A virus we can treat- treating Hepatitis C in the office

Plenary Session- McGill Refresher Course 2022

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Disclosures and Conflicts

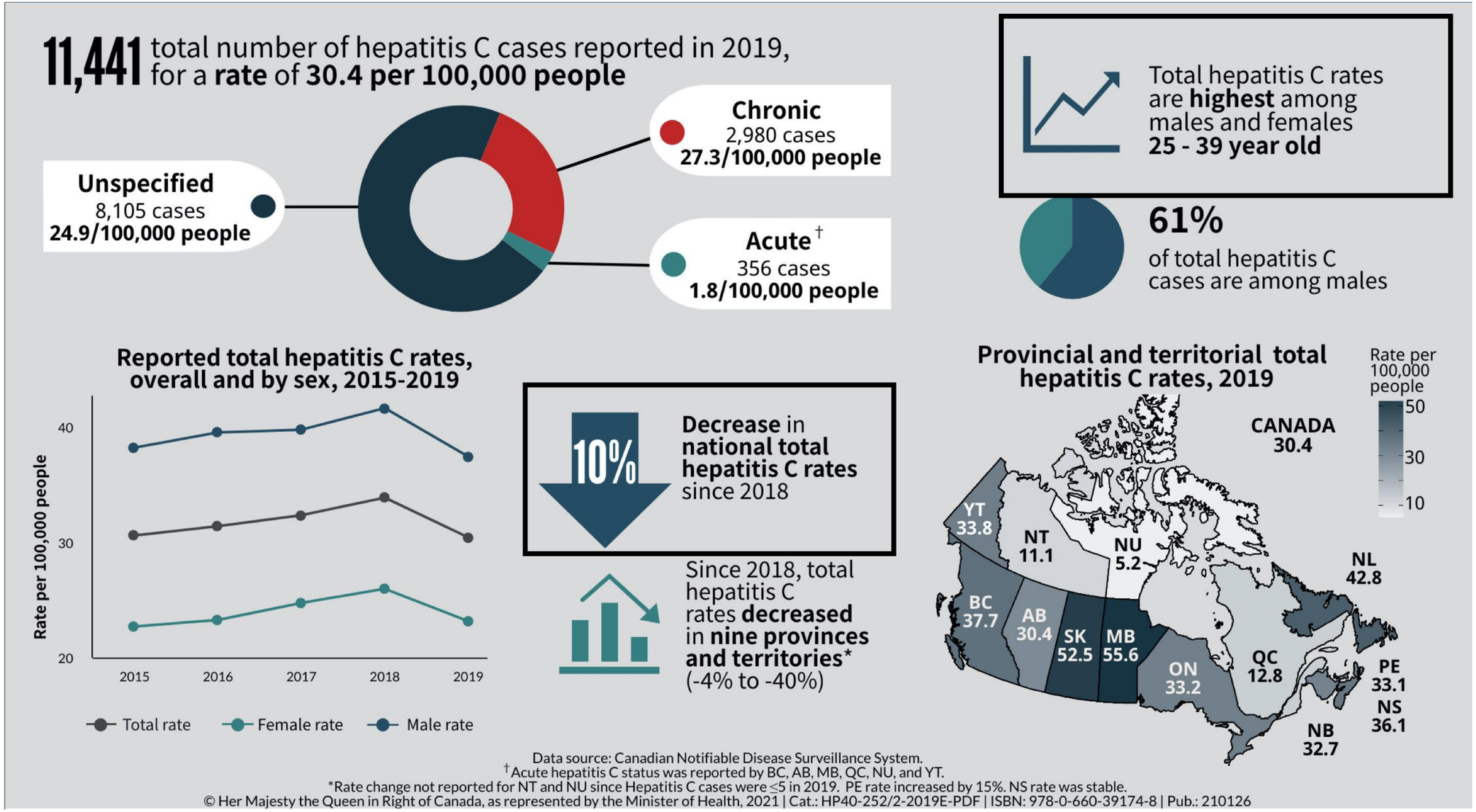
I have no disclosures to make

- I have worked with Abbvie and Gilead for Hepatitis C treatments for this patient population.
- I have worked with Indivior and participated in an advisory board for their products in May 2021.

Learning Objectives

- Able to understand the prevalence and risk factors for Hepatitis C.
- To feel comfortable screening for and diagnosing Hepatitis C.
- Review a simplified algorithm for the treatment of Hepatitis C.
- Understand post treatment care for patients with Hepatitis C.

Some statistics on Hepatitis C



Data source: Canadian Notifiable Disease Surveillance System.
†Acute hepatitis C status was reported by BC, AB, MB, QC, NU, and YT.
*Rate change not reported for NT and NU since Hepatitis C cases were ≤5 in 2019. PE rate increased by 15%. NS rate was stable.

https://www.canada.ca/content/dam/phac-aspc/documents/services/publications/diseases-conditions/hepatitis-c-2019-surveillance-data/hepatitis-c-2019-surveillance-data.pdf

Some statistics on Hepatitis C

Looking at the high risk groups

Based on national hepatitis C estimates and a few Canadian surveillance systems:

- 66.0% of people who inject drugs and 28.5% of people who formerly injected drugs were antibody positive for hepatitis C (2011).[1]
- 24.0% of federal prisoners and 23.3% of provincial prisons were antibody positive for hepatitis C (2011).[1]
- 3.0% of people living in nursing homes and long-term care hospitals were antibody positive for hepatitis C (2011).[1]
- 1.9% of people born in a country outside of Canada were antibody positive for hepatitis C (2011).[1] Data on prevalence rates among specific immigrant populations is not available; however, immigrants from countries where hepatitis C is more prevalent may have higher hepatitis C rates upon entry to Canada. Since hepatitis C testing is not done upon entry to Canada, there may be immigrants living with hepatitis C who are not aware of their infection.
- 5% of gay men and other men who have sex with men were antibody positive for hepatitis C (2005–2007).[2]
- 5% of street-involved youth were antibody positive for hepatitis C (2005-2006)[3] and 2.3% of people who are homeless (who do not inject drugs) were antibody positive for hepatitis C (2011).[1]

https://www.catie.ca/the-epidemiology-of-hepatitis-c-in-canada-0

Hepatitis C- who to screen

Canadian Task Force on Preventive Health Care

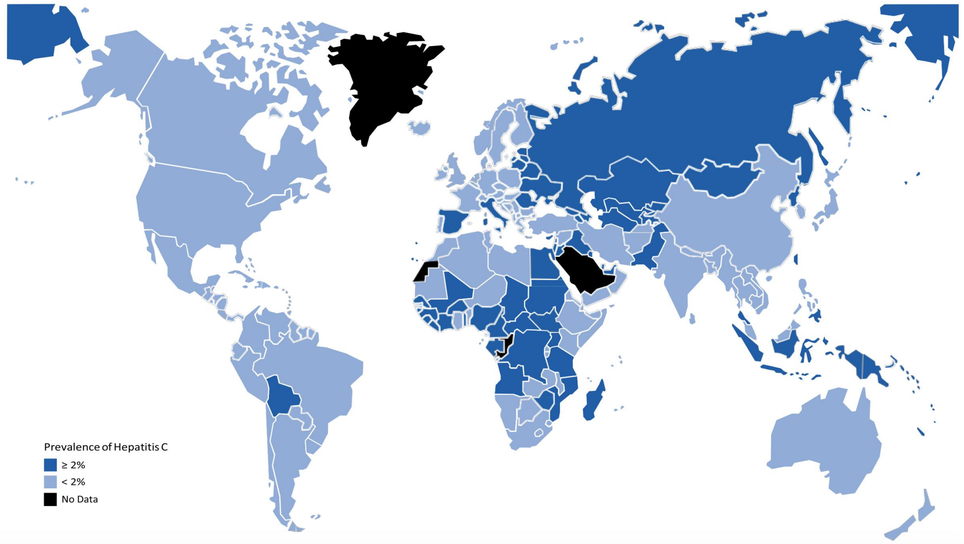
2017

Summary of recommendations for clinicians and policy-makers

We recommend against screening for HCV in adults who are not at elevated risk (strong recommendation, very low-quality evidence).

This recommendation applies only to adults who are not at elevated risk for HCV. It does not apply to pregnant women[24] or adults who are at elevated risk for hepatitis C,[14] such as:

- Individuals with current or history of injection drug use
- Individuals who have been incarcerated
- Individuals who were born, travelled or resided in HCV-endemic countries (Appendix 6)
- Individuals who have received health care where there is a lack of universal precautions
- Recipients of blood transfusions, blood products or organ transplant before 1992 in Canada
- Patients on hemodialysis
- Individuals who have had needle-stick injuries
- Individuals who have engaged in other risks sometimes associated with HCV exposure, such as high-risk sexual behaviours, homelessness, intranasal and inhalation drug use, tattooing, body piercing or sharing sharp instruments or personal hygiene materials with someone who is HCV positive
- Anyone with clinical clues suspicious for HCV infection (and above risk factors)



https://canadiantaskforce.ca/guidelines/published-guidelines/hepatitis-c/

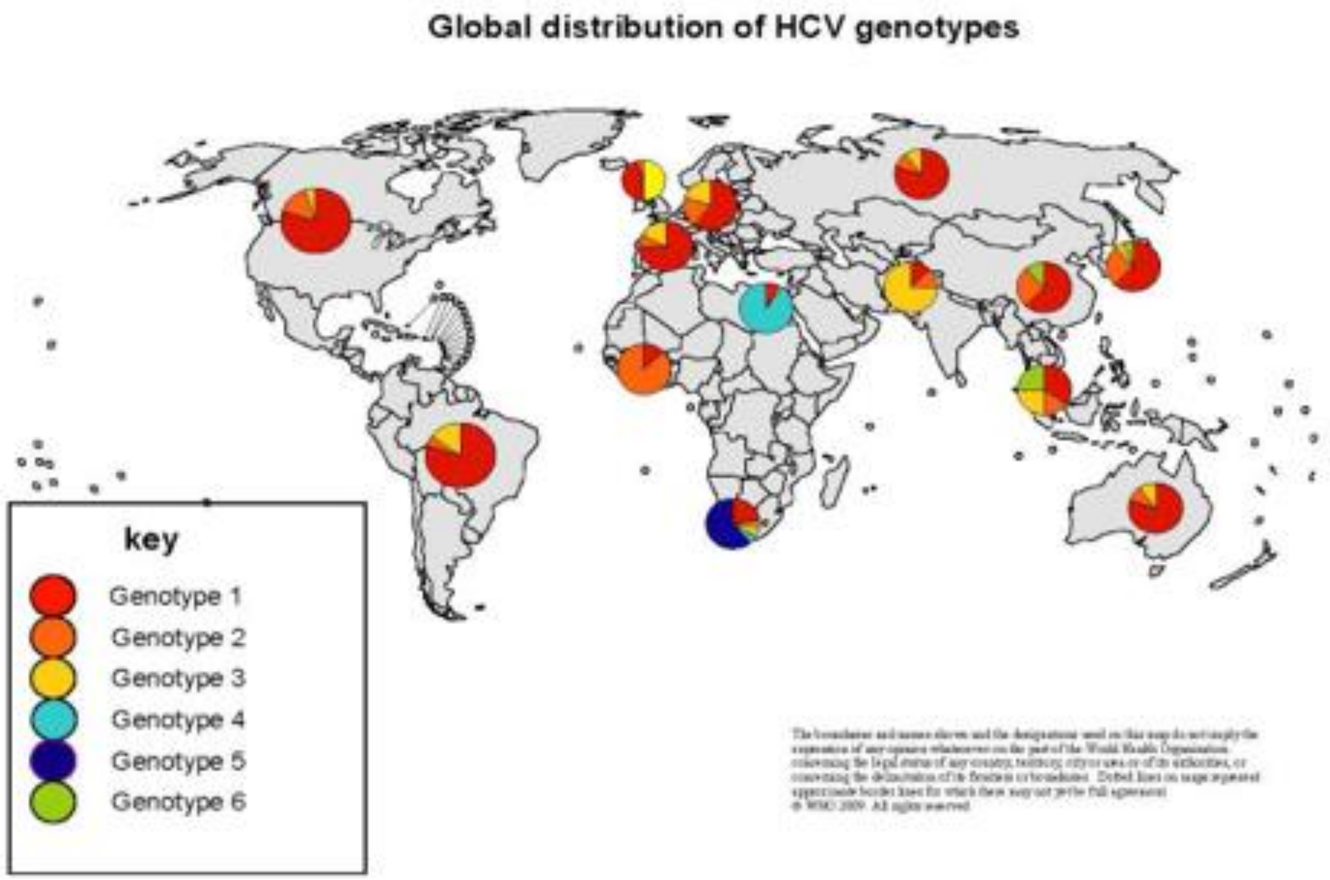
Hepatitis C- who to screen

USPSTF 2020

- Universal hepatitis C screening:
  - Hepatitis C screening at least once in a lifetime for all adults aged ≥18 years, except in settings where the prevalence of HCV infection (HCV RNA-positivity) is <0.1%
  - Hepatitis C screening for all pregnant women during each pregnancy, except in settings where the prevalence of HCV infection (HCV RNA-positivity) is <0.1%
- One-time hepatitis C testing regardless of age or setting prevalence among persons with recognized risk factors or exposures:
  - Persons with HIV
  - Persons who ever injected drugs and shared needles, syringes, or other drug preparation equipment, including those who injected once or a few times many years ago
  - Persons with selected medical conditions, including persons who ever received maintenance hemodialysis and persons with persistently abnormal ALT levels
  - Prior recipients of transfusions or organ transplants, including persons who received clotting factor concentrates produced before 1987, persons who received a transfusion of blood or blood components before July 1992, persons who received an organ transplant before July 1992, and persons who were notified that they received blood from a donor who later tested positive for HCV infection
  - Health care, emergency medical, and public safety personnel after needle sticks, sharps, or mucosal exposures to HCV-positive blood
  - Children born to mothers with HCV infection
- Routine periodic testing for persons with ongoing risk factors, while risk factors persist:
  - Persons who currently inject drugs and share needles, syringes, or other drug preparation equipment
  - Persons with selected medical conditions, including persons who ever received maintenance hemodialysis
- Any person who requests hepatitis C testing should receive it, regardless of disclosure of risk, because many persons might be reluctant to disclose stigmatizing risks

https://jamanetwork.com/journals/jama/fullarticle/2762184

Hepatitis C- the facts



Modes of transmission of Hepatitis C and symptoms:

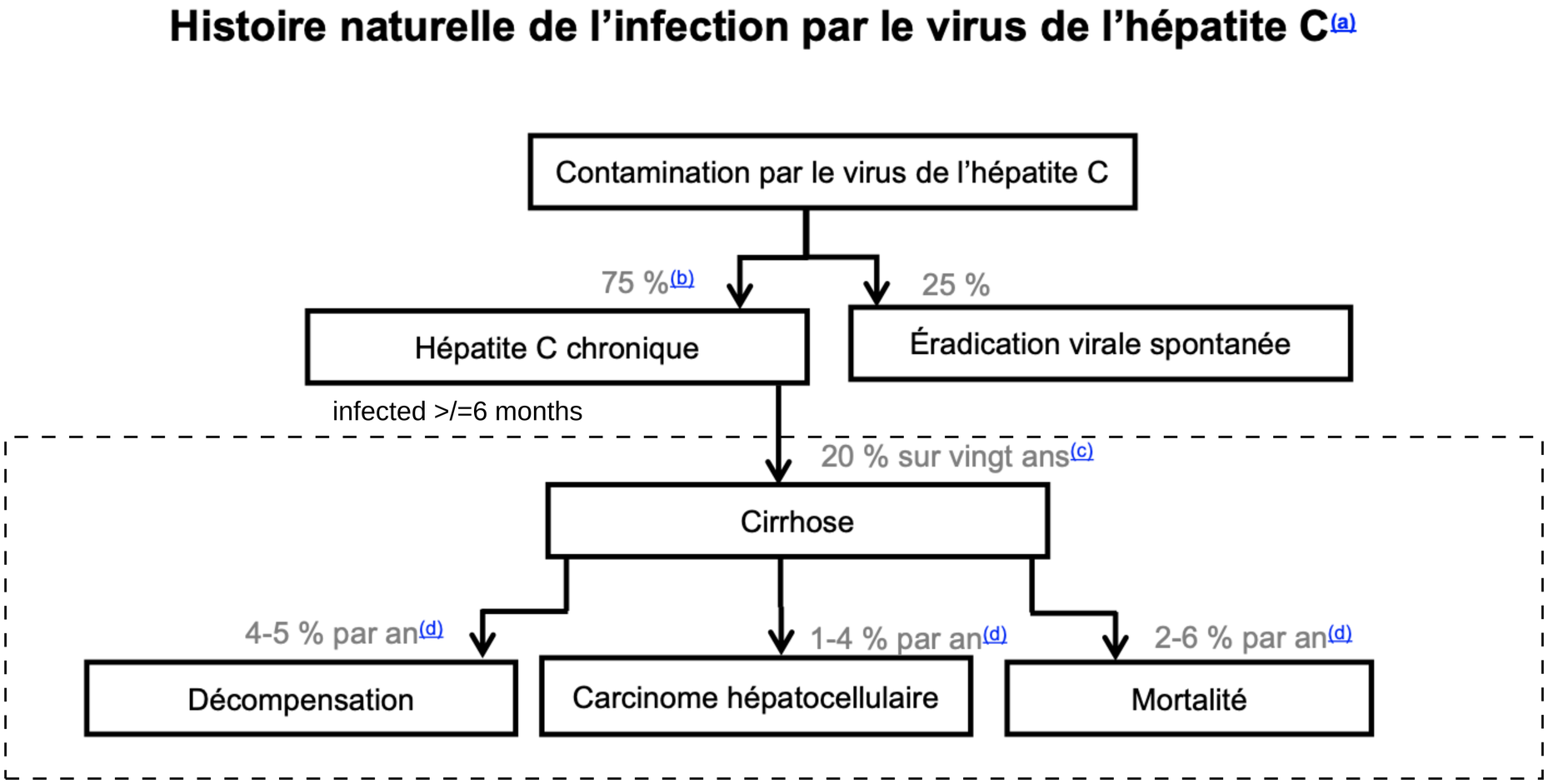
Blood contact with an infected person

Patients are often asymptomatic from Hepatitis C infection, can sometimes present with fatigue and myalgia with arthritis and of course liver issues if goes untreated for long enough**.**

Genotype 3 is associated with the fastest progression to fibrosis.

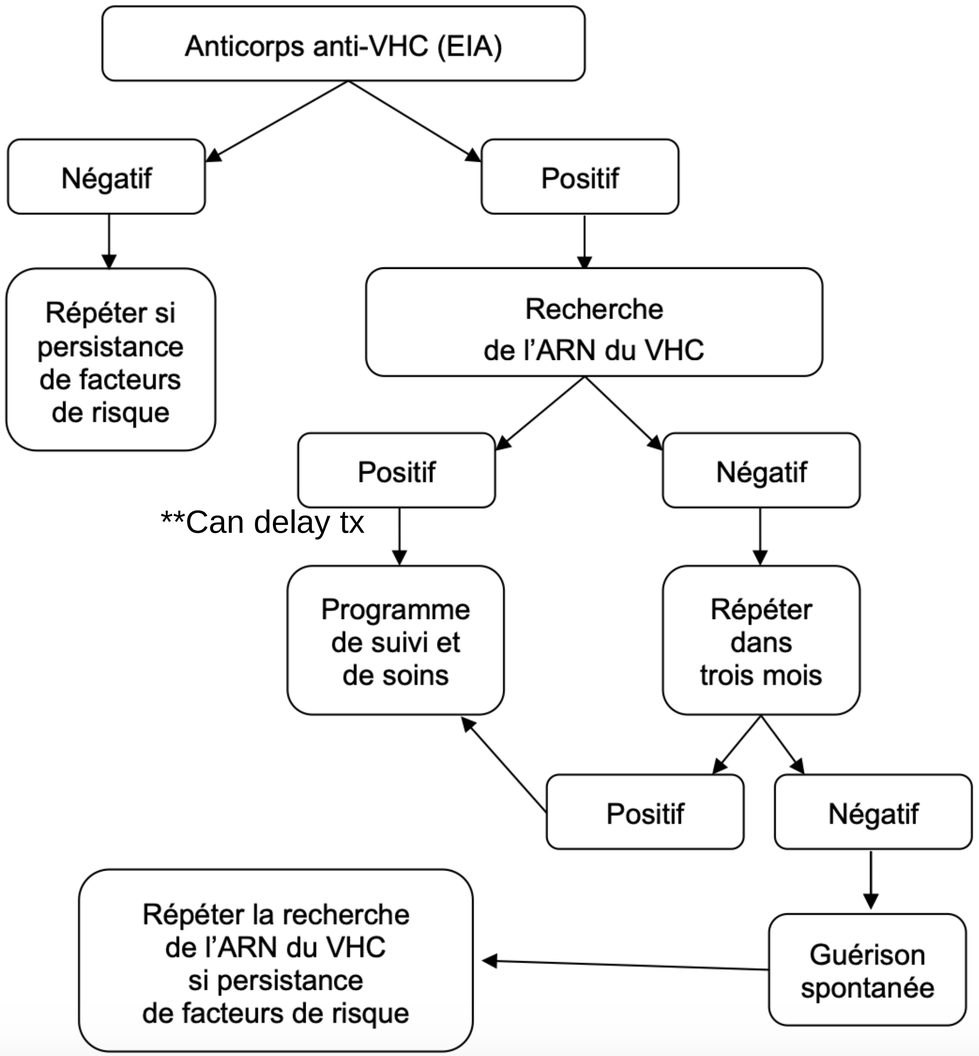
http://hepctrust.org.uk/information/about-hepatitis-c-virus/genotypes-hepatitis-c

Hepatitis C- Why treat it?

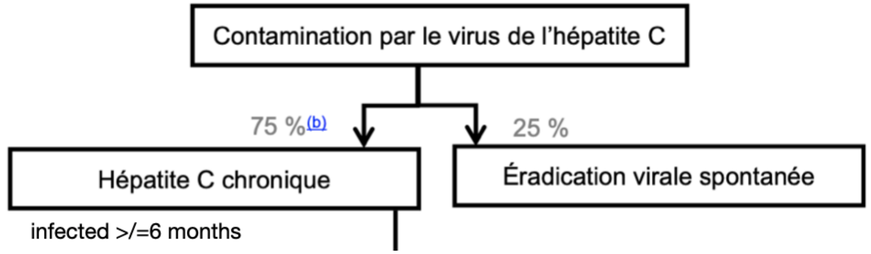


https://publications.msss.gouv.qc.ca/msss/fichiers/2022/22-267-01W.pdf

Diagnosis of Hepatitis C



Histoire naturelle de l'infection par le virus de l'hépatite C[(a)]



Hepatitis C is a reportable disease in Quebec and a MADO should be filled in.

https://publications.msss.gouv.qc.ca/msss/fichiers/2022/22-267-01W.pdf

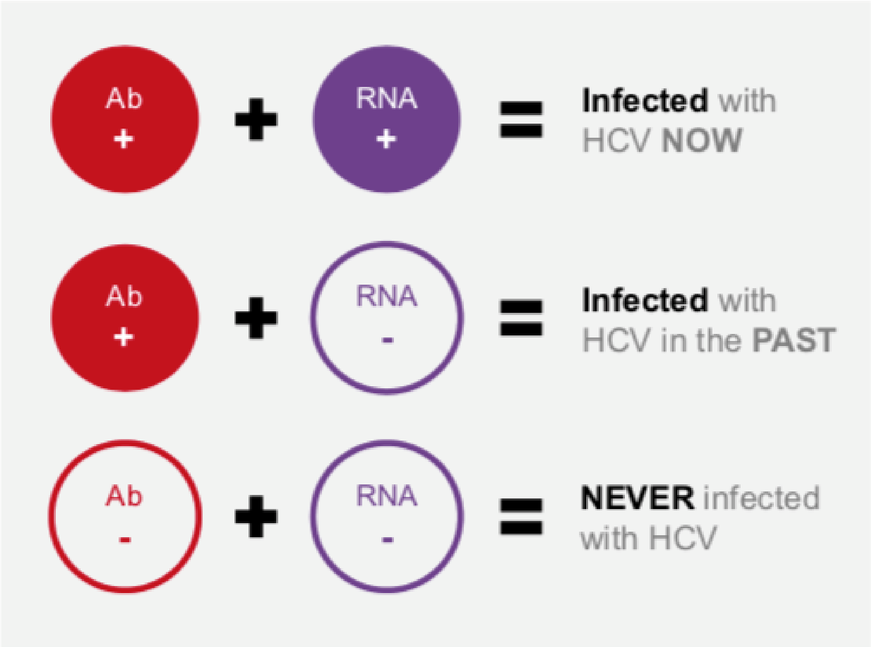
Hepatitis C- Diagnosis

Testing for Hepatitis C

There are two blood tests:

Ab
Antibody positive if EVER exposed to HCV

RNA
Viral Load present if infected with the virus NOW



Hep C Ab+ does not give the patient immunity to Hepatitis C

Hep C Ab can also be done on a capillary blood test and results present in 20-40 minus.

Window period- can be 6-12 weeks after the infection.
**Immunocompromised patients (HIV) may never develop anti Hep C Ab.

Hepatitis C- Pre treatment blood work

What needs to be ordered:
CBC
INR
albumin
creatinine
bilirubin
AST (need to include reason)
ALT
Hep B sAb
Hep B sAg
Hep B cAb
Hep A IgG
HIV
beta hcg (if woman of child bearing age)

Optional:
Genotype of HCV

EASL HCV treatment recommendations 2020

Simplified treatment algorithm

- Improving access to HCV therapy has become a worldwide priority
- When genotype/subtype determination is not available, not affordable and/or limits access, simplified treatment should be used to facilitate the cascade of care
- Groups who will benefit from a streamlined care pathway:

PWID	Prisoners	Homeless individuals	Migrants	Rural communities with poor access to care
People with mental health disorders	People with substance use disorders	MSM	Sex workers	Indigenous populations

"Pangenotypic HCV drug regimens can be used to treat individuals without identifying the HCV genotype and subtype"

Genotype/subtype determination-based algorithm

- Where available and affordable, and access to care would not be limited, genotype/subtype determination could optimise results in some groups:

GT 1b | GT 3a CC

- If sequence analysis of the NS5B coding region is available and affordable it should be performed in:

Patients born in sub-Saharan Africa, China or South-East Asia

1l | 4r | 3b | 3g | 6u | 6v

EASL CPG HCV. J Hepatol 2020; https://doi.org/10.1016/j.jhep.2020.08.018

Before starting treatment- how bad is the fibrosis?

- Can be done with biochemical values (using pre treatment blood work) and special calculators/scores.
- Can also be done with a fibroscan machine (usually done by GI).

https://bodymeasure.ca/fibroscan

Hepatitis C- fibrosis scores

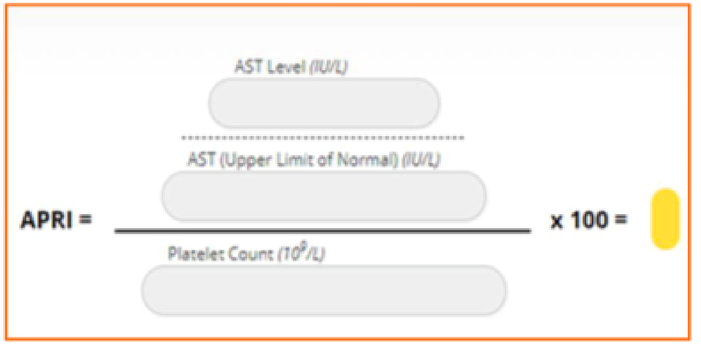
Staging Liver Disease: Diagnosing Cirrhosis

AAR (AST/ALT Ratio):

AST/ALT

APRI (AST Platelet Ratio Index) Score:

(AST/upper limit of normal)/platelet count (expressed as platelets × 10^9/L) × 100



Modified APRI Score:

[Age (y) x (AST/upper limit of normal] / [Serum albumin (g/dl) x platelet count (expressed as platelets × 10^9/L) × 100]

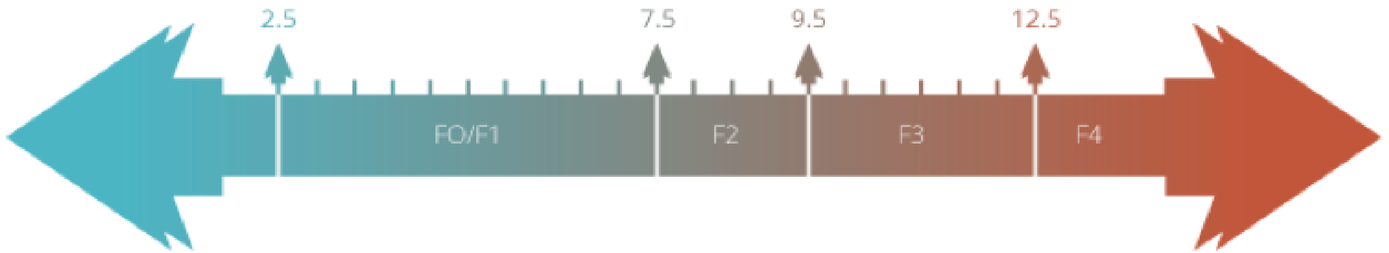
FIB-4:

Age (y) × AST (IU/l) /platelet count (×10^9/litre) ×√ALT (IU/l))

You don't need to remember these formulas - there are online calculators which make this easy!

Hepatitis C- fibroscan

The diagram below show what FibroScan® scores mean.



Score	2.5 – 7.4	7.5 – 9.4	9.5 – 12.4	> 12.5
Indicates	F0/F1	F2	F3	F4
	No/Mild fibrosis	Moderate fibrosis	Severe fibrosis	Cirrhosis
	Indicates no or minimal liver fibrosis and no evidence of progressive liver disease	Indicates significant liver fibrosis and evidence of progressive liver disease	Indicates severe liver fibrosis and high risk progression to cirrhosis	Indicates extensive liver fibrosis consistent with cirrhosis

Evaluating fibrosis (using QC guidelines)

Figure 4. Algorithme pragmatique pour la détermination du stade de la fibrose hépatique

ASSOCIER DEUX TESTS NON INVASIFS D'ÉVALUATION DE LA FIBROSE[90]

- **Associer FibroScan® ET un test biologique de fibrose (approche idéale)**

OU

- **Associer deux tests biologiques de fibrose, soit APRI ET Fib-4 (approche pragmatique)**

  •APRI < 1 ET Fib-4 < 1,45 → **FibroScan® non nécessaire**

N.B. Lorsque le contexte est particulièrement propice à l'instauration d'un traitement antiviral, un score APRI < 1 OU un score Fib-4 < 1,45 permet d'exclure une cirrhose du foie avec une bonne valeur prédictive négative. Ce traitement pourra commencer sans délai et un FibroScan® n'est alors pas nécessaire.

https://publications.msss.gouv.qc.ca/msss/fichiers/2022/22-267-01W.pdf

Hepatitis C- when to refer patients

When to Refer Patients to a Specialist

- Patients with **advanced fibrosis or cirrhosis** FIB4 > 1.45 AND APRI>1
- Patients with **extrahepatic manifestations**
- Patients with **complex co-morbidities**
- Patients with **renal impairment**
- Patients with **HIV/HCV or HBV/HCV coinfection**
- Patients who **failed first line DAA**

Hepatitis C- Treatment with DAAs

- Highly effective and have a cure rate of greater than 95%.

Genotype	Regimen	Dose	Duration of Treatment	Pills per Day	Administration
All	GLE/PIB (Maviret®)	100/40 mg	8-16 weeks	3	With food
All	SOF/VEL (Epclusa®)	400/100 mg	12 weeks	1	
1, 4, 5, 6	SOF/LDV (Harvoni®)	90/400 mg	8-24 weeks	1	**Need genotype and viral load

All of these medications are medicament d'exception for RAMQ. Very easy to get approved.

How to check drug interactions

IMM de SOF/VEL et GLE/PIB

Liverpool Website-
https://www.hep-druginteractions.org/checker

	Epclusa	Maviret
	SOF/VEL	**GLE/PIB**
Statines		
Atorvastatine		
Simvastatine		
Pravastatine		
Rosuvastatine		
Agents anti-VIH		
Atazanavir		
Darunavir		
Ritonavir		
Éfavirenz		
TAF		
Médicaments contenant de l'éthinylestradiol		
Amiodarone		

	Epclusa	Maviret
	SOF/VEL	**GLE/PIB**
Agents acidoréducteurs		
Antiacides		
Antagonistes du récepteur H_2		
IPP		
Immunodépresseurs		
Cyclosporine		
Tacrolimus		
Azathioprine		
Mycophénolate		

Aucune interaction

Interaction possible

Faible interaction possible

Non recommandé

IPP : inhibiteurs de la pompe à protons; TAF : ténofovir alafénamide

Université de Liverpool, www.hep-druginteractions.org (en anglais seulement)

Side effects of DAA (direct acting antiviral) medications

- Biggest side effects: headache, fatigue, nausea and GI issues. Can also have rashes and itchy skin. Usually these side effects decrease or go away within a couple of weeks.

- Although usually very well tolerated.

Hepatitis C treatment- old and new

Advances in HCV Therapeutics

	Past therapy: Peg Interferon+Ribavirin	Current therapy: Direct Acting Antivirals (DAAs) - Interferon Free
Efficacy	40-80%	**>95%**
Dosing	Injection (weekly) + oral (daily)	**Oral (daily)**
Toxicity	Significant	**Minimal**
Duration	24-48 weeks	**8-16 weeks**
Uptake	Low	**High**

During treatment- no real follow up needed

This can be a telemedicine visit to ensure there are no side effects or that there is good compliance.

Tableau 7. Suivi du patient durant et après un traitement par agents antiviraux à action directe[a]

	PRÉ-TRAITEMENT	DURANT LE TRAITEMENT[b]			POST-TRAITEMENT	
	Dans les 12 semaines précédant le Tx	Sem. 2	Sem. 4	Chaque mois jusqu'à la fin du Tx	4 sem. post-Tx	12 sem. post-Tx
FSC	X	Si RBV	Si RBV ou PRN[c]	Si RBV ou PRN[c]	Si RBV ou PRN[c]	PRN[c]
RNI[b], [d]	X		PRN[c]	PRN[c]	PRN[c]	PRN[c]
Bilirubine totale et libre[b]	X		PRN[c]	PRN[c]	PRN[c]	PRN[c]
AST	X		PRN[c]	PRN[c]	PRN[c]	PRN[c]
ALT[b]	X		PRN[c]	PRN[c]	PRN[c]	X
P. alc[b]	X		PRN[c]	PRN[c]	PRN[c]	PRN[c]
Albumine	X		PRN[c]	PRN[c]	PRN[c]	PRN[c]
Débit de filtration glomérulaire estimé	X		PRN[c]	PRN[c]	PRN[c]	PRN[c]
Créatinine	X		PRN[c]	PRN[c]	PRN[c]	PRN[c]
Test de grossesse chez la femme en âge de procréer	X		Si RBV	Si RBV	Si RBV	Si RBV
ARN du VHC quantitatif	X		Optionnel[e]			X[f]
ADN du VHB			PRN[g]	PRN[g]	PRN[g]	PRN[g]
Visite clinique	PRN[h]		X	PRN[i]	PRN[i]	X

***Theoretical risk of reactivation of Hep B on HCV treatment. Hep B cAb +, LFTs needed once per month on treatment.

https://publications.msss.gouv.qc.ca/msss/fichiers/2022/22-267-01W.pdf

After treatment

- A 12 week post treatment SVR (sustained virology response) is needed to ensure clearance of the virus. You need to order a viral RNA to make sure it is negative.
- It is also recommended to do an ALT value at this time.

Hepatitis C- Post treatment

Hepatitis A and hepatitis B vaccination responses in persons with chronic hepatitis C infections: A review of the evidence and current recommendations

Jane A Buxton, MBBS MHSc[1,2] and Jin Hee Kim, MD BSc[1]

- They should get Hepatitis A and B vaccines if needed.They should have their immunity checked after getting the complete Hepatitis vaccines. Should also be up to date on pneumococcal and influenza vaccines.

- If patient is continuing to engage in high risk behaviour, they need to be retested q3-6 months. Remember to write on the requisition that they will be Hep C Ab positive and that you need the RNA.

- If they are considered to have cirrhosis, they need U/S q6 months with AFP blood work. They should be followed by GI for gastroscopy and esophageal varices prophylaxis.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2605862/

Counselling for patients with Hepatitis C

CONSEILS À DONNER AUX PERSONNES ATTEINTES D'UNE CIRRHOSE HÉPATIQUE

La meilleure prévention des complications de la cirrhose est d'en corriger durablement les causes : hépatites virales B et C, abus d'alcool, obésité et syndrome métabolique.

HABITUDES DE VIE

- Éviter la consommation d'alcool, de drogue et de tabac.
- Adopter des pratiques de consommation de drogue sécuritaires afin de prévenir une réinfection virale.
- Maintenir un poids santé idéal (indice de masse corporelle de 20-25 kg/m^2) et un tour de taille idéal (femme : < 88 cm ; homme : < 102 cm).

ALIMENTATION

- Pas de restriction protéique.
- S'assurer un apport de protéines de 1,2 à 1,5 g/kg/jour.
- Prendre une collation protéinée avant le coucher (fromage, noix, etc…).
- Déjeuner dès le lever.
- Pas de restriction hydrique.
- Si inappétence : prendre des petits repas fréquemment, des suppléments oraux (Boost®, Ensure®).
- Si ascite : suivre une diète pauvre en sel (cuisiner sans sel, éviter les mets préparés commerciaux).

VACCINATION

- Référer à une infirmière en vaccination adulte en CLSC pour « mise à jour vaccination chez patient avec cirrhose ».
- Vacciner contre l'hépatite A (vaccin monovalent contre l'hépatite A) si non réalisée antérieurement.
- Faire vérifier son immunité contre l'hépatite B (anti-HBs > 10 UI/mL) et vacciner selon résultats (vaccin monovalent contre l'hépatite B).
- Se faire vacciner une fois contre les infections à pneumocoque (Pneumovax® et Prevnar®).
- Se faire vacciner contre l'influenza chaque année.

MÉDICATION

Éviter

- Anti-inflammatoires non stéroïdiens (AINS) : risque de néphrotoxicité et de saignement gastro-intestinal.
- Inhibiteurs de l'enzyme de conversion de l'angiotensine (IECA) et bloqueurs des récepteurs de l'angiotensine (BRA) : risque de néphrotoxicité.

Faire attention

- Benzodiazépines, opiacés, qui peuvent précipiter l'encéphalopathie hépatique ;
- Inhibiteurs de la pompe à protons (IPP), dont l'indication doit être vérifiée régulièrement ;
- Antidépresseurs, dont la dose initiale et la dose maximale doivent être réduites de 50 %.

Prendre au besoin, sans dépasser la dose sécuritaire

- Acétaminophène : de 2 à 3 grammes par jour.

- Treat HIV and HBV if present.
- Pregnancy counselling.
- Education about spread of the virus and re infection risk.

https://publications.msss.gouv.qc.ca/msss/fichiers/2022/22-267-01W.pdf

Summary of Hepatitis C diagnosis and treatment

VISIT 1

Screen as per guidelines and risk factors with Hep C Ab

Hep C Ab + → order RNA → VISIT 2 (depending on centre) Hep C Ab positive and RNA positive

VISIT 3

Pre treatment blood work (do not need genotype)

Calculate FIB4 and APRI score

If FIB4< 1.45 **OR** APRI<1

NO → If fibrosis is suspicious, refer for fibroscan and likely treatment by a specialist

VISIT 4

Choose treatment Maviret or Epclusa (patients choice).
Apply for med exception.

optional VISIT

VISIT 5

SVR at 12 weeks post treatment with ALT

Vaccination and counselling. Screen q3-6 months based on risk factors for reinfection

Take home points and conclusions

- Screening for Hepatitis C should be done in the population with risk factors as needed.
- Hepatitis C treatment is effective, well tolerated and simple.
- Post treatment care and counselling is important to prevent re infection.

Questions and comments

- You can also contact me at vanessa.pasztor@mail.mcgill.ca

Bibliography

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