to their infant is approximately 4% to 7% per pregnancy. Transmission occurs at the time of birth, and no prophylaxis is available to prevent it. The risk is significantly higher if the mother has a high viral load or is coinfected with HIV. Most infants infected with HCV at birth have no symptoms and do well during childhood. More research is needed to find out the long-term effects of perinatal HCV infection (27).

Should a woman with HCV infection be advised against breastfeeding?

No. There is no evidence that breastfeeding spreads HCV. While there is currently not enough information on the risks of transmission through breastfeeding by HCV-positive mothers with cracked or bleeding nipples, precautions may be considered (28).

When should children born to HCV-infected mothers be tested to see if they were infected at birth?

Children should be tested for anti-HCV no sooner than age 18 months because anti-HCV from the mother might last until this age. If diagnosis is desired before the child reaches 18 months, testing for HCV RNA can be performed at or after the infant's first well-child visit at age 1–2 months. HCV RNA testing should then be repeated at a subsequent visit, independent of the initial HCV RNA test result (29).

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National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention (/nchhstp)

Viral Hepatitis

Hepatitis C medications: A review and update for patients

Last reviewed/updated: February 14, 2017

CONTENTS

How is hepatitis C treated?

Hepatitis C virus is treated with all-oral medications. These pills, called **antiviral medications**, are usually taken once per day. These antiviral medications are extremely good at attacking the virus and preventing it from multiplying.

Antiviral medications were not the original treatment for hepatitis C. Before 2014, the only treatment for hepatitis C was called interferon and ribavirin, taken as weekly injections under the skin, plus pills. Interferon treatment caused many unpleasant side effects and was not usually successful. Today's antiviral treatments are extremely successful at curing the virus and have very minimal side effects.

Ribavirin (without interferon) is sometimes prescribed to be taken along with the new antiviral medicines. Most patients do not need ribavirin, but for certain patients, ribavirin is needed as extra help for the antiviral medications to have the best chance at curing the hepatitis C virus. Ribavirin has some mild-moderate side effects. Ribavirin is a pill taken twice per day, as 2 or 3 pills in the morning plus 2 or 3 pills at night, depending on the patient's body weight.

Why should people take antiviral medications for hepatitis C?

The purpose of taking antiviral medications for hepatitis C is to:

- remove (or clear) all the hepatitis C virus from your body permanently
- stop or slow down the damage to your liver
- reduce the risk of developing cirrhosis (advanced scarring of the liver)
- reduce the risk of developing liver cancer (hepatocellular carcinoma)
- reduce the risk of liver failure and the need for a liver transplant

What does it mean to have a successful treatment? What is a Sustained Virologic Response (SVR)?

In an untreated state, the hepatitis C virus infects the cells of the liver and then continuously lives there, making copies of itself that circulate in the bloodstream. When antiviral medications are used, they can destroy the way the virus reproduces. The amount of virus in the bloodstream then decreases. The amount of virus in the blood is measured by a **viral load** (also called HCV RNA).

Treatment is successful when the viral load drops to **undetectable** levels, which means the virus cannot be detected in the bloodstream at all. The viral load becomes undetectable during treatment and remains undetected after treatment has ended. If there is still no detectable virus in the blood 12 weeks after the end of the treatment, the treatment was successful. This is called a Sustained Virologic Response (SVR).

THIS MEANS THEY SHOULD HAVE BEEN Doing Blood work During Course OF TREATMENT

A patient who has achieved an SVR is considered to be cured of the hepatitis C virus.

What are the names of the medications for treating hepatitis C?

There are many antiviral medications that are used to treat hepatitis C. Some are used alone, some are used in combination with each other, and ribavirin can be added to any of the medications on this list.

Antiviral medications in alphabetical order (not in order of preference):

- Daclatasvir (Daklinza) + Sofosbuvir (Solvaldi)
- Elbasvir/Grazoprevir (Zepatier)
- Ombitasvir/paritaprevir/ritonavir + Dasabuvir (Viekira is the name of the entire combination)
- Sofosbuvir (Solvaldi) + ribavirin
- Sofosbuvir/Ledipasvir (Harvoni)
- Sofosbuvir/Velpatasvir (Epclusa)
- Sofosbuvir (Solvaldi) + Simeprevir (Olysio)

There are also more medications expected to be developed and approved.

How long is the treatment?

Most of the time, treatment is 12 weeks long. Sometimes treatment can be 8 weeks long, and occasionally it needs to be either 16 or 24 weeks long.

How likely is it that the treatment will cure my hepatitis C virus?

In general, hepatitis C treatment regimens have extremely high success rates. Many of the regimens are successful in curing more than 90 percent of people and some of the regimens are successful in 95 to 99 percent of people. **All patients with hepatitis C should be evaluated for treatment.**

Some patients may have a somewhat lower likelihood of success. For patients who may have a lower chance of successful treatment, their provider may tell them to take the medication for longer and/or add ribavirin to the medications that are used.

The medications may not work as well in some patients who:

- have genotype 3 infection
- were treated previously but not cured, which is called "treatment experienced"
- have cirrhosis
- have changes in their virus, called "mutations," that cause the virus to be resistant to medications. Mutations can prevent the medications from working as well.

REASON I SHOULD HAVE BEEN REEVALUATED + HCV RNA VIRAL LOAD AFTER SEVEN MONTH DELAY

How quickly will the medications work?

The medications will usually cause a very big drop in the viral load within the first two weeks. Some patients will see their viral load become undetectable very early, such as by the fourth week. For other patients, it can take longer until their viral load becomes undetectable. If the drop in the viral load is very slow then the provider may add ribavirin, and/or extend the number of weeks for the treatment.

AND AGAIN, WHY I SHOULD HAVE HAD BLOOD WORK THROUGHOUT TREATMENT + HCV RNA VIRAL LOAD TESTED

What can people do to help the medications work best?

- ✓ Take the medications every day
- ✓ Stay in touch with pharmacy to be sure that all refills are ready on time
- ✓ Take the medications exactly as prescribed (in terms of timing with food or other medicines)
- ✓ Do not skip doses
- Get all blood tests done on time — HAD NO TEST AT ALL
- Go to all visits with providers as recommended — DID NOT SEE ANY ONE FOR VISIT
- ✓ Tell the provider about all other medications that are being taken - including over-the-counter medicines, vitamins, herbs, and supplements
- ✓ Complete the entire course of medication

What does it mean to relapse?

Relapse means that the treatment did not succeed in curing the virus. The medicine was able to clear the virus for a time, but then the virus came back. Re-treatment options should then be discussed with the provider.

How will my doctor monitor me during the treatment?

Your provider will meet with you during treatment to review how well you are tolerating treatment and review laboratory results. Laboratory tests help keep tabs on your health, track the viral load, and determine your response to treatment. You will be given specific dates to go get your blood tested at the lab during and after the treatment. NONE OF THIS HAPPENED

Side effects of antiviral medications

Hepatitis C antivirals have very mild or no side effects. Some of the side effects may be:

- Nausea
- Fatigue
- Headache
- Rash
- Disturbed sleep (insomnia)

Side effects of ribavirin

Ribavirin can have side effects that are more noticeable and more common. These side effects are reversible so they will stop when the ribavirin is stopped.

- Drop in red blood cell count (anemia)
- Cough
- Shortness of breath
- Chest pain
- Rash
- Birth defects (harm to embryo or fetus of pregnant patients)

Ribavirin and birth defects

Ribavirin can cause birth defects, harming the embryo or fetus of pregnant patients, so ribavirin should **not be taken during pregnancy**. In addition, both the patient and their sexual partner must use birth control during the ribavirin treatment and for 6 months after it is completed.

What about patients with hepatitis C who also have hepatitis B?

Hepatitis B virus can flare in patients who are co-infected with hepatitis B and hepatitis C and are taking medication for hepatitis C. This has been reported as a potential risk for patients who are taking hepatiis C treatment and have underlying hepatitis B as well. The flare usually occurs within a few weeks after the patient starts taking medication for hepatitis C. Therefore, patients who have both hepatitis B and hepatitis C should be seen by a hepatitis expert *before* starting treatment of the hepatitis C; they may need to start taking hepatitis B treatment to avoid a hepatitis B flare.

Are there ways to cure hepatitis C other than with medications?

Patients sometimes ask whether there are ways to treat hepatitis C other than taking medicines. Currently, there are no vaccines to prevent hepatitis C. Once a person is infected, the only way to treat it is with prescribed antiviral medications.

Some patients worry that having hepatitis C means they will need a liver transplant. Only a very small fraction of people with hepatitis C require a liver transplant. By far, most people with hepatitis C never need a liver transplant. A transplant is performed **only** when damage to the liver is extremely advanced and the liver is unable to perform its basic functions. A transplant provides a new working liver, but a transplant does not get rid of the hepatitis C virus in the patient. Patients with a liver transplant still need antiviral medication to cure their virus.

Helpful tips while taking hepatitis C medications

- Always follow your health care providers' advice, particularly the instructions on taking your medicine.
- If you have to cancel an appointment, call your doctor and schedule a new one as soon as possible.
- Take good care of yourself. Eat well, drink 8 to 10 glasses of water each day, and try to get a full night's sleep.
- Learn about the hepatitis C medications you are taking. This includes special risks and warnings.
- If taking ribavirin, use sunscreen, wear long sleeves and a hat, and limit sun exposure.
- Write down your doctor's name and phone number. Carry this information with you at all times.
- Write the names and amounts of the medicines you are taking. Carry this information with you at all times.

More information

For more about hepatitis C treatment, see our patient information (/patient/hcv/treat/index.asp), contact the Centers for Disease Control and Prevention (CDC) Hepatitis Toll-Free Information Line at 1-888-4 HEPCDC (1-888-443-7232), or visit the CDC website at http://www.cdc.gov/hepatitis/index.htm (https://www.cdc.gov/hepatitis/index.htm).

Rena K. Fox, MD (/patient/faqs/expert-bios.asp#rena)
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Last updated February 14, 2018

AASLD IDSA

AASLD AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

HCV Guidance: Recommendations for Testing, Managing, and Treating Hepatitis C

IDSA

HCV Testing and Linkage to Care

One-Time Hepatitis C Testing

Recommendations for One-Time Hepatitis C Testing	
RECOMMENDED	**RATING**
One-time hepatitis C testing is recommended for persons born* from 1945 through 1965 without prior ascertainment of risk.	I, B
Other persons should be screened for HCV infection risk factors. One-time testing should be performed for all persons with behaviors, exposures, and conditions or circumstances associated with an increased risk of HCV infection.	
Risk Behaviors	
Injection-drug use (current or ever, including those who injected only once)	
Intranasal illicit drug use	
Risk Exposures	
Persons on long-term hemodialysis (ever)	
Persons with percutaneous/parenteral exposures in an unregulated setting	
Healthcare, emergency medical, and public safety workers after needle-stick, sharps, or mucosal exposures to HCV-infected blood	
Children born to HCV-infected women	
Prior recipients of transfusions or organ transplants, including persons who:	I, B
Were notified that they received blood from a donor who later tested positive for HCV	
Received a transfusion of blood or blood components, or underwent an organ transplant before July 1992	
Received clotting factor concentrates produced before 1987	
Persons who were ever incarcerated	
Other Conditions and Circumstances	
HIV infection	
Sexually-active persons about to start pre-exposure prophylaxis (PreP) for HIV	
Unexplained chronic liver disease and/or chronic hepatitis, including elevated alanine aminotransferase (ALT) levels	
Solid organ donors (deceased and living)	

* Regardless of country of birth

There are an estimated 3.5 million HCV-infected persons in the United States, including 2.7 million in the general noninstitutionalized population ( ) and 800,000 incarcerated, institutionalized, or homeless persons ( ). Approximately 50% of all infected people are unaware that they have HCV ( ); ( ).

HCV testing is recommended in select populations based on demographics, possible exposures, high-risk behaviors, and medical conditions. Testing recommendations are based on HCV prevalence in these populations; proven benefits of care and treatment in reducing the risk of hepatocellular carcinoma and

Exhibit G

all-cause mortality; and the potential public health benefit of reducing transmission through early treatment, viral clearance, and reduced risk behaviors ( ); ( ); ( ).

HCV is primarily transmitted through percutaneous exposure to infected blood. Other modes of transmission include mother-to-infant and contaminated devices shared for noninjection drug use. Sexual transmission also occurs but generally seems inefficient except among HIV-infected men who have unprotected sex with men ( ).

Injection drug use poses the most significant risk for HCV infection, accounting for at least 60% of acute HCV infections in the United States. Healthcare exposures are important sources of transmission, including the receipt of blood products prior to 1992 (after which routine screening of the blood supply was implemented); receipt of clotting factor concentrates before 1987; long-term hemodialysis; needle-stick injuries among healthcare workers; and patient-to-patient transmission resulting from poor infection control practices.

Other risk factors include having been born to an HCV-infected mother, having been incarcerated, and percutaneous or parenteral exposures in an unregulated setting. Examples of these settings include tattoos received outside of licensed parlors and medical procedures done internationally or domestically where strict infection control procedures may not have been followed (eg, surgery before implementation of universal precautions) ( ).

The importance of these risk factors might differ based on geographic location and population ( ); ( ). An estimated 29% of incarcerated persons in North America are HCV-antibody –positive, supporting the recommendation to screen this population for HCV ( ).

Because of shared transmission modes, persons with HIV infection are at risk for HCV. Sexual transmission is a particular risk for HIV-infected men who have unprotected sex with men ( ); ( ). Screening sexually active, non-HIV-infected persons before they start pre-exposure prophylaxis (PreP) for HIV infection prevention should also be considered ( ).

Recent data support testing in all deceased and living solid organ donors because of the risk of HCV infection posed to the recipient ( ); ( ). Although hepatitis C testing guidelines from the US Centers for Disease Control and Prevention (CDC) and the US Preventive Services Task Force (USPSTF) do not specifically recommend testing immigrants from countries with a high prevalence of HCV infection (eg, Egypt and Pakistan), such persons should be tested if they were born from 1945 through 1965, or if they have risk factors for infection (see).

CDC established risk-based HCV testing guidelines in 1998 ( ). These guidelines were expanded in 2012 with a recommendation to offer a one-time HCV testing to all persons born from 1945 through 1965 without prior ascertainment of HCV risk factors (see). This recommendation was supported by evidence demonstrating that a risk-based strategy alone failed to identify more than 50% of HCV infections, due in part to patient underreporting of their risk and provider limitations in ascertaining risk factor information. Furthermore, persons in the 1945 through 1965 birth cohort account for nearly 75% of all HCV infections, with a 5-fold higher prevalence (3.25%) than other adults. This reflects a higher incidence of HCV infections in the 1970s and 1980s (peaking at 230,000 annually in the US, compared to an estimated 30,500 in 2014) ( ). A retrospective analysis published in 2013 showed that 68% of persons with HCV infection would have been identified with a birth cohort testing strategy, whereas only 27% would have been screened with the risk-based approach ( ). The cost-effectiveness of one-time birth cohort testing is comparable to that of current risk-based screening strategies ( ).

Both CDC and the USPSTF recommend a one-time HCV test in asymptomatic persons belonging to the 1945 through 1965 birth cohort, as well as other individuals based on exposures, behaviors, and conditions or circumstances that increase HCV infection risk.

HCV Testing for Persons With Ongoing Risk Factors

Recommendation for HCV Testing for Persons With Ongoing Risk Factors	
RECOMMENDED	RATING
Annual HCV testing is recommended for persons who inject drugs and for HIV-infected men who have unprotected sex with men. Periodic testing should be offered to other persons with ongoing risk factors for HCV exposure.	IIa, C

Evidence regarding the frequency of testing in persons at risk for ongoing exposures to HCV is lacking. Therefore, clinicians should determine the periodicity of testing based on the risk of infection or reinfection. Because of the high incidence of HCV infection among persons who inject drugs and HIV-infected men who have unprotected sex with men, HCV testing at least annually is recommended for these populations ( ); ( ); ( ); ( ); ( ); ( ).

Implementation of clinical decision support tools or prompts for HCV testing in electronic health records could facilitate reminding clinicians of HCV testing when indicated ( ); ( ); ( ).

Initial HCV Testing and Follow-Up

Recommendations for Initial HCV Testing and Follow-Up	
RECOMMENDED	RATING
An HCV-antibody test is recommended for initial HCV testing. If the result is positive, current infection should be confirmed by a sensitive HCV-RNA test.	I, A
Among persons with a negative HCV-antibody test who are suspected of having liver disease, testing for HCV RNA or follow-up testing for HCV antibody is recommended if exposure to HCV occurred within the past 6 months; testing for HCV RNA can also be considered for persons who are immunocompromised.	I, C
Among persons at risk of reinfection after previous spontaneous or treatment-related viral clearance, initial HCV-RNA testing is recommended because an HCV-antibody test is expected to be positive.	I, C
Quantitative HCV-RNA testing is recommended prior to initiation of antiviral therapy to document the baseline level of viremia (ie, baseline viral load).	I, A
HCV genotype testing is recommended to guide selection of the most appropriate antiviral regimen.	I, A
Persons found to have a positive HCV-antibody test and negative results for HCV RNA by polymerase chain reaction (PCR) should be informed that they do not have evidence of current (active) HCV infection.	I, A

All persons recommended for HCV screening should initially be tested for HCV antibody ( ); ( ) using an assay approved by the US Food and Drug Administration (FDA). FDA-approved tests include laboratory-based assays and a point-of-care assay (ie, OraQuick HCV Rapid Antibody Test [OraSure Technologies]) ( ). The latter is an indirect immunoassay with a sensitivity and specificity similar to those of laboratory-based HCV-antibody assays.

A positive test result for HCV antibody indicates either current (active) HCV infection (acute or chronic), past infection that has resolved, or a false-positive result ( ). Therefore, an HCV nucleic acid test (NAT) to detect viremia is necessary to confirm active HCV infection and guide clinical management, including initiation of HCV treatment. HCV-RNA testing should also be performed in persons with a negative HCV-antibody test who are either immunocompromised (eg, persons receiving chronic hemodialysis) ( ) or who might have been exposed to HCV within the last 6 months because these persons may be HCV-antibody–negative. An HCV-RNA test is also needed to detect reinfection in HCV-antibody–positive persons after previous spontaneous or treatment-related viral clearance.

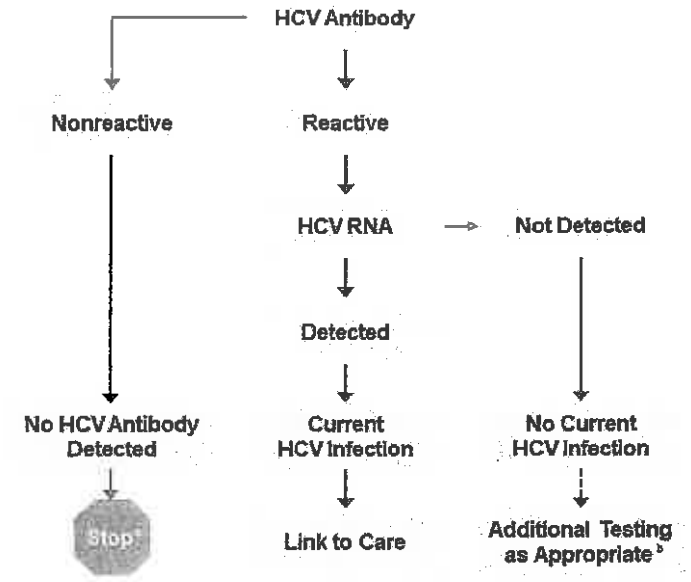
An FDA-approved quantitative or qualitative NAT with a detection level of 25 IU/mL or lower should be used to detect HCV RNA. Table 1 lists FDA-approved, commercially available HCV-antibody screening assays. Figure 1 shows the CDC-recommended testing algorithm.

Table 1. FDA-Approved HCV-Antibody Screening Assays

Assay	Manufacturer	Format
Abbott HCV EIA 2.0	Abbott Laboratories Abbott Park, IL, USA	EIA[a] (manual)
Advia Centaur HCV	Siemens Healthcare Malvern, PA, USA	CIA[b] (automated)
Architect Anti-HCV	Abbott Laboratories Abbott Park, IL, USA	CMIA[c] (automated)
AxSYM Anti-HCV	Abbott Laboratories Abbott Park, IL, USA	MEIA[d] (automated)
OraQuick HCV Rapid Antibody Test	OraSure Technologies, Inc. Bethlehem, PA, USA	Immunochromatographic (manual)
Ortho HCV Version 3.0 ELISA Test System	Ortho-Clinical Diagnostics, Inc. Raritan, NJ, USA	EIA[a] (manual)
VITROS Anti-HCV	Ortho-Clinical Diagnostics, Inc. Raritan, NJ, USA	CIA[b] (automated)

[a] EIA: enzyme immunoassay
[b] CIA: chemiluminescent immunoassay
[c] CMIA: chemiluminescent microparticle immunoassay
[d] MEIA: microparticle enzyme immunoassay
Table prepared by Saleem Kamili, PhD, Centers for Disease Control and Prevention.

Figure 1. CDC-Recommended Testing Sequence for Identifying Current HCV Infection



[a] For persons who might have been exposed to HCV within the past 6 months, testing for HCV RNA or follow-up testing for HCV antibody should be performed. For persons who are immunocompromised, testing for HCV RNA should be performed.

[b] To differentiate past, resolved HCV infection from biologic false positivity for HCV antibody, testing with another HCV-antibody assay can be considered. Repeat HCV-RNA testing if the person tested is suspected to have had HCV exposure within the past 6 months or has clinical evidence of HCV disease, or if there is concern regarding the handling or storage of the test specimen.

Adapted from Centers for Disease Control and Prevention (CDC), 2013 ([illegible])

Persons who have a positive HCV-antibody test and negative results for HCV RNA by polymerase chain reaction (PCR) should be informed that they do not have laboratory evidence of current HCV infection. Additional HCV testing is typically unnecessary. The HCV-RNA test can be repeated when there is a high index of suspicion for recent infection or in patients with ongoing HCV infection risk.

Clinicians (or patients) may seek additional testing to determine whether a positive HCV-antibody test represents a remote HCV infection that has resolved or a false positive. For patients with no apparent risk for HCV infection, the likelihood of a false-positive HCV-antibody test is directly related to the HCV prevalence in the tested population. False-positive HCV-antibody tests most commonly occur in populations with a low prevalence of HCV infection ( ). If further testing is desired to distinguish between a true positive vs biologic false positivity for HCV antibody, repeat testing may be done with a different FDA-approved, HCV-antibody assay. A biologic false result should not occur with two different assays ( ); ( ).

Prior to initiation of antiviral therapy, quantitative HCV-RNA testing may be used to determine the baseline level of viremia (ie, viral load), which may affect treatment duration with certain regimens. The degree of viral load decline after initiation of treatment is less predictive of sustained virologic response (SVR) in the era of direct-acting antiviral (DAA) therapy compared to previous interferon-based treatment (see). Testing for HCV genotype helps guide selection of the most appropriate antiviral regimen.

Counseling Persons With Active HCV Infection

Recommendations for Counseling Persons With Active HCV Infection	
RECOMMENDED	RATING
Persons with current HCV infection should receive education and interventions aimed at reducing liver disease progression and preventing HCV transmission.	IIa, B
Abstinence from alcohol and, when appropriate, interventions to facilitate cessation of alcohol consumption should be advised for all persons with HCV infection.	IIa, B
Evaluation for other conditions that may accelerate liver fibrosis, including hepatitis B and HIV infections, is recommended for all persons with active HCV infection.	IIb, B
Evaluation for advanced fibrosis using liver biopsy, imaging, and/or noninvasive markers is recommended for all persons with HCV infection to facilitate an appropriate decision regarding HCV treatment strategy, and to determine the need for initiating additional measures for cirrhosis management (eg, hepatocellular carcinoma screening) (see section).	I, A
Vaccination against hepatitis A and hepatitis B is recommended for all susceptible persons with HCV infection.	IIa, C
Vaccination against pneumococcal infection is recommended for all patients with cirrhosis.	IIa, C
All persons with HCV infection should be provided education about how to avoid HCV transmission to others.	I, C

In addition to receiving antiviral therapy, HCV-infected persons should be educated about how to prevent further liver damage. Most important is prevention of the potential deleterious effect of alcohol. Numerous studies have found a strong association between excess alcohol use and the development or progression of liver fibrosis, and the development of hepatocellular carcinoma ( ); ( ); ( ); ( ); ( ); ( ); ( ).

Daily consumption of more than 50 grams of alcohol has a high likelihood of worsening fibrosis. Some studies indicate that daily consumption of smaller amounts of alcohol also has a deleterious effect on the liver; however, these data are controversial ( ); ( ); ( ). Excess alcohol intake may also cause steatohepatitis. Alcohol screening and brief interventions, such as those outlined by the , have been demonstrated to reduce alcohol consumption and episodes of binge drinking in the general population and among HCV-infected persons who consume alcohol heavily ( ); ( ); ( ). Persons identified as abusing alcohol and having alcohol dependence require treatment and consideration for referral to an addiction specialist.

Hepatitis B virus (HBV) and HIV coinfection have been associated with a poorer HCV prognosis in cohort studies ( ); ( ); ( ); ( ). Because of overlapping risk factors for these infections and benefits associated with their identification and treatment, HCV-infected persons should be tested for HIV antibody and hepatitis B surface antigen (HBsAg) using standard screening assays ( ); ( ); (see and). Patients should also be counseled about how to reduce their risk of acquiring these infections, including through HBV vaccination.

Patients with obesity and metabolic syndrome having underlying insulin resistance are at increased risk for nonalcoholic fatty liver disease, which is a risk factor for accelerated fibrosis progression in HCV-infected persons ( ); ( ). Therefore, HCV-infected persons who are overweight or obese (defined by a body mass index of 25 to 29.9 kg/m², and ≥30 kg/m², respectively) should be counseled regarding strategies to reduce body weight and improve insulin resistance via diet, exercise, and medical therapies ( ); ( ). HCV-infected patients with hyperlipidemia or cardiovascular comorbidities may also benefit from lipid-lowering drugs. Prospective studies have demonstrated the safety and efficacy of statins in patients with chronic HCV and others with compensated chronic liver disease ( ); ( ). Therefore, these agents should not be withheld from HCV-infected patients.

The severity of liver disease associated with chronic HCV infection is a key factor in determining the initial and follow-up evaluation of patients. Although patients with more advanced disease may have a lower response to HCV therapy, they are also most likely to derive the greatest survival benefit ( ). A liver biopsy can provide objective, semiquantitative information regarding the amount and pattern of collagen or scar tissue in the liver, which can help inform the development of treatment and monitoring plans. The Metavir fibrosis score (F0 to F4) and Ishak fibrosis score (0 to 6) are commonly used to quantify the amount of hepatic collagen. A liver biopsy can also help assess the severity of liver inflammation and hepatic steatosis, and aid in excluding competing causes of liver injury ( ). However, the procedure has a low but real risk of complications, and sampling artifact makes its serial use in most patients less desirable ( ).

Noninvasive methods frequently used to estimate liver disease severity include:

- Liver-directed physical exam (normal in most patients)
- Routine blood tests (eg, ALT, AST, albumin, bilirubin, international normalized ratio [INR], and CBC with platelet count)
- Serum fibrosis marker panels
- Liver imaging (eg, ultrasound, or CT scan)
- Transient elastography

Simple calculations derived from routine blood tests—such as the serum AST-to-platelet ratio index ( ) ( ) and fibrosis-4 ( ) ( )—as well as assessment of liver surface nodularity and spleen size by liver ultrasound or other cross-sectional imaging modalities can help determine if patients with HCV have occult portal hypertension. The presence of portal hypertension is associated with a greater likelihood of developing future hepatic complications in untreated patients ( ); ( ).

Liver elastography provides instant information regarding liver stiffness at the point of care and can reliably distinguish patients with a high versus low likelihood of cirrhosis ( ); ( ). A more detailed discussion regarding fibrosis assessment is found in the section.

Because persons with known or suspected bridging fibrosis and cirrhosis are at increased risk of developing complications of advanced liver disease, they require frequent follow-up. They should also avoid hepatotoxic drugs, such as excessive acetaminophen (>2 g/d) and certain herbal supplements. Nephrotoxic drugs, such as nonsteroidal anti-inflammatory drugs, should also be avoided. Ongoing imaging surveillance for liver cancer and gastroesophageal varices is also recommended for these patients ( ); ( ). Persons with cirrhosis are more susceptible to invasive pneumococcal infection ( ) and should receive pneumococcal vaccination ( ).

Exposure to infected blood is the primary mode of HCV transmission. HCV-infected persons must be informed of the precautions needed to avoid exposing others to infected blood. This is particularly important for persons who use injection drugs given that HCV transmission in this population primarily results from sharing needles and other contaminated drug injection equipment. Epidemics of acute HCV due to sexual transmission in HIV-infected men who have sex with men have also been described recently ( ); ( ); ( ). Table 2 outlines measures to avoid HCV transmission. HCV is not spread by sneezing, hugging, holding hands, coughing, or sharing eating utensils or drinking glasses, nor is it transmitted through food or water.

Table 2. Measures to Prevent HCV Transmission

HCV-infected persons should be counseled to avoid sharing toothbrushes and dental or shaving equipment, and be cautioned to cover any bleeding wound to prevent the possibility of others coming into contact with their blood.
Persons should be counseled to stop using illicit drugs and enter substance abuse treatment. Those who continue to inject drugs should be counseled to:

Avoid reusing or sharing syringes, needles, water, cotton, and other drug preparation equipment. Use new sterile syringes and filters, and disinfected cookers. Clean the injection site with a new alcohol swab. Dispose of syringes and needles after 1 use in a safe, puncture-proof container.
Persons with HCV infection should be advised not to donate blood and to discuss HCV serostatus prior to donation of body organs, other tissue, or semen.
Persons with HIV infection and those with multiple sexual partners or sexually transmitted infections should be encouraged to use barrier precautions to prevent sexual transmission. Other persons with HCV infection should be counseled that the risk of sexual transmission is low and may not warrant barrier protection.
Household surfaces and implements contaminated with visible blood from an HCV-infected person should be cleaned using a dilution of 1 part household bleach to 9 parts water. Gloves should be worn when cleaning up blood spills.

Linkage to Care

Recommendation for Linkage to Care	
RECOMMENDED	RATING
All persons with active HCV infection should be linked to a clinician who is prepared to provide comprehensive management.	IIa, C

Improvement in identification of active HCV infection and advances in treatment regimens will have limited impact on HCV-related morbidity and mortality without concomitant improvement in linkage to care. All patients with current HCV infection and a positive HCV-RNA test result should be evaluated by a clinician with expertise in assessment of liver disease severity and HCV treatment. Subspecialty care and consultation are required for persons with HCV infection who have advanced fibrosis or cirrhosis (Metavir stage ≥F3), including possible referral for consideration of liver transplantation.

In the United States, only an estimated 13% to 18% of HCV-infected persons had received treatment by 2013 ( ). Lack of appropriate clinician assessment and delays in linkage to care can result in negative health outcomes. Furthermore, patients who are lost to follow-up fail to benefit from evolving evaluation and treatment options.

Commonly cited patient-related barriers to treatment initiation include contraindications to treatment (eg, medical or psychiatric comorbidities); lack of acceptance of treatment (eg, asymptomatic nature of disease, competing priorities, low treatment efficacy, long treatment duration, and adverse effects); and lack of access to treatment (eg, cost and distance to specialist) ( ); ( ); ( ).

Common clinician-related barriers include perceived patient-related barriers (eg, fear of adverse effects, treatment duration, cost, and effectiveness); lack of expertise in HCV treatment; lack of specialty referral resources; resistance to treating persons currently using illicit drugs or alcohol; and concern about the cost of HCV treatment ( ); ( ); ( ).

Data are lacking to support exclusion of HCV-infected persons from considerations for hepatitis C therapy based on the amount of alcohol intake or use of illicit drugs. Based on data from interferon-based treatment, SVR rates among people who inject drugs are comparable to those among people who do not inject drugs ( ). Some possible strategies to address barriers to HCV treatment are listed in Table 3.

Table 3. Common Barriers to HCV Treatment and Potential Strategies

Barrier	Strategy
Contraindications to treatment (eg, comorbidities, substance abuse, and psychiatric disorders)	Conduct counseling and education Refer for services (eg, psychiatry and opioid substitution therapy) Optimize treatment with simpler, less toxic regimens
Competing priorities and loss to follow-up	Conduct counseling and education Engage case managers and patient navigators (HIV model) Co-localize services (eg, primary care, medical homes, and drug treatment)
Long treatment duration and adverse effects	Optimize treatment with simpler, better tolerated regimens Conduct appropriate education and monitoring Utilize directly observed therapy (tuberculosis model)
Lack of access to treatment (eg, high cost, lack of insurance, geographic distance, and/or lack of availability of specialists)	Leverage expansion of coverage through the Patient Protection and Affordable Care Act Participate in models of care involving close collaboration between primary care clinicians and specialists Liaise with pharmaceutical patient assistance programs Co-localize services (primary care, medical homes, drug treatment)
Lack of practitioner expertise	Collaborate with specialists (eg, Project ECHO-like models and telemedicine) Develop accessible, clear HCV treatment guidelines Develop electronic health record performance measures and clinical decision support tools (eg, pop-up reminders and standing orders)

One strategy that addresses several barriers is co-localization (integrated care) of HCV screening, evaluation, and treatment with other medical or social services. Co-localization has already been applied to settings with a high prevalence of HCV infection (eg, correctional facilities, needle exchange programs, substance abuse treatment centers, and methadone maintenance facilities) but this type of care is not uniformly available ( ); ( ); ( ). A study conducted by Ho and colleagues demonstrated that integrated care—consisting of multidisciplinary care coordination and patient case management—increased the proportion of patients with HCV infection and psychiatric illness or substance use who begin antiviral therapy and achieve a sustained virologic response, without serious adverse events ( ).

A strategy that addresses lack of access to specialists—a primary barrier to hepatitis C care—is participation in models involving close collaboration between primary care practitioners and subspecialists ( ); ( ); ( ). Such collaborations have used telemedicine and knowledge networks to overcome geographic distances to specialists ( ); ( ). For example, Project ECHO ( ) uses videoconferencing to enhance primary care practitioner capacity in rendering HCV care and treatment to New Mexico's large rural and underserved population ( ). Through case-based learning and real-time feedback from a multidisciplinary team of specialists (gastroenterology, infectious disease, pharmacology, and psychiatry practitioners), Project ECHO has expanded access to HCV treatment in populations that might have otherwise remained untreated. The short duration of treatment and few serious adverse events associated with DAA therapy present an opportunity to expand the number of midlevel practitioners and primary care physicians engaged in the management and treatment of HCV infection.

Additional strategies for enhancing linkage to and retention in care could be adapted from other fields, such as tuberculosis and HIV. For example, use of directly observed therapy has enhanced adherence to tuberculosis treatment, and use of case managers and patient navigators has reduced loss of follow-up in

HIV care ( ). Recent hepatitis C testing and care programs have identified the use of patient navigators or care coordinators as important interventions in overcoming challenges associated with linkage to and retention in care ( ); ( ). Ongoing assessment of efficacy and comparative effectiveness of this and additional strategies is a crucial area of future research for patients with HCV infection. Replication and expansion of best practices and new models for linkage to HCV care will also be crucial to maximize the public health impact of newer treatment paradigms.

Related References

Last update: September 21, 2017

◂ Previous Page Next Page ▸

AST to Platelet Ratio Index (APRI) Calculator

Share

This is an AST to Platelet Ratio Index (APRI) calculator tool. Enter the required values to calculate the APRI value. The APRI Score will appear in the oval on the far right (highlighted in yellow). Most experts recommend using 40 IU/L as the value for the AST upper limit of normal when calculating an APRI value.

AST Level *(IU/L)*

AST (Upper Limit of Normal) *(IU/L)*

APRI = ______________________ **x 100 =**

Platelet Count *(10^9/L)*

Interpretation

In a meta-analysis of 40 studies, investigators concluded that an APRI score greater than 1.0 had a sensitivity of [illegible] greater than 0.7 had a sensitivity of 77% and specificity of 72% for predicting significant hepatic fibrosis.[1]
For detection of cirrhosis, using an APRI cutoff score of 2.0 was more specific (91%) but less sensitive (46%). The lower the APRI score (less than 0.5), the greater the negative predictive value (and ability to rule out cirrhosis) and the higher the [illegible] greater the positive predictive value (and ability to rule in cirrhosis); midrange values are less helpful. The APRI alone is likely not sufficiently sensitive to rule out significant disease. Some evidence suggests that the use of multiple indices in combination (such as APRI plus FibroTest) or an algorithmic approach may [illegible] diagnostic accuracy than using APRI alone.[2]

Sources

1. Lin ZH, Xin YN, Dong QJ, et al. Performance of the aspartate aminotransferase-to-platelet ratio index for the staging of hepatitis C-related fibrosis: an updated meta-analysis. Hepatology. 2011;53:726-36.
2. Chou R, Wasson N. Blood tests to diagnose fibrosis or cirrhosis in patients with chronic hepatitis C virus infection: a systematic review. Ann Intern Med. 2013;158:807-20.

Related Activities

You may find more information and a scenario for which you can use this calculator in the following activities from our course:

- [illegible]

This calculator operates entirely from your device.
No input variables or data is transmitted between your computer and our servers.

Funded by a grant from the Centers for Disease Control and Prevention

Exhibit H

Clinical Calculators

Clinical Calculators
CTP Calculator
APRI Calculator
BMI Calculator
CrCl Calculator
FIB-4 Calculator
Glasgow Coma Scale
GFR Calculator
MELD Calculator
SAAG Calculator

Substance Use Screening Tools
AUDIT-C Questionnaire
CAGE Questionnaire

Fibrosis-4 (FIB-4) Calculator

Share

The Fibrosis-4 score helps to estimate the amount of scarring in the liver. Enter the required values to calculate the FIB-4 value. It will appear in the oval on the far right (highlighted in yellow).

$$\text{FIB-4} = \frac{\text{Age (years)} \times \text{AST Level (U/L)}}{\text{Platelet Count } (10^9/L) \times \sqrt{\text{ALT (U/L)}}}$$

Interpretation:

Using a lower cutoff value of 1.45, a FIB-4 score <1.45 had a negative predictive value of 90% for advanced fibrosis [illegible]

Sources

Sterling RK, Lissen E, Clumeck N, et. al. Development of a simple noninvasive index to predict significant fibrosis patients with HIV/HCV co-infection. Hepatology 2006;43:1317-1325.

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Clinical Calculators

Clinical Calculators

CTP Calculator

APRI Calculator

BMI Calculator

CrCl Calculator

FIB-4 Calculator

Glasgow Coma Scale

GFR Calculator

MELD Calculator

SAAG Calculator

Substance Use Screening Tools

AUDIT-C Questionnaire

CAGE Questionnaire

Child-Turcotte-Pugh (CTP) Calculator

Share

Use the Child-Turcotte-Pugh Classification for Severity of Cirrhosis calculator to estimate the cirrhosis severity. Select the applicable Clinical and Lab Criterias, then check the classification at the bottom.

Clinical and Lab Criteria			Points
Encephalopathy			
	O	None	+1
	O	Mild to moderate (grade 1 or 2)	+2
	O	Severe (grade 3 or 4)	+3
Ascites			
	O	None	+1
	O	Mild to moderate (diuretic responsive)	+2
	O	Severe (diuretic refractory)	+3
Bilirubin (mg/dL)			
	O	< 2	+1
	O	2-3	+2
	O	> 3	+3
Albumin (g/dL)			
	O	> 3.5	+1
	O	2.8-3.5	+2
	O	< 2.8	+3
International normalized ratio			
	O	< 1.7	+1
	O	1.7-2.3	+2
	O	> 2.3	+3

Child-Turcotte-Pugh Class obtained by adding score for each parameter (total points)

Related Activities

You may find more information and a scenario for which you can use this calculator in the following activities from our course:

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Section Contents

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When and in Whom to Initiate HCV Therapy

Successful hepatitis C treatment results in sustained virologic response (SVR), which is tantamount to virologic cure and, as such, is expected to benefit nearly all chronically infected persons. When the US Food and Drug Administration (FDA) approved the first interferon-sparing treatment for HCV infection, many patients who had previously been "warehoused" sought treatment. The infrastructure (ie, experienced practitioners, budgeted healthcare dollars, etc) did not yet exist to treat all patients immediately. Thus, the panel offered guidance for prioritizing treatment first for those with the greatest need.

Since that time, there have been opportunities to treat many of the highest-risk patients and accumulate real-world experience regarding the tolerability and safety of interferon-free HCV regimens. More importantly, from a medical standpoint, data continue to accumulate that demonstrate the many benefits, both intrahepatic and extrahepatic, that accompany HCV eradication. Therefore, the panel continues to recommend treatment for all patients with chronic HCV infection, except those with a short life expectancy that cannot be remediated by HCV treatment, liver transplantation, or another directed therapy. Accordingly, prioritization tables have been removed from this section.

Despite the strong recommendation for treatment of nearly all HCV-infected patients, pretreatment assessment of a patient's understanding of treatment goals and provision of education about adherence and follow-up are essential. A well-established therapeutic relationship between clinician and patient remains crucial for optimal outcomes with direct-acting antiviral (DAA) therapies. Additionally, in certain settings there remain factors that impact access to medications and the ability to deliver them to patients. In these settings, clinicians may still need to decide which patients should be treated first. The descriptions of unique populations discussed in this section may help physicians make more informed treatment decisions for these groups. For additional information, see unique patient populations: , and .

Goal of Treatment	
RECOMMENDED	RATING
The goal of treatment of HCV-infected persons is to reduce all-cause mortality and liver-related health adverse consequences, including end-stage liver disease and hepatocellular carcinoma, by the achievement of virologic cure as evidenced by a sustained virologic response.	I, A

Recommendation for When and in Whom to Initiate Treatment	
RECOMMENDED	RATING
Treatment is recommended for all patients with chronic HCV infection, except those with a short life expectancy that cannot be remediated by HCV therapy, liver transplantation, or another directed therapy. Patients with a short life expectancy owing to liver disease should be managed in consultation with an expert.	I, A

Clinical Benefit of Cure

Exhibit I

The proximate goal of HCV therapy is SVR (virologic cure), defined as the continued absence of detectable HCV RNA for at least 12 weeks after completion of therapy. SVR is a marker for cure of HCV infection and has been shown to be durable in large prospective studies in more than 99% of patients followed-up for ≥5 years ( ); ( ). Patients in whom SVR is achieved have HCV antibodies but no longer have detectable HCV RNA in serum, liver tissue, or mononuclear cells, and achieve substantial improvement in liver histology ( ); ( ); ( ). Assessment of viral response, including documentation of SVR, requires use of an FDA-approved quantitative or qualitative nucleic acid test (NAT) with a detection level of ≤25 IU/mL.

Patients who are cured of their HCV infection experience numerous health benefits, including a decrease in liver inflammation as reflected by improved aminotransferase levels (ie, alanine aminotransferase [ALT] and aspartate aminotransferase [AST]), and a reduction in the rate of liver fibrosis progression ( ). Among 3,010 treatment-naive patients from 4 randomized trials who had pretreatment and posttreatment liver biopsies (separated by a mean of 20 months) and were treated with 10 different interferon-based regimens, 39% to 73% of participants who achieved SVR had improvement in liver fibrosis and necrosis ( ). Additionally, cirrhosis resolved in 49% of the cases. Portal hypertension, splenomegaly, and other clinical manifestations of advanced liver disease also improved. Among HCV-infected persons, SVR is associated with a >70% reduction in the risk of liver cancer (hepatocellular carcinoma [HCC]), and a 90% reduction in the risk of liver-related mortality and liver transplantation ( ); ( ); ( ).

Cure of HCV infection also reduces symptoms and mortality from severe extrahepatic manifestations, including cryoglobulinemic vasculitis, a condition affecting 10% to 15% of HCV-infected patients ( ); ( ); ( ). HCV-infected persons with non-Hodgkin lymphoma and other lymphoproliferative disorders achieve complete or partial remission in up to 75% of cases following successful therapy for HCV infection ( ); ( ); ( ); ( ); ( ). These reductions in disease severity contribute to dramatic reductions in all-cause mortality ( ); ( ). Furthermore, patients who achieve SVR have a substantially improved quality of life, which spans their physical, emotional, and social health ( ); ( ); ( ); ( ). Because of the many benefits associated with successful HCV treatment, clinicians should treat HCV-infected patients with antiviral therapy with the goal of achieving SVR, preferably early in the course of chronic HCV infection before the development of severe liver disease and other complications.

Benefits of Treatment at Early Fibrosis Stages (Metavir Stage Less Than F2)

Initiating therapy in patients with lower-stage fibrosis augments the benefits of SVR. In a long-term follow-up study, 820 patients with biopsy-confirmed Metavir stage F0 or F1 fibrosis were followed for up to 20 years ( ). The 15-year survival rate was significantly better for those who experienced SVR than for those whose treatment failed or for those who remained untreated (93%, 82%, and 88%, respectively; P=.003). The study results argue for consideration of earlier initiation of treatment. Several modeling studies also suggest a greater mortality benefit if treatment is initiated at fibrosis stages prior to F3 ( ); ( ); ( ).

Treatment delay may decrease the benefit of SVR. In a report from France, 820 patients with biopsy-confirmed Metavir stage F0 or F1 fibrosis were followed for as long as 20 years ( ). The authors noted rapid progression of fibrosis in 15% of patients during follow-up, and in patients treated successfully, long-term survival was better. Specifically, at 15 years, survival rate was 92% for those with SVR versus 82% for treatment failures and 88% for those not treated. In a Danish regional registry study, investigators modeled treatment approaches with the aim of evaluating the benefit to the region in terms of reductions in morbidity and mortality and HCV prevalence ( ). Although they note that in their situation of low HCV prevalence (0.4%) with approximately 50% undiagnosed, a policy that restricts treatment to those with Metavir fibrosis stage F3 or higher would decrease mortality from HCC and cirrhosis, the number needed to treat to halve the prevalence of the disease is lower if all eligible patients receive treatment at diagnosis.

A modeling study based on the Swiss HIV cohort study also demonstrated that waiting to treat HCV infection until Metavir fibrosis stages F3 and F4 resulted in 2- and 5-times higher rates of liver-related mortality, respectively, compared with treating at Metavir stage F2 ( ). A US Veterans Administration dataset analysis that used very limited end points of virologic response dating from the interferon-treatment era suggested that early initiation of therapy (at a fibrosis-4 [FIB-4] score of <3.25) increased the benefit attained with respect to likelihood of treatment success and mortality reduction, and ultimately decreased the number of patients needed to treat to preserve 1 life by almost 50% ( ).

Considerations in Specific Populations

Despite the recommendation for treatment of nearly all patients with HCV infection, it remains important for clinicians to understand patient- and disease-related factors that place individuals at risk for HCV-

related complications (liver and extrahepatic) as well as for HCV transmission. Although these groups are no longer singled out for high prioritization for treatment, it is nonetheless important that clinicians recognize the unique dimensions of HCV disease and its natural history in these populations. The discussions offered below may assist clinicians in making compelling cases for insurance coverage of treatment when necessary.

Persons With Advanced Liver Disease

For persons with advanced liver disease (Metavir stage F3 or F4), the risk of developing complications of liver disease, such as hepatic decompensation (Child-Turcotte-Pugh [CTP] class B or C [ ]) or HCC, is substantial and may occur in a relatively short timeframe. A large prospective study of patients with cirrhosis resulting from HCV infection examined the risk of decompensation—including HCC, ascites, jaundice, bleeding, and encephalopathy—and found that the overall annual incidence rate was 3.9% ( ). The National Institutes of Health (NIH)-sponsored HALT–C study included a group of 220 patients with cirrhosis resulting from HCV infection who were observed for approximately 8 years. A primary outcome of death, hepatic decompensation, HCC, or an increase in CTP score ≥2 occurred at a rate of 7.5% per year ( ); ( ). Patients with a CTP score of ≥7 experienced a death rate of 10% per year.

Numerous studies have demonstrated that hepatitis C therapy and the achievement of SVR in this population results in dramatic decreases in hepatic decompensation events, HCC, and liver-related mortality ( ); ( ); ( ); ( ); ( ). In the HALT-C study, patients with advanced fibrosis secondary to HCV infection who achieved SVR, compared with patients with similarly advanced liver fibrosis who did not achieve SVR, had a decreased need for liver transplantation (HR, 0.17; 95% CI, 0.06-0.46), decreased development of liver-related morbidity and mortality (HR, 0.15; 95% CI, 0.06-0.38), and decreased HCC (HR, 0.19; 95% CI, 0.04-0.80) ( ). Importantly, persons with advanced liver disease also require long-term follow-up and HCC surveillance regardless of treatment outcome (see).

Given the clinical complexity and need for close monitoring, patients with advanced liver disease that has already decompensated (CTP class B or C [ ]) should be treated by physicians with experience treating HCV in conjunction with a liver transplantation center, if possible (see).

Persons Who Have Undergone Liver Transplantation

In HCV-infected individuals, HCV infection of the liver allograft occurs universally in those with viremia at the time of transplantation. Histologic features of hepatitis develop in about 75% of recipients within the first 6 months following liver transplantation ( ). By the fifth postoperative year, up to 30% of untreated patients have progressed to cirrhosis ( ); ( ). A small proportion of patients (4% to 7%) develop an accelerated course of liver injury (cholestatic hepatitis C, associated with very high levels of viremia) with subsequent rapid allograft failure. Recurrence of HCV infection post transplantation is associated with decreased graft survival for recipients with HCV infection compared to recipients who undergo liver transplantation for other indications ( ).

Effective HCV therapy prior to transplantation resulting in SVR (virologic cure) prevents HCV recurrence post transplantation ( ). In addition, complete HCV viral suppression prior to transplantation prevents recurrent HCV infection of the graft in the majority of cases ( ); ( ). Preliminary data from a study of patients with complications of cirrhosis secondary to HCV infection who were wait-listed for liver transplantation (included patients with MELD scores up to 14 and CTP scores up to 8) found that treatment with sofosbuvir and weight-based ribavirin for up to 48 weeks was well tolerated and associated with an overall posttransplant SVR rate of 70% ( ). Posttransplant SVR was nearly universal among patients who had undetectable HCV RNA for 28 days or longer prior to transplantation.

Treatment of established HCV infection post transplantation also yields substantial improvements in patient and graft survival ( ); ( ). The availability of effective, interferon-free antiviral therapy has addressed the major hurdles to treating HCV recurrence post transplantation—poor tolerability and efficacy. A multicenter, open-label study evaluated the efficacy of sofosbuvir plus ribavirin to induce virologic suppression in 40 patients after liver transplantation with compensated recurrence of HCV infection. Daily sofosbuvir plus ribavirin for 24 weeks achieved SVR12 in 70% of these patients ( ). No deaths, graft losses, or episodes of rejection occurred. Six patients had serious adverse events, all of which were considered unrelated to the study treatment. There were no drug interactions reported between sofosbuvir and any of the concomitant immunosuppressive agents. In contrast, treatment with sofosbuvir plus ribavirin, with or without peginterferon, in 64 patients with severe, decompensated cirrhosis resulting from recurrence of HCV infection following liver transplantation was associated with an overall SVR12 rate of 59% and a mortality rate of 13% ( ). On an intent-to-treat basis, treatment was associated with clinical improvement in 57% and stable

disease in 22% of patients. Given the clinical complexity (including drug interactions and the need for close monitoring), patients with liver transplant should be treated by physicians with experience in treating this population (see).

Persons at Increased Risk for Rapidly Progressive Fibrosis and Cirrhosis

Fibrosis progression is variable across different patient populations as well as within the same individual over time. Many of the components that determine fibrosis progression and development of cirrhosis in an individual are unknown. However, certain factors, such as coinfection with HIV or the hepatitis B virus (HBV) and prevalent coexistent liver diseases (eg, nonalcoholic steatohepatitis [NASH]), are well-recognized contributors to accelerated fibrosis progression (see below).

HIV/HCV Coinfection

HIV coinfection accelerates fibrosis progression among HCV-infected persons ( ); ( ); ( ), although control of HIV replication and restoration of CD4 cell count may mitigate this to some extent ( ); ( ). However, antiretroviral therapy is not a substitute for HCV treatment. In the largest paired-biopsy study, 282 HIV/HCV-coinfected patients with 435 paired biopsies were prospectively evaluated ( ). Thirty-four percent of patients showed fibrosis progression of at least 1 Metavir stage at a median of 2.5 years. Importantly, 45% of patients with no fibrosis on initial biopsy had progression. Finally, a more rapid progression to death following decompensation combined with lack of widespread access to liver transplantation and poor outcomes following transplantation highlight the need for HCV treatment in this population regardless of current fibrosis stage (see) ( ); ( ); ( ).

HBV/HCV Coinfection

The prevalence of HBV/HCV coinfection is estimated at 1.4% in the United States and 5% to 10% globally ( ); ( ). Persons with HBV/HCV coinfection and detectable viremia of both viruses are at increased risk for disease progression, decompensated liver disease, and the development of HCC. HBV/HCV-coinfected individuals are susceptible to a process called viral interference wherein one virus may interfere with the replication of the other virus. Thus, when treating one or both viruses with antiviral drugs, periodic retesting of HBV DNA and HCV RNA levels during and after therapy is prudent, particularly if only one of the viruses is being treated at a time. Treatment of HCV infection in such cases utilizes the same genotype-specific regimens as are recommended for HCV monoinfection (see). HBV infections in such cases should be treated as recommended for HBV monoinfection ( ).

Other Coexistent Liver Diseases

Persons with other chronic liver diseases who have coincident chronic HCV infection should be considered for HCV therapy given the potential for rapid liver disease progression. An interferon-free regimen is generally preferred for immune-mediated liver diseases, such as autoimmune hepatitis, because of the potential for interferon-related exacerbation.

Persons With Extrahepatic Manifestations of Chronic HCV Infection

Cryoglobulinemia

Chronic hepatitis C is associated with a syndrome of cryoglobulinemia, an immune complex and lymphoproliferative disorder that leads to arthralgias, fatigue, palpable purpura, renal disease (eg, membranoproliferative glomerulonephritis), neurologic disease (eg, peripheral neuropathy, central nervous system vasculitis), and reduced complement levels ( ). Because patients with chronic hepatitis C frequently have laboratory evidence of cryoglobulins (>50% in some series), antiviral treatment is imperative for those with the syndrome of cryoglobulinemia and symptoms or objective evidence of end-organ manifestations. Interferon-based regimens can produce clinical remission; however, the adverse effects of interferon may mimic manifestations of cryoglobulinemia ( ).

Glomerular disease results from deposition of HCV-related immune complexes in the glomeruli ( ). Successful treatment of HCV using interferon-based regimens can reverse proteinuria and nephrotic syndrome but usually does not fully ameliorate azotemia ( ). There is building new evidence of effective resolution of cryoglobulinemia upon clearance of HCV in most patients, making a strong case for HCV treatment in this clinical setting.

Diabetes

The relationship between chronic hepatitis C and diabetes (most notably type 2 diabetes and insulin resistance) is complex and incompletely understood. The prevalence and incidence of diabetes is increased in the context of hepatitis C ( ). In the United States, type 2 diabetes occurs more frequently in HCV-infected patients, with a >3-fold greater risk in persons older than 40 years ( )

). The positive correlation between quantity of plasma HCV RNA and established markers of insulin resistance confirms this relationship ( ). Insulin resistance and type 2 diabetes are independent predictors of accelerated liver fibrosis progression ( ). Patients with type 2 diabetes and insulin resistance are also at increased risk for HCC ( ).

Successful antiviral treatment has been associated with improved markers of insulin resistance and a greatly reduced incidence of new-onset type 2 diabetes and insulin resistance in HCV-infected patients ( ). Most recently, antiviral therapy for HCV infection has been shown to improve clinical outcomes related to diabetes. In a large prospective cohort from Taiwan, the incidence rates of end-stage renal disease, ischemic stroke, and acute coronary syndrome were greatly reduced in HCV-infected patients with diabetes who received antiviral therapy compared with untreated, matched controls ( ). Therefore, antiviral therapy may prevent progression to diabetes in HCV-infected patients with prediabetes, and may reduce renal and cardiovascular complications in HCV-infected patients with established diabetes.

Fatigue

Fatigue is the most frequently reported symptom in patients with chronic hepatitis C, and has a major effect on quality of life and activity level as evidenced by numerous measures of impaired quality of life ( ). The presence and severity of fatigue appears to correlate poorly with disease activity, although it may be more common and severe in HCV-infected individuals with cirrhosis ( ). Despite difficulties in separating fatigue symptoms associated with hepatitis C from those associated with other concurrent conditions (eg, anemia, depression), numerous studies have reported a reduction in fatigue after cure of HCV infection ( ). In the Virahep-C study, 401 patients with HCV infection were evaluated for fatigue prior to and after treatment, using validated scales to assess the presence and severity of fatigue ( ). At baseline, 52% of patients reported having fatigue, which was more frequent and severe in patients with cirrhosis than in those without cirrhosis. Achieving SVR was associated with a substantial decrease in the frequency and severity of fatigue.

A recent analysis of 413 patients from the NEUTRINO and FUSION trials who were treated with a sofosbuvir-containing regimen and achieved SVR12 demonstrated improvement in patient fatigue (present in 12%) from the pretreatment level ( ). After achieving SVR12, participants had marked improvements in fatigue over their pretreatment scores, measured by 3 separate validated questionnaires. Additional studies support and extend these findings beyond fatigue, with improvements in overall health-related quality of life and work productivity observed following successful HCV therapy ( ); ( ); ( ); ( ); ( ); ( ).

Dermatologic Manifestations

The reported prevalence of HCV infection in patients with porphyria cutanea tarda approximates 50% and occurs disproportionately in those with cirrhosis ( ). The treatment of choice for active porphyria cutanea tarda is iron reduction by phlebotomy and maintenance of a mildly iron-reduced state without anemia. However, although improvement of porphyria cutanea tarda during HCV treatment with interferon has frequently been described ( ), there are currently insufficient data to determine whether treating HCV infection with DAAs and achievement of SVR results in porphyria cutanea tarda improvement.

Lichen planus is characterized by pruritic papules involving mucous membranes, hair, and nails. HCV antibodies are present in 10% to 40% of patients with lichen planus but a causal link with chronic HCV infection is not established. Resolution of lichen planus has been reported with interferon-based regimens, but there have also been reports of exacerbation with these treatments. Although it is unknown whether DAAs will have more success against lichen planus, treatment with interferon-free regimens would appear to be a more advisable approach to addressing this disorder ( ); ( ).

Benefit of Treatment to Reduce Transmission

Persons who have successfully achieved SVR (virologic cure) no longer transmit the virus to others. As such, successful treatment of HCV infection benefits public health. Several health models have shown that even modest increases in successful treatment of HCV infection among persons who inject drugs can decrease prevalence and incidence ( ); ( ); ( ); ( ); ( ). Models developed to estimate the impact of HCV testing and treatment on the burden of hepatitis C at a country level reveal that large decreases in HCV prevalence and incidence are possible as more persons are successfully treated ( ).

There are also benefits to eradicating HCV infection between couples and among families, thus eliminating the perception that an individual might be contagious. In addition, mother-to-child transmission of HCV does not occur if the woman is not viremic, providing an additional benefit of curing

a woman before she becomes pregnant ( ). However, the safety and efficacy of treating women who are already pregnant to prevent transmission to the fetus have not yet been established; thus, treatment is not recommended for pregnant women.

The Society for Healthcare Epidemiology of America (SHEA) advises that healthcare workers who have substantial HCV viral replication (≥10^4 genome equivalents/mL) be restricted from performing procedures that are prone to exposure ( ) and that all healthcare workers with confirmed chronic HCV infection should be treated. For reasons already stated, the achievement of SVR in such individuals will not only eliminate the risk of HCV transmission to patients but also decrease circumstantial loss of experienced clinicians. Given concerns about underreporting of infection and transmission ( ), the availability of effective, all-oral regimens should lead to greater willingness on the part of exposure-prone clinicians to be tested and treated.

Successful treatment of HCV-infected persons at greatest risk for transmission represents a formidable tool to help stop HCV transmission in those who continue to engage in high-risk behaviors. To guide implementation of hepatitis C treatment as a prevention strategy, studies are needed to define the best candidates for treatment to stop transmission, the additional interventions needed to maximize the benefits of HCV treatment (eg, preventing reinfection), and the cost-effectiveness of the strategies when used in target populations.

Persons Who Inject Drugs

Injection drug use (IDU) is the most common risk factor for HCV infection in the United States and Europe, with an HCV seroprevalence rate of 10% to 70% ( ); ( ). IDU also accounts for the majority of new HCV infections (approximately 70%) and is the key driving force in the perpetuation of the epidemic. Given these facts and the absence of an effective vaccine against HCV, testing and linkage to care combined with treatment of HCV infection with potent interferon-free regimens has the potential to dramatically decrease HCV incidence and prevalence ( ). However, treatment-based strategies to prevent HCV transmission have yet to be studied, including how to integrate hepatitis C treatment with other risk-reduction strategies (eg, opiate substitution therapy, and needle and syringe exchange programs) ( ).

In studies of interferon-based treatments in persons who inject drugs, adherence and efficacy rates are comparable to those of patients who do not use injected drugs. A meta-analysis of treatment with peginterferon, with or without ribavirin, in active or recent injection drug users showed SVR rates of 37% and 67% for genotype 1 or 4 and 2 or 3, respectively ( ). With the introduction of shorter, better-tolerated, and more efficacious interferon-free therapies, these SVR rates are expected to improve. Importantly, the rate of reinfection in this population is lower (2.4/100 person-years of observation) than that of incident infection in the general population of injection drug users (6.1 to 27.2/100 person-years), although reinfection increases with active or ongoing IDU (6.44/100 person-years) and available data on follow-up duration are limited ( ); ( ).

Ideally, treatment of HCV-infected persons who inject drugs should be delivered in a multidisciplinary care setting with services to reduce the risk of reinfection and for management of the common social and psychiatric comorbidities in this population ( ); ( ); ( ); ( ). Regardless of the treatment setting, recent or active IDU should not be seen as an absolute contraindication to HCV therapy. There is strong evidence from various settings in which persons who inject drugs have demonstrated adherence to treatment and low rates of reinfection, countering arguments that have been commonly used to limit treatment access in this patient population ( ); ( ); ( ). Indeed, combining HCV treatment with needle exchange and opioid agonist therapy programs in this population with a high prevalence of HCV infection has shown great value in decreasing the burden of HCV disease. Elegant modeling studies illustrate high return on the modest investment of addressing this often-ignored segment of the HCV-infected population ( ). These conclusions were drawn before the introduction of the latest DAA regimens. Conversely, there are no data to support the utility of pretreatment screening for illicit drug or alcohol use in identifying a population more likely to successfully complete HCV therapy. These requirements should be abandoned because they create barriers to treatment, add unnecessary cost and effort, and potentially exclude populations that are likely to obtain substantial benefit from therapy. Scaling up HCV treatment in persons who inject drugs is necessary to positively impact the HCV epidemic in the US and globally.

HIV-Infected Men Who Have Sex With Men

Since 2000, a dramatic increase in incident HCV infections among HIV-infected men who have sex with men (MSM) who did not report IDU as a risk factor has been demonstrated in several US cities ( ); ( ). Recognition and treatment of HCV infection (including acute infection) in this population may represent an important step in preventing subsequent infections ( ). As with persons who inject drugs, HIV/HCV-coinfected MSM who engage in ongoing high-risk sexual practices should be treated for their HCV infection in conjunction with continued education about risk-reduction strategies. In particular, safer-sex strategies should be emphasized given the high rate of reinfection after

SVR, which may approach 30% over 2 years in HIV-infected MSM with acute HCV infection (.
).

Incarcerated Persons

Among incarcerated individuals, the rate of HCV seroprevalence ranges from 30% to 60% ( ) and the rate of acute infection is approximately 1% ( ). Screening for HCV infection is relatively uncommon in state prison systems. Treatment uptake has historically been limited, in part because of the toxic effects and long treatment duration of older interferon-based therapies as well as concerns about cost ( ). In particular, truncation of HCV treatment owing to release from prison has been cited as a major limitation to widespread, effective HCV treatment in correctional facilities ( ); ( ). Shorter HCV treatment duration with DAAs reduces stay-related barriers to HCV treatment in prisons. Likewise, the improved safety of DAA regimens diminishes concerns about toxic effects. Coordinated treatment efforts within prison systems would likely rapidly decrease the prevalence of HCV infection in this at-risk population ( ), although research is needed in this area.

Persons on Hemodialysis

The prevalence rate of HCV infection is markedly elevated in persons on hemodialysis, ranging from 2.6% to 22.9% in a large multinational study ( ). Studies in the US found a similarly elevated prevalence rate of 7.8% to 8.9% ( ); ( ). Importantly, the seroprevalence of HCV was found to increase with time on dialysis, suggesting that nosocomial transmission, among other risk factors, plays a role in HCV acquisition in these patients ( ). Improved education and strict adherence to universal precautions can drastically reduce nosocomial HCV transmission risk for persons on hemodialysis ( ), but clearance of HCV viremia through treatment-induced SVR eliminates the potential for transmission.

HCV-infected persons on hemodialysis have a decreased quality of life and increased mortality compared with those who are uninfected ( ); ( ); ( ). HCV infection in this population also has a deleterious impact on kidney transplantation outcomes with decreased patient and graft survival ( ). The increased risk for nosocomial transmission and the substantial clinical impact of HCV infection in those on hemodialysis are compelling arguments for HCV therapy as effective antiviral regimens that can be used in persons with advanced renal failure are now available (see).

Patients Unlikely to Benefit From HCV Treatment

Patients with a limited life expectancy that cannot be remediated by HCV treatment, liver transplantation, or another directed therapy do not require antiviral treatment. Patients with a short life expectancy owing to liver disease should be managed in consultation with an expert. Chronic hepatitis C is associated with a wide range of comorbid conditions ( ); ( ). Little evidence exists to support initiation of HCV treatment in patients with a limited life expectancy (<12 months) owing to nonliver-related comorbid conditions. For these patients, the benefits of HCV treatment are unlikely to be realized and palliative care strategies should take precedence ( ); ( ).

Pretreatment Assessment

Recommendation for Pretreatment Assessment	
RECOMMENDED	RATING
Evaluation for advanced fibrosis using liver biopsy, imaging, and/or noninvasive markers is recommended for all persons with HCV infection, to facilitate decision making regarding HCV treatment strategy and to determine the need for initiating additional measures for the management of cirrhosis (eg, hepatocellular carcinoma screening) (see).	I, A

An accurate assessment of fibrosis remains vital as the degree of hepatic fibrosis is one of the most robust prognostic factors used to predict HCV disease progression and clinical outcomes ( ). Individuals with severe fibrosis require surveillance monitoring for liver cancer, esophageal varices, and hepatic function ( ); ( ). In some instances, the recommended duration of treatment is also longer.

Although liver biopsy is the diagnostic standard, sampling error and observer variability limit test performance, particularly when inadequate sampling occurs. Up to one-third of bilobar biopsies had a difference of at least 1 stage between the lobes ( ). In addition, the test is invasive and minor complications are common, limiting patient and practitioner acceptance. Although rare, serious complications such as bleeding are well recognized.

Noninvasive tests to stage the degree of fibrosis in patients with chronic HCV infection include models incorporating indirect serum biomarkers (routine tests), direct serum biomarkers (components of the extracellular matrix produced by activated hepatic stellate cells), and vibration-controlled transient liver elastography. No single method is recognized to have high accuracy alone, and each test must be interpreted carefully. A publication from the Agency for Healthcare Research and Quality found evidence in support of a number of blood tests; however, at best, they are only moderately useful for identifying clinically significant fibrosis or cirrhosis ( ).

Vibration-controlled transient liver elastography is a noninvasive way to measure liver stiffness and correlates well with measurement of substantial fibrosis or cirrhosis in patients with chronic HCV infection. The measurement range, however, overlaps between stages ( ); ( ); ( ).

The most efficient approach to fibrosis assessment is to combine direct biomarkers and vibration-controlled transient liver elastography ( ); ( ). A biopsy should be considered for any patient who has discordant results between the 2 modalities that would affect clinical decision making (eg, one shows cirrhosis and the other does not). The need for liver biopsy with this approach is markedly reduced.

Alternatively, if direct biomarkers or vibration-controlled transient liver elastography are not available, the AST-to-platelet ratio index (APRI) or fibrosis-4 (FIB-4) index score can prove helpful—although neither is sensitive enough to rule out substantial fibrosis ( ); ( ); ( ). Biopsy should be considered for those in whom more accurate fibrosis staging would impact treatment decisions. Individuals with clinically evident cirrhosis do not require additional staging (biopsy or noninvasive assessment).

Recommendation for Repeat Liver Disease Assessment	
RECOMMENDED	RATING
Ongoing assessment of liver disease is recommended for persons in whom therapy is deferred.	I, C

Ongoing assessment of liver disease is especially important in patients for whom therapy has been deferred. In line with evidence-driven recommendations for treatment of nearly all HCV-infected patients, several factors must be taken into consideration if treatment deferral is entertained or mandated by lack of medication access. As noted, strong and accumulating evidence argue against deferral because of decreased all-cause morbidity and mortality, prevention of onward transmission, and quality-of-life improvements for patients treated regardless of baseline fibrosis. Additionally, treatment of HCV infection may improve or prevent extraheptatic complications, including diabetes mellitus, cardiovascular disease, renal disease, and B-cell non-Hodgkin lymphoma ( ); ( ); ( ), which are not tied to fibrosis stage ( ); ( ). Deferral practices based on fibrosis stage alone are inadequate and shortsighted.

Fibrosis progression varies markedly between individuals based on host, environmental, and viral factors ( ); ( ). Fibrosis may not progress linearly. Some individuals (often those aged >50 years) may progress slowly for many years followed by an acceleration of fibrosis progression. Others may never develop substantial liver fibrosis despite longstanding infection. The presence of existing fibrosis is a strong risk factor for future fibrosis progression. Fibrosis results from chronic hepatic necroinflammation; thus, a higher activity grade on liver biopsy and higher serum transaminase values are associated with more rapid fibrosis progression ( ). However, even patients with normal ALT levels may develop substantial liver fibrosis over time ( ); ( ). The limitations of transient elastography and liver biopsy in ascertaining the progression of fibrosis must be recognized.

Host factors associated with more rapid fibrosis progression include male sex, longer duration of infection, and older age at the time of infection ( ). Many patients have concomitant nonalcoholic fatty liver disease. The presence of hepatic steatosis (with or without steatohepatitis) on liver biopsy, elevated body mass index, insulin resistance, and iron overload are associated with fibrosis progression ( ); ( ). Chronic alcohol use is an important risk factor because alcohol consumption has been associated with more rapid fibrosis progression ( ). A safe amount of alcohol consumption has not been established. Cigarette smoking may also lead to more rapid fibrosis progression. For more counseling recommendations, see .

Immunosuppression leads to more rapid fibrosis progression, particularly in the settings of HIV/HCV coinfection and solid organ transplantation ( ); ( ); ( ). Therefore, immunocompromised patients should be treated even if they have mild liver fibrosis at presentation.

Level of HCV RNA does not correlate with stage of disease (degree of inflammation or fibrosis). Available data suggest that fibrosis progression occurs most rapidly in patients with genotype 3 infection ( ); ( ). Aside from coinfection with HBV or HIV, no other viral factors are consistently associated with disease progression.

Although an ideal interval for assessment has not been established, annual evaluation is appropriate to discuss modifiable risk factors and update testing for hepatic function and markers for disease progression. For all individuals with advanced fibrosis, liver cancer screening dictates a minimum of evaluation every 6 months.

Table. Factors Associated With Accelerated Fibrosis Progression

Host	Viral
Nonmodifiable	Genotype 3 infection
Fibrosis stage	Coinfection with hepatitis B virus or HIV
Inflammation grade	
Older age at time of infection	
Male sex	
Organ transplant	
Modifiable	
Alcohol consumption	
Nonalcoholic fatty liver disease	
Obesity	
Insulin resistance	

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MMWR

Recommendations and Reports

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Recommendations for Prevention and Control of Hepatitis C Virus (HCV) Infection and HCV-Related Chronic Disease

Terms and Abbreviations Used in This Publication Acute hepatitis C Newly acquired symptomatic hepatitis C virus

(HCV) infection. ALT Alanine aminotransferase. Anti-HCV Antibody to HCV that develops in response to HCV

infection; detectable in persons with acute, chronic, and resolved infection. AST Aspartate aminotransferase. Chronic (persistent) HCV infection Persistent infection with HCV;

characterized by detection of HCV RNA greater than or equal to 6 months after newly acquired infection. Chronic hepatitis C Liver inflammation in patients with chronic

HCV infection; characterized by abnormal levels of liver enzymes. CSTE Council of State and Territorial Epidemiologists. DNA Deoxyribonucleic acid. EIA Enzyme immunoassay. FDA U.S. Food and Drug Administration. HBV Hepatitis B virus. HCC Hepatocellular carcinoma. HCV Hepatitis C virus. HCV-positive Positive for anti-HCV as verified by supplemental

testing or positive for HCV RNA. HCV RNA Hepatitis C virus ribonucleic acid. HIV Human immunodeficiency virus. IG Immune globulin. IM Intramuscular. IV Intravenous. MSM Men who have sex with men. NHANES III Third National Health and Nutrition Examination

Survey. NIH National Institutes of Health. Positive predictive value Probability that a positive screening

test is truly positive; dependent on prevalence of disease in a population. Qualitative RT-PCR for HCV RNA Test to detect HCV RNA by

amplification of viral genetic sequences. Quantitative assays for HCV RNA Tests to detect HCV RNA concentration (viral load) by amplification of viral genetic

sequences or by signal amplification. Resolved HCV infection Recovery following hepatitis C virus

infection; characterized by sustained disappearance of serum HCV RNA and normalization of liver enzymes. RIBATM Recombinant immunoblot assay. RNA Ribonucleic acid. RT-PCR Reverse transcriptase polymerase chain reaction. STD Sexually transmitted disease. Supplemental anti-HCV test Additional test (i.e.,RIBATM) used to

verify a positive anti-HCV result obtained by EIA.

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Summary

These recommendations are an expansion of previous recommendations for the prevention of hepatitis C virus (HCV) infection that focused on screening and follow-up of blood, plasma, organ, tissue, and semen donors (CDC. Public Health Service inter-agency guidelines for screening donors of blood, plasma, organs, tissues, and semen for evidence of hepatitis B and hepatitis C. MMWR 1991;40{No. RR-4};1-17). The recommendations in this report provide broader guidelines for a) preventing transmission of HCV; b) identifying, counseling, and testing persons at risk for HCV infection; and c) providing appropriate medical evaluation and management of HCV-infected persons. Based on currently available knowledge, these recommendations were developed by CDC staff members after consultation with experts who met in Atlanta during July 15-17, 1998. This report is intended to serve as a resource for health-care professionals, public health officials, and organizations involved in the development, delivery, and evaluation of prevention and clinical services.

INTRODUCTION

Hepatitis C virus (HCV) infection is the most common chronic bloodborne infection in the United States. CDC staff estimate that during the 1980s, an average of 230,000 new infections occurred each year (CDC, unpublished data). Although since 1989 the annual number of new infections has declined by greater than 80% to 36,000 by 1996 (1,2), data from the Third National Health and Nutrition Examination Survey (NHANES III), conducted during 1988-1994, have indicated that an estimated 3.9 million (1.8%) Americans have been infected with HCV (3). Most of these persons are chronically infected and might not be aware of their infection because they are not clinically ill. Infected persons serve as a source of transmission to others and are at risk for chronic liver disease or other HCV-related chronic diseases during the first two or more decades following initial infection.

Chronic liver disease is the tenth leading cause of death among adults in the United States, and accounts for approximately 25,000 deaths annually, or approximately 1% of all deaths (4). Population-based studies indicate that 40% of chronic liver disease is HCV-related, resulting in an estimated 8,000-10,000 deaths each year (CDC, unpublished data). Current estimates of medical and work-loss costs of HCV-related acute and chronic liver disease are greater than $600 million annually (CDC, unpublished data), and HCV-associated end-stage liver disease is the most frequent indication for liver transplantation among adults. Because most HCV-infected persons are aged 30-49 years (3), the number of deaths attributable to HCV-related chronic liver disease could increase substantially during the next 10-20 years as this group of infected persons reaches ages at which complications from chronic liver disease typically occur.

HCV is transmitted primarily through large or repeated direct percutaneous exposures to blood. In the United States, the relative importance of the two most common exposures associated with transmission of HCV, blood transfusion and injecting-drug use, has changed over time (Figure_1) (2,5). Blood transfusion, which accounted for a substantial proportion of HCV infections acquired greater than 10 years ago, rarely accounts for recently acquired infections. Since 1994, risk for transfusion-transmitted HCV infection has been so low that CDC's sentinel counties viral hepatitis surveillance system* has been unable to detect any transfusion-associated cases of acute hepatitis C, although the risk is not zero. In contrast, injecting-drug use consistently has accounted for a substantial proportion of HCV infections and currently accounts for 60% of HCV transmission in the United States. A high proportion of infections continues to be associated with injecting-drug use, but for reasons that are unclear, the dramatic decline in incidence of acute hepatitis C since 1989 correlates with a decrease in cases among injecting-drug users.

Reducing the burden of HCV infection and HCV-related disease in the United States requires implementation of primary prevention activities to reduce the risk for contracting HCV infection and secondary prevention activities to reduce the risk for liver and other chronic diseases in HCV-infected persons. The recommendations contained in this report were developed by reviewing currently available data and are based on the opinions of experts. These recommendations provide broad guidelines for a) the prevention of transmission of HCV; b) the identification, counseling, and testing of persons at risk for HCV infection; and c) the appropriate medical evaluation and management of HCV-infected persons.

BACKGROUND

Prospective studies of transfusion recipients in the United States demonstrated that rates of posttransfusion hepatitis in the 1960s exceeded 20% (6). In the mid-1970s, available diagnostic tests indicated that 90% of posttransfusion hepatitis was not caused by hepatitis A or hepatitis B viruses and that the move to all-volunteer blood donors had reduced risks for posttransfusion hepatitis to 10% (7-9). Although non-A, non-B hepatitis (i.e., neither type A nor type B) was first recognized because of its association with blood transfusion, population-based sentinel surveillance demonstrated that this disease accounted for 15%-20% of community-acquired viral hepatitis in the United States (5). Discovery of HCV by molecular cloning in 1988 indicated that non-A, non-B hepatitis was primarily caused by HCV infection (5,10-14).

Epidemiology Demographic Characteristics

HCV infection occurs among persons of all ages, but the highest incidence of acute hepatitis C is found among persons aged 20-39 years, and males predominate slightly (5). African Americans and whites have similar incidence of acute disease; persons of Hispanic ethnicity have higher rates. In the general population, the highest prevalence rates of HCV infection are found among persons aged 30-49 years and among males (3). Unlike the racial/ethnic pattern of acute disease, African Americans have a substantially higher prevalence of HCV infection than do whites (Figure 2).

Prevalence of HCV Infection in Selected Populations in the United States

The greatest variation in prevalence of HCV infection occurs among persons with different risk factors for infection (15) (Table 1). Highest prevalence of infection is found among those with large or repeated direct percutaneous exposures to blood (e.g., injecting-drug users, persons with hemophilia who were treated with clotting factor concentrates produced before 1987, and recipients of transfusions from HCV-positive donors) (12,13,16-22). Moderate prevalence is found among those with frequent but smaller direct percutaneous exposures (e.g., long-term hemodialysis patients) (23). Lower prevalence is found among those with inapparent percutaneous or mucosal exposures (e.g., persons with evidence of high-risk sexual practices) (24-28) or among those with small, sporadic percutaneous exposures (e.g., health-care workers) (29-33). Lowest prevalence of HCV infection is found among those with no high-risk characteristics (e.g., volunteer blood donors) (34; personal communication, RY Dodd, Ph.D., Head, Transmissible Diseases Department, Holland Laboratory, American Red Cross, Rockville, MD, July 1998). The estimated prevalence of persons with different risk factors and characteristics also varies widely in the U.S. population (Table 1) (3; 35-39; CDC, unpublished data).

Transmission Modes

Most risk factors associated with transmission of HCV in the United States were identified in case-control studies conducted during 1978-1986 (40,41). These risk factors included blood transfusion, injecting-drug use, employment in patient care or clinical laboratory work, exposure to a sex partner or household member who has had a history of hepatitis, exposure to multiple sex partners, and low socioeconomic level. These studies reported no association with military service or exposures resulting from medical, surgical, or dental procedures, tattooing, acupuncture, ear piercing, or foreign travel. If transmission from such exposures does occur, the frequency might be too low to detect.

Transfusions and Transplants. Currently, HCV is rarely transmitted by blood transfusion. During 1985-1990, cases of transfusion-associated non-A, non-B hepatitis declined by greater than 50% because of screening policies that excluded donors with human immunodeficiency virus (HIV) infection and donors with surrogate markers for non-A, non-B hepatitis (5,42). By 1990, risk for transfusion-associated HCV infection was approximately 1.5%/recipient or approximately 0.02%/unit transfused (42). During May 1990, routine testing of donors for evidence of HCV infection was initiated, and during July 1992, more sensitive -- multiantigen

- testing was implemented, reducing further the risk for infection to 0.001%/ unit transfused (43).

Receipt of clotting factor concentrates prepared from plasma pools posed a high risk for HCV infection (44) until effective procedures to inactivate viruses, including HCV, were introduced during 1985 (Factor VIII) and 1987 (Factor IX). Persons with hemophilia who were treated with products before inactivation of those products have prevalence rates of HCV infection as high as 90% (20-22). Although plasma derivatives (e.g., albumin and immune globulin {IG} for intramuscular {IM} administration) have not been associated with transmission of HCV infection in the United States, intravenous (IV) IG that was not virally inactivated was the source of one outbreak of hepatitis C during 1993-1994 (45,46). Since December 1994, all IG products – IV and IM – commercially available in the United States must undergo an inactivation procedure or be negative for HCV RNA (ribonucleic acid) before release.

Transplantation of organs (e.g., heart, kidney, or liver) from infectious donors to the organ recipient also carried a high risk for transmitting HCV infection before donor screening (47,48). Limited studies of recipients of transplanted tissue have implicated transmission of HCV only from nonirradiated bone tissue of unscreened donors (49,50). As with blood-donor screening, use of anti-HCV-negative organ and tissue donors has virtually eliminated risks for HCV transmission from transplantation.

Injecting and Other Illegal Drug Use. Although the number of cases of acute hepatitis C among injecting-drug users has declined dramatically since 1989, both incidence and prevalence of HCV infection remain high in this group (51,52). Injecting-drug use currently accounts for most HCV transmission in the United States, and has accounted for a substantial proportion of HCV infections during past decades (2,5,53). Many persons with chronic HCV infection might have acquired their infection 20-30 years ago as a result of limited or occasional illegal drug injecting. Injecting-drug use leads to HCV transmission in a manner similar to that for other bloodborne pathogens (i.e., through transfer of HCV-infected blood by sharing syringes and needles either directly or through contamination of drug preparation equipment) (54,55). However, HCV infection is acquired more rapidly after initiation of injecting than other viral infections (i.e., hepatitis B virus {HBV} and HIV), and rates of HCV infection among young injecting-drug users are four times higher than rates of HIV infection (19). After 5 years of injecting, as many as 90% of users are infected with HCV. More rapid acquisition of HCV infection compared with other viral infections among injecting-drug users is likely caused by high prevalence of chronic HCV infection among injecting-drug users, which results in a greater likelihood of exposure to an HCV-infected person.

A study conducted among volunteer blood donors in the United States documented that HCV infection has been independently associated with a history of intranasal cocaine use (56). (The mode of transmission could be through sharing contaminated straws.) Data from NHANES III indicated that 14% of the general population have used cocaine at least once (CDC, unpublished data). Although NHANES III data also indicated that cocaine use was associated with HCV infection, injecting-drug use histories were not ascertained. Among patients with acute hepatitis C identified in CDC's sentinel counties viral hepatitis surveillance system since 1991, intranasal cocaine use in the absence of injecting-drug use was uncommon (2). Thus, at least in the recent past, intranasal cocaine use rarely appears to have contributed to transmission. Until more data are available, whether persons with a history of noninjecting illegal drug use alone (e.g., intranasal cocaine use) are likely to be infected with HCV remains unknown.

Nosocomial and Occupational Exposures. Nosocomial transmission of HCV is possible if infection-control techniques or disinfection procedures are inadequate and contaminated equipment is shared among patients. Although reports from other countries do document nosocomial HCV transmission (57-59), such transmission rarely has been reported in the United States (60), other than in chronic hemodialysis settings (61). Prevalence of antibody to HCV (anti-HCV) positivity among chronic hemodialysis patients averages 10%, with some centers reporting rates greater than 60% (23). Both incidence and prevalence studies have documented an association between anti-HCV positivity and increasing years on dialysis, independent of blood transfusion (62,63). These studies, as well as investigations of dialysis-associated outbreaks of hepatitis C (64), indicate that HCV transmission might occur among patients in a hemodialysis center because of incorrect implementation of infection-control practices, particularly sharing of medication vials and supplies (65).

Health-care, emergency medical (e.g., emergency medical technicians and paramedics), and public safety workers (e.g., fire-service, law-enforcement, and correctional facility personnel) who have exposure to blood in the workplace are at risk for being infected with bloodborne pathogens. However, prevalence of HCV infection among health-care workers, including orthopedic, general, and oral surgeons, is no greater than the general population, averaging 1%-2%, and is 10 times lower than that for HBV infection (29-33). In a single study that evaluated risk factors for infection, a history of unintentional needle-stick injury was the only occupational risk factor independently associated with HCV infection (66).

The average incidence of anti-HCV seroconversion after unintentional needle sticks or sharps exposures from an HCV-positive source is 1.8% (range: 0%-7%) (67-70), with one study reporting that transmission occurred only from hollow-bore needles compared with other sharps (69). A study from Japan reported an incidence of HCV infection of 10% based on detection of HCV RNA by reverse transcriptase polymerase chain reaction (RT-PCR) (70). Although no incidence studies have documented transmission associated with mucous membrane or nonintact skin exposures, transmission of HCV from blood splashes to the conjunctiva have been described (71,72).

The risk for HCV transmission from an infected health-care worker to patients appears to be very low. One published report exists of such transmission during performance of exposure-prone invasive procedures (73). That report, from Spain, described HCV transmission from a cardiothoracic surgeon to five patients, but did not identify factors that might have contributed to transmission. Although factors (e.g., virus titer) might be related to transmission of HCV, no methods exist currently that can reliably determine infectivity, nor do data exist to determine threshold concentration of virus required for transmission.

Percutaneous Exposures in Other Settings. In other countries, HCV infection has been associated with folk medicine practices, tattooing, body piercing, and commercial barbering (74-81). However, in the United States, case-control studies have reported no association between HCV infection and these types of exposures (40,41). In addition, of patients with acute hepatitis C who were identified in CDC's sentinel counties viral hepatitis surveillance system during the past 15 years and who denied a history of injecting-drug use, only 1% reported a history of tattooing or ear piercing, and none reported a history of acupuncture (41; CDC, unpublished data). Among injecting-drug users, frequency of tattooing and ear piercing also was uncommon (3%).

Although any percutaneous exposure has the potential for transferring infectious blood and potentially transmitting bloodborne pathogens (i.e., HBV, HCV, or HIV), no data exist in the United States indicating that persons with exposures to tattooing and body piercing alone are at increased risk for HCV infection. Further studies are needed to determine if these types of exposures and settings in which they occur (e.g., correctional institutions, unregulated commercial establishments), are risk factors for HCV infection in the United States.

Sexual Activity. Case-control studies have reported an association between exposure to a sex contact with a history of hepatitis or exposure to multiple sex partners and acquiring hepatitis C (40,41). In addition, 15%-20% of patients with acute hepatitis C who have been reported to CDC's sentinel counties surveillance system, have a history of sexual exposure in the absence of other risk factors. Two thirds of these have an anti-HCV-positive sex partner, and one third reported greater than 2 partners in the 6 months before illness (2).

In contrast, a low prevalence of HCV infection has been reported by studies of long-term spouses of patients with chronic HCV infection who had no other risk factors for infection. Five of these studies have been conducted in the United States, involving 30-85 partners each, in which average prevalence of HCV infection was 1.5% (range: 0% to 4.4%) (56,82-85). Among partners of persons with hemophilia coinfected with HCV and HIV, two studies have reported an average prevalence of HCV infection of 3% (83,86). One additional study evaluated potential transmission of HCV between sexually transmitted disease (STD) clinic patients, who denied percutaneous risk factors, and their steady partners (28). Prevalence of HCV infection among male patients with an anti-HCV-positive female partner (7%) was no different than that among males with a negative female partner (8%). However, female patients with an anti-HCV-positive partner were almost fourfold more likely to have HCV infection than females with a negative male partner (10% versus 3%, respectively). These data indicate that, similar to other bloodborne viruses, sexual transmission of HCV from males to females might be more efficient than from females to males.

Among persons with evidence of high-risk sexual practices (e.g., patients attending STD clinics and female prostitutes) who denied a history of injecting-drug use, prevalence of anti-HCV has been found to average 6% (range: 1%-10%) (24-28,87). Specific factors associated with anti-HCV positivity for both heterosexuals and men who have sex with men (MSM) included greater numbers of sex partners, a history of prior STDs, and failure to use a condom. However, the number of partners associated with infection risk varied among studies, ranging from greater than 1 partner in the previous month to greater than 50 in the previous year. In studies of other populations, the number of partners associated with HCV infection also varied, ranging from greater than 2 partners in the 6 months before illness for persons with acute hepatitis C (41), to greater than or equal to 5 partners/year for HCV-infected volunteer blood donors (56), to greater than or equal to 10 lifetime partners for HCV-infected persons in the general population (3).

Only one study has documented an association between HCV infection and MSM activity (28), and at least in STD clinic settings, the prevalence rate of HCV infection among MSM generally has been similar to that of heterosexuals. Because sexual transmission of bloodborne viruses is recognized to be more efficient among MSM compared with heterosexual men and women, why HCV infection rates are not substantially higher among MSM compared with heterosexuals is unclear. This observation and the low prevalence of HCV infection observed among long-term spouses of persons with chronic HCV infection have raised doubts regarding the importance of sexual activity in transmission of HCV. Unacknowledged percutaneous risk factors (i.e., illegal injecting-drug use) might contribute to increased risk for HCV infection among persons with high-risk sexual practices.

Although considerable inconsistencies exist among studies, data indicate overall that sexual transmission of HCV appears to occur, but that the virus is inefficiently spread through this manner. More data are needed to determine the risk for, and factors related to, transmission of HCV between long-term steady partners as well as among persons with high-risk sexual practices, including whether other STDs promote transmission of HCV by influencing viral load or modifying mucosal barriers.

Household Contact. Case-control studies also have reported an association between nonsexual household contact and acquiring hepatitis C (40,41). The presumed mechanism of transmission is direct or inapparent percutaneous or permucosal exposure to infectious blood or body

fluids containing blood. In a recent investigation in the United States, an HCV-infected mother transmitted HCV to her hemophilic child during performance of home infusion therapy, presumably when she had an unintentional needle stick and subsequently used the contaminated needle in the child (88).

Although prevalence of HCV infection among nonsexual household contacts of persons with chronic HCV infection in the United States is unknown, HCV transmission to such contacts is probably uncommon. In studies from other countries of nonsexual household contacts of patients with chronic hepatitis C, average anti-HCV prevalence was 4% (15). Although infected contacts in these studies reported no other commonly recognized risk factors for hepatitis C, most of these studies were done in countries where exposures commonly experienced in the past from contaminated equipment used in traditional and nontraditional medical procedures might have contributed to clustering of HCV infections in families (75,76,79).

Perinatal. The average rate of HCV infection among infants born to HCV-positive, HIV-negative women is 5%-6% (range: 0%-25%), based on detection of anti-HCV and HCV RNA, respectively (89-101). The average infection rate for infants born to women coinfected with HCV and HIV is higher -- 14% (range: 5%-36%) and 17%, based on detection of anti-HCV and HCV RNA, respectively (90,96,98-104). The only factor consistently found to be associated with transmission has been the presence of HCV RNA in the mother at the time of birth. Although two studies of infants born to HCV-positive, HIV-negative women reported an association with titer of HCV RNA, each study reported a different level of HCV RNA related to transmission (92,93). Studies of HCV/HIV-coinfected women more consistently have indicated an association between virus titer and transmission of HCV (102).

Data regarding the relationship between delivery mode and HCV transmission are limited and presently indicate no difference in infection rates between infants delivered vaginally compared with cesarean-delivered infants. The transmission of HCV infection through breast milk has not been documented. In the studies that have evaluated breastfeeding in infants born to HCV-infected women, average rate of infection was 4% in both breastfed and bottle-fed infants (95,96,99,100,105,106).

Diagnostic criteria for perinatal HCV infection have not been established. Various anti-HCV patterns have been observed in both infected and uninfected infants of anti-HCV-positive mothers. Passively acquired maternal antibody might persist for months, but probably not for greater than 12 months. HCV RNA can be detected as early as 1 to 2 months.

Persons with No Recognized Source for Their Infection. Recent studies have demonstrated that injecting-drug use currently accounts for 60% of HCV transmission in the United States (2). Although the role of sexual activity in transmission of HCV remains unclear, less than or equal to 20% of persons with HCV infection report sexual exposures (i.e., exposure to an infected sexual partner or to multiple partners) in the absence of percutaneous risk factors (2). Other known exposures (occupational, hemodialysis, household, perinatal) together account for approximately 10% of infections. Thus, a potential risk factor can be identified for approximately 90% of persons with HCV infection. In the remaining 10%, no recognized source of infection can be identified, although most persons in this category are associated with low socioeconomic level. Although low socioeconomic level has been associated with several infectious diseases and might be a surrogate for high-risk exposures, its nonspecific nature makes targeting prevention measures difficult.

Screening and Diagnostic Tests Serologic Assays

The only tests currently approved by the U.S. Food and Drug Administration (FDA) for diagnosis of HCV infection are those that measure anti-HCV (Table 2) (107). These tests detect anti-HCV in greater than or equal to 97% of infected patients, but do not distinguish between acute, chronic, or resolved infection. As with any screening test, positive predictive value of enzyme immunoassay (EIA) for anti-HCV varies depending on prevalence of infection in the population and is low in populations with an HCV-infection prevalence of less than 10% (1,34). Supplemental testing with a more specific assay (i.e., recombinant immunoblot assay {RIBATM}) of a specimen with a positive EIA result prevents reporting of false-positive results, particularly in settings where asymptomatic persons are being tested.

Supplemental test results might be reported as positive, negative, or indeterminate. An anti-HCV-positive person is defined as one whose serologic results are EIA-test-positive and supplemental-test-positive. Persons with a negative EIA test result or a positive EIA and a negative supplemental test result are considered uninfected, unless other evidence exists to indicate HCV infection (e.g., abnormal ALT levels in immunocompromised persons or persons with no other etiology for their liver disease). Indeterminate supplemental test results have been observed in recently infected persons who are in the process of seroconversion, as well as in persons chronically infected with HCV. Indeterminate anti-HCV results also might indicate a false-positive result, particularly in those persons at low risk for HCV infection.

Nucleic Acid Detection

The diagnosis of HCV infection also can be made by qualitatively detecting HCV RNA using gene amplification techniques (e.g., RT-PCR) (Table 2) (108). HCV RNA can be detected in serum or plasma within 1-2 weeks after exposure to the virus and weeks before the onset of alanine aminotransferase (ALT) elevations or the appearance of anti-HCV. Rarely, detection of HCV RNA might be the only evidence of HCV infection. Although RT-PCR assay kits for HCV RNA are available for research purposes from various manufacturers of diagnostic reagents, none have been approved by FDA. In addition, numerous laboratories perform RT-PCR using in-house laboratory methods and reagents.

Although not FDA-approved, RT-PCR assays for HCV infection are used commonly in clinical practice. Most RT-PCR assays have a lower limit of detection of 100-1,000 viral genome copies/mL. With adequate optimization of RT-PCR assays, 75%-85% of persons who are anti-HCV-positive and greater than 95% of persons with acute or chronic hepatitis C will test positive for HCV RNA. Some HCV-infected persons might be only intermittently HCV RNA-positive, particularly those with acute hepatitis C or with end-stage liver disease caused by hepatitis C. To minimize false-negative results, serum must be separated from cellular components within 2-4 hours after collection, and preferably stored frozen at -20 C or -70 C (109). If shipping is required, frozen samples should be protected from thawing. Because of assay variability, rigorous quality assurance and control should be in place in clinical laboratories performing this assay, and proficiency testing is recommended.

Quantitative assays for measuring the concentration (titer) of HCV RNA have been developed and are available from commercial laboratories (110), including a quantitative RT-PCR (Amplicor HCV MonitorTM, Roche Molecular Systems, Branchburg, New Jersey) and a branched DNA (deoxyribonucleic acid) signal amplification assay (QuantiplexTM HCV RNA Assay {bDNA}, Chiron Corp., Emeryville, California) (Table 2). These assays also are not FDA-approved, and compared with qualitative RT-PCR assays, are less sensitive with lower limits of detection of 500 viral genome copies/mL for the Amplicor HCV MonitorTM to 200,000 genome equivalents/mL for the QuantiplexTM HCV RNA Assay (111). In addition, they each use a different standard, which precludes direct comparisons between the two assays. Quantitative assays should not be used as a primary test to confirm or exclude diagnosis of HCV infection or to monitor the endpoint of treatment. Patients with chronic hepatitis C generally circulate virus at levels of 105-107 genome copies/mL. Testing for level of HCV RNA might help predict likelihood of response to antiviral therapy, although sequential measurement of HCV RNA levels has not proven useful in managing patients with hepatitis C.

At least six different genotypes and greater than 90 subtypes of HCV exist (112). Approximately 70% of HCV-infected persons in the United States are infected with genotype 1, with frequency of subtype 1a predominating over subtype 1b. Different nucleic acid detection methods are available commercially to group isolates of HCV, based on genotypes and subtypes (113). Evidence is limited regarding differences in clinical features, disease outcome, or progression to cirrhosis or hepatocellular carcinoma (HCC) among persons with different genotypes. However, differences do exist in responses to antiviral therapy according to HCV genotype. Rates of response in patients infected with genotype 1 are substantially lower than in patients with other genotypes, and treatment regimens might differ on the basis of genotype. Thus, genotyping might be warranted among persons with chronic hepatitis C who are being considered for antiviral therapy.

Clinical Features and Natural History Acute HCV Infection

Persons with acute HCV infection typically are either asymptomatic or have a mild clinical illness; 60%-70% have no discernible symptoms; 20%-30% might have jaundice; and 10%-20% might have nonspecific symptoms (e.g., anorexia, malaise, or abdominal pain) (13,114,115). Clinical illness in patients with acute hepatitis C who seek medical care is similar to that of other types of viral hepatitis, and serologic testing is necessary to determine the etiology of hepatitis in an individual patient. In less than or equal to 20% of these patients, onset of symptoms might precede anti-HCV seroconversion. Average time period from exposure to symptom onset is 6-7 weeks (116-118), whereas average time period from exposure to seroconversion is 8-9 weeks (114; personal communication, HJ Alter, M.D., Chief, Department of Transfusion Medicine, Clinical Center, National Institutes of Health, Bethesda, MD, September 1998). Anti-HCV can be detected in 80% of patients within 15 weeks after exposure, in greater than or equal to 90% within 5 months after exposure, and in greater than or equal to 97% by 6 months after exposure (14,114). Rarely, seroconversion might be delayed until 9 months after exposure (14,119).

The course of acute hepatitis C is variable, although elevations in serum ALT levels, often in a fluctuating pattern, are its most characteristic feature. Normalization of ALT levels might occur and suggests full recovery, but this is frequently followed by ALT elevations that indicate progression to chronic disease (14). Fulminant hepatic failure following acute hepatitis C is rare (120,121).

Chronic HCV Infection

After acute infection, 15%-25% of persons appear to resolve their infection without sequelae as defined by sustained absence of HCV RNA in serum and normalization of ALT levels (122; personal communication, LB Seeff, M.D., Senior Scientist {Hepatitis C}, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, July 1998). Chronic HCV infection develops in most persons (75%-85%)(14,122-124), with persistent or fluctuating ALT elevations indicating active liver disease developing in 60%-70% of chronically infected persons (12-15,116,122-124). In the remaining 30%-40% of chronically infected persons, ALT levels are normal. No clinical or epidemiologic features among patients with acute infection have been found to be predictive of either persistent infection or chronic liver disease. Moreover, various ALT patterns have been observed in these patients during follow-up, and patients might have prolonged periods (greater than or equal to 12 months) of normal ALT activity even though they have histologic-confirmed chronic hepatitis (14). Thus, a single ALT determination cannot be used to exclude ongoing hepatic injury, and long-term follow-up of patients with HCV infection is required to determine their clinical outcome or prognosis.

The course of chronic liver disease is usually insidious, progressing at a slow rate without symptoms or physical signs in the majority of patients during the first two or more decades after infection. Frequently, chronic hepatitis C is not recognized until asymptomatic persons are identified as HCV-positive during blood-donor screening, or elevated ALT levels are detected during routine physical examinations. Most studies have reported that cirrhosis develops in 10%-20% of persons with chronic hepatitis C over a period of 20-30 years, and HCC in 1%-5%, with striking geographic variations in rates of this disease (124-128). However, when cirrhosis is established, the rate of development of HCC might be as high as 1%-4%/year. In contrast, a study of greater than 200 women 17 years after they received HCV-contaminated Rh factor IG reported that only 2.4% had evidence of cirrhosis and none had died (129). Thus, longer term follow-up studies are needed to assess lifetime consequences of chronic hepatitis C, particularly among those who acquired their infection at young ages.

Although factors predicting severity of liver disease have not been well-defined, recent data indicate that increased alcohol intake, being aged greater than 40 years at infection, and being male are associated with more severe liver disease (130). In particular, among persons with alcoholic liver disease and HCV infection, liver disease progresses more rapidly; among those with cirrhosis, a higher risk for development of HCC exists (131). Furthermore, even intake of moderate amounts (greater than 10 g/day) of alcohol in patients with chronic hepatitis C might enhance disease progression. More severe liver injury observed in persons with alcoholic liver disease and HCV infection possibly is attributable to alcohol-induced enhancement of viral replication or increased susceptibility of cells to viral injury. In addition, persons who have chronic liver disease are at increased risk for fulminant hepatitis A (132).

Extrahepatic manifestations of chronic HCV infection are considered to be of immunologic origin and include cryoglobulinemia, membranoproliferative glomerulonephritis, and porphyria cutanea tarda (131). Other extrahepatic conditions have been reported, but definitive associations of these conditions with HCV infection have not been established. These include seronegative arthritis, Sjogren syndrome, autoimmune thyroiditis, lichen planus, Mooren corneal ulcers, idiopathic pulmonary fibrosis (Hamman-Rich syndrome), polyarteritis nodosa, aplastic anemia, and B-cell lymphomas.

Clinical Management and Treatment

HCV-positive patients should be evaluated for presence and severity of chronic liver disease (133). Initial evaluation for presence of disease should include multiple measurements of ALT at regular intervals, because ALT activity fluctuates in persons with chronic hepatitis C. Patients with chronic hepatitis C should be evaluated for severity of their liver disease and for possible treatment (133-135).

Antiviral therapy is recommended for patients with chronic hepatitis C who are at greatest risk for progression to cirrhosis (133). These persons include anti-HCV-positive patients with persistently elevated ALT levels, detectable HCV RNA, and a liver biopsy that indicates either portal or bridging fibrosis or at least moderate degrees of inflammation and necrosis.

In patients with less severe histologic changes, indications for treatment are less clear, and careful clinical follow-up might be an acceptable alternative to treatment with antiviral therapy (e.g., interferon) because progression to cirrhosis is likely to be slow, if it occurs at all. Similarly, patients with compensated cirrhosis (without jaundice, ascites, variceal hemorrhage, or encephalopathy) might not benefit from interferon therapy. Careful assessment should be made, and the risks and benefits of therapy should be thoroughly discussed with the patient.

Patients with persistently normal ALT values should not be treated with interferon outside of clinical trials because treatment might actually induce liver enzyme abnormalities (136). Patients with advanced cirrhosis who might be at risk for decompensation with therapy and pregnant women also should not be treated. Interferon treatment is not FDA-approved for patients aged less than 18 years, and more data are needed regarding treatment of persons aged less than 18 years or greater than 60 years. Treatment of patients who are drinking excessive amounts of

alcohol or who are injecting illegal drugs should be delayed until these behaviors have been discontinued for greater than or equal to 6 months. Contraindications to treatment with interferon include major depressive illness, cytopenias, hyperthyroidism, renal transplantation, and evidence of autoimmune disease.

Most clinical trials of treatment for chronic hepatitis C have been conducted using alpha-interferon (134,135,137,138). When the recommended regimen of 3 million units administered subcutaneously 3 times/week for 12 months is used, approximately 50% of treated patients have normalization of serum ALT activity (biochemical response), and 33% have a loss of detectable HCV RNA in serum (virologic response) at the end of therapy. However, greater than or equal to 50% of these patients relapse when therapy is stopped. Thus, 15%-25% have a sustained response as measured by testing for ALT and HCV RNA greater than or equal to 1 years after therapy is stopped, many of whom also have histologic improvement. For patients who do not respond by the end of therapy, retreatment with a standard dose of interferon is rarely effective. Patients who have persistently abnormal ALT levels and detectable HCV RNA in serum after 3 months of interferon are unlikely to respond to treatment, and interferon treatment should be discontinued. These persons might be considered for participation in clinical trials of alternative treatments. Decreased interferon response rates (less than 15%) have been found in patients with higher serum HCV RNA titers and HCV genotype 1 (the most common strain of HCV in the United States); however, treatment should not be withheld based solely on these findings.

Therapy for hepatitis C is a rapidly changing area of clinical practice. Combination therapy with interferon and ribavirin, a nucleoside analogue, is now FDA-approved for treatment of chronic hepatitis C in patients who have relapsed following interferon treatment and might be approved soon for patients who have not been treated previously. Studies of patients treated with a combination of ribavirin and interferon have demonstrated a substantial increase in sustained response rates, reaching 40%-50%, compared with response rates of 15%-25% with interferon alone (139,140). However, as with interferon alone, combination therapy in patients with genotype 1 is not as successful, and sustained response rates among these patients are still less than 30%.

Most patients receiving interferon experience flu-like symptoms early in treatment, but these symptoms diminish with continued treatment. Later side effects include fatigue, bone marrow suppression, and neuropsychiatric effects (e.g., apathy, cognitive changes, irritability, and depression). Interferon dosage must be reduced in 10%-40% of patients and discontinued in 5% -15% because of severe side effects. Ribavirin can induce hemolytic anemia and can be problematic for patients with preexisting anemia, bone marrow suppression, or renal failure. In these patients, combination therapy should be avoided or attempts should be made to correct the anemia. Hemolytic anemia caused by ribavirin also can be life-threatening for patients with ischemic heart disease or cerebral vascular disease. Ribavirin is teratogenic, and female patients should avoid becoming pregnant during therapy.

Other treatments, including corticosteroids, ursodiol, and thymosin, have not been effective. High iron levels in the liver might reduce the efficacy of interferon. Use of iron-reduction therapy (phlebotomy or chelation) in combination with interferon has been studied, but results have been inconclusive. Because patients are becoming more interested in alternative therapies (e.g., traditional Chinese medicine, antioxidants, naturopathy, and homeopathy), physicians should be prepared to address questions regarding these topics.

Postexposure Prophylaxis and Follow-Up

Available data regarding the prevention of HCV infection with IG indicate that IG is not effective for postexposure prophylaxis of hepatitis C (67,141). No assessments have been made of postexposure use of antiviral agents (e.g., interferon) to prevent HCV infection. Mechanisms of the effect of interferon in treating patients with hepatitis C are poorly understood, and an established infection might need to be present for interferon to be an effective treatment (142). As of the publication of this report, interferon is FDA-approved only for treatment of chronic hepatitis C.

The immediate postexposure setting provides opportunity to identify persons early in the course of their HCV infection. Studies indicate that interferon treatment begun early in the course of HCV infection is associated with a higher rate of resolved infection (143). However, no data exist indicating that treatment begun during the acute phase of infection is more effective than treatment begun early during the course of chronic HCV infection. In addition, as stated previously, interferon is not FDA-approved for this indication. Determination of whether treatment of HCV infection is more beneficial in the acute phase than in the early chronic phase will require evaluation with well-designed research protocols.

PREVENTION AND CONTROL RECOMMENDATIONS Rationale

Reducing the burden of HCV infection and HCV-related disease in the United States requires implementation of primary prevention activities that reduce risks for contracting HCV infection and secondary prevention activities that reduce risks for liver and other chronic diseases in HCV-infected persons. In addition, surveillance and evaluation activities are required to determine the effectiveness of prevention programs in reducing incidence of disease, identifying persons infected with HCV, providing appropriate medical follow-up, and promoting healthy lifestyles and behaviors.

Primary prevention activities can reduce or eliminate potential risk for HCV transmission from a) blood, blood components, and plasma derivatives; b) such high-risk activities as injecting-drug use and sex with multiple partners; and c) percutaneous exposures to blood in health care and other (i.e., tattooing and body piercing) settings. Immunization against HCV is not available; therefore, identifying persons at risk but not infected with HCV provides opportunity for counseling on how to reduce their risk for becoming infected.

Elements of a comprehensive strategy to prevent and control hepatitis C virus (HCV) infection and HCV-related disease

- Primary prevention activities include
  - screening and testing of blood, plasma, organ, tissue, and semen donors
  - virus inactivation of plasma-derived products;
  - risk-reduction counseling and services; and
  - implementation and maintenance of infection-control practices.
- Secondary prevention activities include
  - identification, counseling, and testing of persons at risk, and
  - medical management of infected persons.

- Professional and public education.
- Surveillance and research to monitor disease trends and the effectiveness of prevention activities and to develop improved prevention methods.

Secondary prevention activities can reduce risks for chronic disease by identifying HCV-infected persons through diagnostic testing and by providing appropriate medical management and antiviral therapy. Because of the number of persons with chronic HCV infection, identification of these persons must be a major focus of current prevention programs. Identification of persons at risk for HCV infection provides opportunity for testing to determine their infection status, medical evaluation to determine their disease status if infected, and antiviral therapy, if appropriate. Identification also provides infected persons opportunity to obtain information concerning how they can prevent further harm to their liver and prevent transmitting HCV to others.

Factors for consideration when making decisions regarding development and implementation of preventive services for a particular disease include the public health importance of the disease, the availability of appropriate diagnostic tests, and the effectiveness of available preventive and therapeutic interventions. However, identification of persons at risk for HCV infection must take into account not only the benefits but also the limitations and drawbacks associated with such efforts. Hepatitis C is a disease of major public health importance, and suitable and accurate diagnostic tests as well as behavioral and therapeutic interventions are available. Counseling and testing can prevent disease transmission and progression through reducing high-risk practices (e.g., injecting-drug use and alcohol intake). However, the degree to which persons will change their high-risk practices based on knowing their test results is not known, and possible adverse consequences of testing exist, including disclosure of test results to others that might result in disrupted personal relationships and possible discriminatory action (e.g., loss of employment, insurance, and educational opportunities). Antiviral treatment is also available, and treatment guidelines have been developed. Such treatment is beneficial for many patients, although sustained response rates and mode of delivery are currently less than ideal.

Persons at risk for HCV infection who receive health-care services in the public and private sectors should have access to counseling and testing. Facilities that provide counseling and testing should include services or referrals for medical evaluation and management of persons identified as infected with HCV. Priorities for implementing new counseling and testing programs should be based on providing access to persons who are most likely to be infected or who practice high-risk behaviors.

PRIMARY PREVENTION RECOMMENDATIONS Blood, Plasma Derivatives, Organs, Tissues, and Semen

Current practices that exclude blood, plasma, organ, tissue, or semen donors determined to be at increased risk for HCV by history or who have serologic markers for HCV infection must be maintained to prevent HCV transmission from transfusions and transplants (1). Viral inactivation of clotting factor concentrates and other products derived from human plasma, including IG products, also must be continued, and all plasma-derived products that do not undergo viral inactivation should be HCV RNA negative by RT-PCR before release.

High-Risk Drug and Sexual Practices

Health-care professionals in all patient care settings routinely should obtain a history that inquires about use of illegal drugs (injecting and noninjecting) and evidence of high-risk sexual practices (e.g., multiple sex partners or a history of STDs). Primary prevention of illegal drug injecting will eliminate the greatest risk factor for HCV infection in the United States (144). Although consistent data are lacking regarding the extent to which sexual activity contributes to HCV transmission, persons having multiple sex partners are at risk for STDs (e.g., HIV, HBV, syphilis, gonorrhea, and chlamydia). Counseling and education to prevent initiation of drug-injecting or high-risk sexual practices is important, especially for adolescents. Persons who inject drugs or who are at risk for STDs should be counseled regarding what they can do to minimize their risk for becoming infected or of transmitting infectious agents to others, including need for vaccination against hepatitis B (144-148). Injecting and noninjecting illegal drug users and sexually active MSM also should be vaccinated against hepatitis A (149).

Prevention messages for persons with high-risk drug or sexual practices

- Persons who use or inject illegal drugs should be advised
  - to stop using and injecting drugs.
  - to enter and complete substance-abuse treatment, including relapse-prevention programs.
  - if continuing to inject drugs,
    - to never reuse or "share" syringes, needles, water, or drug preparation equipment; if injection equipment has been used by other persons, to first clean the equipment with bleach and water;
    - to use only sterile syringes obtained from a reliable source (e.g., pharmacies);
    - to use a new sterile syringe to prepare and inject drugs;
    - if possible, to use sterile water to prepare drugs; otherwise to use clean water from a reliable source (such as fresh tap water).
    - to use a new or disinfected container ("cooker") and a new filter ("cotton") to prepare drugs;
    - to clean the injection site before injection with a new alcohol swab; and
    - to safely dispose of syringes after one use.
  - to get vaccinated against hepatitis B and hepatitis A.
- Persons who are at risk for sexually transmitted diseases should be advised
  - that the surest way to prevent the spread of human immunodeficiency virus infection and other sexually transmitted diseases is to have sex with only one uninfected partner or not to have sex at all.

- to use latex condoms correctly and every time to protect themselves and their partners from diseases spread through sexual activity.
- to get vaccinated against hepatitis B, and if appropriate, hepatitis A.

Counseling of persons with potential or existing illegal drug

use or high-risk sexual practices should be conducted in the setting in which the patient is identified. If counseling services cannot be provided on-site, patients should be referred to a convenient community resource, or at a minimum, provided easy-to-understand health-education material. STD and drug-treatment clinics, correctional institutions, and HIV counseling and testing sites should routinely provide information concerning prevention of HCV and HBV infection in their counseling messages. Based on the findings of multiple studies, syringe and needle-exchange programs can be an effective part of a comprehensive strategy to reduce the incidence of bloodborne virus transmission and do not encourage the use of illegal drugs (150-153). Therefore, to reduce the risk for HCV infection among injecting-drug users, local communities can consider implementing syringe and needle-exchange programs.

Percutaneous Exposures to Blood in Health Care and Other Settings Health-Care Settings

Health-care, emergency medical, and public safety workers should be educated regarding risk for and prevention of bloodborne infections, including the need to be vaccinated against hepatitis B (154-156). Standard barrier precautions and engineering controls should be implemented to prevent exposure to blood. Protocols should be in place for reporting and follow-up of percutaneous or permucosal exposures to blood or body fluids that contain blood.

Health-care professionals responsible for overseeing patients receiving home infusion therapy should ensure that patients and their families (or caregivers) are informed of potential risk for infection with bloodborne pathogens, and should assess their ability to use adequate infection-control practices consistently (88). Patients and families should receive training with a standardized curriculum that includes appropriate infection-control procedures, and these procedures should be evaluated regularly through home visits.

Currently, no recommendations exist to restrict professional activities of health-care workers with HCV infection. As recommended for all health-care workers, those who are HCV-positive should follow strict aseptic technique and standard precautions, including appropriate use of hand washing, protective barriers, and care in the use and disposal of needles and other sharp instruments (154,155).

In chronic hemodialysis settings, intensive efforts must be made to educate new staff and reeducate existing staff regarding hemodialysis-specific infection-control practices that prevent transmission of HCV and other bloodborne pathogens (65,157). Hemodialysis-center precautions are more stringent than standard precautions. Standard precautions require use of gloves only when touching blood, body fluids, secretions, excretions, or contaminated items. In contrast, hemodialysis-center precautions require glove use whenever patients or hemodialysis equipment is touched. Standard precautions do not restrict use of supplies, instruments, and medications to a single patient; hemodialysis-center precautions specify that none of these items be shared among any patients. Thus, appropriate use of hemodialysis-center precautions should prevent transmission of HCV among chronic hemodialysis patients, and isolation of HCV-positive patients is not necessary or recommended.

Routine precautions for the care of all hemodialysis patients

- Patients should have specific dialysis stations assigned to them, and chairs and beds should be cleaned after each use.
- Sharing among patients of ancillary supplies such as trays, blood pressure cuffs, clamps, scissors, and other nondisposable items should be avoided.
- Nondisposable items should be cleaned or disinfected appropriately between uses.
- Medications and supplies should not be shared among patients, and medication carts should not be used.
- Medications should be prepared and distributed from a centralized area.
- Clean and contaminated areas should be separated (e.g., handling and storage of medications and hand washing should not be done in the same or an adjacent area to that where used equipment or blood samples are handled).

Other Settings

Persons who are considering tattooing or body piercing should be informed of potential risks of acquiring infection with bloodborne and other pathogens through these procedures. These procedures might be a source of infection if equipment is not sterile or if the artist or piercer does not follow other proper infection-control procedures (e.g., washing hands, using latex gloves, and cleaning and disinfecting surfaces).

SECONDARY PREVENTION RECOMMENDATIONS Persons for Whom Routine HCV Testing Is Recommended

Testing should be offered routinely to persons most likely to be infected with HCV who might require medical management, and testing should be accompanied by appropriate counseling and medical follow-up. In addition, anyone who wishes to know or is concerned regarding their HCV-infection status should be provided the opportunity for counseling, testing, and appropriate follow-up. The determination of which persons at risk to recommend for routine testing is based on various considerations, including a known epidemiologic relationship between a risk factor and acquiring HCV infection, prevalence of risk behavior or characteristic in the population, prevalence of infection among those with a risk behavior or characteristic, and the need for persons with a recognized exposure to be evaluated for infection.

Persons who should be tested routinely for hepatitis C virus (HCV) infection based on their risk for infection

- Persons who ever injected illegal drugs, including those who injected once or a few times many years ago and do not consider themselves as drug users.
- Persons with selected medical conditions, including
  - persons who received clotting factor concentrates produced before 1987;

- persons who were ever on chronic (long-term) hemodialysis; and
- persons with persistently abnormal alanine aminotransferase levels.

- Prior recipients of transfusions or organ transplants, including
  - persons who were notified that they received blood from a donor who later tested positive for HCV infection;
  - persons who received a transfusion of blood or blood components before July 1992; and
  - persons who received an organ transplant before July 1992.

Persons who should be tested routinely for HCV-infection based on a recognized exposure

- Healthcare, emergency medical, and public safety workers after needle sticks, sharps, or mucosal exposures to HCV-positive blood.
- Children born to HCV-positive women.

Persons Who Have Ever Injected Illegal Drugs

Health-care professionals in primary-care and other appropriate settings routinely should question patients regarding their history of injecting-drug use, and should counsel, test, and evaluate for HCV infection, persons with such histories. Current injecting-drug users frequently are not seen in the primary health-care setting and might not be reached by traditional media; therefore, community-based organizations serving these populations should determine the most effective means of integrating appropriate HCV information and services into their programs.

Testing persons in settings with potentially high proportions of injecting-drug users (e.g., correctional institutions, HIV counseling and testing sites, or drug and STD treatment programs) might be particularly efficient for identifying HCV-positive persons. HCV testing programs in these settings should include counseling and referral or arrangements for medical management. However, limited experience exists in combining HCV programs with existing HIV, STD, or other established services for populations at high risk for infection with bloodborne pathogens. Persons at risk for HCV infection through limited or occasional drug use, particularly in the remote past, might not be receptive to receiving services in such settings as HIV counseling and testing sites and drug and STD treatment programs. In addition, whether a substantial proportion of this group at risk can be identified in these settings is unknown. Studies are needed to determine the best approaches for reaching persons who might not identify themselves as being at risk for HCV infection.

Persons with Selected Medical Conditions

Persons with hemophilia who received clotting factor concentrates produced before 1987 and long-term hemodialysis patients should be tested for HCV infection. Educational efforts directed to health-care professionals, patient organizations, and agencies who care for these patients should emphasize the need for these patients to know whether they are infected with HCV and encourage testing for those who have not been tested previously. Periodic testing of long-term hemodialysis patients for purposes of infection control is currently not recommended (61). However, issues surrounding prevention of HCV and other bloodborne pathogen transmission in long-term hemodialysis settings are currently undergoing discussion, and updating recommendations for this setting is under development.

Persons with persistently abnormal ALT levels are often identified in medical settings. As part of their medical work-up, health-care professionals should test routinely for HCV infection persons with ALT levels above the upper limit of normal on at least two occasions. Persons with other evidence of liver disease identified by abnormal serum aspartate aminotransferase (AST) levels, which is common among persons with alcohol-related liver disease, should be tested also.

Prior Recipients of Blood Transfusions or Organ Transplants

Persons who might have become infected with HCV through transfusion of blood and blood components should be notified. Two types of approaches should be used -- a) a targeted, or directed, approach to identify prior transfusion recipients from donors who tested anti-HCV positive after multiantigen screening tests were widely implemented (July 1992 and later); and b) a general approach to identify all persons who received transfusions before July 1992. A targeted notification approach focuses on a specific group known to be at risk, and will reach persons who might be unaware they were transfused. However, because blood and blood-component donor testing for anti-HCV before July 1992 did not include confirmatory testing, most of these notifications would be based on donors who were not infected with HCV because their test results were falsely positive. A general education campaign to identify persons transfused before July 1992 has the advantage of not being dependent on donor testing status or availability of records, and potentially reaches persons who received HCV-infected blood from donors who tested falsely negative on the less sensitive serologic test, as well as from donors before testing was available.

- Persons who received blood from a donor who tested positive for HCV infection after multiantigen screening tests were widely implemented. Persons who received blood or blood components from donors who subsequently tested positive for anti-HCV using a licensed multiantigen assay should be notified as provided for in guidance issued by FDA. For specific details regarding this notification, readers should refer to the FDA document, Guidance for Industry. Current Good Manufacturing Practice for Blood and Blood Components: (1) Quarantine and Disposition of Units from Prior Collections from Donors with Repeatedly Reactive Screening Tests for Antibody to Hepatitis C Virus (Anti-HCV); (2) Supplemental Testing, and the Notification of Consignees and Blood Recipients of Donor Test Results for Anti-HCV. (This document is available on the Internet at .)

Blood-collection establishments and transfusion services should work with local and state health agencies to coordinate this notification effort. Health-care professionals should have information regarding the notification process and HCV infection so that they are prepared to discuss with their patients why they were notified and to provide appropriate counseling, testing, and medical evaluation. Health-education material sent to recipients should be easy to understand and include information concerning where they can be tested, what hepatitis C means in terms of their day-to-day living, and where they can obtain more information.

- Persons who received a transfusion of blood or blood components (including platelets, red cells, washed cells, and fresh frozen plasma) or a solid-organ transplant (e.g., heart, lung, kidney, or liver) before July 1992. Patients with a history of blood transfusion or solid-organ transplantation before July 1992 should be counseled, tested, and evaluated for HCV infection. Health-care professionals in primary-care and other appropriate settings routinely should ascertain their patients' transfusion and transplant histories either through questioning their

patients, including such risk factors for transfusion as hematologic disorders, major surgery, trauma, or premature birth, or through review of their medical records. In addition, transfusion services, public health agencies, and professional organizations should provide to the public, information concerning the need for HCV testing in this population. Health-care professionals should be prepared to discuss these issues with their patients and provide appropriate counseling, testing, and medical evaluation.

Health-Care, Emergency Medical, and Public Safety Workers After Needle Sticks, Sharps, or Mucosal Exposures to HCV-Positive Blood

Individual institutions should establish policies and procedures for HCV testing of persons after percutaneous or permucosal exposures to blood and ensure that all personnel are familiar with these policies and procedures (see text box on next page) (141). Health-care professionals who provide care to persons exposed to HCV in the occupational setting should be knowledgeable regarding the risk for HCV infection and appropriate counseling, testing, and medical follow-up.

IG and antiviral agents are not recommended for postexposure prophylaxis of hepatitis C. Limited data indicate that antiviral therapy might be beneficial when started early in the course of HCV infection, but no guidelines exist for administration of therapy during the acute phase of infection. When HCV infection is identified early, the individual should be referred for medical management to a specialist knowledgeable in this area.

Children Born to HCV-Positive Women

Because of their recognized exposure, children born to HCV-positive women should be tested for HCV infection (158). IG and antiviral agents are not recommended for postexposure prophylaxis of infants born to HCV-positive women. Testing of infants for anti-HCV should be performed no sooner than age 12 months, when passively transferred maternal anti-HCV declines below detectable levels. If earlier diagnosis of HCV infection is desired, RT-PCR for HCV RNA may be performed at or after the infant's first well-child visit at age 1-2 months. Umbilical cord blood should not be used for diagnosis of perinatal HCV infection because cord blood can be contaminated by maternal blood. If positive for either anti-HCV or HCV RNA, children should be evaluated for the presence or development of liver disease, and those children with persistently elevated ALT levels should be referred to a specialist for medical management.

Postexposure follow-up of health-care, emergency medical, and public safety workers for hepatitis C virus (HCV) infection

- For the source, baseline testing for anti-HCV.*
- For the person exposed to an HCV-positive source, baseline and follow-up testing including
  - baseline testing for anti-HCV and ALT activity; and
  - follow-up testing for anti-HCV (e.g., at 4 6 months) and ALT activity. (If earlier diagnosis of HCV infection is desired, testing for HCV RNAÝ may be performed at 4 6 weeks.)
- Confirmation by supplemental anti-HCV testing of all anti-HCV results reported as positive by enzyme immunoassay.

Persons for Whom Routine HCV Testing Is Not Recommended

For the following persons, routine testing for HCV infection is not recommended unless they have risk factors for infection.

Persons for whom routine hepatitis C virus (HCV) testing is not recommended

- Health-care, emergency medical, and public safety workers.
- Pregnant women.
- Household (nonsexual) contacts of HCV-positive persons.
- The general population.

Health-Care, Emergency Medical, and Public Safety Workers

Routine testing is recommended only for follow-up for a specific exposure.

Pregnant Women

Health-care professionals in settings where pregnant women are evaluated or receive routine care should take risk histories from their patients designed to determine the need for testing and other prevention measures, and those health-care professionals should be knowledgeable regarding HCV counseling, testing, and medical follow-up.

Household (Nonsexual) Contacts of HCV-Positive Persons

Routine testing for nonsexual household contacts of HCV-positive persons is not recommended unless a history exists of a direct (percutaneous or mucosal) exposure to blood.

Persons for Whom Routine HCV Testing Is of Uncertain Need

For persons at potential (or unknown) risk for HCV infection, the need for, or effectiveness of, routine testing has not been determined.

Persons for whom routine hepatitis C virus (HCV) testing is of uncertain need

- Recipients of transplanted tissue (e.g., corneal, musculoskeletal, skin, ova, sperm).
- Intranasal cocaine and other noninjecting illegal drug users.

- Persons with a history of tattooing or body piercing.
- Persons with a history of multiple sex partners or sexually transmitted diseases.
- Long-term steady sex partners of HCV-positive persons.

Recipients of Transplanted Tissue

On the basis of currently available data, risk for HCV transmission from transplanted tissue (e.g., corneal, musculoskeletal, skin, ova, or sperm) appears to be rare.

Intranasal Cocaine and Other Noninjecting Illegal Drug Users

Currently, the strength of the association between intranasal cocaine use and HCV infection does not support routine testing based solely on this risk factor.

Persons with a History of Tattooing or Body Piercing

Because no data exist in the United States documenting that persons with a history of such exposures as tattooing and body piercing are at increased risk for HCV infection, routine testing is not recommended based on these exposures alone. In settings having a high proportion of HCV-infected persons and where tattooing and body piercing might be performed in an unregulated manner (e.g., correctional institutions), these types of exposures might be a risk factor for HCV infection. Data are needed to determine the risk for HCV infection among persons who have been exposed under these conditions.

Persons with a History of Multiple Sex Partners or STDs

Although persons with a history of multiple sex partners or treatment for STDs and who deny injecting-drug use appear to have an increased risk for HCV infection, insufficient data exist to recommend routine testing based on these histories alone. Health-care professionals who provide services to persons with STDs should use that opportunity to take complete risk histories from their patients to ascertain the need for HCV testing, provide risk-reduction counseling, offer hepatitis B vaccination, and, if appropriate, hepatitis A vaccination.

Long-Term Steady Sex Partners of HCV-Positive Persons HCV-positive persons with long-term steady partners do not need to change their sexual practices. Persons with HCV infection should discuss with their partner the need for counseling and testing. If the partner chooses to be tested and tests negative, the couple should be informed of available data regarding risk for HCV transmission by sexual activity to assist them in making decisions about precautions (see section regarding counseling messages for HCV-positive persons). If the partner tests positive, appropriate counseling and evaluation for the presence or development of liver disease should be provided.

Testing for HCV Infection Consent for testing should be obtained in a manner consistent with that for other medical care and services provided in the same setting, and should include measures to prevent unwanted disclosure of test results to others. Persons should be provided with information regarding

- exposures associated with the transmission of HCV, including behaviors or exposures that might have occurred infrequently or many years ago;
- the test procedures and the meaning of test results;
- the nature of hepatitis C and chronic liver disease;
- the benefits of detecting infection early;
- available medical treatment; and
- potential adverse consequences of testing positive, including disrupted personal relationships and possible discriminatory action (e.g., loss of employment, insurance, and educational opportunities).

Comprehensive information regarding hepatitis C should be provided before testing; however, this might not be practical when HCV testing is performed as part of a clinical work-up or when testing for anti-HCV is required. In these cases, persons should be informed that a) testing for HCV infection will be performed, b) individual results will be kept confidential, and c) appropriate counseling and referral will be offered if results are positive.

Testing for HCV infection can be performed in various settings, including physicians' offices, other health-care facilities, health department clinics, and HIV or other freestanding counseling and testing sites. Such settings should be prepared to provide appropriate information regarding hepatitis C and provide or offer referral for additional medical care or other needed services (e.g., drug treatment), as warranted. Facilities providing HCV testing should have access to information regarding referral resources, including availability, accessibility, and eligibility criteria of local medical care and mental health professionals, support groups, and drug-treatment centers. The diagnosis of HCV infection can be made by detecting either anti-HCV or HCV RNA. Anti-HCV is recommended for routine testing of asymptomatic persons, and should include use of both EIA to test for anti-HCV and supplemental or confirmatory testing with an additional, more specific assay (Figure 3). Use of supplemental antibody testing (i.e., RIBATM) for all positive anti-HCV results by EIA is preferred, particularly in settings where clinical services are not provided directly.

Supplemental anti-HCV testing confirms the presence of anti-HCV (i.e., eliminates false-positive antibody results), which indicates past or current infection, and can be performed on the same serum sample collected for the EIA (i.e., routine serology). Confirmation or exclusion of HCV infection in a person with indeterminate anti-HCV supplemental test results should be made on the basis of further laboratory testing, which might include repeating the anti-HCV in two or more months or testing for HCV RNA and ALT level.

In clinical settings, use of RT-PCR to detect HCV RNA might be appropriate to confirm the diagnosis of HCV infection (e.g., in patients with abnormal ALT levels or with indeterminate supplemental anti-HCV test results) although RT-PCR assays are not currently FDA-approved. Detection of HCV RNA by RT-PCR in a person with an anti-HCV-positive result indicates current infection. However, absence of HCV RNA in a person with an anti-HCV-positive result based on EIA testing alone (i.e., without supplemental anti-HCV testing) cannot differentiate between resolved infection and a false-positive anti-HCV test result. In addition, because some persons with HCV infection might experience intermittent viremia, the meaning of a single negative HCV RNA result is difficult to interpret, particularly in the absence of additional clinical information.

If HCV RNA is used to confirm anti-HCV results, a separate serum sample will need to be collected and handled in a manner suitable for RT-PCR. If the HCV RNA result is negative, supplemental anti-HCV testing should be performed so that the anti-HCV EIA result can be interpreted before the result is reported to the patient.

Laboratories that perform HCV testing should follow the recommended anti-HCV testing algorithm, which includes use of supplemental testing. Having assurances that the HCV testing is performed in accredited laboratories whose services adhere to recognized standards of good laboratory practice is also necessary. Laboratories that perform HCV RNA testing should review routinely their data regarding internal and external proficiency testing because of great variability in accuracy of HCV RNA testing.

Prevention Messages and Medical Evaluation HCV-specific information and prevention messages should be provided to infected persons and individuals at risk by trained personnel in public and private health-care settings. Health-education materials should include a) general information about HCV infection; b) risk factors for infection, transmission, disease progression, and treatment; and c) detailed prevention messages appropriate for the population being tested. Written materials might also include information about community resources available for HCV-positive patients for medical evaluation and social support, as appropriate.

Persons with High-Risk Drug and Sexual Practices

Regardless of test results, persons who use illegal drugs or have high-risk sexual practices or occupations should be provided with information regarding how to reduce their risk for acquiring bloodborne and sexually transmitted infections or of potentially transmitting infectious agents to others (see section regarding primary prevention).

Negative Test Results

If their exposure was in the past, persons who test negative for HCV should be reassured.

Indeterminate Test Results

Persons whose HCV test results are indeterminate should be advised that the result is inconclusive, and they should receive appropriate follow-up testing or referral for further testing (see section regarding testing for HCV infection).

Positive Test Results

Persons who test positive should be provided with information regarding the need for a) preventing further harm to their liver; b) reducing risks for transmitting HCV to others; and c) medical evaluation for chronic liver disease and possible treatment.

- To protect their liver from further harm, HCV-positive persons should be advised to
  - not drink alcohol;
  - not start any new medicines, including over-the-counter and herbal medicines, without checking with their doctor; and
  - get vaccinated against hepatitis A if liver disease is found to be present.
- To reduce the risk for transmission to others, HCV-positive persons should be advised to
  - not donate blood, body organs, other tissue, or semen;
  - not share toothbrushes, dental appliances, razors, or other personal-care articles that might have blood on them; and
  - cover cuts and sores on the skin to keep from spreading infectious blood or secretions.
- HCV-positive persons with one long-term steady sex partner do not need to change their sexual practices. They should
  - discuss the risk, which is low but not absent, with their partner (If they want to lower the limited chance of spreading HCV to their partner, they might decide to use barrier precautions {e.g., latex condoms}); and
  - discuss with their partner the need for counseling and testing.
- HCV-positive women do not need to avoid pregnancy or breastfeeding. Potential, expectant, and new parents should be advised that
  - approximately 5 out of every 100 infants born to HCV-infected women become infected (This occurs at the time of birth, and no treatment exists that can prevent this from happening);
  - infants infected with HCV at the time of birth seem to do very well in the first years of life (More studies are needed to determine if these infants will be affected by the infection as they grow older);
  - no evidence exists that mode of delivery is related to transmission; therefore, determining the need for cesarean delivery versus vaginal delivery should not be made on the basis of HCV infection status;
  - limited data regarding breastfeeding indicate that it does not transmit HCV, although HCV-positive mothers should consider abstaining from breastfeeding if their nipples are cracked or bleeding;
  - infants born to HCV-positive women should be tested for HCV infection and if positive, evaluated for the presence or development of chronic liver disease (see section regarding routine testing of children born to HCV-positive women); and
  - if an HCV-positive woman has given birth to any children after the woman became infected with HCV, she should consider having the children tested.
- Other counseling messages
  - HCV is not spread by sneezing, hugging, coughing, food or water, sharing eating utensils or drinking glasses, or casual contact.

- Persons should not be excluded from work, school, play, child-care or other settings on the basis of their HCV infection status.
- Involvement with a support group might help patients cope with hepatitis C.

- HCV-positive persons should be evaluated (by referral or consultation, if appropriate) for presence or development of chronic liver disease including
  - assessment for biochemical evidence of chronic liver disease;
  - assessment for severity of disease and possible treatment according to current practice guidelines in consultation with, or by referral to, a specialist knowledgeable in this area (see excerpts from NIH Consensus Statement in the following section); and
  - determination of need for hepatitis A vaccination.

NIH Consensus Statement Regarding Management of Hepatitis C (Excerpted)

The NIH "Consensus Statement on Management of Hepatitis C" was based on data available in March 1997 (133). Because of advances in the field of antiviral therapy for chronic hepatitis C, standards of practice might change, and readers should consult with specialists knowledgeable in this area.

Persons Recommended for Treatment

Treatment is recommended for patients with chronic hepatitis C who are at greatest risk for progression to cirrhosis, as characterized by

- persistently elevated ALT levels;
- detectable HCV RNA; and
- a liver biopsy indicating either portal or bridging fibrosis or at least moderate degrees of inflammation and necrosis.

Persons for Whom Treatment Is Unclear Included are

- patients with compensated cirrhosis (without jaundice, ascites, variceal hemorrhage, or encephalopathy);
- patients with persistent ALT elevations, but with less severe histologic changes (i.e., no fibrosis and minimal necroinflammatory changes) (In these patients, progression to cirrhosis is likely to be slow, if at all; therefore, observation and serial measurements of ALT and liver biopsy every 3-5 years is an acceptable alternative to treatment with interferon); and
- patients aged less than 18 years or greater than 60 years (note that interferon is not approved for patients aged less than 18 years).

Persons for Whom Treatment Is Not Recommended Included are

- patients with persistently normal ALT values;
- patients with advanced cirrhosis who might be at risk for decompensation with therapy;
- patients who are currently drinking excessive amounts of alcohol or who are injecting illegal drugs (treatment should be delayed until these behaviors have been discontinued for greater than or equal to 6 months); and
- persons with major depressive illness, cytopenias, hyperthyroidism, renal transplantation, evidence of autoimmune disease, or who are pregnant.

PUBLIC HEALTH SURVEILLANCE

The objectives of conducting surveillance for hepatitis C are to

- identify new cases and determine disease incidence and trends;
- determine risk factors for infection and disease transmission patterns;
- estimate disease burden; and
- identify infected persons who can be counseled and referred for medical follow-up.

Various surveillance approaches are required to achieve these objectives because of limitations of diagnostic tests for HCV infection, the number of asymptomatic patients with acute and chronic disease, and the long latent period between infection and chronic disease outcome.

Surveillance for Acute Hepatitis C

Surveillance for acute hepatitis C -- new, symptomatic infections -- provides the information necessary for determining incidence trends, changing patterns of transmission and persons at highest risk for infection. In addition, surveillance for new cases provides the best means to evaluate effectiveness of prevention efforts and to identify missed opportunities for prevention. Acute hepatitis C is one of the diseases mandated by the Council of State and Territorial Epidemiologists (CSTE) for reporting to CDC's National Notifiable Diseases Surveillance System. However, hepatitis C reporting has been unreliable to date because most health departments do not have the resources required for case investigations to determine if a laboratory report represents acute infection, chronic infection, repeated testing of a person previously reported, or a false-positive result. Historically, the most reliable national data regarding acute disease incidence and transmission patterns have come from sentinel surveillance (i.e., sentinel counties study of acute viral hepatitis). As hepatitis C prevention and control programs are implemented, federal, state, and local agencies will need to determine the best methods to effectively monitor new disease acquisition.

Laboratory Reports of Anti-HCV-Positive Tests

Although limitations exist for the use of anti-HCV-positive laboratory reports to identify new cases and to monitor trends in disease incidence, they potentially are an important source from which state and local health departments can identify infected persons who need counseling and medical follow-up. Development of registries of persons with anti-HCV-positive laboratory results might facilitate efforts to provide counseling and medical follow-up and these registries could be used to provide local, state, and national estimates of the proportion of persons with HCV infection who have been identified. If such registries are developed, the confidentiality of individual identifying information should be ensured according to applicable laws and regulations.

Serologic Surveys

Serologic surveys at state and local levels can characterize regional and local variations in prevalence of HCV infection, identify populations at high risk, monitor trends, and evaluate prevention programs. Existing laboratory-based reporting of HCV-positive test results cannot provide this information because persons who are tested will not be representative of the population as a whole, and certain populations at high risk might be underrepresented. Thus, data from newly designed or existing serologic surveys will be needed to monitor trends in HCV infection and evaluate prevention programs at state and local levels.

Surveillance for Chronic Liver Disease

Surveillance for HCV-related chronic liver disease can provide information to measure the burden of disease, determine natural history and risk factors, and evaluate the effect of therapeutic and prevention measures on incidence and severity of disease. Until recently, no such surveillance existed, but a newly established sentinel surveillance pilot program for physician-diagnosed chronic liver disease will provide baseline data and a template for a comprehensive sentinel surveillance system for chronic liver disease. As the primary source of data regarding the incidence and natural history of chronic liver disease, this network will be pivotal for monitoring the effects of education, counseling, other prevention programs, and newly developed therapies on the burden of the disease.

FUTURE DIRECTIONS

To prevent chronic HCV infection and its sequelae, prevention of new HCV infections should be the primary objective of public health activities. Achieving this objective will require the integration of HCV prevention and surveillance activities into current public health infrastructure. In addition, several questions concerning the epidemiology of HCV infection remain, and the answers to those questions could change or modify primary prevention activities. These questions primarily concern the magnitude of the risk attributable to sexual transmission of HCV and to illegal noninjecting-drug use.

Identification of the large numbers of persons in the United States with chronic HCV infection is resource-intensive. The most efficient means to achieve this identification is unknown, because the prevention effectiveness of various implementation strategies has not been evaluated. However, widespread programs to identify, counsel, and treat HCV-infected persons, combined with improvements in the efficacy of treatment, are expected to lower the morbidity and mortality from HCV-related chronic liver disease substantially. Monitoring the progress of these activities to determine their effectiveness in achieving a reduction in HCV-related chronic disease is important.

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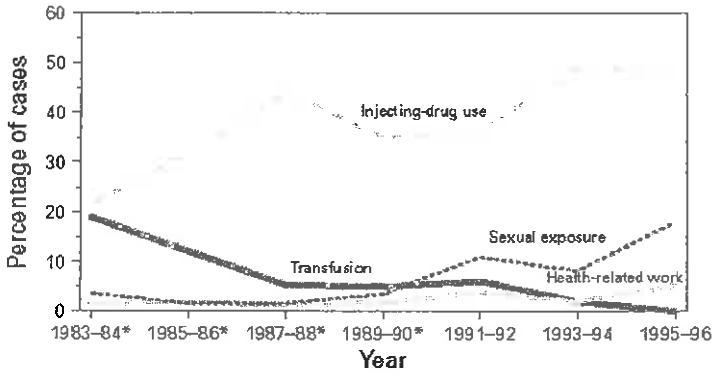
* Sentinel counties viral hepatitis surveillance system identifies all persons w symptomatic acute viral hepatitis reported through stimulated passive surveillan participating county health departments (four during 1982-1995 and six during 19 These counties are demographically representative of the U.S. population. Serum from reported cases are tested for all viral hepatitis markers, and case-patient interviewed extensively for risk factors for infection.

Figure_1

FIGURE 1. Reported cases of acute hepatitis C by selected risk factors — United States, 1983–1996



*Data presented for non-A, non-B hepatitis.
Source: Centers for Disease Control and Prevention.

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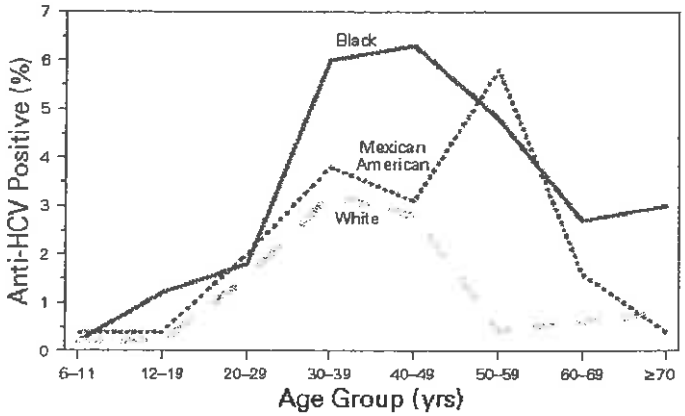
Figure_2

FIGURE 2. Prevalence of hepatitis C virus (HCV) infection by age and race/ethnicity — United States, 1988–1994



Source: Third National Health and Nutrition Examination Survey, CDC.

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Table_1

Note: To print large tables and graphs users may have to change their printer settings to landscape and use a small font size.

TABLE 1. Estimated average prevalence of hepatitis C virus (HCV) infection in the United States by various characteristics and estimated prevalence of persons with these characteristics in the population

Characteristic	HCV-infection prevalence %	HCV-infection prevalence (range, %)	Prevalence of persons with characteristic, %
Persons with hemophilia treated with products made before 1987	87	(74-90)	<0.01
Injecting-drug users			
current	79	(72-86)	0.5
history of prior use	No Data		5
Persons with abnormal alanine aminotransferase levels	15	(10-18)	5
Chronic hemodialysis patients	10	(0-64)	0.1
Persons with multiple sex partners (lifetime)			
>=50	9	(6-16)	4
10-49	3	(3-4)	22
2-9	2	(1-2)	52
Persons reporting a history of sexually transmitted diseases	6	(1-10)	17
Persons receiving blood transfusions before 1990	6	(5-9)	6
Infants born to infected mothers	5	(0-25)	0.1
Men who have sex with men	4	(2-18)	5
General population	1.8	(1.5-2.3)	NA*
Health-care workers	1	(1-2)	9
Pregnant women	1	--	1.5
Military personnel	0.3	(0.2-0.4)	0.5
Volunteer blood donors	0.16	--	5

* Not applicable.

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Table_2

Note: To print large tables and graphs users may have to change their printer settings to landscape and use a small font size.

TABLE 2. Tests for hepatitis C virus (HCV) infection

Test/Type	Application	Comments
-- Hepatitis C virus antibody (anti-HCV)		
-- EIA (enzyme immunoassay)	-- Indicates past or present infection but does not differentiate between acute chronic or resolved infection -- All positive EIA results should be verified with a supplemental assay	-- Sensitivity >=97% -- EIA alone has low-positive predictive value in low-prevalence population
HCV RNA (hepatitis C virus ribonucleic acid)		
Qualitative tests*†		
-- Reverse transcriptase polymerase chain reaction (RT-PCR) amplification of HCV RNA by in-house or commercial assays (e.g. Amplicor HCV)	-- Detect presence of circulating HCV RNA -- Monitor patients on antiviral therapy	-- Detect virus as early as 1-2 weeks after exposure -- Detection of HCV RNA during course of infection might be intermittent; a single negative RT-PCR is not conclusive -- False-positive and false-negative results might occur
Quantitative tests*†		
-- RT-PCR amplification of HCV RNA by in-house or commercial assays (e.g. Amplicor HCV Monitor) -- Branched chain DNAs (bDNA) assays (e.g., Quantiplex HCV RNA Assay)	-- Determine concentration of HCV RNA -- Might be useful for assessing the likelihood of response to antiviral	-- Less sensitive than qualitative RT-PCR -- Should not be used to *exclude* the diagnosis of HCV infection or to determine treatment endpoint
Genotype*†		
-- Several methodologies available (e.g. hybridization sequencing)	-- Group isolates of HCV based on genetic differences into 6 genotypes and >90 subtypes -- With new therapies, length of treatment might vary based on genotype	-- Genotype 1 (subtypes 1a and 1b) most common in United States and associated with lower response to antiviral activity
Serotype*		
-- EIA based on immunoreactivity to synthetic peptides (e.g. Murex HCV Serotyping 1-6 Assay)	-- No clinical utility	-- Cannot distinguish between subtypes

* Currently not U.S. Food and Drug Administration approved; lack standardization.
† Samples require special handling (e.g., serum must be separated within 2-4 hours of collection and stored frozen (-20 C or -70C); frozen samples should be shipped on dry ice).
& Deoxyribonucleic acid.

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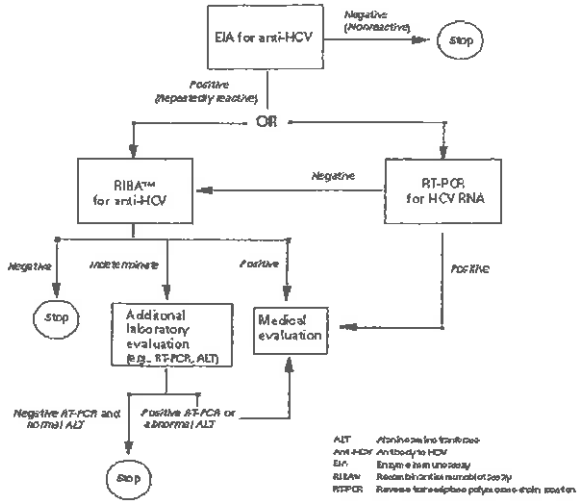
Figure_3

FIGURE 3. Hepatitis C virus (HCV)-infection–testing algorithm for asymptomatic persons



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New York State
Department of Corrections and Community Supervision
Division of Health Services

Hepatitis C Primary Care Practice Guideline

INTRODUCTION

These practice guidelines represent an approach to the current management of hepatitis C disease, consistent with community and FDA standards, and appropriate in our correctional setting.

This field of science has been evolving very rapidly. New information and treatment agents have resulted in shorter, safer therapeutic options with high cure rates. As new information becomes available, these guidelines will be periodically reviewed and updated.

Acute Hepatitis C is defined as infection manifesting itself within 6 months of exposure. The average incubation period for acute hepatitis C is 6 to 12 weeks, but may range from 2 to 26 weeks. Persons with acute disease are typically asymptomatic or have a mild clinical illness with a self-limiting course. Fulminant hepatic failure in acute disease is extremely rare.

It is estimated that 15-25% of patients with acute hepatitis C will spontaneously clear the virus within 12 weeks (and no later than 20 weeks) from the onset of symptoms. Those who do not clear the virus go on to develop chronic hepatitis C.

If there is clinical suspicion of acute hepatitis C or a significant exposure has occurred, an HCV RNA assay (BioReference # 3376) along with HCV antibodies must be ordered to make the diagnosis. HCV RNA usually is detected in the serum within 8 weeks post exposure, but can be delayed up to 6 months. It is therefore recommended that HCV RNA be checked at baseline, 4 weeks, 12 weeks and 6 months post exposure.

HCV antibodies are not present in the serum during the acute phase of the disease, and do not become positive until 8 weeks post exposure: usually between 2 and 6 months.

Generally hepatitis C should not be treated in the acute phase in order to allow for spontaneous clearing of the virus. Treatment of acute hepatitis C will only be done after consultation with IFD (infectious disease specialty), and should be deferred for at least 12 weeks from the onset of symptoms.

Chronic Hepatitis C: Of the approximately 75-85% who develop chronic hepatitis C, about 20% will eventually develop cirrhosis over a period of 20 to 30 years. The progression to chronic liver disease in the majority of patients is insidious, advancing without symptoms or physical signs. HIV co-infected and diabetic patients may have an accelerated course. Frequently, chronic hepatitis C is not recognized until symptoms appear with the development of advanced liver disease.

Once cirrhosis has developed, up to 3% per year will develop hepatocellular carcinoma. In the U.S., chronic hepatitis C is the most common cause of end stage liver disease and the leading indication for a liver transplant.

Patients with chronic hepatitis C are at higher risk for morbidity and mortality if they develop either acute hepatitis A or B. Determination of immunity status to both hepatitis A and B is important and lack of immunity should prompt vaccination.

Epidemiology and Pathogenesis

The hepatitis C virus (HCV) was identified in the late 1980s. It is a small, enveloped single stranded RNA virus of the Flaviviridae family. It includes a heterogeneous group of viruses. There are several different genotypes and subtypes. Prevalence of the different genotypes varies worldwide. Genotype 1 is responsible for 70-80% of chronic hepatitis C in the US. Genotypes 2 and 3 are also seen, while other genotypes are rare in the US.

In 1999 the WHO estimated there was a worldwide prevalence of HCV of 170 million people.
In the US:

- There are about 3 million people currently infected with chronic hepatitis C.
- The peak prevalence is among those born between 1945 and 1965, accounting for approximately 75% of HCV cases. This prevalence is tied to an increase in IV drug use during the 70s and 80s.
- HCV infection is responsible for 8,000 to 13,000 deaths per year. It is the leading cause of chronic liver disease and hepatocellular cancer, and it accounts for the majority of liver transplants.
- There has been a significant decline in the number of new cases of HCV disease since the 1980s. The decline is mostly due to changes in practices of IV drug users and improved screening of blood products.
- Approximately 30% of the patients with HIV are co-infected with hepatitis C.
- An estimated 10-25% of the adult prison population is infected with chronic hepatitis C.

HCV is transmitted through the percutaneous exposure of infectious blood or blood products, or body fluids contaminated with infectious blood.

Risk factors for acquiring HCV infection are:

- Foremost IV drug abuse and needle sharing
- Receipt of contaminated blood or blood products, or organ transplantation prior to 1992
- Infusion of clotting factor before 1987
- Needle sticks in healthcare workers
- Sharing personal care items like razors or toothbrushes
- Tattoos and body piercings with unsterile equipment

Less commonly:

- Intranasal cocaine use
- Sex with multiple partners

- Transmission between monogamous heterosexual partners and perinatal transmission from mother to child are rare.

The hepatitis C virus is not directly cytopathic to the liver cells, but it is the host's immune response that causes both the hepatic and extra-hepatic manifestations of the disease. In the majority of cases, despite the host's immune response, the virus is not cleared from the body and this leads to chronic hepatitis. Factors that play a role in the outcome of the disease are age, gender, alcohol abuse, viral characteristics and genetic makeup of the host.

Because of its high genetic variability, patients who have recovered from an acute infection or have been cured from a chronic infection can again become infected if re-exposed to the hepatitis C virus.

To date there is no vaccine against HCV, nor is there any pre or post- exposure prophylaxis in the way of medications or immunoglobulins.

SCREENING (Attachment 1)

Inmates that are at risk for hepatitis C should be screened for the presence of antibodies to HCV. **Also, all adults born between 1945 and 1965 should be offered a once in a lifetime screening test for HCV.**

Screening is done with an enzyme immunoassay blood test (EIA).

Inmates with the following risk factors should be screened for HCV:

- Born between 1945 and 1965
- History of IV drug use
- HIV infection
- Intranasal cocaine use
- STD's
- Unprotected sex with multiple sexual partners or known HCV infected sexual partner
- Blood transfusions or solid organ transplant before 1992
- Hemodialysis
- Infusion of clotting factor before 1987
- Tattoos or body piercing with unsterile equipment
- Sharing of personal items like razors or toothbrushes
- Unexplained elevated LFT's or signs/symptoms of hepatitis
- Children of mothers with HCV infection
- Known exposure to HCV
- Needle stick or mucosal exposure to HCV infected blood

DIAGNOSIS

If the screening test for hepatitis C is positive, then a confirmatory test needs to be done. All confirmatory tests directly detect HCV RNA. **Note that a positive hepatitis C antibody screen alone does not indicate hepatitis C disease.**

A positive HCV RNA (viral load- VL) will confirm the diagnosis of chronic hepatitis C. A negative result indicates either a resolved infection with hepatitis C or a false positive screening test.

If the screening test for HCV is positive; but viral RNA is negative and there is a strong suspicion for HCV disease, then the patient can be retested for viral RNA after several months. This test should be repeated only once.

An indeterminate screening test should be worked up as a positive screen.

In immune-compromised patients (including those with HIV, patients on hemodialysis, transplant recipients) and in those recently exposed to HCV, the HCV antibody may not be detected in the screening test. In these patients, if hepatitis C is strongly suspected, then a quantitative HCV RNA needs to be done despite a negative screening test.

The confirmatory quantitative test used in DOCCS is the **COBAS/TaqMan HCV RNA PCR assay** (BioReference # 3376).

Confirmatory testing will be recorded in the FHS1 medical problem list, utilizing the problem codes listed in the next section. The blue "Hepatitis C Data Flow Sheet," Form 3132, can also be utilized for documentation.
HCV education, risk reduction, and treatment options will be discussed with the patient and documented in the ambulatory health record (AHR). (Patient information sheets: English, Spanish).

REPORTING AND DOCUMENTATION

Persons who have hepatitis C disease must be reported to the county health department using the procedure outlined in Health Services Policy 8.01. In the policy you will find links to the appropriate forms that need to be completed and sent to the local DOH.

DOCCS' Regional Infection Control Nurse will be notified.

Along with regular AHR visit notes, entries will be made on the FHS1 Problem List to document HCV disease and management.

The following FHS1 problem list codes are to be utilized to document test results and hepatitis C management:

0701 - Hep C Disease
0702 - Hep C Antibody Positive
0703 - Hep C Rx Initiated
0704 - Hep C Rx Discontinued, Medical
0705 - Hep C Rx Discontinued, Other
0706 - Hep C Rx Completed
0707 - Hep C Rx Refused
0708 - Hep C Rx Contraindicated
072A - Hep C AB pos, Viral RNA neg
072B - Hep C testing refused
0725 - Hep C Rx Deferred
0726 - Hep C Genotype Known
0727 - Hep C Antibody Negative
0728 - Hep C Sustained Viral Response
0729 - Hep C trt. failure/relapse

Note the following:

- If the screening test is indeterminate, it will be treated as a positive screen and code 0702 will be used (Hepatitis C Antibody Positive"); add a notation in the comment section that the screening test was indeterminate.
- Code 0701 ("Hepatitis C Disease") will be added **only** if the HCV RNA is also positive. If the screening test is positive (or indeterminate), but the confirmatory HCV RNA is negative, then code 072A ("Hep C AB pos, Viral RNA neg") should be entered.
- When code 0703 is entered (Hepatitis C Rx initiated), add regimen used and length of treatment in the comment section.
- If viral RNA is not detected after treatment, this indicates a Sustained Virologic Response (SVR) and should be coded as such (code # 0728). Code # 072A should not be used after successful treatment.
- Code 0701 (Hepatitis C Disease) should be inactivated once a patient has achieved SVR. Such patients are considered cured and no longer need to be followed for hepatitis C disease unless there are indications of re-infection or relapse. Patients with advanced liver disease need monitoring as outlined in other sections of these guidelines.

EVALUATING HEPATITIS C

Once the diagnosis of chronic hepatitis C and has been confirmed, then the genotype needs to be determined. Identifying the genotype is important for determining both the type and length of treatment. Management of chronic hepatitis C depends on the genotype, stage of disease, the presence or absence of cirrhosis, and whether or not the patient was previously treated.

A liver biopsy is not routinely needed to determine eligibility for treatment. However the presence or absence of cirrhosis needs to be determined in order to decide the course of treatment. Staging of the disease can be done with the use of clinical, laboratory and other non-invasive data. If a liver biopsy has not been performed, patients that are being considered for treatment will have a FibroSure test (BioReference code # 6124) to determine fibrosis stage. Patients with suspected cirrhosis (stage 4 fibrosis) will also undergo an abdominal/liver ultrasound with portal vein doppler to determine the extent of liver disease and/or the presence of portal hypertension. Patients with cirrhosis may require a different regimen than those who do not. Patients with decompensated cirrhosis are not eligible for treatment with many current regimens.

In addition, the APRI (AST to Platelet Ratio Index) score can also be calculated to help determine the stage of fibrosis and presence of cirrhosis. It is based on the AST elevation and the platelet count, and is calculated by the following formula:

[(AST/ULN) ÷ Platelet count in thousands] x 100

Where ULN stands for the upper limit of normal of the AST value for the lab. Platelet count is reported in thousands.

A score > 0.5 indicates probable fibrosis, a score between 0.5 and 1.5 correlates to a Metavir stage of 1 to 3, and a score > 1.5 indicates cirrhosis.

(See attachments 2, 3 and 4 for scoring systems for hepatic fibrosis, FibroSure conversion table and APRI score).

Initial work up for HCV disease includes:

Any time prior to treatment:

- HCV RNA VL (Ultra-sensitive HCV RNA by PCR, BioReference # 3376)- **if** a regimen lasting less than 12 weeks is considered in GT 1 then an HCV VL must be repeated within 3 months of treatment to determine patient eligibility
- HCV genotype
- HIV screen
- FibroSure assay (BioReference # 6124)
- Liver ultrasound with portal vein Doppler (stage 4 disease only)
- Hepatitis A & B screen
- If screening for hepatitis A or B is negative, the patient will be vaccinated. Treatment can be initiated before the vaccination series is completed.
- Testing for viral resistance **only** in select patients. Resistance testing should be done after approval of the designated RMD. Recommendations as follows:
    - NS5A polymorphism testing in GT 1a if Zepatier regimen considered (BioReference # J242)
    - Q80K polymorphism testing in GT 1a with cirrhosis if SIM/SOF regimen considered (Bioreference # B610)

Within 12 weeks of treatment:

- CBC with differential
- SMA-C
- PT-PTT/INR
- NOTE: a repeat HCV RNA VL should be repeated **ONLY IF** a regimen of Harvoni lasting less than 12 weeks is considered in GT 1

Just prior to initiating treatment:

- HCG in females
- Drug-drug interactions especially in HIV patients

Note: Psychiatric evaluation prior to treatment is no longer routinely required.
IFD consult is to be obtained once the work up is complete.

PATIENT SELECTION

Side effects have improved with newer regimens. However, hepatitis C treatment still carries a significant incidence of adverse reactions, some life threatening, especially when ribavirin is used. Treatment regimens have been simplified, but compliance is necessary to achieve a sustained virologic response (SVR) and a committed patient that is highly motivated to adhere to the treatment program is of utmost importance. Patients who have previously exhibited non-adherence to medical care may not be good candidates for HCV treatment.

Patients need to be carefully screened and counseled before therapy is contemplated. The decision of when to treat depends on several factors including genotype, stage and natural history of disease, history of prior treatment, adverse reactions, expected efficacy and ability to tolerate an appropriate regimen.

Newer, safer, more effective drugs are continuously being developed, and patients with earlier stages of fibrosis, based on a risk assessment for progression of hepatitis C, may be given the option to monitor their disease and to defer treatment.

Some of the risk factors predictive of severity and more rapid progression of disease are:

- viral characteristics
- presence of liver fibrosis
- host genetic variations and immune status
- male gender
- age >50 at time of infection
- duration of infection >20 years
- ETOH abuse
- co-infection with HIV or Hepatitis B
- co-morbidities such as diabetes mellitus, steatosis and obesity

Patients not treated at this time will be counseled about disease progression, communicability, and risk reduction. They will be evaluated periodically for progression of fibrosis as outlined in the patient monitoring section below.

All patients with chronic hepatitis C disease should be worked up and evaluated for treatment. In DOCCS priority in treatment will be given to those with more advanced fibrosis (F3 and F4), and to those with either immuno-compromising conditions (e.g. HIV, DM) or severe extra-hepatic manifestations of hepatitis C.

The following criteria will be considered when deciding whom to treat:

- Must be 18 or older
- Eligible patients may be hepatitis C **treatment naïve** or hepatitis C **treatment experienced: relapsers** (achieved an undetectable viral load after treatment, but did not have a SVR after 24 weeks), **partial responders** (achieved a 2-log drop in HCV VL by week 12, but still had a detectable VL at week 24 of treatment), **null-responders** (did not achieve at least a 2-log drop in HCV VL at week 12 of treatment)
- Patients with stage 3 and 4 fibrosis will be treated
- Patients with serious extra-hepatic manifestations of HCV infection, regardless of fibrosis stage, will be treated
- Patients with earlier stages of fibrosis will be evaluated on an individual basis and risk indicators for rapid progression of disease or other compelling reasons to treat will be considered
- Decompensated liver disease- Child-Turcotte-Pugh class B and C (Attachment 5) and candidates for liver transplant will be referred to a transplant center for management of their hepatitis C as most current regimens are contraindicated in this population (Note: Epclusa has been FDA approved for use in patients with decompensated cirrhosis)

- End stage kidney disease, stage IV (GFR<30) and kidney transplant patients should be carefully evaluated on a case-by-case basis with a consultant as only some regimens are approved for use in such patients and careful monitoring is required (Zepatier has been FDA approved for use in patients with end stage renal disease including those on hemodialysis)
- Pregnant females and females that may become pregnant cannot be on treatment. A negative HCG in women of childbearing age is required, and **two methods of effective contraception must be used during treatment and, if Ribavirin used, for six months after completion**
- Male patients, if taking ribavirin, must inform their female partner of childbearing age that **two methods of effective contraception must be used during treatment and for six months after completion**
- Risk of re-infection including using or possessing syringes, tattoo equipment or documented chronic noncompliance with medical care will be considered when making treatment decisions
- Evidence of substance abuse (drug and/or alcohol) in the past 6 months shall not per se serve as exclusion for any care or treatment. Evidence of such substance abuse may only be considered as one factor among all others in assessing and evaluating each individual's needs and suitability for care and treatment. Such evidence may be noted, but shall not in any case be used to prevent any initial work up and/or referral to the IFD specialist. All patients who qualify for hepatitis C treatment, regardless of a drug or alcohol related incident in the past 6 months, will have an initial work up and appropriate testing for HCV disease and will be referred to IFD for an evaluation.
- Psychiatric clearance is no longer needed. It is required **ONLY** if an interferon regimen is considered. However, DOCCS no longer supports using interferon in treating HCV.

Before treatment is initiated the following must be obtained:

- Evaluation and recommendation by IFD
- Approval of Deputy Commissioner/Chief Medical Officer
- Signed consent addressing risks/benefits, and agreeing to comply with treatment regimen
- Male patients on ribavirin considering conjugal visits, must sign a consent to inform their female partner of childbearing age of the teratogenic effects of therapy

OBTAINING APPROVAL & MEDICATIONS FOR TREATMENT

Therapy for Hepatitis C will not be started without an evaluation by an IFD consultant and prior approval by the Deputy Commissioner/Chief Medical Officer.

Steps for obtaining treatment:

1. Referral to IFD through FHS1, screen 4.1 (only patients that have been screened, worked up, and eligible for treatment should be referred to IFD).

2. Treatment approval and medication order via the "Hep C Treatment Request" form found in the Forms and Attachment portion of the Health Exchange shared drive. Indicate at the bottom, in the comment section, what treatment regimen is being requested. This form will automatically go to the CMO for review then forwarded to central pharmacy to obtain requested drugs.

TREATMENT

The field of Hep C therapy has been evolving rapidly. New drugs have recently been approved and others are being developed. All oral regimens, that are highly effective and safe, are now available for all genotypes and more will be approved in the near future.

These treatment guidelines have been drafted mostly following recommendations by the American Association for the Study of Liver Diseases (AASLD) and are in compliance with FDA guidelines. They are meant to establish a standard approach to Hep C treatment in DOCCS in order to improve continuity of care and patient outcomes. The latest AASLD guidelines can be accessed at www.hcvguidelines.org.

It should be noted that the treatment of hepatitis C is not "one size fits all," and therapy should be individualized on a case-by-case basis in consultation with IFD and prior approval by the DOCCS Deputy Commissioner/Chief Medical Officer.

The FDA has approved new oral medications that are direct acting antivirals (DAA) against the hepatitis C virus. They are used in combination therapy for the treatment of chronic hepatitis C.

Monotherapy with DAAs should never be used for the treatment of hepatitis C.

Dose adjustments of the DAAs should not be made (except for daclatasvir if recommended by consultant). If stopped because of adverse reactions, they should not be restarted. Any modification or discontinuation of therapy must be first discussed with a consultant.

There are currently four classes of DAAs:

1. Nonstructural protein NS3/4A protease inhibitors (PIs)
2. NS5B nucleotide analog polymerase inhibitors (NPIs)
3. NS5B non-nucleotide analog polymerase inhibitors (NNPIs)
4. NS5A protein inhibitors

NONSTRUCTURAL PROTEIN NS3/4A PROTEASE INHIBITORS (PIs)

First Generation PIs

Telaprevir and Boceprevir (TVR and BOC) were the first PIs available and were used in combination therapy for the treatment of chronic hepatitis C genotype 1. They are no longer recommended because of their serious adverse reactions, significant drug-drug interactions, high potential for resistance and cumbersome administration schedule.

Second Generation PIs

These are better tolerated compared to the first generation PIs with less adverse reactions, less drug-drug interactions, better efficacy, lower potential for resistance and easier to administer. Most adverse reactions occur in combination therapy especially when ribavirin is used. PIs can cause elevation of liver function tests (LFTs) and worsening liver failure in patients with cirrhosis. Careful monitoring of LFTs in such patients is imperative. Any elevation of ALT or other LFTs will prompt an immediate referral to IFD. A 10-fold elevation requires discontinuation of therapy and immediate IFD evaluation.

Grazoprevir- available as a fixed-dose oral combination with elbasvir (Zepatier). It is FDA approved for use in Genotypes 1 or 4.

Paritaprevir- available as a fixed-dose oral combination tablet with low dose ritonavir and ombitasvir (Technivie, Viekira Pak). It is FDA approved for the treatment of genotype 1 and 4 when used in combination therapy.

Simeprevir (SIM)- dosing is 150 mg daily given by mouth with food. It is used in combination therapy with sofosbuvir +/- ribavirin for the treatment of genotype 1 or 4. When used in genotype 1a, testing for the presence of Q80K mutation may be necessary. Simeprevir is generally well tolerated. Common side effects are fatigue, headache, nausea and skin reactions including photosensitivity especially in the first four weeks. Sun exposure should be avoided and sun protection used. Symptomatic bradycardia requiring pacemaker placement has been reported in patients where simeprevir was co-administered with sofosbuvir and amiodarone. Hepatic decompensation and deaths have occurred in patients with moderate or severe liver disease (Child-Pugh Class B or C) and use in such patients is not recommended. (Prescribing Information – Simeprevir)

NS5B NUCLEOTIDE ANALOG POLYMERASE INHIBITORS (NPIs)

This class of DAAs is active across all genotypes and has a high barrier to resistance.

Sofosbuvir (SOF)- dosing is 400 mg given daily by mouth with or without food. It is used in genotypes 1, 2, 3 and 4 in combination therapy with ledispasvir (Harvoni), velpatasvir (Epclusa), or simeprevir +/- ribavirin. It is well tolerated. Adverse reactions occur mostly in combination with ribavirin. Symptomatic bradycardia requiring pacemaker placement has been reported when sofosbuvir is co-administered with amiodarone and another HCV direct acting antiviral. (Prescribing Information - Sofosbuvir)

NS5B NON-NUCLEOTIDE ANALOG POLYMERASE INHIBITORS (NNPIs)

This class of DAAs is less potent and more genotype specific when compared to the NPIs, they also have a lower barrier to resistance.

Dasabuvir- is used in combination therapy with the fixed-dose combination of paritaprevir, ritonavir and ombitasvir (Viekira Pak). It is given with food as a single 250 mg oral tablet twice a day as part of a regimen for the treatment of genotype 1.

NS5A PROTEIN INHIBITORS

This class of DAAs is highly effective against all genotypes of the hepatitis C virus, but has a low barrier to resistance.

Daclatasvir- dosing is 60 mg given daily by mouth with or without food. It is given in combination therapy with sofosbuvir +/- ribavirin. It is FDA approved for the treatment of genotypes 1 or 3, but effective for other genotypes. Dose of Daclatasvir may need to be modified when co-administered with certain medications; this should be done in consultation with a specialist expert in managing such drug interactions. Symptomatic bradycardia requiring pacemaker placement has been reported in patients where daclatasvir was co-administered with amiodarone and sofosbuvir. (Prescribing Information – Daclatasvir)

Elbasvir- available as a fixed-dose oral combination with grazoprevir (Zepatier).

Ledipasvir- available as a fixed-dose oral combination tablet with sofosbuvir (Harvoni).

Ombitasvir- available as a fixed-dose oral combination tablet with paritepravir and ritonavir (Technivie, Viekira Pak).

Velpatasvir- available as a fixed-dose oral combination tablet with sofosbuvir (Epclusa).

FIXED-DOSE COMBINATION DRUGS

The following fixed-dose combination drugs are currently FDA approved for use in the treatment of hepatitis C.

Epclusa- contains a fixed dose combination of velpatasvir 100 mg and sofosbuvir 400 mg. It is given orally as a single dose tablet once a day with or without food in the treatment of chronic hepatitis C genotypes 1, 2, 3, 4, 5 or 6. Epclusa may be used in patients with decompensated cirrhosis in combination with ribavirin. It is generally well tolerated, most common side effects are fatigue and headache. Symptomatic bradycardia requiring pacemaker placement has been reported in patients with underlying cardiac disease in whom Epclusa was co-administered with amiodarone. (Prescribing Information – Epclusa)

Harvoni- combination tablet containing ledipasvir 90 mg and sofosbuvir 400 mg. It is given orally as a single dose tablet once a day with or without food.

Harvoni is approved for the treatment of genotype 1 and 4 and is well tolerated. Symptomatic bradycardia requiring pacemaker placement has been reported in patients with underlying cardiac disease in whom Harvoni was co-administered with amiodarone. (Prescribing Information – Harvoni)

Technivie- combination tablet containing paritaprevir 75 mg, ritonavir 50 mg and ombitasvir 12.5 mg. It is used in combination with ribavirin for the treatment of genotype 4. Technivie may cause worsening liver function tests and patients need to be closely monitored. It can result in serious liver injury and death in patients with cirrhosis and use in this population is to be avoided if possible. Any elevation of ALT or other LFTs will prompt an immediate referral to IFD. A 10-fold elevation requires discontinuation of therapy and immediate IFD evaluation. Technivie should not be used in women on ethinyl estradiol. (Prescribing Information - Technivie)

Viekira Pak- contains a fixed-dose oral combination tablet containing paritaprevir 75 mg, ritonavir 50 mg and ombitasvir 12.5 mg plus a tablet containing dasabuvir 250 mg. Recommended dosage is two combination tablets paritaprevir/ritonavir/ombitasvir in the morning and one dasabuvir tablet twice daily. It should be given with food. Viekira is FDA approved for use in GT1 in combination with ribavirin.

Viekira may cause worsening liver function tests and patients need to be closely monitored. It can result in serious liver injury and death in patients with cirrhosis and use in this population is to be avoided if possible. Any elevation of ALT or other LFTs will prompt an immediate referral to IFD. A 10-fold elevation requires discontinuation of therapy and immediate IFD evaluation. Viekira should not be used in women on ethinyl estradiol. (Prescribing Information - Viekira)

Zepatier- fixed-dose oral combination tablet containing elbasvir 50 mg and grazoprevir 100mg. It is FDA approved for the treatment of HCV genotypes 1 and 4. Dosing is one tablet daily, with or without ribavirin. It can be given with or without food. When used in genotype 1a, testing for the presence of NS5A resistance polymorphism is required to determine length of therapy. Zepatier is generally well tolerated. Elevations in ALT have been reported and close monitoring of LFTs is mandatory. Any elevation of ALT or other LFTs will prompt an immediate referral to IFD. A 10-fold elevation requires discontinuation of therapy and immediate IFD evaluation. Zepatier is contraindicated in patients with moderate or severe hepatic impairment (Child-Pugh class B or C). It can be given without dose adjustment to patients with renal impairment, including those on hemodialysis. (Prescribing Information – Zepatier)

NON-DIRECT ACTING DRUGS

Peginterferon and ribavirin are two older drugs used in the treatment of hepatitis C. Their role in the treatment of hepatitis C is through their antiviral, immunomodulatory and anti-inflammatory properties. Although done in past, **dual therapy with PEG/RIBA alone should never be used.**

Pegasys, peginterferon alfa 2a (PEG)- Pegasys was used in the treatment of hepatitis C for many years and was associated with significant adverse reactions including serious infections, anemia, thrombocytopenia, neuropsychiatric decompensation, worsening hepatitis and autoimmune disorders. Because of these serious potentially life-threatening adverse reactions and the availability of safer all oral regimens, DOCCS will no longer recommend using Pegasys in the treatment of hepatitis C. Patients with autoimmune disorders, severe depression, platelet count <50K, decompensated cirrhosis, hepatocellular cancer and solid organ transplant are not eligible to receive Pegasys. (Prescribing Information - Pegasys)

Ribavirin (RIBA) – weight based when used in combination therapy. It is given in a divided BID dose: 1000 mg po daily for patients <75 kg, 400 mg in AM, 600 mg in PM; 1200 mg po daily for patients >75 kg, 600 mg BID. Ribavirin can cause anemia and is highly teratogenic. Dose adjustments of ribavirin may become necessary in managing anemia. The use of erythropoietin has not been FDA approved for the treatment of anemia in patients undergoing Hep C treatment, and it is not recommended as first line therapy. Reduction of RIBA should be done first.

-**Ribavirin dose adjustments in anemia** (Attachment 6):

- Hgb between 8.5 and 10 (or a drop of 2 gm or more during any 4 week period in patients with cardiac disease)- decrease RIBA to 600 mg daily (200 mg q AM, 400 mg q PM)
- Hgb< 8.5- discontinue RIBA. In patients with cardiac disease, discontinuing RIBA should be considered if Hgb < 12 despite 4 weeks of dose reduction.

Once RIBA has been stopped because of an adverse reaction, it may be restarted at 600 mg daily; if tolerated it can be increased to 800 mg daily, but never to its original dose (1000 or 1200 mg/day).

Ribavirin is highly teratogenic and two forms of effective contraception must be used during treatment, and for six months after treatment has ended, when either males or females are on an HCV regimen containing ribavirin. (Prescribing Information - Ribavirin)

TREATMENT REGIMENS

There are several interferon free, all oral DAA containing regimens available that are both effective and safe. Treatment options for HCV should be reviewed with a consultant and approved by DOCCS' CMO. Regimens are determined by the following factors:

1. HCV genotype
2. Previous treatment experience
3. Presence or absence of cirrhosis
4. Renal function
5. Patient co-morbidities
6. Presence or absence of viral resistance-associated variants (eg. NS5A mutation)
7. Drug- drug interaction
8. HIV co-infection. Many medications used in HIV cannot be used or need dose adjustment when combined with HCV regimens. Therapeutic regimens need to be carefully selected and modified in conjunction with an HIV specialist when treating HIV/HCV co-infected patients. It is not recommended that HIV treatment be interrupted to allow for HCV treatment.
9. Regimen toxicity

Genotype 1

Genotype (GT) 1 is further subdivided into GT 1a and GT 1b. Patients with GT 1 that cannot be subtyped should be treated as GT 1a. In general GT 1a has a higher relapse rate than GT 1b when certain regimens are used. Length of therapy will vary depending on many factors: specific regimen, viral mutations, the presence or absence of cirrhosis, whether or not the patient is treatment naïve or treatment experienced and pretreatment viral load (HCV RNA). For GT 1a only, if Zepatier is being considered for treatment, then testing for NS5A polymorphism must be done to determine regimen and/or length of therapy (BioReference #J242).

The following regimens are used in the treatment of hepatitis C GT1 in order of preference for DOCCS:

Genotype 1a- (Attachment 7)

Treatment Naïve, GT 1a- (test for NS5A polymorphism)

No cirrhosis

No NS5A polymorphism present

- Zepatier for 12 weeks

NS5A polymorphism present

- Harvoni for 8 weeks- this regimen may be considered in selected patients with no co-morbidities **ONLY IF** pre-treatment HCV RNA < 6 million IU/ml and only if recommended by specialist
- Harvoni for 12 weeks if pre-treatment HCV RNA > 6 million IU/ml or comorbid conditions
- Viekira Pak + RIBA for 12 weeks
- Zepatier + RIBA for 16 weeks
- Epclusa for 12 weeks

- Daclatasvir + SOF for 12 weeks
- SIM + SOF for 12 weeks

<u>With compensated cirrhosis</u>

No NS5A polymorphism present

- Zepatier for 12 weeks

NS5A polymorphism present

- Harvoni for 12 weeks
- Zepatier + RIBA for 16 weeks
- Epclusa for 12 weeks (Note: Epclusa may also be used in patients with decompensated cirrhosis)
- Daclatasvir + SOF +/- RIBA for 24 weeks (consider NS5A resistance)
- SIM + SOF +/- RIBA for 24 weeks **IF** no Q80K polymorphism present
- Viekira Pak + RIBA for 24 weeks (not recommended; monitor LFTs frequently if used)

<u>Treatment Experienced</u> (Failed PEG/RIBA)- **GT 1a** (test for NS5A polymorphism)

<u>No cirrhosis</u>

No NS5A polymorphism present

- Zepatier for 12 weeks

NS5A polymorphism present

- Harvoni for 12 weeks
- Viekira Pak + RIBA for 12 weeks
- Zepatier + RIBA for 16 weeks
- Epclusa for 12 weeks
- Daclatasvir + SOF for 12 weeks
- SIM + SOF for 12 weeks

<u>With compensated cirrhosis</u>

No NS5A polymorphism present

- Zepatier for 12 weeks

NS5A polymorphism present

- Harvoni + RIBA for 12 weeks
- Zepatier + RIBA for 16 weeks
- Epclusa for 12 weeks (Note: Epclusa may also be used in patients with decompensated cirrhosis)

- Harvoni for 24 week
- Daclatasvir + SOF +/- RIBA for 24 weeks (consider NS5A resistance)
- SIM + SOF +/- RIBA for 24 weeks IF no Q80K polymorphism present
- Viekira Pak + RIBA for 24 weeks (not recommended; monitor LFTs frequently if used)

Treatment Experienced (Failed Protease Inhibitor)- **GT 1a** (test for NS5A polymorphism)

No cirrhosis

No NS5A polymorphism present

- Zepatier + RIBA for 12 weeks

NS5A polymorphism present

- Harvoni for 12 weeks
- Zepatier + RIBA for 16 weeks
- Epclusa for 12 weeks
- Daclatasvir + SOF for 12 weeks

With compensated cirrhosis

No NS5A polymorphism present

- Zepatier + RIBA for 12 weeks

NS5A polymorphism present

- Harvoni + RIBA for 12 weeks
- Zepatier + RIBA for 16 weeks
- Epclusa for 12 weeks (Note: Epclusa may also be used in patients with decompensated cirrhosis)
- Harvoni for 24 week
- Daclatasvir + SOF +/- RIBA for 24 weeks (consider NS5A resistance)

Treatment Experienced (Failed Sofosbuvir/RIBA)- **GT 1a**

No cirrhosis

- Harvoni + RIBA for 12 weeks

With compensated cirrhosis

- Harvoni + RIBA for 24 weeks

Genotype 1b- (Attachment 8)

Treatment Naïve- GT 1b

No cirrhosis

- Harvoni for 8 weeks- this regimen may be considered in selected patients with no co-morbidities **ONLY IF** pre-treatment HCV RNA < 6 million IU/ml and only if recommended by specialist
- Zepatier for 12 weeks
- Harvoni for 12 weeks if pre-treatment HCV RNA > 6 million IU/ml or comorbid conditions
- Viekira Pak for 12 weeks
- Epclusa for 12 weeks
- Daclatasvir + SOF for 12 weeks
- SIM + SOF for 12 weeks

With compensated cirrhosis

- Zepatier for 12 weeks
- Harvoni for 12 weeks
- Epclusa for 12 weeks (Note: Epclusa may also be used in patients with decompensated cirrhosis)
- Daclatasvir + SOF +/- RIBA for 24 weeks
- SIM + SOF +/- RIBA for 24 weeks
- Viekira Pak for 12 weeks (not recommended; monitor LFTs frequently if used)

Treatment Experienced (Failed PEG/RIBA)- **GT 1b**

No cirrhosis

- Zepatier for 12 weeks
- Harvoni for 12 weeks
- Viekira Pak for 12 weeks
- Epclusa for 12 weeks
- Daclatasvir + SOF for 12 weeks
- SIM + SOF for 12 weeks

With compensated cirrhosis

- Zepatier for 12 weeks
- Harvoni + RIBA for 12 weeks
- Epclusa for 12 weeks (Note: Epclusa may also be used in patients with decompensated cirrhosis)
- Harvoni for 24 weeks
- Daclatasvir + SOF +/- RIBA for 24 weeks
- SIM + SOF +/- RIBA for 24 weeks

- Viekira Pak for 12 weeks (not recommended; monitor LFTs frequently if used)

Treatment Experienced (Failed Protease Inhibitor)- **GT 1b**

No cirrhosis

- Zepatier + RIBA for 12 weeks
- Harvoni for 12 weeks
- Epclusa for 12 weeks
- Daclatasvir + SOF for 12 weeks

With compensated cirrhosis

- Zepatier + RIBA for 12 weeks
- Harvoni + RIBA for 12 weeks
- Epclusa for 12 weeks (Note: Epclusa may also be used in patients with decompensated cirrhosis)
- Harvoni for 24 week
- Daclatasvir + SOF +/- RIBA for 24 weeks

Treatment Experienced (Failed Sofosbuvir/RIBA)- **GT 1b**

No cirrhosis

- Harvoni + RIBA for 12 weeks

With compensated cirrhosis

- Harvoni + RIBA for 24 weeks

Treatment Experienced (Failed regimens that include an NS5A inhibitor) **GT 1a and 1b**

Clinical and scientific data is very limited on retreating HCV patients that have failed regimens containing an NS5A polymerase inhibitor (Harvoni, Viekira, Zepatier, Epclusa) and studies are ongoing. As such DOCCS recommends deferring treatment until more data or newer agents become available. Patients with cirrhosis, that cannot wait to be retreated, will be considered for retreatment on an individual basis under the recommendations of a consultant. Prior to treatment these patients will need to be tested for resistance-associated variants for NS5A inhibitor and for Q80k as per direction of a consultant and RMD approval. Therapy will then be tailored according to drug resistance patterns.

Genotype 2- (Attachment 9)

Treatment Naïve GT 2

No cirrhosis

- Epclusa for 12 weeks
- Daclatasvir + SOF for 12 weeks (not FDA approved)

With compensated cirrhosis

- Epclusa for 12 weeks (Note: Epclusa may also be used in patients with decompensated cirrhosis)
- Daclatasvir + SOF for 16-24 weeks (not FDA approved)

Treatment Experienced (Failed Peg/RIBA)- **GT 2**

No cirrhosis

- Epclusa for 12 weeks

With compensated cirrhosis

- Epclusa for 12 weeks (Note: Epclusa may also be used in patients with decompensated cirrhosis)

Treatment Experienced (Failed Sofosbuvir/RIBA)- **GT 2**

No cirrhosis or with compensated cirrhosis

- Epclusa + RIBA for 12 weeks (Note: Epclusa may also be used in patients with decompensated cirrhosis)
- Daclatasvir + SOF +/- RIBA for 24 weeks (limited data, not FDA approved; consider only if cannot take RIBA)

Genotype 3- (Attachment 10)

Treatment Naïve – GT 3

No cirrhosis

- Epclusa for 12 weeks
- Daclatasvir + SOF for 12 weeks

With compensated cirrhosis

- Epclusa for 12 weeks (studies are ongoing looking into resistance patterns and the need to add RIBA; can be used in decompensated cirrhosis)
- Daclatasvir + SOF +/- RIBA for 24 weeks (latest data no longer supports the FDA approved 12 week regimen)

Treatment Experienced (Failed Peg/RIBA)- GT3

No cirrhosis

- Epclusa for 12 weeks
- Daclatasvir + SOF for 12 weeks

With compensated cirrhosis

- Epclusa for 12 weeks (AASLD recommends adding RIBA in this population based on preliminary data; can be used in decompensated cirrhosis)
- Daclatasvir + SOF + RIBA for 24 weeks (latest data no longer supports the FDA approved 12 week regimen)

Treatment Experienced (Failed Sofosbuvir/RIBA)- GT3

No cirrhosis or with compensated cirrhosis

- Epclusa + RIBA for 12 weeks (recommended by AASLD, but no data available)
- Daclatasvir + SOF + RIBA for 24 weeks (limited data, not FDA approved)

Studies are ongoing and better options may be available soon for GT 3 treatment experienced patients. It may be beneficial for those with earlier stages of fibrosis to defer treatment at this time.

There are no retreatment recommendations at this time for patients with GT 3 who have failed an NS5A inhibitor regimen. Unless urgent treatment is necessary, treatment of these patients should also be deferred.

Genotype 4- (Attachment 11)

Studies are still ongoing for the treatment of HCV GT 4 and some of the regimens used are off label and not FDA approved. Limited data is available especially in retreating treatment experienced patients with GT 4.

Treatment Naïve- GT 4

No cirrhosis

- Zepatier for 12 weeks
- Harvoni for 12 weeks
- Technivie + RIBA for 12 weeks
- Epclusa for 12 weeks

With compensated cirrhosis

- Zepatier for 12 weeks
- Harvoni for 12 weeks
- Epclusa for 12 weeks (Note: Epclusa may also be used in patients with decompensated cirrhosis)
- Technivie + RIBA for 12 weeks (not recommended; monitor LFTs frequently if used)

Treatment Experienced (Failed PEG/RIBA)- GT 4

No cirrhosis

- Technivie + RIBA for 12 weeks
- Epclusa for 12 weeks
- Harvoni for 12 weeks
- Zepatier for 12 weeks (Preliminary studies indicate treatment with Zepatier should be extended to 16 weeks and RIBA added if there was prior virologic failure on treatment)

With compensated cirrhosis

- Epclusa for 12 weeks (Note: Epclusa may also be used in patients with decompensated cirrhosis)
- Harvoni + RIBA for 12 weeks
- Zepatier for 12 weeks (Preliminary studies indicate treatment with Zepatier should be extended to 16 weeks and RIBA added if there was prior virologic failure on treatment)
- Harvoni for 24 weeks
- Technivie + RIBA for 12 weeks (not recommended; monitor LFTs frequently if used)

DRUG INTERACTIONS

Prior to initiating treatment for hepatitis C, a careful review of DRUG-DRUG interactions should be conducted, especially in HIV co-infection.

Many drugs co-administered with HCV treatment may require dose modification and/or specific timing of administration around HCV medications. It is recommended that each drug given during HCV treatment be individually researched and medical necessity established prior to initiating treatment. Dose modification of HCV drugs (other than daclatasvir, if recommended by consultant) should not be done.

HIV co-infected patients may require drug dose modification or regimen change when treated for HCV. HIV therapy should not be suspended when treating HCV.
Refer to the links and lists provided below as a guide on drug interactions.
However, remember that new interactions present themselves regularly and such lists may not be complete. A detailed individual search for drug-drug interaction should be done just before therapy is initiated.

Daclatasvir (Daklinza)- (Daclatasvir Drug Interactions)
Is a substrate of CYP3A and an inhibitor of P-glycoprotein transporter (P-gp). Drugs that are inducers of CYP3A may decrease plasma levels of daclatasvir; inhibitors of CYP3A may increase plasma levels of daclatasvir. Also daclatasvir may increase plasma levels of drugs that are substrates of P-gp. Dosage modification of daclatasvir may be required when using such drugs.

Daclatasvir is contraindicated for use with the following:

- **Alpha 1-adrenoreceptor antagonists:** silodosin
- **Antiarrhythmics:** amiodarone (co-administration of amiodarone with daclatasvir in combination with sofosbuvir may cause life-threatening symptomatic bradycardia)
- **Anticonvulsants:** carbamazepine, phenobarbital, phenytoin
- **Antigout agents:** colchicine
- **Antimicrobials:** rifampin
- **Antineoplastic agents:** topotecan, vincristine (liposomal)
- **HCV Drugs:** grazoprevir
- **Herbal Supplements:** St. John's Wort

Epclusa (sofosbuvir/velpatasvir)- (Epclusa Drug interactions)
Sofosbuvir and velpatasvir are both substrates of the drug transporter systems P-gp and breast cancer resistance protein (BCRP). Velpatasvir also of CYP. Epclusa is not recommended for use with drugs that are P-gp inducers or moderate to strong CYP inducers as they may decrease efficacy of sofosbuvir and/or velpatasvir. Epclusa may be co-administered with P-gp, BCRP and CYP inhibitors. Velpatasvir is an inhibitor P-gp and BCRP. Co-administration of Epclusa with drugs that are substrates to these transporters may increase the therapeutic levels of these drugs, and dose adjustments of such drugs may be necessary.

Epclusa is contraindicated with the following:

- **Acid reducing agents:** antacids, H2 blockers, PPIs may reduce plasma levels of velpatasvir. PPIs should not be used. If other acid reducing drugs given, these will need to be given at a lower dose and timing of administration carefully established
- **Alpha 1-adrenoreceptor antagonists:** silodosin
- **Antiarrhythmics:** amiodarone (co-administration of amiodarone with Epclusa may cause life-threatening symptomatic bradycardia); digoxin (if medically necessary digoxin levels should be carefully monitored and dose adjustment may be necessary)
- **Anticonvulsants:** carbamazepine, oxcarbazepine, phenobarbital, phenytoin
- **Antigout agents:** colchicine
- **Antimicrobials:** rifampin, rifabutin, rifapentine
- **Antineoplastic agents:** doxorubicin (conventional), topotecan, vincristine (liposomal)
- **CNS stimulators:** modafinil
- **HCV Drugs:** simeprevir, grazoprevir
- **Herbal Supplements:** St. John's Wort
- **HIV Antiretrovirals:** (IFD input is mandatory when modifying HIV regimens)
  - efavirenz (Sustiva)
  - lopinavir/ritonavir (Kaletra)
  - tipranavir/ritonavir (Aptivus)
  - HIV regimens containing tenofovir DF combinations
- **Statins:** rosuvastatin, atorvastatin; other statins may be used if necessary, but need dose reduction and careful monitoring for signs of myopathy. Pravastatin may be used.

Harvoni (sofosbuvir/ledipasvir)- (Harvoni Drug Interactions)
Sofosbuvir and ledipasvir are substrates of the drug transporter system P-gp and BCRP. P-gp inducers may decrease plasma levels of both sofosbuvir and ledipasvir leading to a reduced therapeutic effect of Harvoni. Harvoni cannot be co-administered with strong P-gp inducers. Ledipasvir is an inhibitor of P-gp and BCRP and may increase intestinal absorption of drugs that are substrates for these transporters.

Harvoni is contraindicated for use with the following:

- **Acid reducing agents:** antacids, H2 blockers, PPIs may reduce plasma levels of ledispasvir. If acid reducing drugs given, these will need to be given at a lower dose and timing of administration carefully established.
- **Alpha 1-adrenoreceptor antagonists:** silodosin
- **Antiarrhythmics:** amiodarone (co-administration of amiodarone with Harvoni may cause life-threatening symptomatic bradycardia); digoxin (if medically necessary digoxin levels should be carefully monitored and dose adjustment may be necessary)
- **Anticonvulsants:** carbamazepine, oxcarbazepine, phenobarbital, phenytoin
- **Antigout agents:** colchicine
- **Antimicrobials:** rifampin, rifabutin, rifapentine
- **Antineoplastic agents:** bosutinib, doxorubicin (conventional), topotecan, vincristine (liposomal)
- **CNS stimulators:** modafinil
- **HCV Drugs:** simeprevir
- **Herbal Supplements:** St. John's Wort
- **HIV Antiretrovirals** (note: some of these HIV drugs may be used individually, but not the combinations listed. IFD input is mandatory):
  - elvitegravir/cobicistat/emtricitabine/tenofovir DF (Stribild)
  - tipranavir/ritonavir (Aptivus)
  - efavirenz/emtricitabine/tenofovir DF (Atripla)
  - HIV regimens containing a protease inhibitor/ritonavir or cobicistat and tenofovir DF combinations:
    atazanavir/ritonavir or cobicistat + emtricitabine/tenofovir DF (Reyataz or Evotaz + Truvada)
    darunavir/ritonavir or cobicistat + emtricitabine/ tenofovir DF (Prezista or Prezcobix + Truvada)
    lopinavir/ritonavir + emtricitabine/tenofovir DF (Kaletra + Truvada);
- **Statins:** rosuvastatin; other statins may be used if necessary, but need dose reduction and careful monitoring for signs of myopathy. Pravastatin may be used.

Pegasys cannot be co-administered with clozapine, telbivudine and tizanidine.

Ribavirin cannot be co-administered with didanosine and zidovudine.

Simeprevir (Olysio) - (Simeprevir Drug Interactions)
Is metabolized through the hepatic CYP3A system; it inhibits the P-gp transporters and is a mild inhibitor of CYP1A2 and CYP3A4 intestinal activity. Drugs that are moderate to strong inhibitors or inducers of CYP3A may significantly affect the plasma level of simeprevir impacting its therapeutic effect and such combination is not recommended.

Co-administration with drugs that are substrates for P-gp transport may result in increased concentration of such drugs, and careful monitoring is needed.

Simeprevir is contraindicated for use with the following:

- **Antiarrhythmics:** amiodarone (co-administration of amiodarone with simeprevir in combination with sofosbuvir may cause life-threatening symptomatic bradycardia)
- **Anticonvulsants:** carbamazepine, oxcarbazepine, phenobarbital, phenytoin
- **Antibiotics:** clarithromycin, erythromycin, telithromycin
- **Antifungals**: fluconazole, itraconazole, ketoconazole, posaconazole, voriconazole
- **Antigout agents:** colchicine
- **Antimicrobials:** rifampin, rifabutin, rifapentine
- **Antineoplastic agents:** bosutinib, doxorubicin (conventional), topotecan, vincristine (liposomal)
- **Corticosteroids:** dexamethasone
- **GI**: cisapride
- **HCV Drugs:** grazoprevir
- **Herbal supplements**: Milk Thistle, St. John's Wort
- **HIV drugs**: cobicistat
- **HIV Integrase Strand Transfer Inhibitors:** elvitegravir
- **HIV Non-Nucleoside Reverse Transcriptase Inhibitors:** delaviridine, efavirenz, etravirine, nevirapine,
- **HIV Protease Inhibitors:** atazanavir, darunavir, fosamprenavir, indinavir, lopinavir, nelfinavir, ritonavir, saquinavir, tipranavir
- **Immunosuppressants** : cyclosporine
- **Statins:** atorvastatin, lovastatin, pitavastatin, pravastatin, rosuvastatin, simvastatin- if medically necessary statins should be given at the lowest possible dose and careful monitoring is needed

Sofosbuvir (Sovaldi) - (Sofosbuvir Drug Interactions)
Is a substrate for the drug transport system P-glucoprotein (P-gp) and breast cancer resistance protein (BCRP). Drugs that are potent intestinal P-gp inducers will decrease sofosbuvir plasma levels and may result in its decreased therapeutic effect. P-gp inducers may not be co-administered with sofosbuvir. On the contrary sofosbuvir may be given with P-gp inhibitors without altering its therapeutic effect.

Sofosbuvir is contraindicated for use with the following:

- **Antiarrhythmics:** amiodarone (co-administration of amiodarone with sofosbuvir in combination with another DAA may cause life-threatening symptomatic bradycardia)
- **Anticonvulsants:** carbamazepine, oxcarbazepine, phenobarbital, phenytoin
- **Antimicrobials:** rifampin, rifabutin, rifapentine
- **CNS stimulators:** modafinil
- **Herbal Supplements**: St. John's Wort
- **HIV Protease Inhibitors:** tipranavir/ritonavir

Technivie (ombitasvir/paritaprevir/ritonavir) - (Tehnivie Drug Interactions)
Many drug interactions exist with Technivie and a careful review of drug-drug interactions should be done before treatment is initiated.

Technivie cannot be co-administered with drugs that are highly dependent on the CYP3A system for clearance, or drugs that are moderate or strong inducers or strong inhibitors of CYP3A and CYP2C8. Drug interactions are also present when Technivie is co-administered with drugs that are substrates or inhibitors of P-gp and BRCP.

Technivie is contraindicated for use with the following:

- **Alpha 1-adrenoreceptor antagonists:** alfuzosin, silodosin, tamsulosin
- **Angiotensin II Receptor Blockers:** losartan, valsartan
- **Anti-angina:** ranolazine
- **Antiarrhytmics:** digoxin
- **Antibiotics:** clarithromycin, erythromycin, telithromycin
- **Anticonvulsants:** carbamazepine, phenobarbital, phenytoin
- **Antifungals:** ketoconazole (systemic)
- **Anti-gout:** colchicine
- **Anti-hyperlipedemics:** gemfibrozil
- **Antimicrobials:** rifampin
- **Antineoplastic agents:** bosutinib, doxorubicin (conventional), topotecan, vincristine (liposomal)
- **Antiplatelet agents:** ticagrelor
- **Beta agonists:** salmeterol
- **Calcium Channel Blockers:** amlodipine, nimodipine
- **Corticosteroids:** systemic budesonide, fluticasone inhaler
- **Ergot derivatives:** bromocriptine, dihydro-ergotamine, ergonovine, ergotamine, methyl-ergonovine
- **Estrogens:** ethinyl estradiol
- **GI:** cisapride
- **HCV Drugs:** daclatasvir, grazoprevir, simeprevir
- **Herbal Supplements:** St. John's Wort
- **HIV Non-Nucleoside Reverse Transcriptase Inhibitors:** efavirenz, rilpivirine
- **HIV Protease Inhibitors:** atazanavir, darunavir, lopinavir
- **Immunosuppressants:** tacrolimus
- **Narcotics:** oxycodone, fentanyl
- **Neuroleptics:** pimozide
- **Phosphodiesterase-5 inhibitors:** sildenafil, tadalafil when used in doses for pulmonary arterial hypertension
- **Sedatives/hypnotics:** oral midazolam, triazolam
- **Statins:** lovastatin, pravastatin, simvastatin; statins should be avoided with Technivie; but if medically necessary, other statins may be given at the lowest possible dose and careful monitoring for signs of myopathy is needed.

Viekira Pak(ombitasvir/paritaprevir/ritonavir + dasabuvir)-(Viekira Drug Interactions)
Many drug interactions exist with Viekira and a careful review of drug-drug interactions should be done before treatment is initiated.
Viekira cannot be co-administered with drugs that are highly dependent on the CYP3A system for clearance, or drugs that are moderate or strong inducers or strong inhibitors of CYP3A and CYP2C8. Drug interactions are also present when Viekira is co-administered with drugs that are substrates or inhibitors of P-gp and BRCP.

Viekira Pak is contraindicated for use with the following:

- **Alpha 1-adrenoreceptor antagonists:** alfuzosin, silodosin, tamsulosin
- **Anti-angina:** ranolazine
- **Antibiotics:** clarithromycin, erythromycin, telithromycin
- **Anticonvulsants:** carbamazepine, phenobarbital, phenytoin
- **Antifungals:** ketoconazole (systemic)
- **Angiotensin II Receptor Blockers:** losartan, valsartan
- **Anti-gout:** colchicine
- **Anti-hyperlipedemics:** gemfibrozil
- **Antimicrobials:** rifampin
- **Antineoplastic agents:** bosutinib, doxorubicin (conventional), topotecan, vincristine (liposomal)
- **Antiplatelet agents:** ticagrelor
- **Beta agonists:** salmeterol
- **Calcium Channel Blockers:** amlodipine, nimodipine
- **Corticosteroids:** systemic budesonide, fluticasone inhaler
- **Ergot derivatives:** bromocriptine, dihydro-ergotamine, ergonovine, ergotamine, methyl-ergonovine
- **Estrogens:** ethinyl estradiol
- **GI:** cisapride
- **HCV Drugs:** daclatasvir, grazoprevir, simeprevir
- **Herbal Supplements:** St. John's Wort
- **HIV Non-Nucleoside Reverse Transcriptase Inhibitors:** efavirenz, rilpivirine
- **HIV Protease Inhibitors:** atazanavir, darunavir, lopinavir
- **Immunosuppressants:** tacrolimus
- **Narcotics:** oxycodone, fentanyl
- **Neuroleptics:** pimozide
- **Phosphodiesterase-5 inhibitors:** sildenafil, tadalafil when used in doses for pulmonary arterial hypertension
- **Sedatives/hypnotics:** oral midazolam, triazolam
- **Statins:** atorvastatin, lovastatin, simvastatin; statins should be avoided with Viekira, but if medically necessary other statins may be given at the lowest possible dose and careful monitoring for signs of myopathy is needed.

Zepatier (elbasvir/grazoprevir) - (Zepatier Drug Interactions)
Zepatier is not recommended for use with drugs that are moderate to strong CYP3A inducers or strong CYP3A or OATP1B1/3 inhibitors.

Zepatier is contraindicated for use with the following:

- **Antibiotics:** nafcillin
- **Anticonvulsants:** carbamazepine, phenobarbital, phenytoin
- **Antifungals:** ketoconazole (systemic)
- **Antimicrobials:** rifampin
- **Antineoplastic agents:** topotecan
- **Herbal Supplements:** St. John's Wort

- **HIV drugs**: cobicistat containing regimens
- **HIV Non-Nucleoside Reverse Transcriptase Inhibitors:** efavirenz, etravirine, nevirapine
- **HIV Protease Inhibitors:** atazanavir, darunavir, fosamprenavir, lopinavir, saquinavir, tipranavir
- **Immunosuppressants** : cyclosporine
- **Neuroleptics**: pimozide
- **Statins**: atorvastatin, rosuvastatin. If medically necessary other statins can be used at a reduced dose and patient closely monitored for signs of myopathy. Pravastatin may be used.

MONITORING PATIENTS ON TREATMENT (Attachment 12)

- A monthly evaluation will be done by the facility physician/PA/NP and be recorded in the AHR.

- Specialty IFD consultation will be mandatory prior to starting HCV therapy, then as clinically indicated. Routine IFD follow up after treatment is initiated and at the end of treatment is not needed.

- Periodic laboratory testing while on treatment will be done as follows:

    - CBC with diff. at week 2, 4 then monthly
    - SMA-C at week 2, 4 then monthly. Patients on a PI containing regimen may need more careful monitoring of LFTs; any elevation of ALT or other LFTs will prompt an immediate referral to IFD. A 10-fold elevation requires discontinuation of all therapy and immediate IFD evaluation.
    - HCV RNA VL should **NOT** be checked during treatment, since there is limited data at this time to support stopping rules for futility
    - HCG monthly in females of childbearing age; if ribavirin used, HCG should also be checked monthly for 6 months after Rx ended

- End of treatment and 12 week post-treatment testing:

    - CBC with diff.
    - SMA-C
    - HCG in females of childbearing age; if ribavirin used, HCG should be checked monthly for 6 months after Rx ended
    - PT-PTT/INR
    - HCV RNA VL (Bioreference # 3376). Patients who have an undetectable VL at 12 weeks post-treatment have achieved a Sustained Virologic Response (SVR) and are considered cured. In such patients HCV RNA monitoring is not necessary after 12 week post treatment and it should not be ordered unless there is clinical suspicion of re-infection with HCV.
    - Clinic evaluation by DOCCS' physician, NP or PA. IFD consultation is not routinely needed during nor at the end of treatment.
    - In patients with an SVR, problem code 0728 (Hep C SVR) is to be added to the problem list and problem code 0701 (Hep C disease) inactivated.
    - Patients who have achieved SVR are considered cured and should be followed as though they were never infected with HCV. Those with advanced liver disease need monitoring as outlined in the section below.

MONITORING PATIENTS NOT TREATED & TREATMENT FAILURES

Patients who are not being treated (treatment contraindicated, refused or deferred) and those who failed to achieve SVR after treatment will be re-evaluated periodically as they have ongoing HCV infection and are at risk of progression of liver disease and disease transmission.

Patient assessment will be done as follows:

- Clinic evaluation by a physician/PA/NP every 6 months at minimum for mild disease, more frequently if clinical decompensation occurs.
- Laboratory testing every 6 months for mild disease, more frequently if needed:
  - CBC with diff
  - SMA-C
  - PT-PTT/INR
- FibroSure assay (BioReference # 6124) will be done annually in patients not treated to determine the progression of fibrosis, earlier if LFTs become elevated or if indicators for rapid fibrosis are present.
- Serial HCV RNA viral load (VL) should **NOT** be done since the VL does not have prognostic value.
- **Patients with cirrhosis need periodic surveillance for hepatocellular carcinoma (HCC).** According to the AASLD guidelines, these patients should be monitored every 6 months with an ultrasound of the liver. A baseline endoscopic evaluation should be done to screen for the presence of esophageal varices and surveillance done as indicated. If the ultrasound is abnormal or there is a palpable abdominal mass or change in clinical condition, a Triple Phase CT scan of the abdomen or contrast MRI should be ordered to screen for HCC. Patients with decompensated cirrhosis should be followed more closely in collaboration with a gastroenterologist or hepatologist. Liver transplantation may need to be considered in end stage cirrhosis.

SPECIAL CONSIDERATIONS- TREATMENT ISSUES

1. Before starting treatment for Hepatitis C, the patient will be counseled about the risks/benefits of therapy. **A signed consent will be obtained** stating the patient has read and understands the risks of therapy and that he/she agrees to the treatment regimen and will comply with all medical follow up (Form #3139/Form #3139SP). **Strict adherence to the regimen is imperative. Three refusals by the patient of either medication, lab work, primary or specialty clinic follow up will be considered criteria for stopping all treatment.**

2. Because of the serious side effect profile of some these drugs and the importance of adherence to therapy, all hepatitis C medications will be administered 1:1 by a nurse, and should not be "self carry."

3. **Ribavirin (RIBA) is highly teratogenic. It is contraindicated in pregnant females and in men whose female partners are, or may become, pregnant.** Pregnancy must be avoided in female patients and female partners of male patients during treatment and up to 6 months after treatment has ended. Female patients must have a negative HCG prior to starting therapy, monthly during therapy, and for 6 months thereafter.

Two forms of effective contraception will be required if conjugal visits are being considered.

Male patients on ribavirin, who wish to engage in conjugal visits, must inform their female partners of the serious risk for birth defects and fetal death should they become pregnant, and must ensure that two effective methods of birth control are being used. Patients who will participate in the family reunion program must agree to inform their spouse they are on treatment for hepatitis C (Family Reunion Letter – for further information refer to directive 4500; Ribavirin Patient Information – Ribavirin Warning Sheet).

4. **Dose adjustments:** When managing adverse reactions or drug interactions, dose adjustment of the DAAs or other HCV drugs should **NOT** be done without specialty consultation. Dose modification of daclatasvir may be necessary when daclatasvir is co-administered with certain other medications. Dose reduction of RIBA or discontinuing therapy may be necessary because of adverse reactions. If RIBA is permanently discontinued the entire regimen should also be stopped.
All dose adjustments and discontinuation of treatment must always be done after consultation with a specialist.

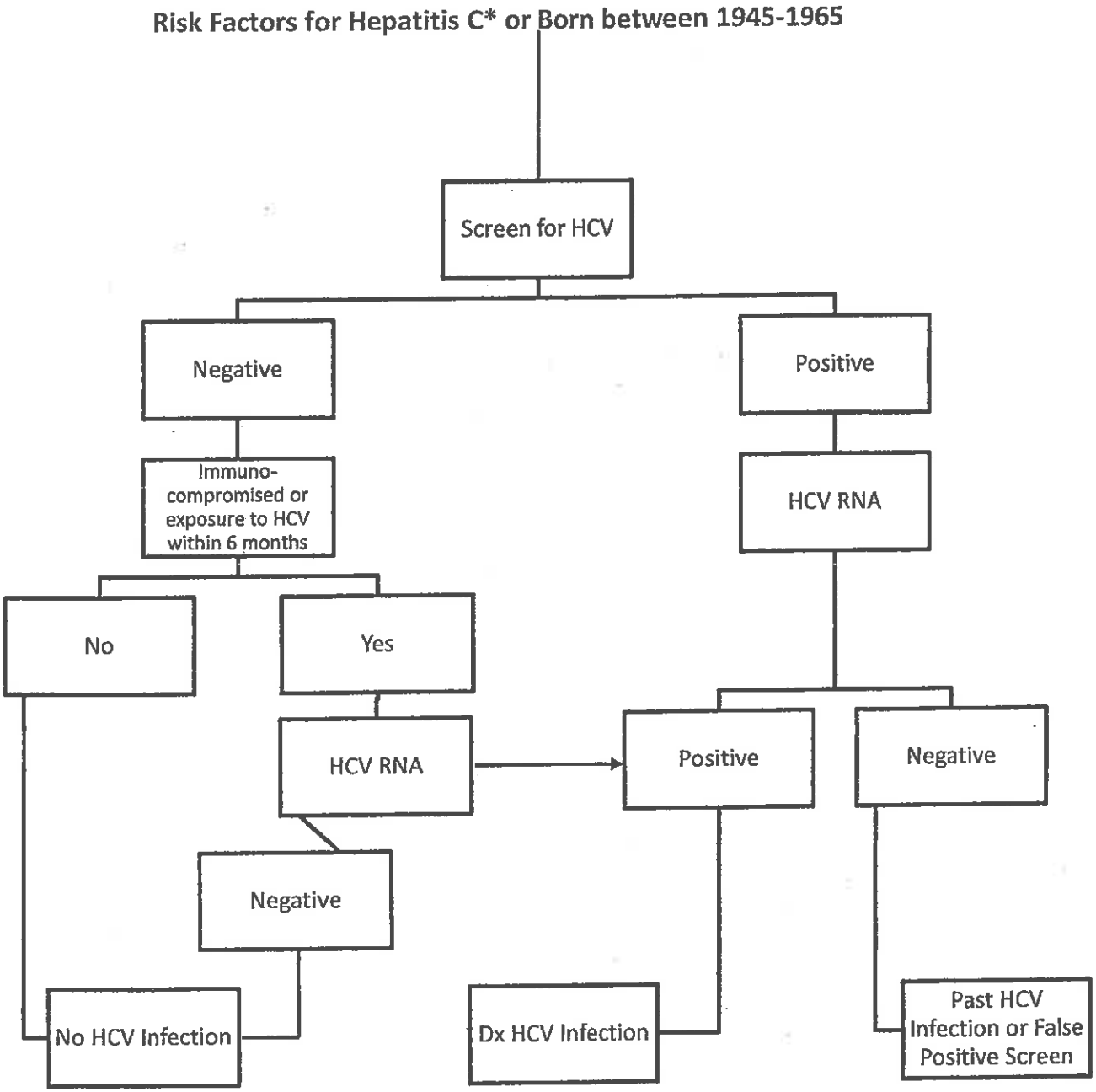
5. Patients on treatment for Hepatitis C should **not be routinely admitted to the infirmary** or any other special designated housing for the purpose of administering medications. Infirmary admissions should be based solely on medical conditions as the need arises.

6. Patients undergoing treatment for Hepatitis C will remain on Facility Hold during the first month of therapy. After that, stable patients may be transferred only after review of laboratory tests and facility primary care evaluation. All transfers and any overnight outside trip (court trips) must be coordinated with the RMD and the medical services of the receiving facility to insure consistent medication availability for the duration of the trip.

7. If there is a possibility that the patient will be released prior to completion of treatment, he/she will have to sign the "Hepatitis C Continuity Program Acceptance," Form #3138/ Form #3138SP.The Regional Infection Control Nurse needs to be contacted to initiate the enrollment process into the continuity program, Form #3131.

8. **The only quantitative HCV RNA assay that will be used in DOCCS for confirming the diagnosis and to monitor response to Hep C treatment is the COBAS/TaqMan HCV RNA PCR assay (BioReference # 3376).**
Viral detection and quantification for this test is as follows: the lower limit of quantification (LLOQ) is 15 IU/ml, the upper limit of quantification (ULOQ) is 50 million IU/ml. Reports will be reported with a numerical value between the two or > 50 million IU/ml if HCV RNA above the ULOQ. When the HCV RNA is below the LLOQ then it will be reported as < 15 ND (not detected) if no virus is detected at all, and < 15 D (detected) if virus is detected but less than 15 IU/ml.

Attachment 1



*HIV, Hx of IV drug abuse, receipt of contaminated blood/blood products or organ transplant prior to 1992, infusion of clotting factor before 1987, needle sticks in health care workers, sharing of razors or toothbrushes, tattoos, intranasal cocaine use, multiple sex partners, hx of STDs, signs of hepatitis, mother with HCV, exposure to HCV, hemodialysis

Scoring System for Hepatic Fibrosis*

Attachment 2

Score	IASL	Metavir	Ishak	Batts & Ludwig
0	No fibrosis	No fibrosis	No fibrosis	No fibrosis
1	Mild fibrosis	Periportal fibrotic expansion	Fibrous expansion of some portal areas, with or w/o short fibrous septa	Fibrous portal expansion
2	Moderate fibrosis	Periportal septa (>1 septum)	Fibrous expansion of most portal area, with or w/o short fibrous septa	Rare bridges or septa
3	Severe fibrosis	Portal-central septa	Fibrous expansion of most portal areas, with occasional portal-portal bridging	Numerous bridges or septa
4	Cirrhosis	Cirrhosis	Fibrous expansion of most area, with marked bridging (portal-portal and portal-central	Cirrhosis
5			Marked bridging (portal-portal and portal-central) with occasional nodules (incomplete cirrhosis)	
6			Cirrhosis, probable or definite	

APRI Score

APRI score = [(AST/ULN) ÷ Platelet count in thousands] x 100

ULN = Upper Limit of Normal of the AST value for the lab.
Platelet count is reported in thousands.

A score > 0.5 indicates probable fibrosis, a score between 0.5 and 1.5 correlates to a Metavir stage of 1 to 3, and a score > 1.5 indicates cirrhosis.

Example: AST 76, Upper Limit of Normal for the lab 35, platelets 120,000

APRI score = [76/35 ÷ 120] x 100 = 1.8 (consistent with cirrhosis)

*Reference:
Ghany et al.; AASLD Practice Guidelines; Diagnosis, Management and Treatment of Hepatitis C: an Update. Hepatology 2009; 49: 1339

Attachment 3

Knodell score (HAI score) of liver biopsy specimens[1]

I. Periportal ± bridging necrosis	Score	II. Intralobular degeneration and focal necrosis[2]	Score	III. Portal inflammation	Score	IV. Fibrosis	Score
None	0	None	0	No portal inflammation	0	No fibrosis	0
Mild piecemeal necrosis	1	Mild (acidophilic bodies, ballooning degeneration and/or scattered foci of hepatocellular necrosis in < 1/3 of lobules or nodules	1	Mild (sprinkling of inflammatory cells in <1/3 of portal tracts)	1	Fibrous portal expansion	1
Moderate piecemeal necrosis (involves less than 50 percent of the circumference of most portal tracts)	3	Moderate (involvement of 1/3 to 2/3 of lobules or nodules)	3	Moderate (increased inflammatory cells in 1/3 to 2/3 of portal tracts)	3	Bridging fiborisis (portal-portal or portal-central linkage)	3
Marked piecemeal necrosis (involves more than 50 percent of the circumference of most portal tracts)	4	Marked (involvement of >2/3 of lobules or nodules)	4	Marked (dense packing of inflammatory cells in >2/3 of portal tracts)	4	Cirrhosis[3]	4
Moderate piecemeal necrosis plus bridging necrosis[4]	5						
Marked piecemeal necrosis plus bridging necrosis	6						
Multilobular necrosis [5]	10						

[1] HAI score is the combined scores for necrosis, inflammation, and fibrosis.
[2] Degeneration-acidophilic bodies, ballooning; focal necrosis-scattered foci of hepatocellular necrosis.
[3] Loss of normal hepatic lobular architecture with fibrous septae separating and surrounding nodules.
[4] Bridging is defined as ≥2 bridges in the liver biopsy specimen; no distinction is made between portal-portal and portal-central linkage.
[5] Two or more contiguous lobules with panlobular necrosis.

Adapted from Knodell, RG, et al. Hepatology 1981; 1:431.

Attachment 4

Conversion of FibroSure Score Into Stages According to Histologic Classification

Fibrosure	Metavir	Knodell/HAI	Ishak
0 – 0.21	F 0	F 0	F 0
0.22 – 0.27	F 0 – F 1	F 0- F 1	F 1
0.28 – 0.31	F 1	F 1	F 2
0.32 – 0.48	F 1- F 2	F 1- F 3	F 2 – F 3
0.49 – 0.58	F 2	F 1 – F 3	F 3
0.59 – 0.72	F 3	F 3	F 4
0.73 – 0.74	F 3 – F 4	F 3 – F 4	F 5
0.75 – 1.0	F 4	F 4	F 6

0 – 0.31: Minimal or absent fibrosis
0.32 – 0.58: Moderate Fibrosis
0.59 – 1.0: Significant fibrosis

References:
BioPredictive website: Fibrotest/Fibrosure
http://www.biopredictive.com/intl/physician/fibrotest-for-hcv/

Attachment 5

Modified Child-Turcotte-Pugh Severity of Liver Disease Worksheet

Clinical and Biochemical Measurements	Points Scored for Increasing Abnormality			
	1	2	3	Score
Encephalopathy (grade)	None	1 or 2 (or precipitant induced)	3 or 4 (or chronic)	
Ascites	Absent	Mild/Moderate (diuretic-responsive)	Moderate/Severe (diuretic-refractory)	
Bilirubin (mg per 100 mL)	<2	2-3	>3	
Albumin (g per 100 mL)	>3.5	2.8-3.5	<2.8	
Prothombin Time (seconds prolonged) or INR	<4 <1.7	4-6 1.7 to 2.3	>6 >2.3	

Total _____

☐ Grade A: Total score or 5 or 6 compensated

☐ Grade B: Total score of 7 to 9 decompensated

☐ Grade C: Total score of 10-15 decompensated

Reference:
Ghany et al.; AASLD Practice Guidelines; Diagnosis, Management and Treatment of Hepatitis C: an Update. Hepatology 2009; 49: 1356

Attachment 6

Ribavirin Treatment Dosing Modifications

Dose adjustments of ribavirin may become necessary during hepatitis C treatment if significant anemia occurs.
Dose reduction of any DAA (direct acting antiviral) or the use of erythropoietin should not be done. Dose adjustment of ribavirin should be done as follows:

Ribavirin dose modification*

Laboratory Values	Reduce Ribavirin Dose to 600 mg/day	Discontinue Ribavirin
Hgb in patients with no cardiac disease	< 10 g/dl	< 8.5 g/dl
Hgb in patients with hx of stable cardiac disease	≥ 2 g/dl decrease in Hgb during any 4 week treatment period	< 12 g/dl despite 4 weeks at reduced dose

*Once Ribavirin has been stopped because of an adverse reaction, it may be restarted at 600 mg daily. If tolerated, it can be increased to 800 mg daily, but never to its original dose.

Attachment 7

TREATMENT OF CHRONIC HEPATITIC C
Genotype 1a

Patient Groups (including both HCV mono-infected and HCV/HIV co-infected individuals)	Treatment Regimens in order of preference	
	No NS5A polymorphism present:	NS5A polymorphism present:
Rx naïve w/o cirrhosis	-Zepatier for 12 weeks	-Harvoni for 12 weeks *(a regimen of Harvoni for 8 weeks may be considered in select patients IF pre-treatment HCV RNA <6 million IU/ml, only if recommended by specialist)* -Viekira Pak + RIBA for 12 weeks -Zepatier + RIBA for 16 weeks -Epclusa for 12 weeks -Daclatasvir + SOF for 12 weeks -SIM + SOF for 12 weeks
Rx naïve with compensated cirrhosis	-Zepatier for 12 weeks	-Harvoni for 12 weeks -Zepatier + RIBA for 16 weeks -Epclusa for 12 weeks (can also be used in decompensated cirrhosis) -Daclatasvir + SOF +/- RIBA for 24 weeks (consider NS5A resistance) -SIM + SOF +/- RIBA for 24 weeks IF no Q80K polymorphism present -Viekira Pak + RIBA for 24 weeks (monitor LFT's frequently)
Failed PEG/RIBA w/o cirrhosis	-Zepatier for 12 weeks	-Harvoni for 12 weeks -Viekira Pak + RIBA for 12 weeks -Zepatier + RIBA for 16 weeks -Epclusa for 12 weeks -Daclatasvir + SOF for 12 weeks -SIM + SOF for 12 weeks
Failed PEG/RIBA with compensated cirrhosis	-Zepatier for 12 weeks	-Harvoni + RIBA for 12 weeks -Zepatier + RIBA for 16 weeks Epclusa for 12 weeks (can also be used in decompensated cirrhosis) -Harvoni for 24 weeks -Daclatasvir + SOF +/- RIBA for 24 weeks (consider NS5A resistance) -SIM + SOF +/- RIBA for 24 weeks IF no Q80K polymorphism present -Viekira Pak + RIBA for 24 weeks (monitor LFTs frequently)
Failed Protease Inhibitor w/o cirrhosis	-Zepatier + RIBA for 12 weeks	-Harvoni for 12 weeks -Zepatier + RIBA for 16 weeks - Epclusa for 12 weeks -Daclatasvir + SOF for 12 weeks
Failed Protease Inhibitor with compensated cirrhosis	-Zepatier + RIBA for 12 weeks	-Harvoni + RIBA for 12 weeks -Zepatier + RIBA for 16 weeks Epclusa for 12 weeks (can also be used in decompensated cirrhosis) -Harvoni for 24 weeks -Daclatasvir + SOF +/- RIBA for 24 weeks (consider NS5A resistance)
Failed SOF/RIBA w/o cirrhosis	Harvoni + RIBA for 12 weeks	
Failed SOF/RIBA with compensated cirrhosis	Harvoni + Riba for 24 weeks	
Failed NS5A Inhibitor regimens	Limited data- defer treatment if possible; refer to consultant	

TREATMENT OF CHRONIC HEPATITIS C

Attachment 8

Genotype 1b

Patient Groups (including both HCV mono-infected and HCV/HIV co-infected individuals)	Treatment Regimens in order of preference
Rx naïve w/o cirrhosis	-Zepatier for 12 weeks -Harvoni for 12 weeks *(a regimen of Harvoni for 8 weeks may be considered in selected patients IF pre-treatment HCV RNA <6 million IU/ml, only if recommended by specialist)* -Viekira Pak for 12 weeks -Epclusa for 12 weeks -Daclatasvir + SOF for 12 weeks -SIM + SOF for 12 weeks
Rx naïve with compensated cirrhosis	-Zepatier for 12 weeks -Harvoni for 12 weeks -Epclusa for 12 weeks (can also be used in decompensated cirrhosis) -Daclatasvir + SOF +/- RIBA for 24 weeks -SIM + SOF +/- RIBA for 24 weeks -Viekira Pak for 12 weeks (monitor LFTs frequently)
Failed PEG/RIBA w/o cirrhosis	-Zepatier for 12 weeks -Harvoni for 12 weeks -Viekira Pak for 12 weeks -Epclusa for 12 weeks -Daclatasvir + SOF for 12 weeks -SIM + SOF for 12 weeks
Failed PEG/RIBA with compensated cirrhosis	-Zepatier for 12 weeks -Harvoni + RIBA for 12 weeks -Epclusa for 12 weeks (can also be used in decompensated cirrhosis) -Harvoni for 24 weeks -Daclatasvir + SOF +/- RIBA for 24 weeks -SIM + SOF +/- RIBA for 24 weeks -Viekira Pak for 12 weeks (monitor LFTs frequently)
Failed Protease Inhibitor w/o cirrhosis	-Zepatier + RIBA for 12 weeks -Harvoni for 12 weeks -Epclusa for 12 weeks -Daclatasvir + SOF for 12 weeks
Failed Protease Inhibitor with compensated cirrhosis	-Zepatier + RIBA for 12 weeks -Harvoni + RIBA for 12 weeks -Epclusa for 12 weeks (can also be used in decompensated cirrhosis) -Harvoni for 24 weeks -Daclatasvir + SOF +/- RIBA for 24 weeks
Failed SOF/RIBA w/o cirrhosis	-Harvoni + RIBA for 12 weeks
Failed SOF/RIBA with compensated cirrhosis	-Harvoni + RIBA for 24 weeks
Failed NS5A inhibitor regimens	Limited data- defer treatment if possible; refer to consultant

Attachment 12

MONITORING TREATMENT

Initial Workup	Week 2	Week 4 then monthly until end of treatment	End of treatment & 12 week follow up
Any time prior to treatment: • HCV RNA[1] • HCV genotype • HIV Screen • Fibrosure assay • Liver US Doppler (for cirrhosis only) • Hep A & B screen • NS5A polymorphism in GT1a only if Zepatier considered • Q80K polymorphism in GT1a with cirrhosis only if SIM/SOF considered Within 12 weeks prior to treatment: • CBC w/diff • SMA-C • PT/INR • IFD consult[2] Just prior to initiating treatment • HCG in females • Facility clinic visit • Drug-drug interactions	CBC w/diff SMA-C	CBC w/diff SMA-C HCG Facility clinic visit[3]	CBC w/diff SMA-C HCG[4] HCV RNA PT/INR Facility clinic visit

[1] HCV RNA (VL) should NOT be monitored during therapy as there are no stopping rules. If a treatment regimen lasting less than 12 weeks is considered, then HCV VL must be repeated within 3 months of starting therapy.

[2] IFD consult is mandatory prior to starting therapy, to be requested after w/u is complete. Subsequent evaluations are as needed.

[3] Monthly clinic evaluations are to be done by a physician, NP, or PA. More frequent evaluations are to be done as needed.

[4] HCG to be checked monthly up to 6 months post treatment if RIBA used.

Ohio Department of Rehabilitation and Correction
Bureau of Medical Services

Protocol: Testing and Treatment Guidelines for Chronic Hepatitis C
Number: C-5

Policy Reference: 68-MED-04, Infectious Disease
67-MNH-02, Mental Health Screening and Assessment Activities
B-1, Consultation Referrals: Initiation, Process, & Follow-up

Responsibility: Medical Directors, Advanced Level Providers, Health Care Administrators, Staff Nurses

DRC Medical Director:

Andrew Eddy, M.D.

Institution Medical Director:

Signature Date: August 9, 2016

Effective Date: August 12, 2016

I. Purpose:

The purpose of this protocol is to provide guidelines for the evaluation and management of inmates with chronic hepatitis C in the Department of Rehabilitation and Correction.

II. Exceptions:

This protocol is not intended to be a substitute for professional judgment by the attending physician, nor should it be used in the treatment of inmates with acute liver disease. The diagnosis of chronic hepatitis C should not deter the physician from considering other liver related diagnoses, if applicable.

III. Definitions:

APRI: AST/Platelet Ratio Index (APRI), a simple ratio of two common lab values. Higher APRI values have been associated with higher stages of liver fibrosis on biopsy. Formula for calculating APRI:
[(AST/upper limits normal AST x 100) /platelet count $x10^3$/ul/1,000]

Copies: The range of viral load reported as the number of the cells infected with the virus within the body. Logs turn large numbers of copies/mL into 'manageable' figures. Refer to the Conversion Spreadsheet (Attachment C).

HCV EIA-2 test: An *in vitro* enzyme immunoassay for the qualitative detection of antibody to Hepatitis C Virus (anti-HCV) in human serum, plasma, or cadaveric serum.

Logs: The range of viral load reported as a measurement of a power of 10 (written as "$\log_{10}$").

Non-Detectable Viral Load: The quantitative measurement of Hepatitis C Virus is below the threshold needed for detection.

Null-Responder: A patient who does not achieve at least a two log decline in their viral load at the treatment midpoint (12 weeks for patients on interferon-based treatment).

Relapser: A patient who has successfully completed anti-viral therapy with a non-detectable viral load at the completion of therapy, but is later found to have a measurable viral load.

Viral Load: The quantitative measurement of Hepatitis C Virus (HCV RNA by PCR).

IV. Directive:

A. Overview:

Hepatitis C is a slowly progressive viral condition that in a limited number of patients will cause long-term complications. The most common complication is the result of progressive liver fibrosis, ultimately resulting in cirrhosis. However, even in the minority of individuals who do develop advanced disease, this process occurs over ten to twenty years or longer.

Among the risk factors that promote disease progression, entry in prison reduces two of the factors: alcohol use and poor nutrition. Because of the slowly progressive nature of the disease and the limited number of individuals who will develop disease complications, ~~many experts~~ recommend that liver biopsy be employed to verify disease progression in order to identify which patients require therapy.

The slowly progressive nature of the disease dictates that hepatitis C should not take precedence over acute illness and that these cases should not receive priority over other medical conditions. Upon diagnosis, patients should be educated about the disease process and evaluation begun to determine their eligibility and need for therapy. Preliminary testing should be completed within six weeks of diagnosis.

B. Screening and Diagnosis:

1. All reception inmates shall be screened for risk factors for hepatitis C infection using the Screening Questionnaire for Possible Hepatitis C Exposure form (DRC5390) or electronic equivalent.

2. Inmates at parent institutions identified with any high risk behaviors may be tested for Hepatitis C Virus (HCV) as medically necessary.

3. Offenders with a positive risk factor assessment (any positive answer on the Screening Questionnaire for Possible Hepatitis C Exposure form (DRC5390) will have an HCV EIA-2 test completed.

4. All positive HCV EIA-2 tests require a HCV viral load to confirm active infection. The viral load should not be repeated unless clinically indicated.

5. Current HCV infection (chronic or acute) will generally be manifest as a positive HCV EIA-2 and a detectable viral load (HCV RNA by PCR).

6. Past HCV infection (immunity) will generally be manifest as a positive HCV EIA-2 and an undetectable viral load (HCV RNA by PCR) in untreated patients.

C. Education and Counseling about HCV Disease:

1. All inmates who test positive for HCV antibody (positive HCV EIA-2 test) and HCV viral load testing shall participate in post-test counseling.

2. Such counseling will consist of:

   a. Natural history of HCV disease
      i. The virus is transmitted through contact with blood or blood products, either in a medical setting, through IV drug abuse and unsterile tattooing. Although the virus can be spread through sexual transmission of blood or blood products, this is considered by the Centers for Disease Control (CDC) to be an ineffective mode of transmission;

      ii. There may be no recognizable acute illness after the virus is initially contracted;

      iii. The natural course of the disease is highly variable and very prolonged, usually measured in decades;

      iv. Although approximately 15-25% of people develop natural immunity, the majority will carry the virus for a lifetime;

      v. Approximately 5-20% of those who carry the virus will develop a wide range of cirrhosis;

      vi. Only 1-5% of those who carry the virus will develop hepatocellular carcinoma;

vii. There is a **significant** increase in the risk of developing chronic liver disease, cirrhosis and Hepatocellular Carcinoma when someone who carries the virus continues to use illicit drugs and alcohol.

b. Mechanism for transmission of HCV
   i. IV or intra-nasal drug use, even once (potential contact with infected blood)
   ii. Blood products, blood transfusion, or organ transplant. (before 1992)
   iii. HIV infection or having a sexual partner with HIV infection
   iv. Hemodialysis
   v. Hemophilia – recipient of concentrated clotting factors
   vi. Sharing intravenous needles
   vii. Sharing tattooing needles or sharps
   viii. Unprotected sex
   ix. Birthed by an HCV infected mother

c. Preventative measures
   i. Stop using illicit drugs and alcohol and enter a substance abuse program
   ii. Never share syringes, needles, tattoo equipment or other drug paraphernalia
   iii. Get vaccinated for hepatitis A and hepatitis B
   iv. Abstain from unprotected sex
   v. Do not share personal items that may be contaminated with blood or body fluids

D. Baseline Evaluation

1. All patients with a positive HCV EIA-2 (positive Hepatitis C antibody) and detectable HCV viral load shall be enrolled into the liver chronic care clinic. Refer to medical protocol A-6, Liver Disease Chronic care Clinic for specifics.

2. A patient with a positive Hepatitis C viral load shall remain enrolled in the liver chronic care clinic and be referred to an Advanced Level Provider (ALP) for evaluation. Refer to medical protocol A-6, Liver Disease Chronic care Clinic for specifics.

3. A patient with a negative Hepatitis C viral load has:

   a. Cleared the virus;
   b. Does not require further treatment;
   c. Is offered counseling, regarding risk behavior and not immune from repeat infection; and
   d. Shall be un-enrolled from the liver chronic care clinic.

4. All HCV viral load positive inmates shall be screened for hepatitis B infections with a full antigen/antibody profile and shall be offered vaccinations if found susceptible.

5. Immunization for Hepatitis A will be offered without antibody screening.

6. An initial Evaluation shall be conducted for all inmates diagnosed with an HCV infection, as outlined in the Assessment for Patients Infected with HCV for Initial and Periodic Evaluations (Attachment A).

7. Periodic evaluations will follow the guidelines detailed in Assessment for Patients Infected with HCV for Initial and Periodic Evaluations (Attachment A).

E. Consideration for Antiviral Treatment

1. Patients with chronic Hepatitis C infection will be prioritized for treatment based on:
   a. Advanced hepatic fibrosis/cirrhosis
   b. Liver transplant recipients
   c. HIV co-infection
   d. Comorbid medical conditions associated with HCV, e.g cryoglobulinemia and certain types of lymphoma
   e. Patients on treatment for chronic HCV infection at time of incarceration

2. The patient must meet all the inclusion criteria and not have any exclusion criteria, as noted in sections F & G of this protocol.

3. Refer to the attached Hepatitis C Chronic Infection Treatment Algorithm (Appendix 1) for a flowchart detailing consideration for treatment.

4. The Hepatitis C Evaluation and Treatment Worksheet (DRC5359) will be used internally at the institution to evaluate for treatment prior to presenting the patient for collegial review. Refer to medical protocol B-1, Consultation Referrals, for collegial review specifics.

F. Treatment Eligibility – Inmates shall be evaluated using both exclusion and inclusion criteria for consideration of antiviral treatment therapy.

1. Exclusion criteria:
   a. Age <18 or >65 will be reviewed on an individual case basis including co-morbidities and life expectancy
   b. Current or planned pregnancy within next 12 months
   c. Substance or alcohol abuse/use/possession or unregulated tattooing in the last 2 years
   d. Platelet count less than 20,000/uL
   e. Decompensated Cirrhosis as indicated by any of the following parameters (↑PT/INR, change in mental status/encephalopathy)
   f. Documented non-adherence to prior therapy, or failure to complete pretreatment evaluations.
   g. Hypersensitivity to interferon, if Hepatitis C treatment regimen includes use of interferon.
   h. Contraindication to any component of treatment regimen.

2. Inclusion criteria:
   a. At least 4 years remaining sentence to complete a course of therapy and follow up.
   b. Persistently elevated ALT levels over a minimum of 6 months and 2 times the upper limit of normal and APRI of 1.5 or greater for consideration of liver biopsy and possible treatment.
   c. Patients over age 45 do not require an elevated ALT level to be eligible for a liver biopsy, but must have an APRI of 1.5 or greater to be considered for biopsy and possible treatment.
   d. Detectable HCV RNA ("viral load"). Viral load testing does not need to be repeated, until just prior to initiation of Hepatitis C antiviral treatment.
   e. Liver biopsy results indicating the presence of liver fibrosis consistent with stage 3 fibrosis or greater on IASL, Batts & Ludwig, or Metavir. scoring systems. Individuals that do not demonstrate significant fibrosis on biopsy will not be treated.
   f. Inmate's signed consent and commitment to lifelong alcohol and substance abuse abstinence.
   g. Inmates with diabetes or hypertension will have dilated retinoscopy performed by the institutional optometrist prior to treatment, if using interferon-based regimen. If found to have poorly controlled disease, the patient may not be a candidate for treatment.
   h. Approved recommendation from Mental Health to start interferon treatment.
   i. Patient's commitment to comply with entire treatment regimen and plan and completion of the Hepatitis C Informed Consent and Treatment Contract (DRC5385) or electronic equivalent.

G. Mental Health Evaluation

1. A mental health evaluation shall be performed by a psychiatrist or a psychologist before prescribing interferon and ribavirin therapy to determine if:

   a. Mental health treatment is warranted prior to antiviral therapy, or
   b. If ongoing mental health assessments are needed during treatment, or
   c. If mental health stabilization is needed prior to treatment with interferon treatment, or
   d. If the patient is too unstable to start interferon treatment.

2. Refer to 67-MNH-02, Mental Health Screening and Assessment Activities, for full details of the mental health evaluation process.

H. Evaluation

1. Once the patient meets all inclusion criteria and has at least 4 years of sentence length remaining and APRI ratio of 1.5 or greater, the patient will be referred for liver biopsy via the collegial review process (see medical protocol B-1, Consultation Referrals for specifics).

2. The liver biopsy will occur before a gastroenterology consult has been obtained.

3. Prior to the liver biopsy, patients will review and initial their signed Hepatitis C Informed Consent & Treatment Contract (DRC5385) or electronic equivalent.

I. Treatment

1. HCV antiviral treatment may be initiated only after obtaining written authority via the non-formulary medication prior authorization process by the ODRC State Medical Director.

2. HCV antiviral therapy may be continued for 14 days for newly arrived reception inmates who were determined to be receiving Hep C antiviral treatment, pending approval via the non-formulary medication prior authorization process by the ODRC State Medical Director.

3. Consultation with Gastroenterology/Hepatology and Requests for liver biopsy will follow the specialty consultation process in accordance with medical protocol B-1, Consultation Referrals: Initiation, Process, & Follow-up.

4. Prior to the start of treatment, patients will review and initial their signed Hepatitis C Informed Consent & Treatment Contract (DRC5385).

5. Patients with biopsy results of stage 3 or 4 on IASL, Batts & Ludwig or Metavir fibrosis scoring systems will have a genotype completed to determine treatment regimen and duration.

6. Treatment regimen will be based on genotype and co-morbidities, in conjunction with Gastroenteriogy/Hepatology services.

7. The request for hepatitis C medications will be completed using the non-formulary medication prior authorization process by the ODRC State Medical Director.

8. The patient will be seen by the ALP to discuss treatment and potential side effects of therapy prior to initiation of antiviral therapy. Refer to the Comparison of Hepatitis C Drugs (Attachment B).

9. Mental health staff is to be notified of the start of interferon therapy for any patient recommended to receive interferon therapy using the Referral to Mental Health Services form (DRC5265).

10. Treatment will commence and continue at the parent institution, unless complications intervene. A nurse will administer all Hepatitis C antiviral medication.

11. Treatment response and continuation will be determined based on genotype and virologic response.

12. Treatment should continue until completion of course of therapy; treatment failure; discontinuation of therapy from side effects; or serious complication from therapy.

J. Monitoring

1. An ALP or nurse shall see the inmate at one week, two weeks, four weeks, and every four weeks thereafter for the duration of treatment.

2. The patient will be questioned about side effects at each monitoring encounter for the duration of treatment. The patient receiving interferon will be questioned specifically about depression, suicidal thoughts, and visual disturbances at each encounter. Patients with side effects will be referred to the ALP.

3. The patient shall be referred to Mental Health services at the start of interferon treatment, so appropriate monitoring can be conducted in accordance with 67-MNH-02, Mental Health Screening and Assessment Activities. A Referral to Mental Health Services (DRC5265) or electronic equivalent will be completed.

4. Specialty consultation follow ups with GE/Hepatology will be completed as clinically indicated.

5. Communication with Gastroenterology Consultation via teleconference, telephone, or telemedicine will be done when significant clinical changes occur or when significant symptoms develop for patients on antiviral therapy, as clinically indicated.

6. Drug testing will be performed; testing will include 7 drugs of abuse panel and ETOH. Any violation of total abstinence will result in the termination of treatment.

7. Those patients who are not eligible, refuse treatment, or have treatment terminated for any reason will be monitored in Chronic Care Clinic (CCC) as clinically indicated for clinical signs of cirrhosis, including jaundice, fluid retention, bruising, and gastrointestinal bleeding. Refer to Common Causes of Abnormal Liver Blood Tests (Appendix 2).

K. Completion of Therapy

1. Patients completing antiviral therapy shall be evaluated with Hepatitis C viral load as requested by Hepatology.

2. Patients with an undetectable viral load at 12 months post therapy shall be considered treatment success and will be discontinued from hepatitis C chronic care and have treatment success noted on the problem list.

3. Patients with a detectable viral load 12 months post therapy shall be considered treatment failures shall be continued to be evaluated in the liver chronic care clinic.

L. Repeat Biopsy

1. Patients who meet the criteria to undergo a liver biopsy but have not met treatment criteria will have annual APRI ratios to determine if further disease progression has occurred.

    a. The APRI ratio shall be completed on these patients annually to assess fibrosis progression.
    b. If the APRI ratio is found to be 1.5 or greater, then repeat biopsy should be considered in 3-5 years.

References:

- Centers for Disease Control, MMWR 1998; 47 (RR19): 1-39.
- Centers for Disease Control, MMWR, 2003; 52 (RR01): 1-33.
- Hepatology, 2003; 38(3), 645-652.
- Federal Bureau of Prisons Clinical Guideline: Evaluation and Treatment of Hepatitis C and Cirrhosis. March 2012. *http://www.bop.gov/news/PDFs/hepatitis_c.pdf*
- Federal Bureau of Prisons Clinical Guideline: Interim Guidance for the Management of Chronic Hepatitis C Infection. June 2014. http://www.bop.gov/resources/pdfs/hepatitis_c_current.pdf

Attached Forms:

Attachment A	Assessment for Patients Infected with HCV for Initial and Periodic Evaluations
Attachment B	Comparison of Hepatitis C Drugs
Attachment C	Conversion Spreadsheet
Appendix 1	Hepatitis C Chronic Infection Treatment Algorithm
Appendix 2	Common Causes of Abnormal Liver Blood Tests
DRC 5265	Referral to Mental Health Services
DRC 5359	Hepatitis C Evaluation and Treatment Worksheet
DRC 5385	Hepatitis C Informed Consent and Treatment Contract
DRC 5390	Screening Questionnaire for Possible Hepatitis C Exposure

ATTACHMENT A
Assessment for Patients Infected with HCV for Initial and Periodic Evaluations

Initial Evaluation:

- **Complete Medical History:**
  - Risk Factor analysis
  - Length of infection history
  - Medication history with attention to previous antiviral therapy
  - OTC, supplements, and herbal remedies
  - History of substance abuse and alcohol consumption
  - Past immunizations
  - History of infection with Hepatitis A or B

- **Physical Assessment:**
  - Height, weight, BMI, &Vital signs
  - HEENT & Neck- attention to JVD, sclera, and thyroid
  - Cardiac exam
  - Lung auscultation
  - Skin examination
  - Abdominal exam for organomegaly, ascites, and venous engorgement
  - Neurological exam for encephalopathy

- **Initial Diagnostic Tests:**
  - Confirmation of HCV antibody positive
  - Plasma HCV RNA (viral load)
  - Complete blood count,
  - Hepatic Profile (AST, ALT, Alk phosphatase, bilirubin)
  - Chem 7 (electrolytes, glucose, creatinine, calculated GFR)
  - APRI calculated
    - [(AST/upper limits normal AST x 100) /platelet count x103/ul/1,000]
  - Hepatitis A & B antibody panels
  - APRI ratio
  - TSH
  - PT/INR
  - bHCG (females)
  - HgbA1C (diabetics)

- **Initial Referrals:**
  - Mental Health Referral (if patient being considered for interferon containing regimen)
  - Substance abuse counseling

- **Initial Prevention Strategies:**
  - HAV and HBV vaccination (depending on serology results)
  - Pneumococcal vaccination (once lifetime)
  - Influenza vaccination
  - Non selective beta-blocker for patients with varices or portal hypertension

Periodic Evaluation:

- **Interval History:**
  - Presence or absence of symptoms
  - Any complications or new complaints
  - General well being
  - Adherence to medical treatment plan
  - Side effects from medications or adverse reactions
  - Dietary adherence
  - Exercise
  - Tobacco use

- **Physical Assessment:**
  - Height, weight, BMI, &Vital signs
  - HEENT & Neck- attention to JVD, sclera, and thyroid
  - Cardiac exam
  - Lung auscultation
  - Skin examination
  - Abdominal exam for organomegaly, ascites, and venous engorgement
  - Neurological exam for encephalopathy

- **Consideration for Antiviral Therapy:**
  - Inclusion criteria met
  - No exclusion criteria
  - Adequate sentence length remaining
  - Consent signed (Hepatitis C Informed Consent and Treatment Contract, DRC 5385)
  - Consent signed
  - APRI ratio result indicates fibrosis 1.5 or greater
  - Absence of substance abuse/use/possession or unregulated tattooing within last 2 years.

- **Periodic Diagnostic Tests:**
  - ALT/AST every 3 months (every 3-6 months if in stable condition)
  - APRI ratio annually
  - Genotype – prior to treatment with antiviral therapy (not repeated)
  - Urine toxicology / ETOH as warranted
  - Liver biopsy (prior to treatment)

- **Periodic Referrals:**
  - Gastroenterologist / Hepatologist for treatment
  - Optometry for Dilated Retinal Exam, before treatment if pre-existing ophthalmological disease if using interferon-based regimen

- **Periodic Prevention Strategies:**
  - HAV and HBV vaccination (depending on serology results)
  - Pneumococcal vaccination (once lifetime)
  - Influenza vaccination annually
  - TB skin testing annually
  - Non selective beta-blocker for patients with varices or portal hypertension

Ohio Department of Rehabilitation and Correction
Office of Correctional Health Care

Protocol: Liver Disease Chronic Care Clinic
Number: A-6

Policy Reference: 68-MED-01, Medical Services
68-MED-19, Chronic Disease Management

Responsibility: Physicians; Advanced Level Providers; Health Care Administrators; Nurses

DRC Medical Director:

Andrew Eddy, M.D.

Institution Chief Medical Officer:

Signature Date: February 28, 2013

Effective Date: March 4, 2013

I. Purpose:

The purposes of this protocol are to:

- Accurately diagnose the underlying cause of the inmate's liver disease in order to plan for appropriate monitoring of these inmates and to provide for appropriate treatment;
- Provide patient education to promote a better understanding of the cause, symptoms and treatment. Additionally, those inmates diagnosed with viral liver infections must be counseled about the potential of transmission to others;
- Reinforce the importance of compliance with the therapeutic regimen.

II. Exceptions:

None

III. Definitions:

Chronic Liver Disease: Ongoing inflammatory process of the liver that does not resolve within 30 days.

Disease Control: The point to which the patient's disease symptoms, complications and progression are managed.

- Good Control: The degree to which disease parameters are correlated with reduced morbidity and mortality.

- Fair Control: The degree to which disease parameters are correlated with increased probability of morbidity and mortality.

- Poor Control: The degree to which disease parameters are correlated with significantly increased morbidity and mortality.

Disease Status: the level at which management of the patient's disease symptoms and disease progression exists.

- Improved Status: indicated when the patient's symptoms and/or baseline laboratory readings, if applicable, have improved since the previously recorded visit.

- Unchanged Status: indicated when the patient's symptoms and/or baseline laboratory readings, if applicable, remain unchanged since the previously recorded visit.

- Worsened Status: indicated when the patient's symptoms and/or baseline laboratory readings, if applicable, have worsened since the previously recorded visit.

IV. Directive:

A. Enrollment in Liver Disease Chronic Care Clinic

1. All inmates who are received at a DRC Reception Center or a parent institution with a diagnosis of a chronic liver disease, or who are subsequently diagnosed with a chronic liver disease as defined by this protocol, shall be referred to the physician or advance healthcare provider for enrollment in Liver Disease Chronic Care Clinic (CCC). Such conditions may include, but are not limited to:

   a. Cirrhosis,

   b. Hepatocellular cancer,

   c. Wilson's disease,

   d. Fatty liver syndrome,

   e. Chronic Hepatitis B,

   f. Chronic Hepatitis C

2. See the attached Evaluation of the Patient with Cirrhosis form (Appendix A) for information pertaining to the above conditions.

3. Physicians and Advanced Level Providers (ALP) who diagnose a patient with a chronic liver disease must write a Doctor's Order (DMH0020) to enroll the patient in Liver Disease CCC.

4. Initial Comprehensive Assessment – to be completed within 30 days of clinic enrollment: at the time of the first chronic care visit, a focused physical exam targeted to the requirements of the specific chronic disease or diseases shall be conducted using the Chronic Care Clinic Baseline Medical Data form (DRC5430) and the Chronic Care Clinic Flow Sheet (DRC5422).

   a. Medical History –history must address the following criteria with regard to chronic liver disease:

      i. Risk factor analysis;

      ii. Known length of disease condition or infection;

      iii. Medication history, with particular attention to prescribed Hepatitis C treatment;

      iv. Use of over-the-counter medications, supplements and herbal remedies;

      v. Past immunizations;

      vi. Known history of infection with Hepatitis A, Hepatitis B or Hepatitis C.

   b. Physical Assessment

      i. Vital signs including temperature, pulse, respiration and blood pressure measurements;

      ii. Height and weight;

      iii. Head and neck – foul breath, jugular venous distention;

      iv. Cardiac examination – dysrhythmias, congestive heart failure;

      v. Lung auscultation;

      vi. Skin examination – dehydration, jaundice, spider angiomas, rash;

      vii. Abdominal examination – ascites, enlarged liver; and

viii. Neurological examination – altered mental status

c. Diagnostic Testing may include:

i. ALT/AST levels,

ii. Hepatitis antibody tests,

iii. Electrolytes,

iv. CBC,

v. PT/INR levels,

vi. FBS,

vii. Serum albumin levels,

viii. Viral RNA levels, if applicable, and

ix. Serum ammonia level, if clinically warranted,

x. Liver ultrasound if cirrhosis present/suspected.

B. Prevention and Wellness

1. Each patient enrolled in Liver Disease Chronic Care Clinic must be offered the following immunizations:

a. Influenza vaccination annually

b. Hepatitis A vaccination series(if not immune); and

c. Hepatitis B vaccination series (if not immune),

d. Pneumococcal (once per lifetime)

e. Patients with cirrhosis should be evaluated for portal hypertension, and if detected, be treated with non-selective beta blockers to prevent gastric varices and variceal bleeding.

2. The ALP will enter the patient's diagnosis on the Inmate Problem List (DRC5374) and shall initiate a liver disease chronic care clinic treatment plan.

C. Treatment Strategies

1. The patient shall be counseled regarding chronic liver disease, the potential for complications or disease progression if untreated, and lifestyle factors that may affect overall health.

2. If medications are indicated, the appropriate drugs shall be selected from the ODRC Formulary and ordered for an initial period not to exceed 110 days.

   a. When the patient is being treated for liver disease with any medication, health care staff must counsel the patient about such medication and any potential side effects.

   b. All medication and other health education given to a patient shall be documented in the medical record.

D. Periodic Evaluations

1. The frequency of subsequent clinic visits shall be determined by the clinician using the following guidelines:

   a. Good control/Improved Disease Status – generally 6 -12 months, no more than every 12 months;

   b. Fair control/Unchanged Disease Status – generally 3- 6 months, but no less than every 6 months;

   c. Poor control/Worsened Disease Status – patients shall be seen as necessary, but at least every month until control improves.

2. The clinician may elect to refer CCC patients to a nurse for an interim visit between regular chronic care visits for additional medication adherence monitoring, counseling, patient education, or lab work monitoring.

3. All periodic evaluations shall contain the following elements:

   a. Interval History – this must include inquiry about the presence or absence of symptoms since the previous visit with particular attention to liver disease symptoms including nausea and vomiting, abdominal pain, fatigue; adherence to the medical treatment plan; dietary adherence (if applicable), exercise; smoking and any other information pertinent to the patient's illness.

   b. Objective data including vital signs and weight, liver and abdominal assessment, jugular venous pressure and skin assessment for jaundice, spider angiomas and other dermatologic signs of liver disease progression.

c. Assessment – clinician shall document, at a minimum, the degree of control and the status of each patient.

d. Completion of the Chronic Care Clinic Follow-up form (DRC5452).

4. Periodic diagnostic studies will be ordered in advance of subsequent clinic visits and may include, if clinically indicated:

a. ALT/AST,

b. Serum albumin levels,

c. PT/INR,

d. WBC; Hgb/Hct, /platelets

e. Liver ultrasound for patients with confirmed diagnosis of cirrhosis every 6 -12 months.

E. Patient Refusal to Participate

1. Inmate patients may choose to refuse any and all Liver Disease CCC care and treatment. Patients who refuse to participate in Liver Disease CCC treatment regimens should be offered a follow-up visit at least every 6 months.

a. The patient shall be advised of treatment options, the risks and benefits of therapy and the health consequences of refusing treatment.

b. If the patient continues to refuse medical treatment recommendations or medications, a Release of Responsibility form (DRC5025) or a Refusal of Medication form (DRC5027) shall be completed and the refusal and counseling shall be documented in the Interdisciplinary Progress Notes (DMH0008).

Attachments

Appendix A	Evaluation of the Patient with Cirrhosis
DRC 5025	Release of Responsibility
DRC 5027	Refusal of Medication
DRC 5422	Chronic Care Clinic Flow Sheet
DRC 5430	Chronic Disease Clinic Baseline Medical Data
DRC 5452	Chronic Care Clinic Follow-up
DRC 5374	Inmate Problem List
DMH 0008	Interdisciplinary Progress Notes
DMH 0020	Doctor's Order

Appendix A
Evaluation of the Patient with Cirrhosis

Disease	Tests and findings
Alcoholic liver disease	History of alcohol abuse
	AST/ALT >2 with both being less than 500 IU/mL if alcoholic hepatitis is present
Chronic hepatitis C	ELISA assay for anti-HCV
	PCR for HCV RNA if confirmatory test is necessary
Primary biliary cirrhosis	Antimitochondrial antibodies as an isolated finding
Primary sclerosing cholangitis	Strong association with inflammatory bowel disease
	Contrastcholangiography to establish the diagnosis
	Antinuclear and antismoothmuscle antibodies and ANCA; these are not diagnostic
Autoimmune hepatitis	Hypergammaglobulinemia
	Antinuclear and antismooth muscle antibodies and ANCA in type 1; anti-LKM-1 in type 2
Chronic hepatitis B	HBsAg and HBeAg and, in some cases, HBV DNA by hybridization or bDNA assay
Hereditary hemochromatosis	Family history of cirrhosis
	Transferrin saturation and plasma ferritin should be performed but may be elevated by liver disease itself
	Diagnosis established by liver biopsy and calculation of hepatic iron index or by genetic testing
Wilson disease	Family or personal history of cirrhosis at a young age
	Serumceruloplasmin reduced in 95 percent of patients
	Liver biopsy showsincreased copper content which may also be seen in cholestatic liver diseases
Alpha-1-antitrypsin deficiency	Family or personal history of cirrhosis at a young age
	Serum AAT; phenotyping if low or borderline values
Nonalcoholic fatty liver disease	History of diabetes mellitus or metabolic syndrome
	Diagnosis maybe suspected by abnormal liver biochemical tests and hepatic imagingshowing fatty infiltration and is confirmed by liver biopsy

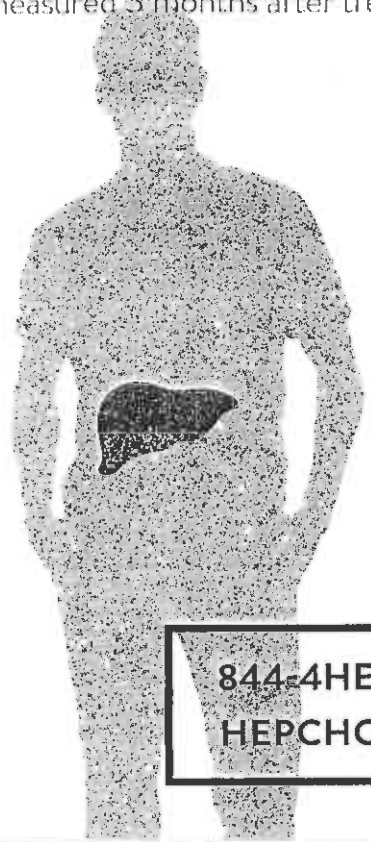
GILEAD

KNOW THE FACTS

AN EDUCATIONAL SERIES BROUGHT TO YOU BY GILEAD SCIENCES

KNOW THE FACTS ABOUT HEP C

It's important to know the facts about hepatitis C (Hep C). Hep C is a serious infection of the liver that is spread through the blood of an infected person. If left untreated, it can cause liver damage or liver cancer. It's important to know that Hep C can be cured. Cure means the virus is not detected in the blood when measured 3 months after treatment is completed.



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FIBROSIS
Scarring in the liver. As Hep C progresses, scar tissue can replace healthy liver tissue. The liver may then stop working as well as it should.

LIVER
Your body's second-largest organ. It weighs about 3 pounds. It is located under your rib cage on your right side.

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HEP C AND YOUR LIVER

YOUR LIVER DOES MANY THINGS FOR YOU

- **CLEANS** YOUR BLOOD
- **PROCESSES SUBSTANCES** THAT MAY BE DAMAGING, LIKE ALCOHOL AND DRUGS
- **TURNS FOOD INTO SUBSTANCES** YOUR BODY NEEDS, LIKE PROTEINS AND NUTRIENTS
- **STORES VITAMINS AND NUTRIENTS** AND RELEASES THEM WHEN YOUR BODY NEEDS THEM
- **HELPS PREVENT** BLOOD CLOTTING
- **DIGESTS** FATS

Hep C causes damage that makes it harder and harder for your liver to do its work. Inflammation increases. Scar tissues builds up. Finally, blood flow to the organ may be blocked. This damage occurs in stages. ▶

THE STAGES OF LIVER DISEASE

HEALTHY LIVER
HELPS DIGEST FOOD. BREAKS DOWN HARMFUL DRUGS AND TOXINS.

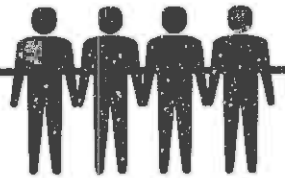
FIBROTIC LIVER
INFLAMMATION FROM HEP C LEADS TO FIBROSIS (SCAR TISSUE) IN THE LIVER.

CIRRHOTIC LIVER
AS SCARRING GETS WORSE, IT BLOCKS BLOOD FLOW IN THE LIVER. THIS IS CALLED CIRRHOSIS.

WHAT TO DO NEXT

START A CONVERSATION

If you have Hep C, or think you may have been exposed to Hep C, the first thing to do is talk with your healthcare provider.



IT'S IMPORTANT TO REMEMBER THAT MANY PEOPLE WITH HEP C HAVE NO SYMPTOMS.

UP TO 75% OF PEOPLE WITH CHRONIC HEP C ARE NOT AWARE THAT THEIR LIVERS ARE BEING DAMAGED.

THE SYMPTOMS OF **HEP C**

Hep C is a **silent disease**. People can live with it for years without symptoms, and most people don't even know they have it. Still, the virus is slowly damaging their livers.

SYMPTOMS OF ACUTE HEP C MAY INCLUDE:

- Fatigue
- Stomach pain
- Nausea/vomiting

SYMPTOMS OF CHRONIC HEP C MAY INCLUDE:

- Loss of appetite
- Dark urine
- Joint pain
- Yellowing of the skin or eyes
- Gray-colored bowel movements

Here are some questions you might ask to get the conversation started:

- AM I AT RISK FOR HEP C?
- HOW MIGHT HEP C AFFECT MY HEALTH?
- HOW DO I KNOW IF MY LIVER IS DAMAGED?
- WHAT SORT OF TESTS DO I NEED?
- IF I HAVE HEP C, CAN I BE CURED?

Cure means the virus is not detected in the blood when measured 3 months after treatment is completed.

TALK TO YOUR HEALTHCARE PROVIDER.

HEP C RESOURCES

There is more to know about Hep C, and a lot of information is available online.

The Hep C Hope program offers resources, tips and personal support to help manage Hep C. **Visit HepcHope.com or talk to a Hep C Educator at 844-4HepcHope who can help register you for the program.**

You also might check out sites like these*:

- hcvadvocate.org
- hepatitis.va.gov
- help4hep.org
- cdc.gov/hepatitis/hcv/patienteduhcv.htm

*These resources are independent third-party organizations and are unaffiliated with Gilead.

ACUTE HEP C INFECTION

When a person is infected with Hep C, they will develop acute Hep C, a short-term viral infection. In approximately 15–25% of people, the body is able to fight off the acute Hep C infection. They are able to get rid of the virus.

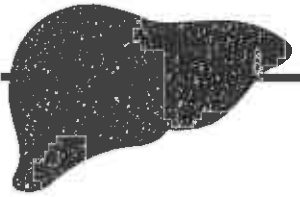
In most people infected with Hep C, the acute infection becomes chronic. They are not able to fight off the virus. It remains in their bodies.

CHRONIC HEP C INFECTION

Chronic Hep C is a serious disease. Chronic Hep C lasts a long time and occurs when the virus remains in a person's body. It causes the liver to swell. Over time, it can damage the liver causing scar tissue to form, making it difficult for the liver to do its job properly. Hep C is the leading cause of liver cancer in the U.S. It is also the number one reason for liver transplants.

Early diagnosis and treatment of Hep C can help prevent liver damage and cirrhosis.

WHAT IS **HEP C?**



1

HEP C IS A VIRUS THAT INFECTS THE LIVER.

2

THE ONLY WAY TO GET HEP C IS IF THE BLOOD OF AN INFECTED PERSON GETS INTO YOUR BLOODSTREAM.

3

IN THE UNITED STATES, HEP C IS THE MOST COMMON VIRUS SPREAD BY BLOOD-TO-BLOOD CONTACT.

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HEP C TERMS

ACUTE HEP C INFECTION

The first stage of Hep C infection. Acute Hep C lasts a short time. It usually occurs within the first 6 months of exposure to the virus.

CHRONIC HEP C INFECTION

In chronic Hep C, the Hep C virus remains in the body after the acute infection. Chronic Hep C can lead to serious liver damage.

CIRRHOSIS

Severe fibrosis or scarring of the liver. Cirrhosis can cause your liver to stop working as it should. Up to 20% of people with chronic Hep C develop cirrhosis.

LEARN MORE ABOUT HEP C

GILEAD

WHY GET TESTED?

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WHY TESTING IS IMPORTANT

Hepatitis C (Hep C) is a serious disease that affects the liver. You can live with it for years, even decades, without symptoms. Many people have the disease and don't know it. But that doesn't mean it's not doing damage. If left untreated, Hep C causes liver damage, and it can even lead to liver cancer. That's why getting tested for Hep C is important.

Hep C is not tested for as part of routine blood work, but the **Centers for Disease Control (CDC) recommends Baby Boomers—people born between 1945 and 1965—get tested**. All it takes is a simple blood test to confirm if you have the Hep C virus. And if you do have Hep C, **Hep C can be cured**. Ask your healthcare provider to get tested.

Cure means the virus is not detected in the blood when measured 3 months after treatment is completed.

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Exhibit C

LIVER

Your body's second-largest organ. It weighs about 3 pounds. It is located under your rib cage on your right side.

LIVER CANCER

The spreading growth of unhealthy cells in the liver. When cancer starts in the liver, it is called liver cancer. Chronic Hep C is one of the leading causes of liver cancer in the U.S.

VIRAL LOAD

The amount of the Hep C virus in your blood. During treatment for Hep C, your healthcare provider may test your blood to find out your viral load. When your treatment is working, the viral load will be dropping.

HEP C TERMS

ACUTE HEP C INFECTION
The first stage of Hep C infection. Acute Hep C lasts a short time. It usually occurs within the first 6 months of exposure to the virus.

ANTIBODY
A chemical released into the bloodstream when you get an infection. The antibody remains in your bloodstream even after the infection goes away.

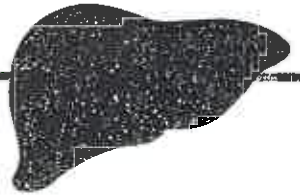
CHRONIC HEP C INFECTION
The Hep C virus that remains in the body after the acute infection, and can lead to serious liver damage.

HEPATITIS
An inflammation (swelling) of the liver. Hep C is one of the causes of hepatitis.

INFLAMMATION
A swelling of part of the body when it is fighting an infection or healing from an injury. Hep C can cause inflammation of the liver. Inflammation of the liver can result in scarring of the liver.

LEARN MORE ABOUT HEP C AND HEP C TESTING

WHAT IS HEP C?



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HOW DO YOU GET HEP C?

The only way to get Hep C is to come in contact with blood from an infected person or contaminated blood. You may be at higher risk if any of the below apply to you:

- ACCIDENTAL NEEDLE STICK
- BEING BORN TO A MOTHER WITH HEP C
- BLOOD TRANSFUSIONS OR RECEIVED BLOOD PRODUCTS BEFORE 1992
- DIALYSIS FOR KIDNEY DISEASE
- HIV
- CERTAIN RECREATIONAL DRUGS
- ORGAN TRANSPLANTS
- VIETNAM-ERA VETERAN
- TATTOOS OR BODY PIERCINGS WITH UNSTERILIZED TOOLS

There are other ways you can get infected.

Sometimes a small amount of infected blood that you cannot see exists on personal items. Sharing items like **razors**, **toothbrushes**, or **unsterilized manicure** and **pedicure tools** could spread Hep C.

Unprotected sex with an infected person is another way to get Hep C.

IF YOU FEEL YOU MAY HAVE BEEN EXPOSED TO HEP C, TALK TO YOUR HEALTHCARE PROVIDER AND ASK TO BE TESTED.

HOW TO GET TESTED

There are two simple blood tests for Hep C ▶

1

THE ANTIBODY TEST

Once you have been exposed to Hep C, the antibodies for the virus will always be in your blood. This test looks for those antibodies.

Note that antibodies cannot be detected right away. It can take as long as 10 weeks for antibodies to show up in your blood. So, if you have just recently been exposed, the test for antibodies may not show it. Also, a positive antibody test does not always mean you have chronic Hep C.

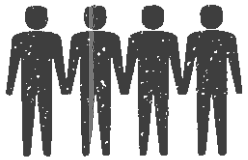
2

THE VIRAL LOAD TEST

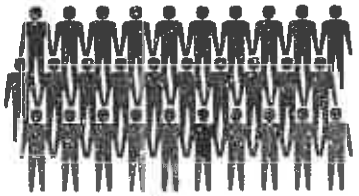
If you have a positive antibody test, the next step is to look for the amount of virus in your blood. The viral load test, also known as the HCV-RNA test, can confirm the presence of chronic Hep C.

HEP C FACTS FOR BABY BOOMERS

Baby Boomers are **5x** more likely to have Hep C



75% of people in the U.S. with Hep C are Baby Boomers



1 in 30 Baby Boomers has Hep C and most don't know it

WHY DO BABY BOOMERS NEED TO GET TESTED?

"Baby Boomers"—people born between 1945 and 1965—are at an increased risk for Hep C. In fact, the CDC recommends that every Baby Boomer be tested.

Why are Baby Boomers at greater risk? No one is 100% sure why Baby Boomers are at a higher risk. The Hep C virus was discovered in 1989 and is spread by blood-to-blood contact. In fact, donated blood was not screened for Hep C until 1992. It's likely that most Baby Boomers were infected before that time and may only be showing symptoms now.

IF YOU ARE A BABY BOOMER, ASK YOUR HEALTHCARE PROVIDER TO TEST YOU FOR HEP C.

Hep C testing is not a routine part of blood work.

ASK YOUR HEALTHCARE PROVIDER TO BE TESTED FOR HEP C.

HEP C RESOURCES

There is more to know about Hep C, and a lot of information is available online.

The Hep C Hope program offers resources, tips and personal support to help manage Hep C. **Visit HepcHope.com or talk to a Hep C Educator at 844-4HepcHope who can help register you for the program.**

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- help4hep.org
- cdc.gov/hepatitis/hcv/patienteduhcv.htm

* These resources are independent third-party organizations and are unaffiliated with Gilead.

THERE ARE SEVERAL TYPES OF HEPATITIS.

"HEPATITIS" is the medical term for inflammation or swelling of the liver. When you have hepatitis, your liver does not work as well as it should.

There are five types of hepatitis viruses: A, B, C, D, and E. Hep C is one of the most serious. When a person is infected with Hep C, some will develop acute Hep C, a short-term viral infection.

For most of those people--about 75--85%--acute Hep C will lead to chronic Hep C. Chronic Hep C is a long-lasting disease.

Chronic Hep C is a serious disease.
Chronic Hep C is the leading cause of liver cancer in the U.S. It's also the number one reason for liver transplants.

BECAUSE HEP C CAN BE SERIOUS AND DAMAGES YOUR LIVER OVER TIME, IT'S IMPORTANT TO GET TESTED.

GILEAD

UNDERSTANDING YOUR DIAGNOSIS

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UNDERSTANDING YOUR HEP C DIAGNOSIS

If you've been diagnosed with chronic (long-lasting) hepatitis C (Hep C), you're not alone. Hep C affects about 3.5 million people in the U.S.

This brochure will help you understand your diagnosis and how to work with your healthcare provider moving forward.

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NOTES

NOTES

LEARN MORE ABOUT HEP C

WHAT TO EXPECT FOLLOWING YOUR DIAGNOSIS

Following your diagnosis, your healthcare provider may refer you to a Hep C Specialist for further testing. **If you need help finding a Hep C Specialist, visit HepcHope.com or call 844-4HepcHope to talk with a Hep C Educator.**

Further testing is needed to help guide your healthcare provider in making decisions about the length and type of Hep C treatment that's right for you.

HCV ANTIBODY (ANTI-HCV) TEST

A blood test that looks for antibodies related to the Hep C virus. If you have ever been infected with Hep C, you will have antibodies.

HEPATITIS

An inflammation of the liver. It can be caused by a number of factors, including Hep C.

VIRAL LOAD

The amount of the Hep C virus in your blood. It is measured with a simple blood test. During treatment, your healthcare provider may test your viral load to see how well your treatment is working.

HEP C TERMS

CHRONIC HEP C INFECTION

In chronic Hep C, the Hep C virus remains in the body after the acute infection. Chronic Hep C can lead to serious liver damage.

CIRRHOSIS

Severe scarring of the liver. Cirrhosis can cause your liver to stop working as well as it should.

CURE

Cure means the virus is not detected in the blood 3 months after treatment is completed.

FIBROSIS

Scarring in the liver. As Hep C progresses, scar tissue can replace healthy liver tissue. The liver may then stop working as well as it should.

GENOTYPE

The Hep C virus has at least six different types called "genotypes." Genotype 1 is the most common in the U.S.

IMPORTANT TESTS TO DIAGNOSE YOUR HEP C

You've probably taken a blood test called an antibody test. It would have shown if you've ever been exposed to the Hep C virus.

You may also be given a test that measures the amount of Hep C virus in your blood—your viral load. This test confirms that you have chronic Hep C.

There is another test that reveals your genotype (the type of Hep C you have). Most people in the U.S. have genotype 1. Other genotypes that have been identified include 2, 3, 4, 5, and 6.

MEASURING LIVER DAMAGE

As Hep C progresses, scar tissue can build up, replacing healthy liver tissue. This is called fibrosis. While fibrosis may not cause any symptoms, it may cause the liver to stop working as well as it once did.

Your "fibrosis score" tells you the amount of scar tissue in your liver. There are many different tests that can determine your fibrosis score. The results of your fibrosis tests will help your healthcare provider make treatment decisions. Fibrosis tests include:

- Blood tests
- Ultrasound
- Liver biopsy

There are several stages of liver damage. The "F" in the chart stands for fibrosis, or scarring. The number after the "F" represents the amount of liver damage. F0 means no damage. F4 means severe liver damage. ▶

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HEP C RESOURCES

There is more to know about Hep C, and a lot of information is available online.

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* These resources are independent third-party organizations and are unaffiliated with Gilead.

THE STAGES OF LIVER DISEASE

STAGE 0 (F0)
THE LIVER IS HEALTHY.

STAGE 1 (F1)
LIVER DAMAGE HAS BEGUN WITH SOME SLIGHT SCARRING.

STAGE 2 (F2)
FIBROSIS BEGINS TO OCCUR. SCAR TISSUE STARTS TO FORM.

STAGE 3 (F3)
MORE DAMAGE. BLOOD FLOW IN THE LIVER HAS BEEN AFFECTED.

STAGE 4 (F4)
CIRRHOSIS HAS OCCURRED. THERE IS SO MUCH SCAR TISSUE THAT THE LIVER IS NOT ABLE TO WORK AS IT SHOULD.

MANAGING YOUR HEP C

The Hep C virus can be unpredictable. Plus, it affects everyone differently. That's why it is so important to keep in close contact with your healthcare provider and get regular checkups.

Some factors that affect how Hep C progresses include:

- YOUR AGE WHEN YOU WERE INFECTED
- WHETHER YOU ARE MALE OR FEMALE
- THE HEALTH OF YOUR IMMUNE SYSTEM
- YOUR USE OF ALCOHOL
- YOUR RACE OR ETHNICITY

BUILD A SUPPORT NETWORK.

This is also a good time to begin building a network of people to support you on your path towards a cure. Family members, friends, and other people living with Hep C are all good choices.

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WHAT TO DO NEXT

KEEP IN TOUCH WITH YOUR HEALTHCARE PROVIDER.

Your healthcare provider and your healthcare team can help you stay healthy as you consider treatment. Have regular checkups with them. Talk with them about your test results, your disease, and any changes in your health. Also talk with your healthcare provider about next steps.

You might ask your healthcare provider:

- CAN MY HEP C BE CURED?
- SHOULD I START TREATMENT FOR MY HEP C?
- WHAT CAN I DO TO GET READY FOR TREATMENT?
- HOW LONG CAN TREATMENT TAKE?
- IS THERE A WAY TO CHECK ON HOW MY HEP C IS PROGRESSING?

Cure means the virus is not detected in the blood when measured 3 months after treatment is completed.

You may be able to help slow down the progression of liver damage. Healthy lifestyle changes may include:

STOP DRINKING ALCOHOL

Alcohol can speed up liver damage.

LOSE WEIGHT

If you are overweight, losing a few pounds may decrease your risk of liver damage. (Fat around your liver can decrease how well your liver works.)

QUIT SMOKING

Smoking increases the risk of liver disease.

CHOOSE HEALTHY FOODS

Fresh vegetables, fruit, whole grains, and lean protein give the liver the nutrients it needs.

STAY ACTIVE

Walk or do some physical activity every day to maintain your overall health. (Talk to your healthcare provider before starting any new physical activity.)

PREVENTING THE SPREAD OF HEP C

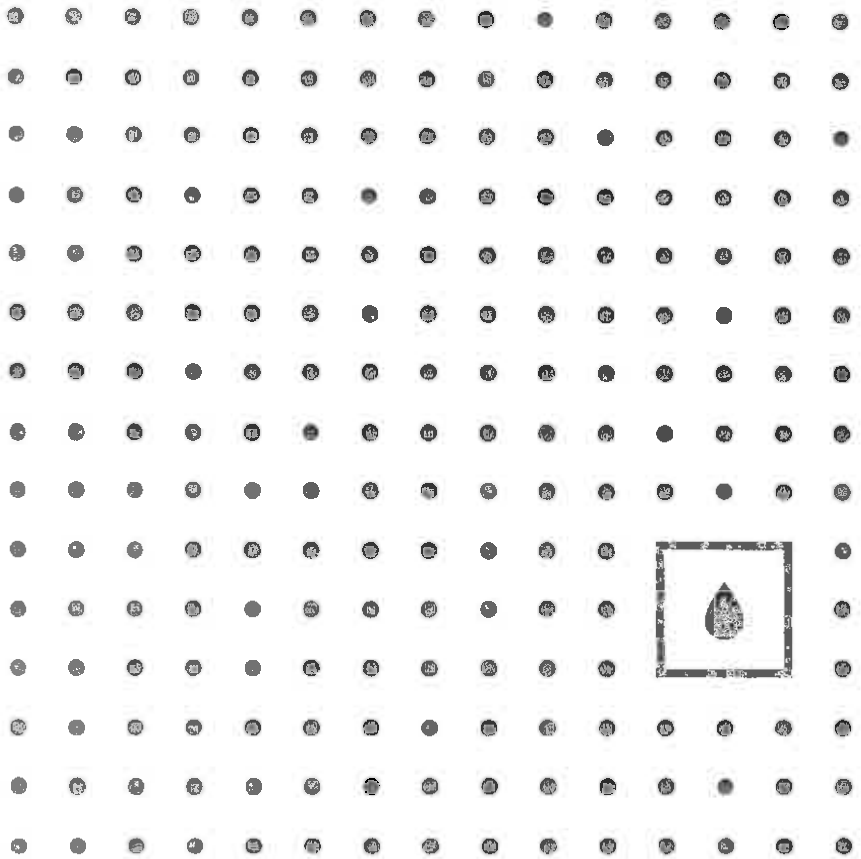
Hep C can only be spread if the blood of an infected person gets into another person's bloodstream.

TAKE THESE SIMPLE STEPS TO AVOID SPREADING HEP C TO YOUR FAMILY AND FRIENDS:

- **Don't share personal items** like toothbrushes, razors, nail clippers, or other manicure tools. Sometimes a small amount of infected blood that you cannot see exists on personal items.
- **Cover cuts** until they heal completely.
- **When you get a cut, don't expose others to your blood.** The Hep C virus can survive on a surface for up to 3 weeks. So make sure you carefully clean and disinfect any surface with blood on it.

Hep C is not spread by casual contact.
ALL OF THESE ACTIVITIES ARE SAFE:

- HUGGING AND KISSING
- SHAKING HANDS OR HOLDING HANDS
- SNEEZING OR COUGHING
- SHARING EATING UTENSILS, FOOD, OR DRINK
- BREASTFEEDING



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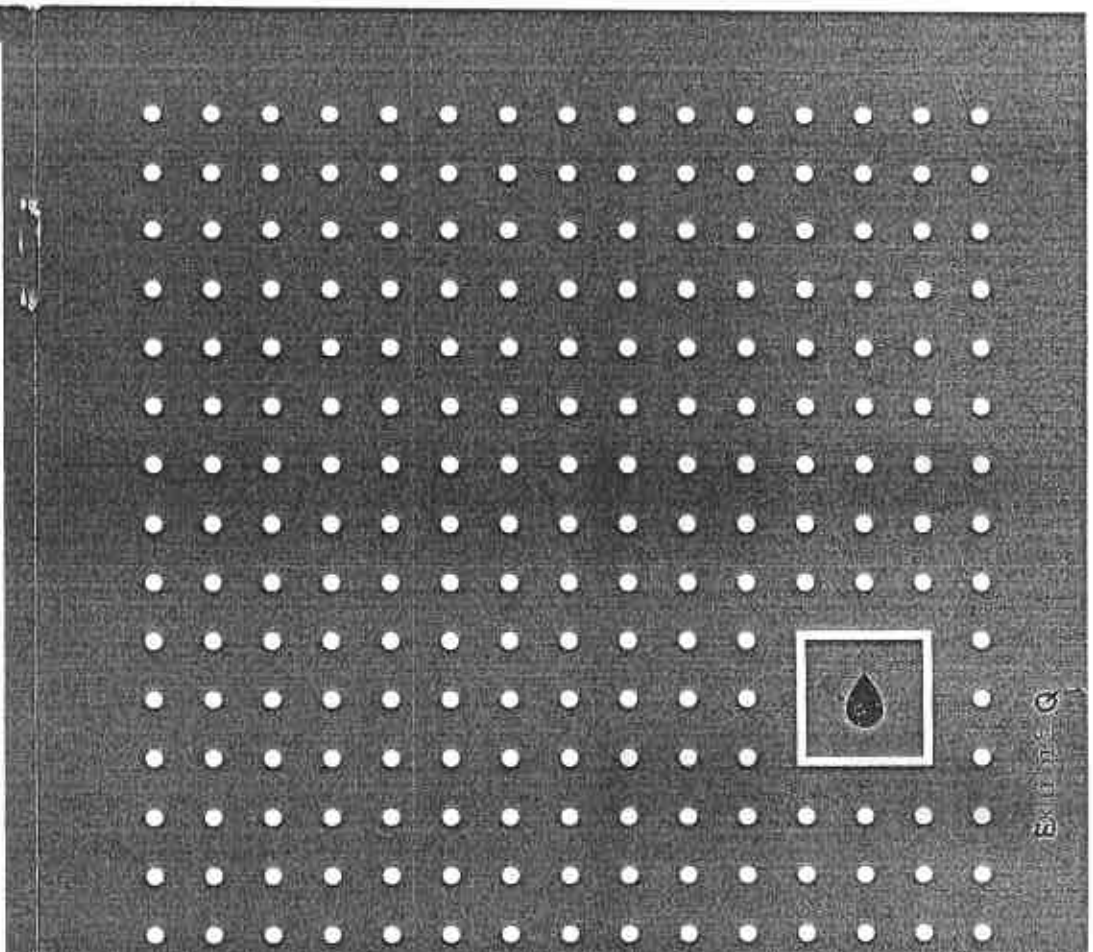

PLANNING FOR TREATMENT

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ADVANCES IN HEP C TREATMENT

There's never been a better time to treat Hep C. Recent scientific advances have led to Hep C treatment options with **cure rates greater than 90%** and shorter treatment regimens than before. In the past few years, it's estimated that **more people have been treated and cured of Hep C than in the previous decade**. You are considered cured if the Hep C virus is not detected in your blood 3 months after your treatment is completed.

It's important to work with your Hep C Specialist to plan your next steps before you begin treatment. If you have questions about what to expect—or need help preparing for a conversation with your Hep C Specialist—**call a Hep C Educator at 844-4HepcHope. Or register for more information at HepcHope.com.**

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NOTES

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NOTES

LEARN MORE ABOUT HEP C

TREATMENT ADVANCES

From 1991 until today there has been great progress in Hep C treatment. Scientific advances have led to shorter treatment options without the harsh side effects of interferon injections.

Today's treatment options are highly effective and cure rates have significantly improved since 2011 with the addition of medicines called direct-acting antivirals (DAAs). DAAs are oral medicines that work against the virus to keep it from multiplying in the body.

Today, more people with Hep C can be treated successfully with just oral therapy. Cure means the virus is not detected in the blood when measured 3 months after treatment is completed.

NOTES

NOTES

THERE HAS NEVER BEEN A BETTER TIME TO BE TREATED FOR HEP C, BECAUSE IT CAN BE CURED. TALK TO YOUR HEP C SPECIALIST ABOUT A TREATMENT PLAN TODAY.

WHAT TO DO NEXT

Talk to your Hep C Specialist about your plan moving forward. It's likely you will have questions for your Hep C Specialist as you consider treatment.

Here are some you might start with:

- HOW MUCH LIVER DAMAGE DO I HAVE?
- CAN MY HEP C BE CURED?
- WHAT ARE MY TREATMENT OPTIONS?
- WHEN SHOULD I START TREATMENT?
- WILL THERE BE ANY SIDE EFFECTS?
- HOW DO I GET MY MEDICINE?
- HOW DO I KNOW IF I'M CURED?

Cure means the virus is not detected in the blood when measured 3 months after treatment is completed.

844-4HEPCHOPE
HEPCHOPE.COM

HEP C RESOURCES

There is more to know about Hep C, and a lot of information is available online.

The Hep C Hope program offers resources, tips and personal support to help manage Hep C. **Visit HepcHope.com or talk to a Hep C Educator at 844-4HepcHope who can help register you for the program.**

You also might check out sites like these*:

- hcvadvocate.org
- hepatitis.va.gov
- help4hep.org
- cdc.gov/hepatitis/hcv/patienteduhcv.htm

* These resources are independent third-party organizations and are unaffiliated with Gilead.

People who follow their treatment plan have a better chance of being cured. It's also important to keep all your appointments with your Hep C Specialist. And don't ever be afraid to ask questions.

You can also learn more about Hep C at HepcHope.com or talk to a Hep C Educator at 844-4HepcHope.

AFTER TREATMENT

WHAT YOU NEED TO KNOW IF YOU GO THROUGH TREATMENT AND ARE CURED

If you and your Hep C Specialist decide to treat your Hep C and if you become cured, there will be Hep C antibodies in your blood. These antibodies show that you once had the virus. Having antibodies is normal. It does not mean you have Hep C. But, because of the antibodies, you will not be able to give blood.

STAYING CURED

The only way you can get re-infected with Hep C is if infected blood gets into your bloodstream. **To help avoid this, follow these rules:**

1

DO NOT SHARE PERSONAL ITEMS LIKE RAZORS OR TOOTHBRUSHES

2

DO NOT INJECT DRUGS OR SHARE NEEDLES

3

DO NOT HAVE UNPROTECTED SEX WITH AN INFECTED PERSON

Smart lifestyle decisions like these can help you stay cured.

ID#: A283016	Name:MANN,JEFFREY	
Form:Appeal	Subject:Health Care	Description:Health Care
Urgent:No	Time left:n/a	Status:Closed

Original Form

5/24/2018 8:25:13 AM : (a283016) wrote

On 5/21/18 I saw Murse Practitioner Beltz and a nurse at the GCI Medical Dept. for a chronic care Hep. C Clinic. I was treated for Hep C, unsuccessfully in 2007 and have been waiting for further treatment ever since. I was told by Ms Beltz that my APRI was .36, and must be at least 1.5 for me to be eligible for treatment. I asked if that number represented the later stage of the disease and was told it does. I stated that it was my understanding that the new drugs are more successful because of earlier diagnosis and earlier treatment, and I was told thats true. So I asked why they would wait until my disease progresses to the later stages when that would reduce my chances of successful treatment. I was told, "Because of the cost of the drugs!". I believe Ms. Beltz, Dr. Douglas, Mr. Hannah the Medical Admin. at GCI, Dr. Eddy and the rest of the doctors on the Collegiate review committee, and all the ODRC medical staff responsible for the medical care I recieve, as well as the policies that influence that care, are Deliberately Indifferent to my medical needs and suffering. Furthermore, I believe it is a violation of my constitutional rights to cause cruel and unusual punishment through the denial of medical care for financial reasons.
To resolve this:
Provide treatment for my Hep C.

Communications

5/25/2018 2:17:15 PM : (Lorie Hanko) wrote

Mr. Mann,
I reviewed your file. It is documented by the advanced licensed provider that there are no signs of advancing disease, and that you will continued to be monitored. There are very specific guidelines and policies regarding the treatment of Hepatitis C. The medical team will review this as needed, and follow the appropriate guidelines. Thanks.

5/25/2018 3:38:45 PM : (a283016) wrote

Everything previously stated in the ICR is incorporated herein. Please provide the name of the staff person that answered the ICR. The answer to the ICR is unacceptable. I have the disease and there is treatment. This is a life threatening disease. It is not acceptable to wait until the disease threatens my life because it is in the late stages before giving me treatment, just because of the cost of the drugs. I recieved treatment in 2007 that was unsuccessful. Am I supposed to believe that I did not need treatment then? That you gave me treatment "Just because"? I do not believe I did not need treatment then.Nor do I believe that 10 years later I do not need treatment for a progressive disease.If you wait until I have an APRI of 1.5 it will significantly reduce my chances of successful treatment.
To resolve this please provide me treatment for my Hep c.

5/29/2018 9:11:57 AM : (Lloyd Brownlee) wrote

Mr. Mann states in his complaint that on 5-21-18 he seen the Nurse Practitioner, Mr. Mann goes on to state that he was treated for Hepatitis C in 2007 unsuccessfully and that in APRI was at .36 and should be at least 1.5. Mr. Mann also states that he was told by the Nurse Practitioner that this represented the later stages of hepatitis C . Mr. Mann also states that he was told by the Nurse Practitioner that the delay in treatment was due to the cost of the drugs.
To investigate this complaint I have interviewed Mrs. Hanko, reviewed medical file, reviewed policy 68-MED-01 and policy 68-MED-04 and protocol C-5.
After reviewing the above mentioned information, medical staff at central office are in charge of reviewing all inmates with hepatitis C and evaluation them under the guidelines of protocol C-5 and decide if each individual meets the criteria to receive medication for hepatitis C. this protocol/procedure was set in place this year (2018).
Your Grievance is denied. This ends Ref # GCI- 0518000476.

5/29/2018 8:02:52 PM : (a283016) wrote

Everything previously stated in the ICR and grievance is incorporated herein by reference. The grievance answer does not answer my complaint.

7/17/2018 10:42:11 AM : (karen stanforth) wrote

Affirmed.
A review of your medical record and treatment plan indicates you have been educated on the current course of action for your condition. Please continue to maintain close contact with your medical providers so they can monitor for any changes in your current health status. The medical staff have followed the appropriate guidelines set forth in 68-MED-01, 68-MED-14, and Medical Protocol C-5. There will be no further action concerning this appeal at this time.
Karen Stanforth, Assistant Chief Inspector, Medical

ID#: A215337	Name:BRAGG,JOHN	
Form:Appeal	Subject:Health Care	Description:Health Care
Urgent:No	Time left:n/a	Status:Closed

Original Form

6/1/2018 9:15:47 AM : (A215337) wrote

This grievance is against Dr. Douglas, Ms. Belts, the nursing staff, & Health Care Administrator Hannah at GCI, along with all those that participate in providing my health care as well as Doctor Eddy, and the Collegiate review Committee and all those who create ODRC Health Car Policies.

In 2007, I recieved treatment for my Hepatitis C, the treatment was unsuccessful. Ever since then I have been waiting for further treatment to no avail. I have been informed by the nurse practioner that basically, I am not recieving treatment due to the cost. I have been on chronic care since 2007.

I have requested treatment for over 11 years and feel that the replies and excuses I have been told are an act of deliberate indifference to my medical needs. It is cruel and unusual punishment to deny me medical care because of the cost. I know that my disease is getting progressively worse. Hepatitis C is a life threatening disease and most successful treatment happens in the early stages. WHY are you waiting to treat me until the disease progresses to the late stages? I'm running out of time...PLEASE provide treatment for my disease.

Communications

6/7/2018 8:39:28 AM : (David Hannah) wrote

Hep C treatment is no long a cost issue. DRC will treat if you APRI score is high enough. This is the standard used by outside hospitals to see if someone qualifies for treatment. It has to be greater than 1.5 and yours is 0.5. You will continue to be followed up and lab work done as ordered.

6/11/2018 7:51:19 PM : (A215337) wrote

Everything previously stated is incorporated herein.

The standard of treatment is 0.5 everywhere but here. Once my APRI reaches 1.5 I will be in the later stages of the disease and treatment will be much less effective. You are condeming me to a reduced chance of success and unnecessary suffering. I believe you are being deliberately indifferent to my medical needs. Please give me treatment for my Hep. C.

6/13/2018 8:25:52 AM : (Lloyd Brownlee) wrote

Mr. Bragg states in his complaint that he received treatment for hepititis C and the treatment was unsuccessfull, Mr. Bragg goes on to state that he has been on chronic care since 2007 and has made request for treatment but has yet to receive proper treatment.

To investigate this complaint I have interviewed Mr. Hannah, reviewed Mr. Bragg's medical files, reviewed policies 68-MED-01 and protocol C5.

After reviewing the above mentioned information I have found the following: you were diagnosed with hepatitis C, The DR&C has a protocol (Medical protocol C5) In place for said treatment. Your APRI score currently is 0.5, in order to receive treatment your APRI score must be at least 1.5. you will still receive evaluations and lab work as ordered by the Medical department.

Your Grievance is denied. This ends Ref # GCI-0618000005.

6/18/2018 7:51:31 PM : (A215337) wrote

Everything previously stated is incorperated herein. In 2007 I received treatment that was unsuccessful. I needed treatment in 2007 and the disease has not gone away so I still need treatment. An APRI of 1.5 condemns me to wait for treatment until the disease is in its late stages and will not be successful. Please provide treatment for my Hep C, there is no reason to deny me treatment other than the cost of the drug. Please provide a list of names of the people who set the APRI level at 1.5. If I met the criteria for treatment in 2007, what makes it different regarding my needing treatment now?

7/17/2018 12:37:42 PM : (karen stanforth) wrote

Affirmed.

A review of your medical record and treatment plan indicates you have been educated on the current course of action for your condition. Please continue to maintain close contact with your medical providers so they can monitor for any changes in your current health status. The medical staff have followed the appropriate guidelines set forth in 68-MED-01, 68-MED-14 and Medical Protocol C-5, "Hepatitis C Treatment Guidelines". There will be no further action concerning this appeal at this time.

Karen Stanforth, Assistant Chief Inspector, Medical

Ref# GCI0718000355	Housing:B60310T	Date Created:07/19/2018
ID#: A655761	Name:PASTRANO,ERIC	
Form:Appeal	Subject:Health Care	Description:Health Care
Urgent:No	Time left:n/a	Status:Closed

Original Form

7/19/2018 9:40:25 AM : (A655761) wrote

This ICR is against Dr. Douglas, Mr. Hannah, the HCA, and all the other doctors and nurses as yet unnamed at GCI involved in my medical care, Dr. Eddy and the collegial review committee members and all those involved in creating and implementing the policies over my health care. Over 6 and a half years ago I was incarcerate in Ohio and I began requesting treatment for my Hepatitis C. Until recently I was on chronic care and had a doctor visit every 6 months. Now I have been informed I will be only be seen once a year. This is a progressive disease, it's not getting betteron its own, its getting worse as time goes by. There are several successful treatments available now. I am requesting treatment for my Hepatitis C. I am being denied medical care that I need. The individuals named above and the policies they created and impose are deliberately indifferent to my medical needs and are causing me cruel and unusual punishment.

Communications / Case Actions

7/19/2018 9:40:25 AM : (A655761) wrote

Form has been submitted

7/23/2018 11:04:49 AM : (Lorie Hanko) wrote

Mr. Pastrano,

I reviewed your records. There are no signs of advanced disease noted. It is important that you follow the recommendations made by our medical team. There are specific guidelines for Hepatitis C treatment. You can refer to protocol A-6 for these guidelines.

7/23/2018 11:04:56 AM : (Lorie Hanko) wrote

Closed inmate form

7/26/2018 11:52:49 AM : (A655761) wrote

Escalated to Grievance

7/26/2018 11:52:49 AM : (A655761) wrote

Everything previously stated is incorporated herein by reference. The answer from Ms. Hanko exemplifies the problem. The DRC policy requires me to be the "ADVANCED" stage of the disease. Obviously if Im not there yet, but they are monitoring me, I will be there eventually. They are avoiding treatment because of cost. Also, by withholding treatment until I am in the "ADVANCED" stage, they virtually guarantee the treatment will be unsuccessful because all the drugs recommend treatment in the early stages. None of their "medical team" have ever given me any recommendations for anything. Ms. Hanko's answer is designed to look good on paper but it is meaningless. I need treatment for my Hepatitis C while it will be effective.

7/27/2018 9:44:20 AM : (Lloyd Brownlee) wrote

Mr. Pastrano states in his complaint that in the 6 years he has been incarcerated in Ohio he has requested treatment for his hepatitis C. Mr. Pastrano goes on to state that he was under the chronic care list and had a health visit every 6 months and that has now changed to only 1 time a year. Mr. Pastrano would like to have treatment and believes that the above mentioned actions is cruel and unusual punishment.

To investigate this complaint I have reviewed medical files. policy 68-MED-19, protocol A 6 and interviewed Mrs. Hanko. After reviewing the above mentioned information I have found that you are still being monitored for your hepatitis C and you are still under chronic care. your numbers hepatitis are based on a system that fail under the guidelines of protocol A-6 which is monitored specifically by medical staff for infectious diseases alone. It should be noted that Dr. Douglas states in medical notes that clinical status is stable with no signs of advancing disease, which is why you are now being seen once a year for said disease.

Your Grievance is denied. This ends Ref # GCI-0718000355.

7/27/2018 9:44:28 AM : (Lloyd Brownlee) wrote

Closed inmate form - Disposition: Denied

8/2/2018 12:48:23 PM : (A655761) wrote

Escalated to Appeal

8/2/2018 12:48:23 PM : (A655761) wrote

Everything previously stated is included herein by reference.

Ref# GCI0718000355	Housing:B60310T	Date Created:07/19/2018

I have not had bloodwork tested in approximately 1 year. There is no way for Dr. Douglas to even know if my disease is progressing. The Inst. Insp. is not qualified to make a medical evaluation of my condition. Because I have not seen the doctor, nobody knows the state of my Hepatitis C. The policy quoted by the isnt. insp. requires me to be in the late stages the disease before I will recieve treatment. The treatment is more effective when given in the early stages of the disease.Consequently, the policy, and policy makers, Dr. Eddy and the rest of the collegiate review committee, are substantially reducing my chances of successful treatment by delaying the care I need for financial reasons.

9/25/2018 12:07:37 PM : (karen stanforth) wrote
Affirmed.
A review of your medical file indicates you are still being monitored for your chronic disease and are being seen in CCC based on your level of control as stated in Medical Protocol A-6. Additionally,Dr. Douglas documented in your medical record your clinical status is stable with no signs of advancing disease, which is why you are now being followed once a year. There will be no further action concerning this disease at this time.
Karen Stanforth, Assistant Chief Inspector, Medical

9/25/2018 12:08:16 PM : (karen stanforth) wrote
Closed inmate form - Disposition: Affirmed with comments