

# The Liver



Dr Fiona H Gordon  
Janki Jethwa

# A Day in the Life...



# Learning Outcomes

- Review the physiology of the liver.
- Understand the effects of alcohol on the liver.
- Learn how hepatitis c affects the liver.
- Consider how community pharmacists can help these patients.

# The Liver

- Largest gland, and largest solid organ, in the body.
- Holds approximately 13% of your total blood supply and has over 500 functions (glucose metabolism, protein metabolism, fat metabolism, vitamin and iron storage, drug metabolism, etc.).
- Blood supply via the hepatic artery and the portal vein.
- Divided into two main lobes (larger right, smaller left) which is further subdivided into lobules.
- 60% of the liver make up of hepatocytes.

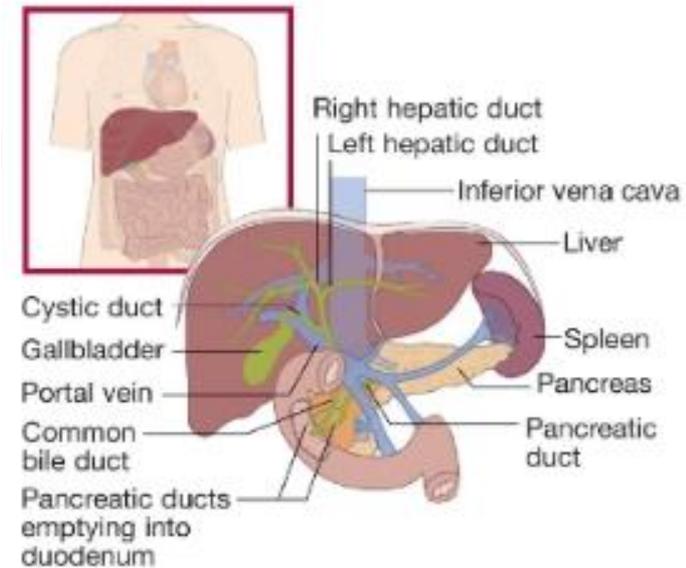
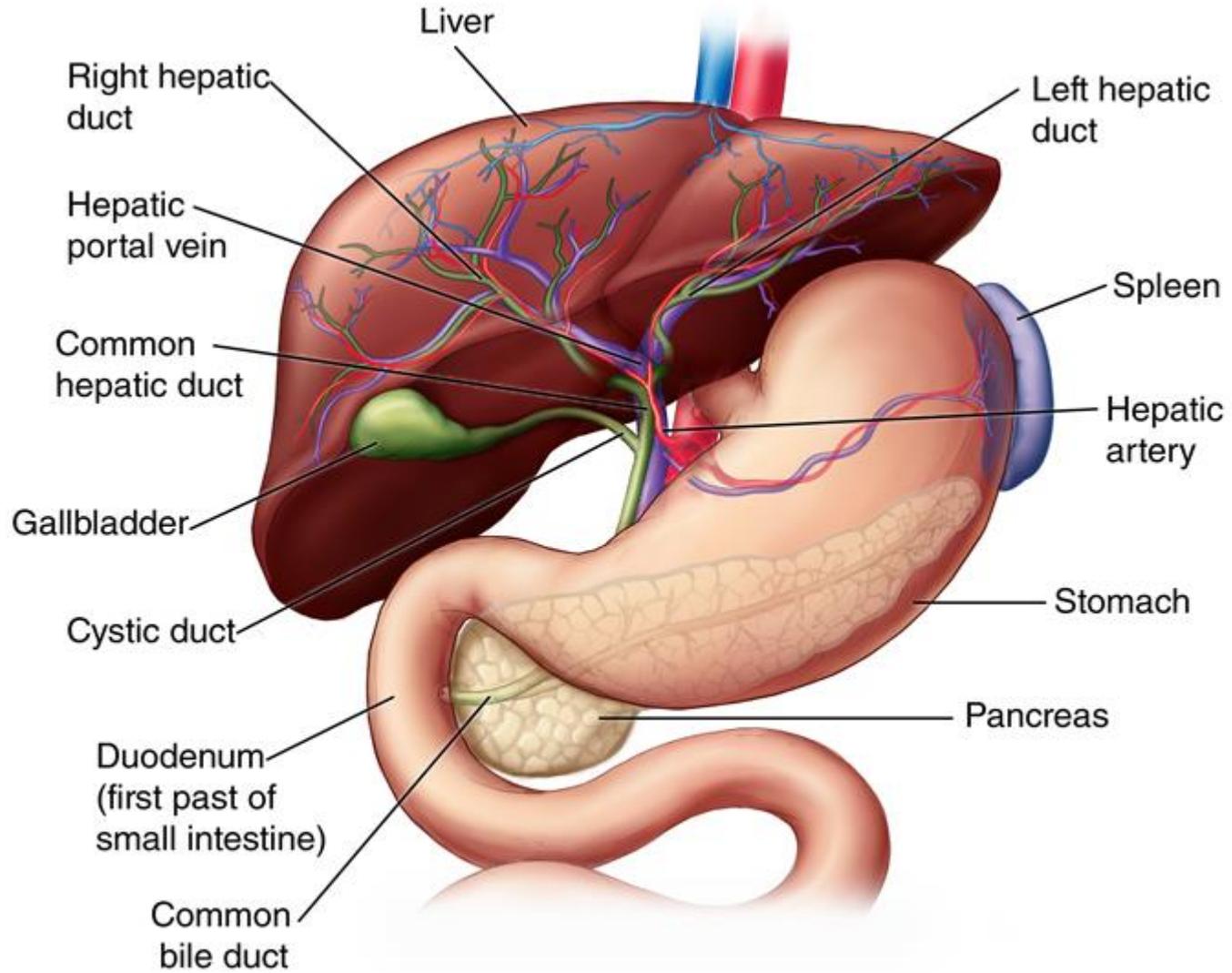
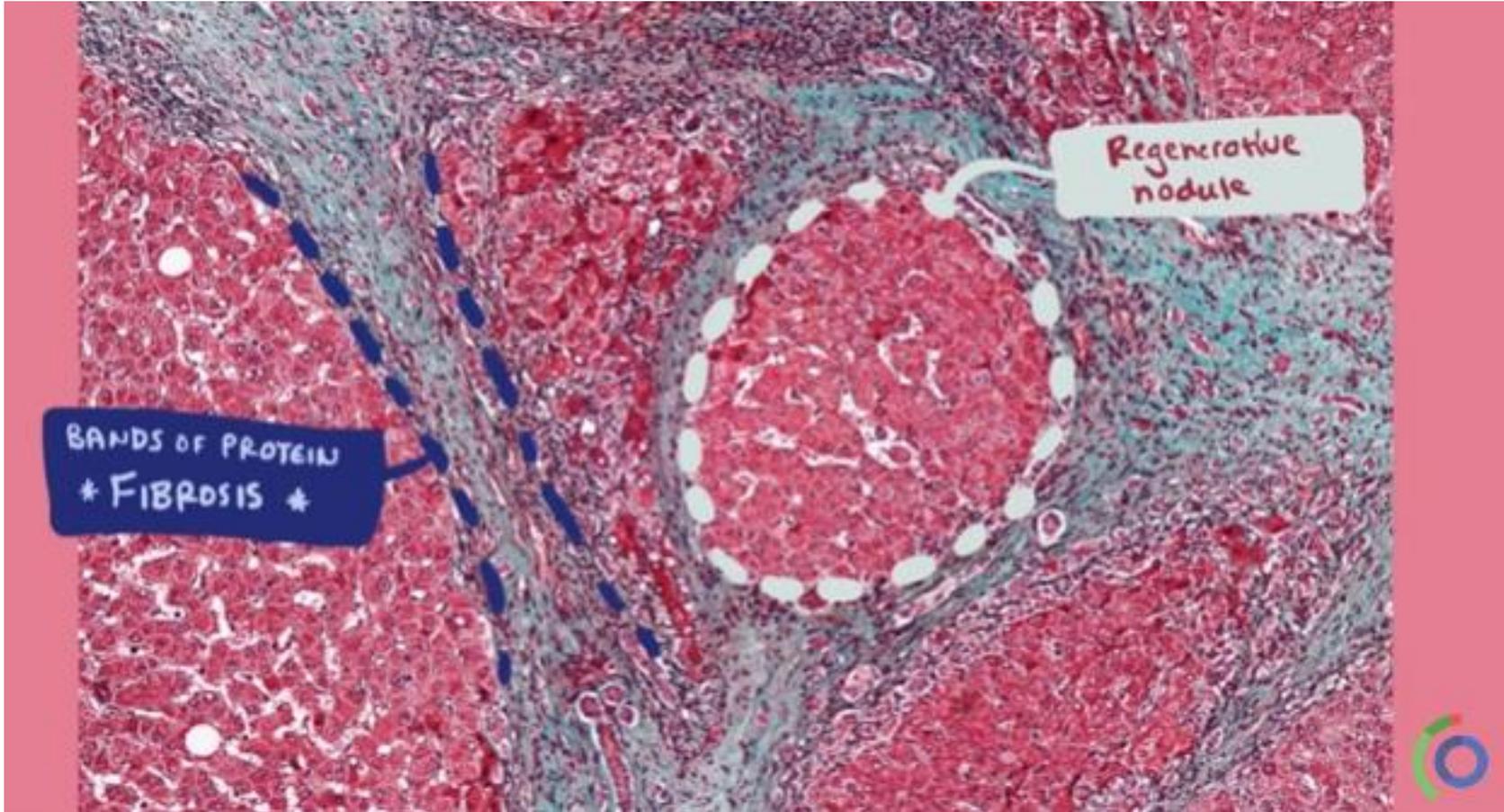


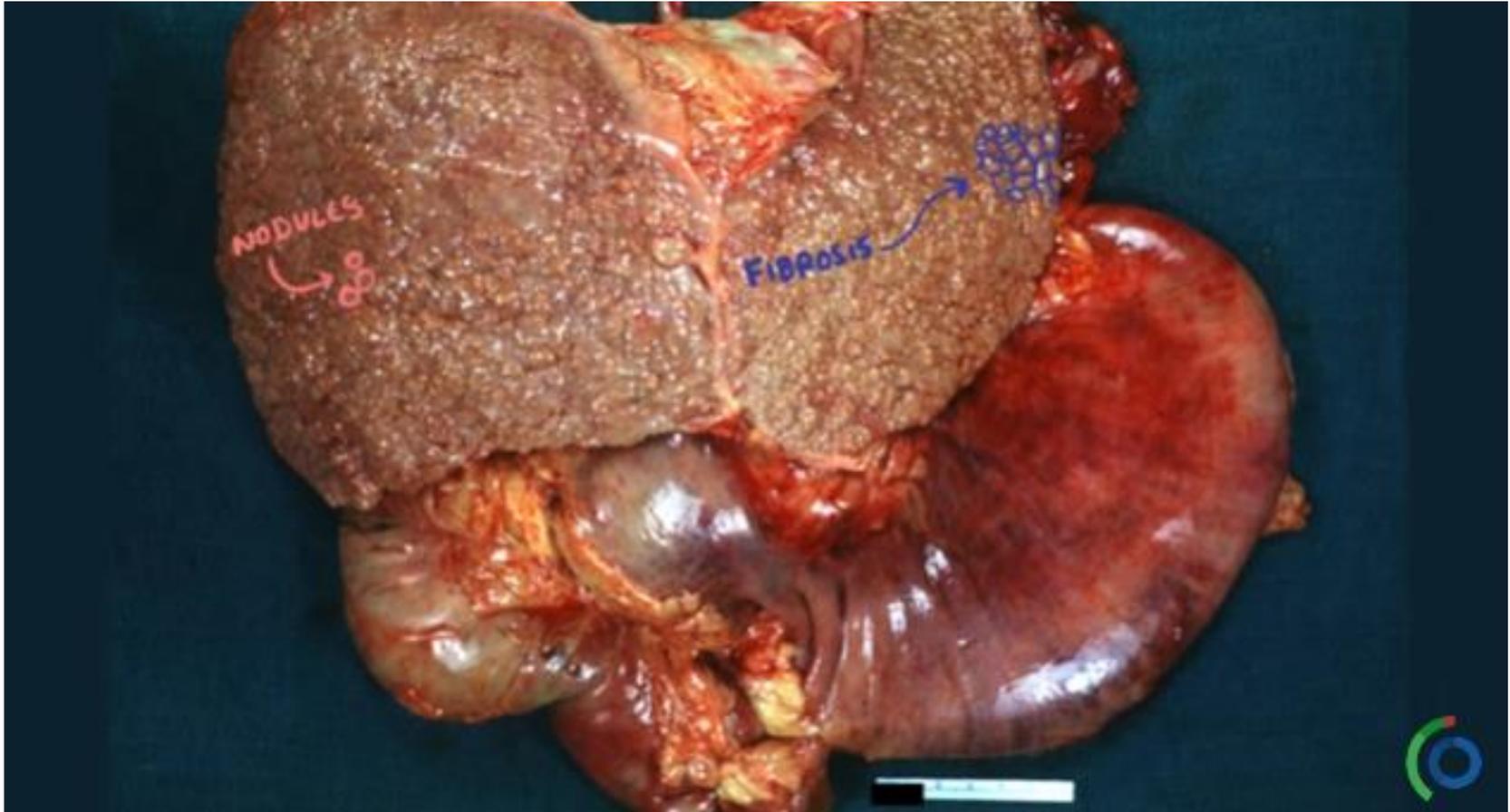
Image from: [www.britishlivertrust.org.uk](http://www.britishlivertrust.org.uk)



# Liver Cirrhosis

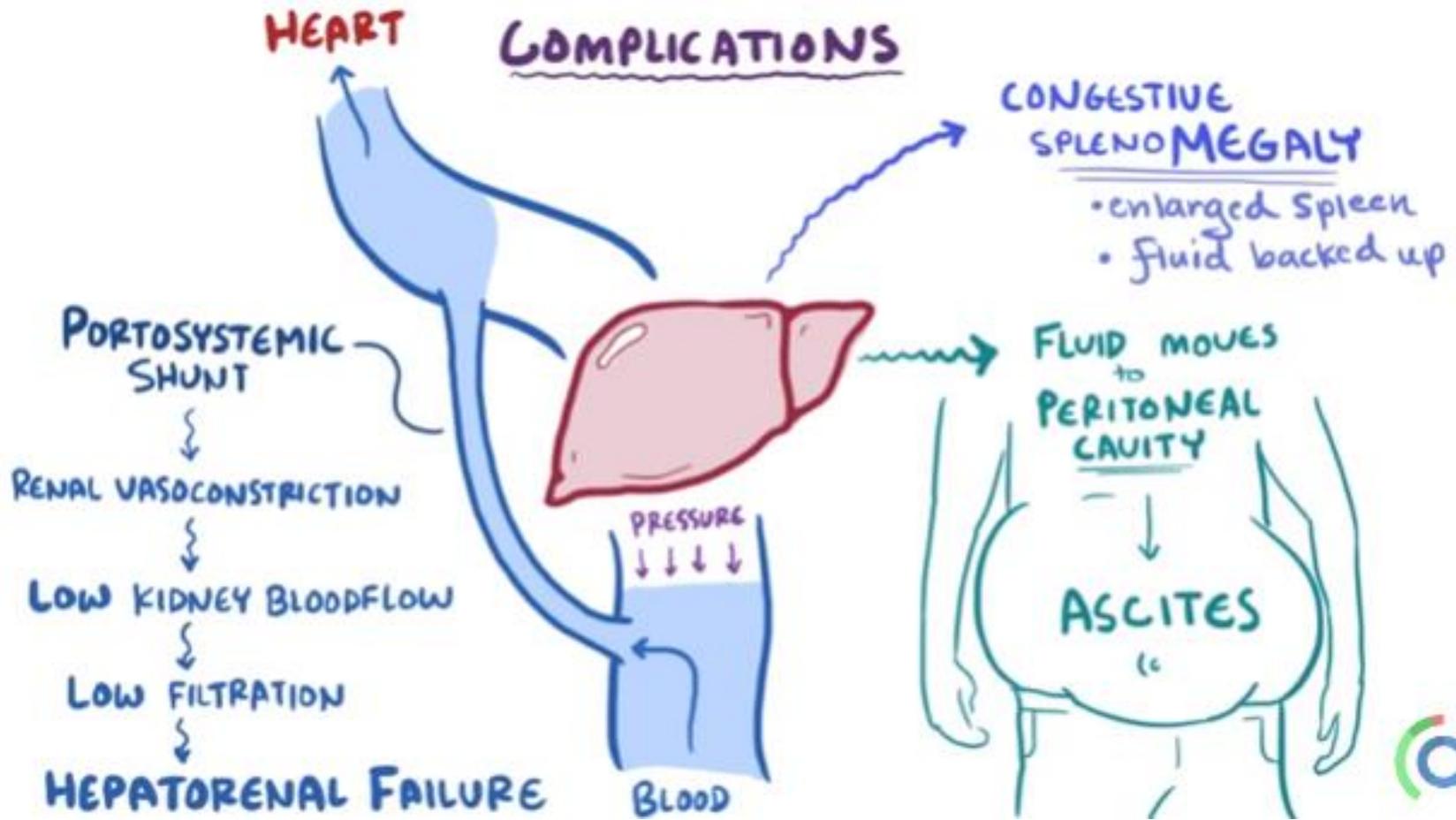
- Functioning hepatocytes become non-functioning stellate cells making collagen.
- Main causes: alcohol, viral, fatty liver disease.
- Sometimes referred to as 'end-stage' liver damage.
- Can be reversed!





# Complications of cirrhosis

- Portal hypertension (high pressure in portal veins)
  - Bleeding varices
  - Ascites
  - Splenomegaly, portosystemic shunt
- Synthetic problems: jaundice, coagulation
- Hepatic encephalopathy
- Hepatoma (hepatocellular carcinoma; HCC)
- Compensated or decompensated



## SYMPTOMS

### \* EARLY ~ SOME FIBROSIS

- └ ASYMPTOMATIC

- └ NON-SPECIFIC

e.g. weight loss, weakness, fatigue

### \* LATER ~ EXTENSIVE FIBROSIS

- └ JAUNDICE & PRURITUS  
(ITCHY SKIN)

- └ ASCITES

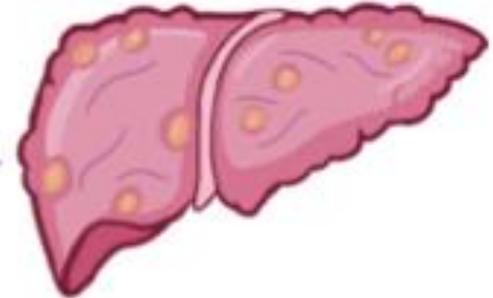
- └ HEPATIC ENCEPHALOPATHY

  - ↳ CONFUSION

- └ EASY BRUISING

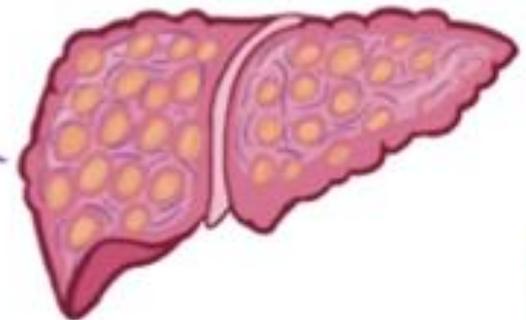
### COMPENSATED

\* STILL DOES ITS JOB \*



### DECOMPENSATED

\* CAN'T FUNCTION \*



# Detecting Cirrhosis

- Blood tests
  - LFTs, Child–Pugh score, Fib4
- Fibroscan
- Ultrasound – not commonly used for Hepatitis C
- Biopsy – to diagnose HCC

# Fibroscan

- Measures liver elastography.
- Propagates a shear wave.
- Measures the velocity of its propagation across liver.



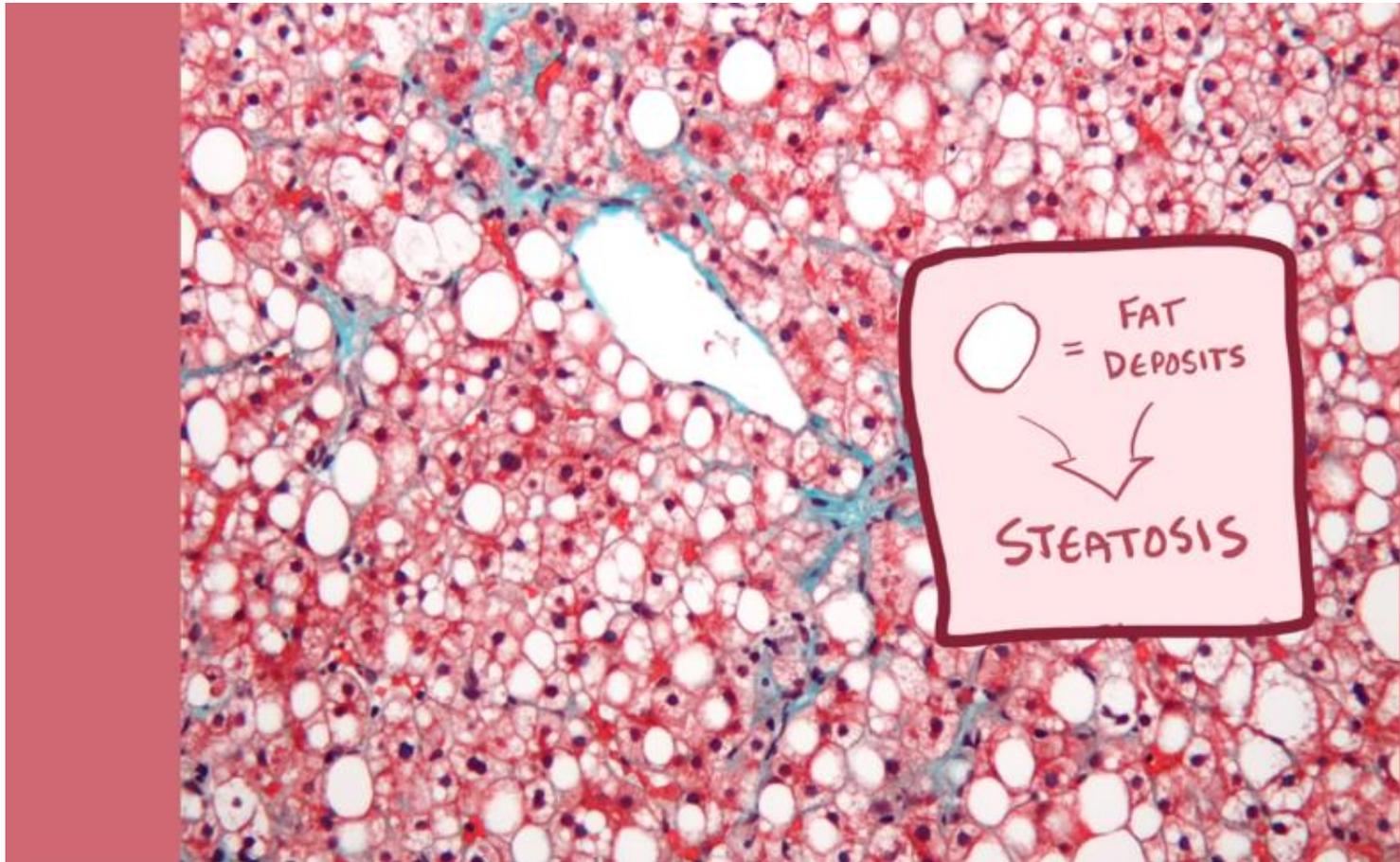
# Alcohol

- Linked to various cancers, GI disease, metabolic problems.
- Physical and emotional problems – dependence and withdrawal.

# Effects of Alcohol on the Liver

- The metabolism of alcohol in the hepatocytes leads to
  - An increase in fat production – steatosis – fatty liver disease.
  - Destruction of hepatocytes by neutrophilic infiltration.
- Alcoholic hepatitis.
- Hepatomegaly, neutrophilic leukocytosis (increased neutrophils in the blood), elevated LFTs.

# Fatty Liver Disease

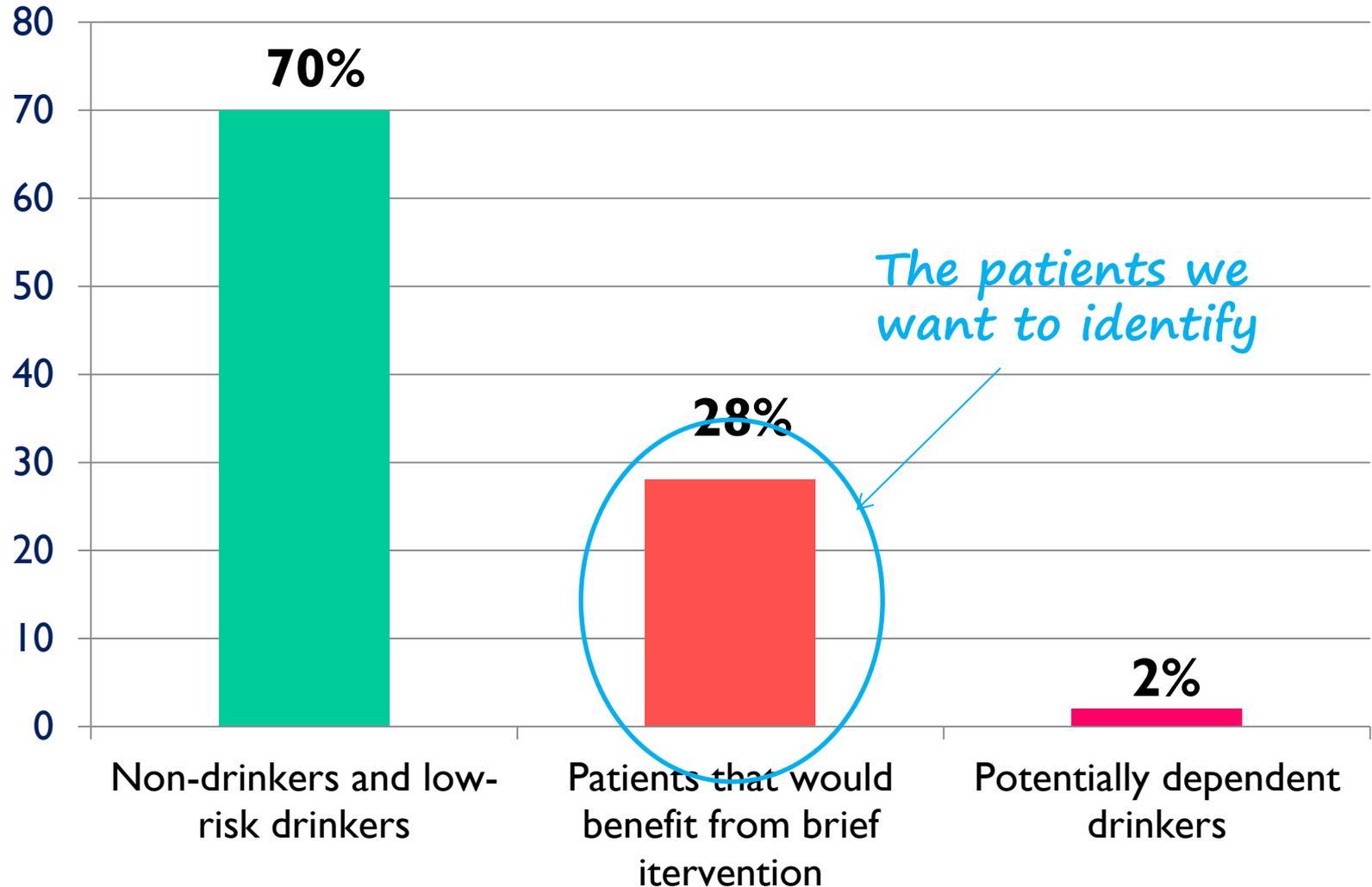




## Each year

- Harmful alcohol consumption costs the NHS an estimated £3.5 billion
- Alcohol contributes to around 1 million hospital admissions
- Alcohol consumption is responsible for an estimated 23,000 premature deaths

## Proportions of the population by level of risk of health harm from alcohol





**8.6  
million**

drinking at  
increasing risk

**1.8  
million**

drinking at  
higher risk

## **INCREASING RISK**

is defined as  
drinking  
14-35 units a week  
for Women  
and  
14-50 units a week  
for men

## **HIGHER RISK**

is defined as  
drinking  
>35 units a week  
for women  
and  
>50 units a week  
for men

# Understanding Units of Alcohol

The formula for calculating units is: 
$$\frac{\text{Volume (in ml)} \times \% \text{ abv}}{1000}$$



# Blood-Alcohol Concentrations

- 0.0% - 0.05%
  - Feeling relaxed and happy
  - Slurred speech
  - Some difficulty with co-ordination and balance
- 0.06% - 0.15%
  - More impairment in speech, memory, attention and co-ordination
  - More aggression and violence
  - Complex tasks become dangerous – illegal to drive if over 0.08%
- 0.16% - 0.3%
  - Alcohol poisoning – amnesia, vomiting, loss of consciousness.

# SYMPTOMS of WITHDRAWAL

- \* ANXIETY
- \* DEPRESSION
- \* IRRITABILITY
- \* FATIGUE
- \* TREMORS
- \* PALPITATIONS
- \* CLAMMY SKIN
- \* DILATED PUPILS
- \* SWEATING
- \* HEADACHES
- \* DIFFICULTY SLEEPING
- \* VOMITING
- \* SEIZURES

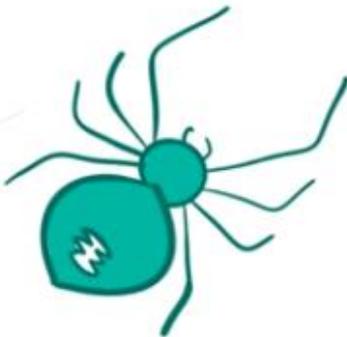
## SYMPTOMS of WITHDRAWAL

a severe complication

### ↳ DELIRIUM TREMENS

- ↳ start a FEW DAYS in
- ↳ HIGH FEVER
- ↳ INTENSE AGITATION
- ↳ visual HALLUCINATIONS
- ↳ tactile HALLUCINATIONS

↳ SYMPTOMS can be DEADLY



# Giving Brief Advice

- ASK
- ADVISE
- REFER
- NICE recommend opportunistically carrying out screening and brief interventions for hazardous and harmful drinking should be an integral part of practice. (QSI I)



**Giving Brief Advice**




## AUDIT-C

### Scoring System<sup>1-4</sup>



How often do you have a drink containing alcohol?	NEVER	MONTHLY OR LESS	2-4 TIMES PER MONTH	2-3 TIMES PER WEEK	4+ TIMES PER WEEK
How many units of alcohol do you drink on a typical day when you are drinking?	1-2	3-4	5-6	7-9	10+
How often have you had 6 or more units if female, or 8 or more if male, on a single occasion in last year?	NEVER	LESS THAN MONTHLY	MONTHLY	WEEKLY	DAILY OR ALMOST DAILY

Name: \_\_\_\_\_

KYOWA KIRIN

# Giving Brief Advice

0-4

## Lower Risk

Congratulate patient on benefits of lower level drinking.

5+

## Increasing to Higher Risk

Give Brief advice to ALL patients drinking above low limits.

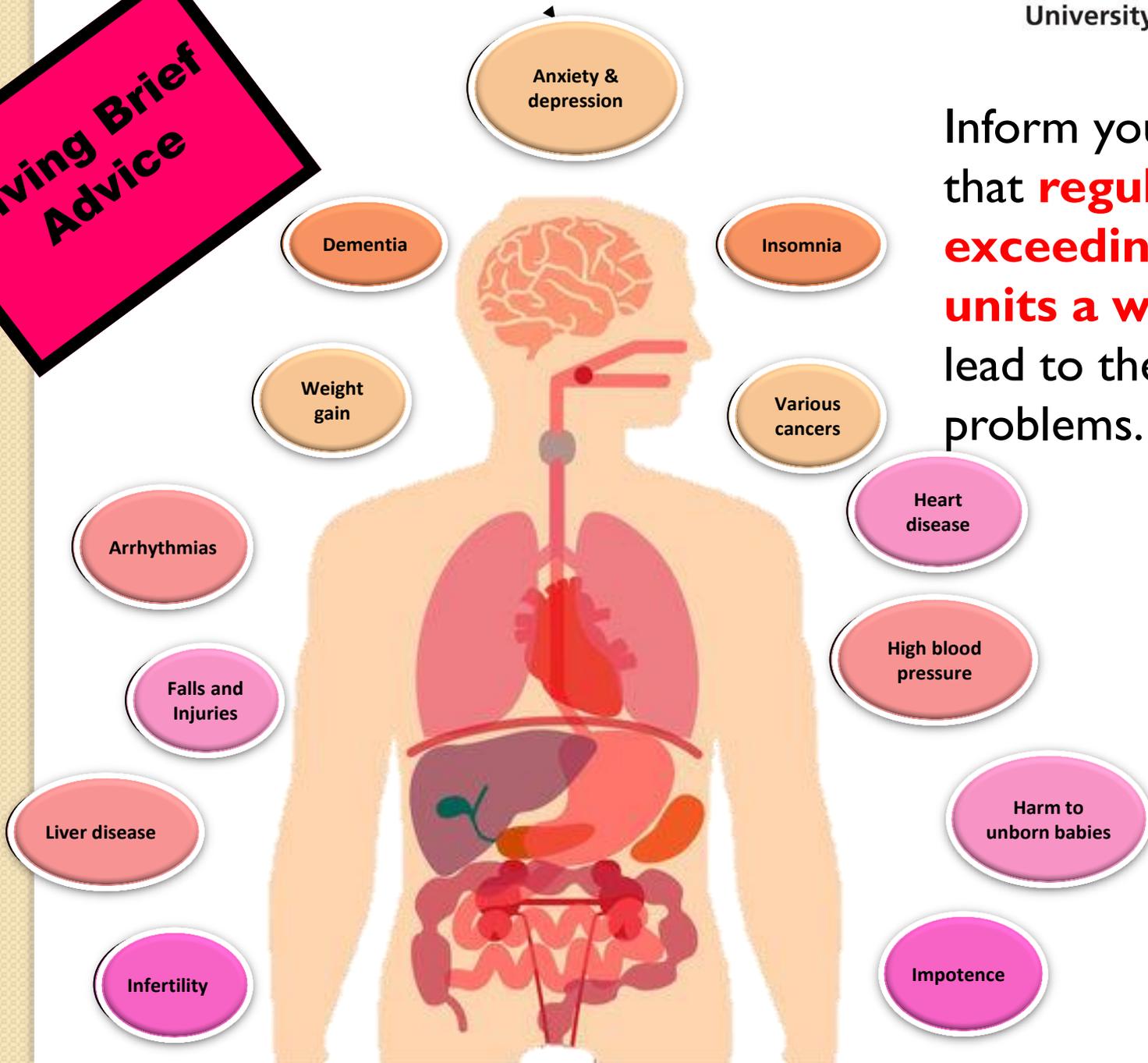
11-12

## Possible Dependence,

Do not advise to stop drinking without medical supervision. Refer to GP.

**Giving Brief Advice**

Inform your patient that **regularly exceeding 14 units a week** can lead to these health problems.



## Giving Brief Advice

- Set *individualised goals*.
- Have several 'drink-free' days when you don't drink at all.
- Set limits and stick to them.
- Have non-alcoholic drinks before and in-between alcoholic drinks
- Avoid drinking in rounds or in large groups.
- Eat before you drink.
- Switch to lower alcohol drinks.
- Avoid going to the pub after work.
- Plan activities for times you would usually drink.
- Have other outlets for when you are bored or stressed

# Clinical Approach

## Be empathetic & non-judgemental

- Bad drinking habits does no equate to being a bad person.
- High risk drinking is not usually permanent.
- Condemnation can damage patient practitioner relationships and may inhibit future discussions.

## Be authoritative

- Be clear and use guidelines
- Don't admit your own transgressions!

## Deflect denial

- Some patients will not be ready to change and that's ok, you may be able to plant a seed that they go away and think about.

## Facilitate

- It is vital to the success of the brief advice session that the patient is in charge of the goal setting and gives their own suggestions on how they could reduce the amount they drink.



# Provide Encouragement

- People drinking at increasing risk are usually not alcohol dependent.
- Changing habits is not easy, patients need to be inspired, empowered and supported to change.
- Be candid about risks, encourage the patient to begin now.



**ROADS 0117440 0540**

**DHI (South Glos): 0154868750**

**ARA (Weston): 0117 930 0282**

**Advocacy services: 0117 965 4444**

**SMART recovery: 0117 914 2208**

**SWAN Project: 0117 914 2208**

**Hawksprings: 0117 964 2859**

**NHS 111**

**Drinkline: 0800 917 8282**

**[www.drinkaware.co.uk](http://www.drinkaware.co.uk)**

**<https://www.e-lfh.org.uk/programmes/alcohol/>**

**[www.nhs.uk/drinkcheck](http://www.nhs.uk/drinkcheck)**

**Apps: NHS DRINK FREE DAYS**



**Signposting**

A vertical decorative bar on the left side of the slide, featuring a textured gold background with a repeating pattern of small squares and larger, overlapping circular motifs in a lighter shade of gold.

# Any questions?

# Viral Hepatitis

- Viral hepatitis is a systemic disease with primary inflammation of the liver caused by a group of hepatotropic viruses.
- Affects over 700,000 people in the UK.
- 5 known types of hepatitis virus: A, B, C, D and E.
- Hepatitis B, C, D and E can develop into chronic infections.
- No specific prophylaxis for hepatitis C and E.
- Diagnosis based on antibody +/- viral PCR.

# VIRAL HEPATITIS

Liver | Inflammation

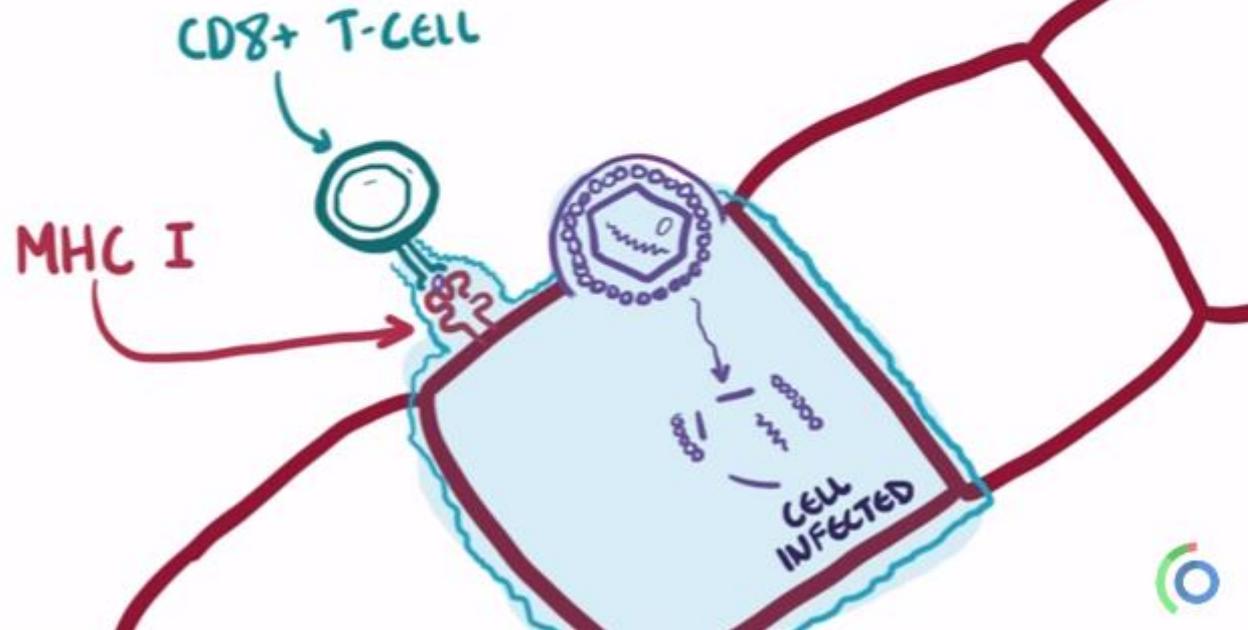
\* CYTOTOXIC KILLING



\* CELL APOPTOSIS



LIVER DAMAGE



# VIRAL HEPATITIS

Liver | Inflammation

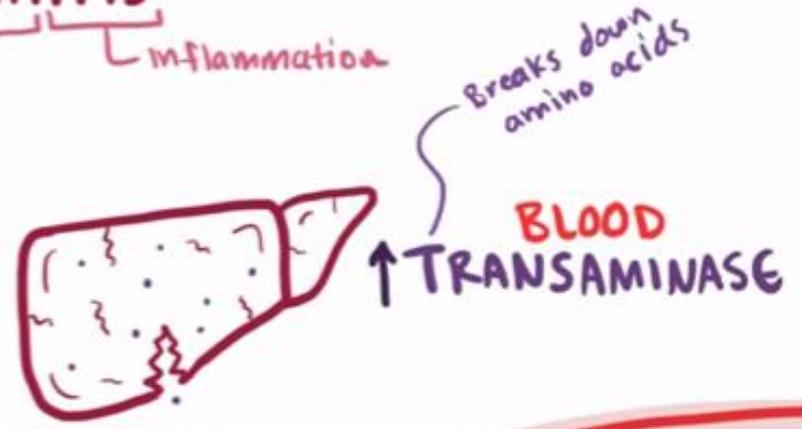
## SYMPTOMS

- Fever, malaise, nausea

- HEPATOMEGALY



- Inflamed
- pain  ~ ouch



↑ Alanine aminotransferase [ALT]  
↑ Aspartate aminotransferase [AST]

## SYMPTOMS

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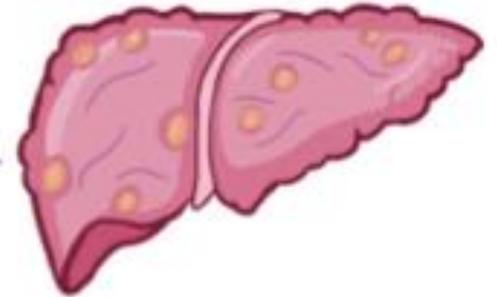
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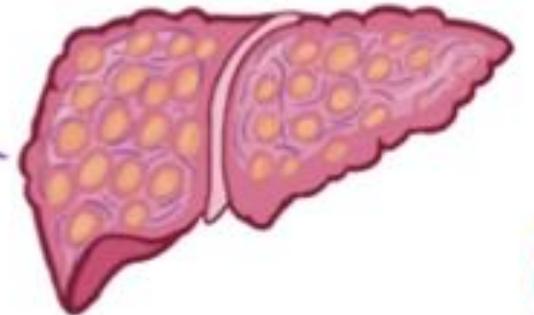
### COMPENSATED

\* STILL DOES ITS JOB \*



### DECOMPENSATED

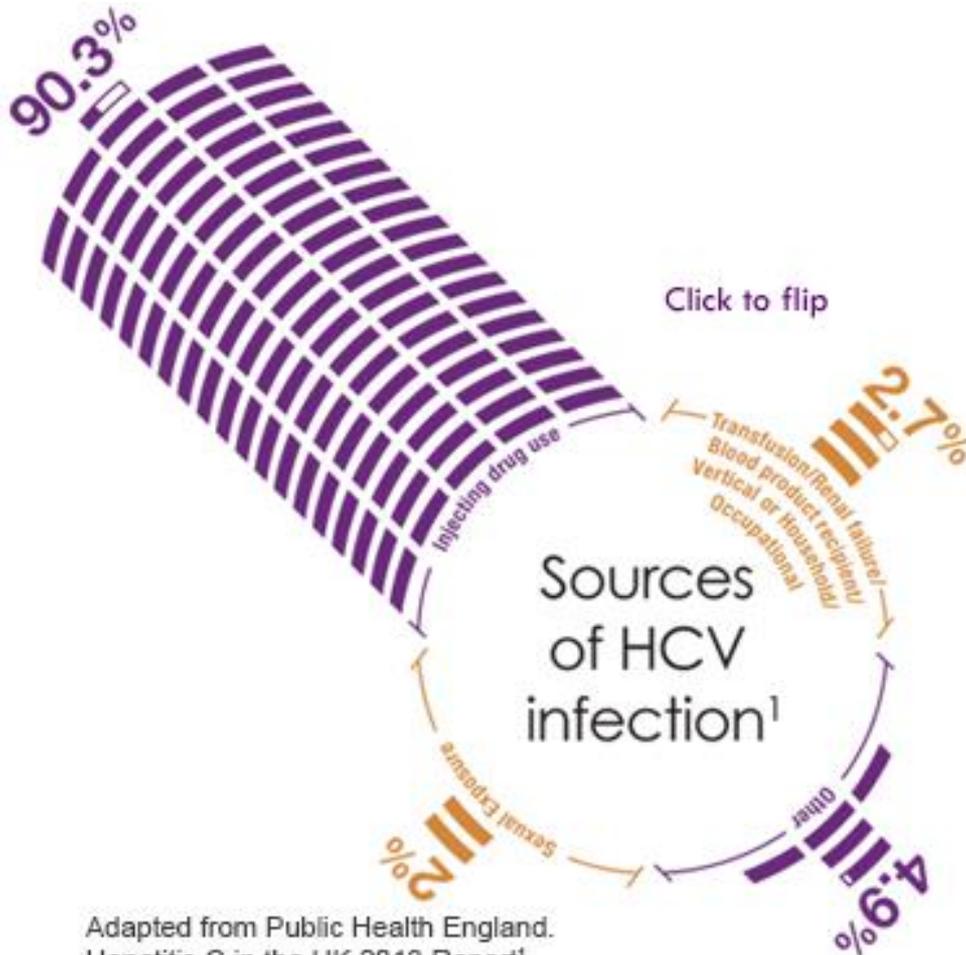
\* CAN'T FUNCTION \*



# Hepatitis C Epidemiology

- 71 million people worldwide. (WHO, 2018)
- Approximately 399,000 deaths each year from hepatitis C.
- No vaccine – in development.
- 160,000 people in England. (PHE, 2017)
- Blood borne virus.
- Majority of patients in England have a history of IV drug use.

# Sources of Infection - UK

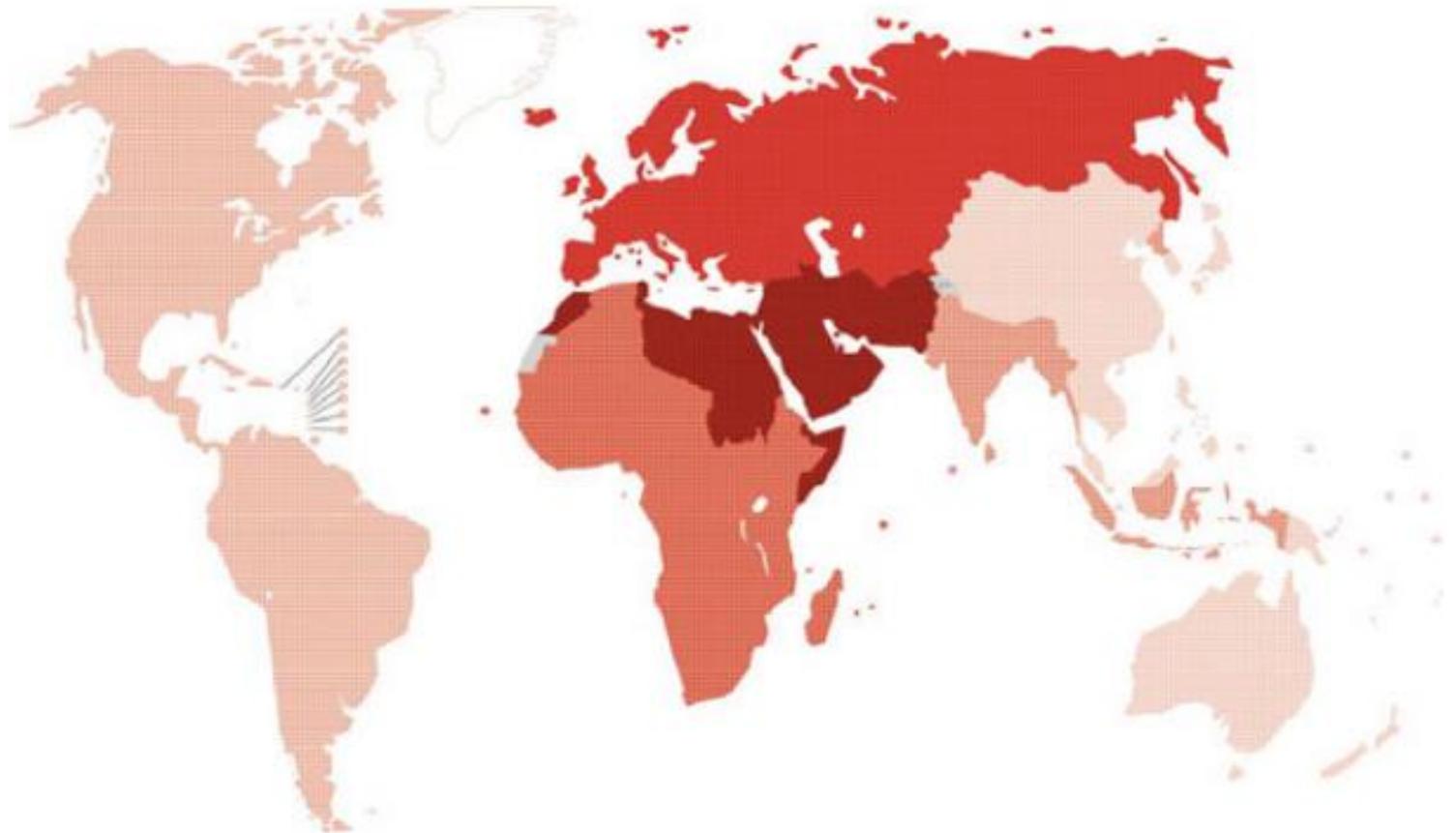


Adapted from Public Health England.  
Hepatitis C in the UK 2013 Report<sup>1</sup>

Injecting drug use is the most common route of transmission in the UK.

# World Prevalence

Table 3 (with map). Incidence of HCV infection in the general population, by WHO region, 2015:  
1.75 million new infections in 2015



Incidence of HCV infection



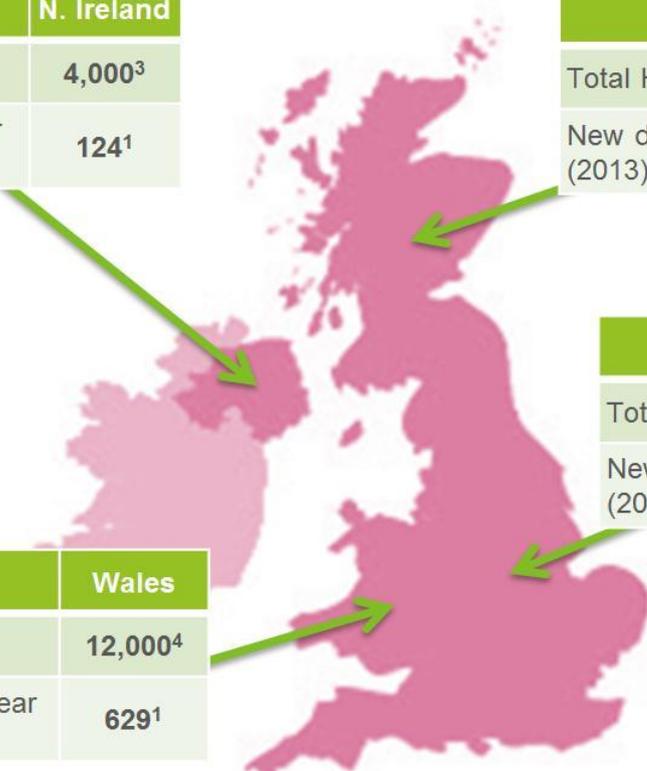
# HCV impacts significant patient numbers in the UK<sup>1</sup>

	N. Ireland
Total HCV Infection	4,000 <sup>3</sup>
New diagnosis per year (2013)	124 <sup>1</sup>

	Scotland
Total HCV Infection	37,000 <sup>1</sup>
New diagnosis per year (2013)	1,903 <sup>1</sup>

	England
Total HCV Infection	160,000 <sup>1</sup>
New diagnosis per year (2013)	11,051 <sup>1</sup>

	Wales
Total HCV Infection	12,000 <sup>4</sup>
New diagnosis per year (2013)	629 <sup>1</sup>



**'Hot-spots' for HCV include<sup>2</sup>**

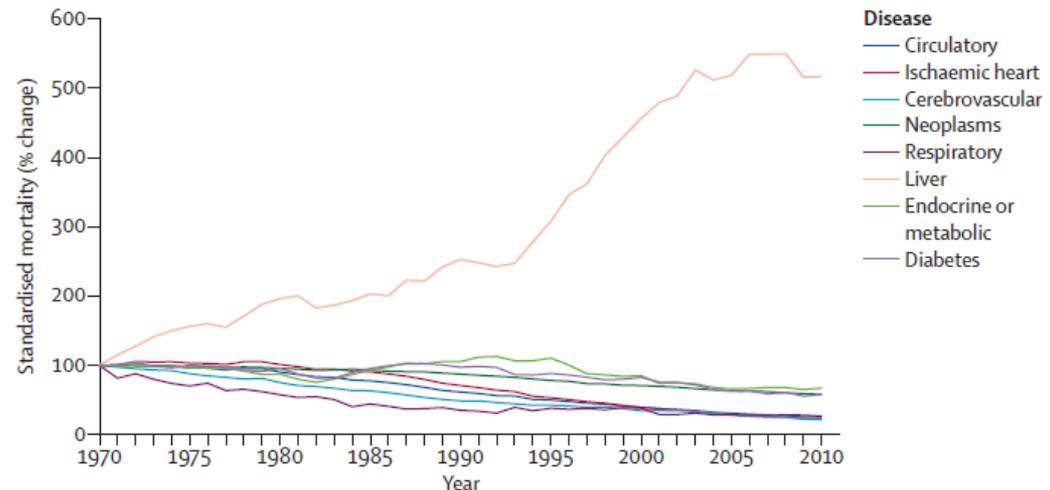
- London
- Manchester
- Bristol
- Lancashire
- Blackburn
- Blackpool
- Liverpool
- Birmingham

HCV = hepatitis C virus

1. Public Health England, Hepatitis C in the UK 2014 report. Available at: [https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/337115/HCV\\_in\\_the\\_UK\\_2014\\_24\\_July.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/337115/HCV_in_the_UK_2014_24_July.pdf) (accessed October 2014). 2. HCV Action, Health and Wellbeing Boards & Hepatitis C. May 2014. Available at: <http://www.hcvaction.org.uk/resource/health-and-wellbeing-boards-hepatitis-c> (accessed October 2014). 3. Health and Safety Executive (HSE) website. Available at <http://www.hse.gov.uk/biosafety/blood-borne-viruses/hepatitis-c.htm> (accessed June 2014). 4. Public Health Wales website. Available at: <http://www.wales.nhs.uk/sitesplus/888/page/43746> (accessed October 2014).

# UK Mortality from Hepatitis C

- Liver disease is the only cause of death still increasing year-on-year.
- Liver disease is 5<sup>th</sup> 'big killer' in England and Wales.
- Between 2005 and 2015 death from hepatitis c related conditions more than doubled from 209 to 468.

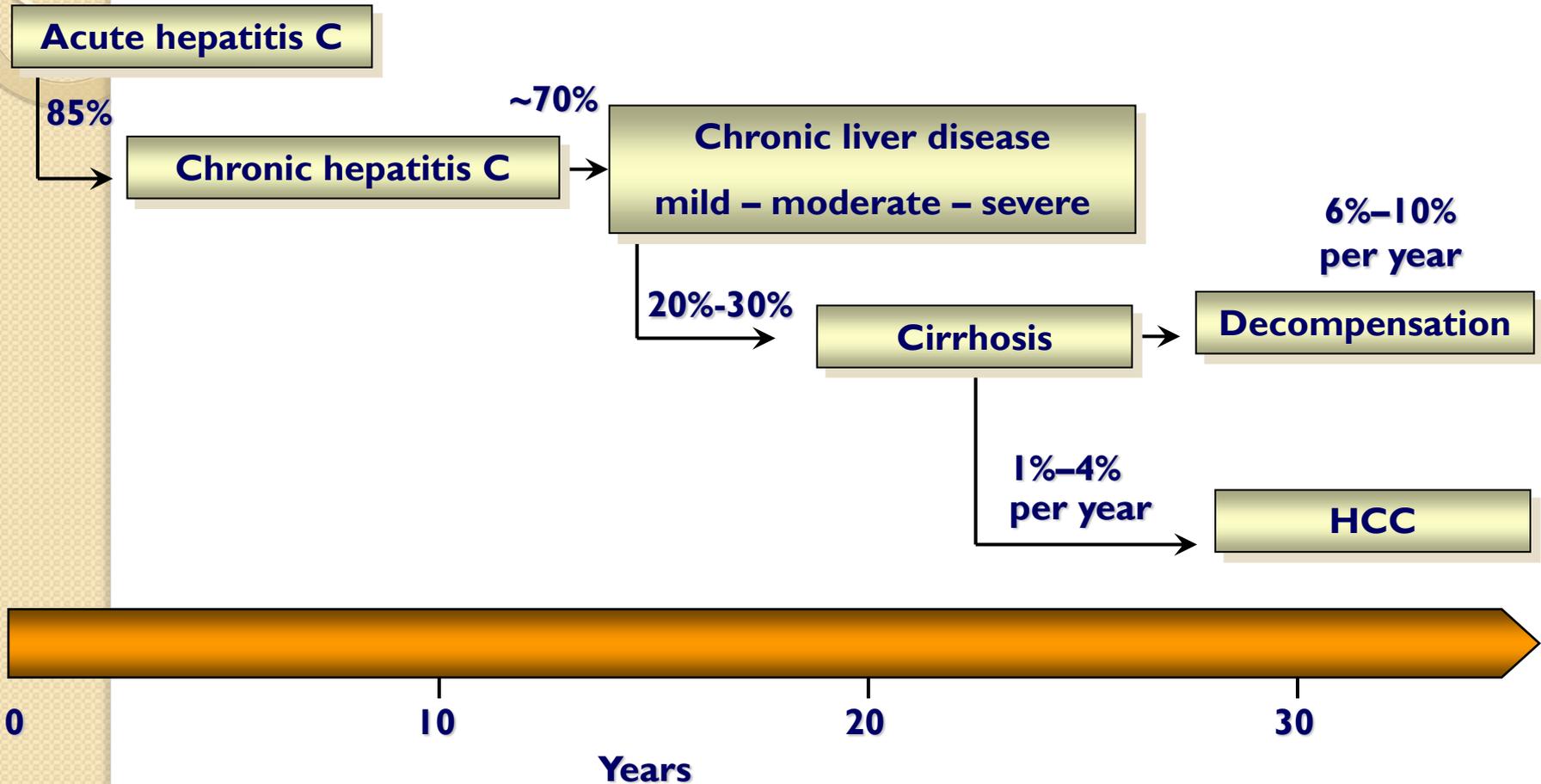


- <https://www.england.nhs.uk/2018/01/hepatitis-c-2/>

# Hepatitis C Infection

- Acute phase – 6 months.
  - Antibodies detectable from 3 weeks after infection.
  - 65% -75% of patients are asymptomatic.
  - Flu like symptoms. (20% develop jaundice)
- Chronic infection.
  - Chronic hepatocyte inflammation.
  - Fibrosis.
  - Cirrhosis.
  - ‘Silent Killer’.

# Natural History of Hepatitis C Infection



Hoofnagle JH. *Hepatology*. 1997;26(suppl 1):15S-20S; Di Bisceglie AM. *Hepatology*. 2000;31: 1014-1018; Di Bisceglie AM. *Hepatology*. 1997;26:34S-38S; Chen SL et al. *Int J Med Sci*. 2006;3:47-52; Alberti A. *Aliment Pharmacol Ther*. 2005 Nov;22(suppl):74-78.

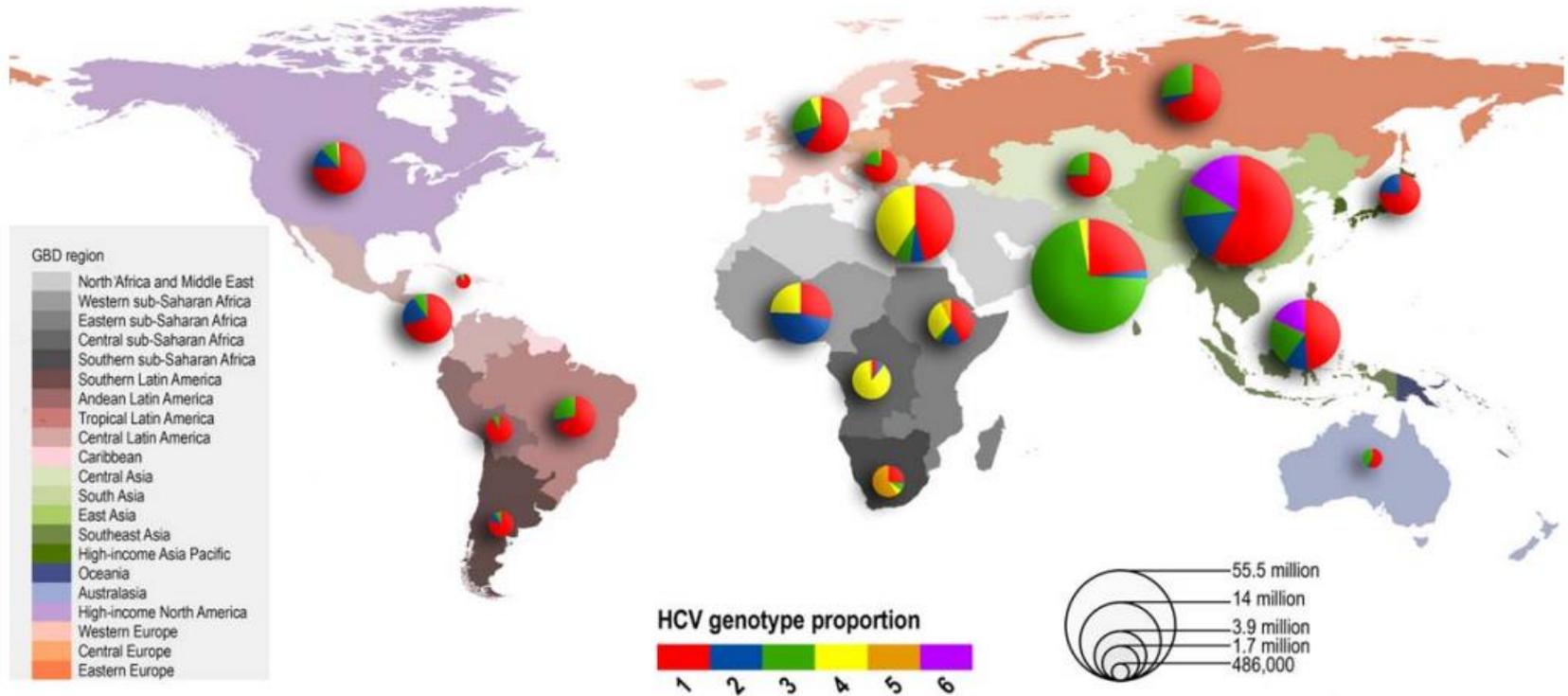
# Presentation

- Blood tests at GP.  
Raised ALT (normal 5-35 units/L).
- Screening of high risk group, e.g. drug recovery agency, prison, sexual health clinics, etc.
- Symptoms of advanced disease: directly to hospitals.

# Diagnosis

- Initially hepatitis C antibodies – can be a dry blood spot test.
- RNA PCR test and viral load.
- Genotype (six main genotypes)
  - Genotype 1 – most common in west.
  - 90% in UK have 1 or 3.
  - Genotype dictates treatment choice.
- LFTs.
- Fibroscan.
- Imaging (if cirrhotic).
- Rarely liver biopsy.

# Genotype Distribution: Global Data (2015)



# Aim of Treatment

- Sustained Viral Response 12 (main endpoint of treatment).
- Preventing transmission.

# Hepatitis C Treatment Options

## Interferon-based treatment

- Pegylated interferon  $\alpha$ 2a and ribavirin.
- **No longer used in Hep C.**

## Direct-acting antivirals (DAA)

- All-oral.
- Non-interferon-based.
- Side-effects minimal.

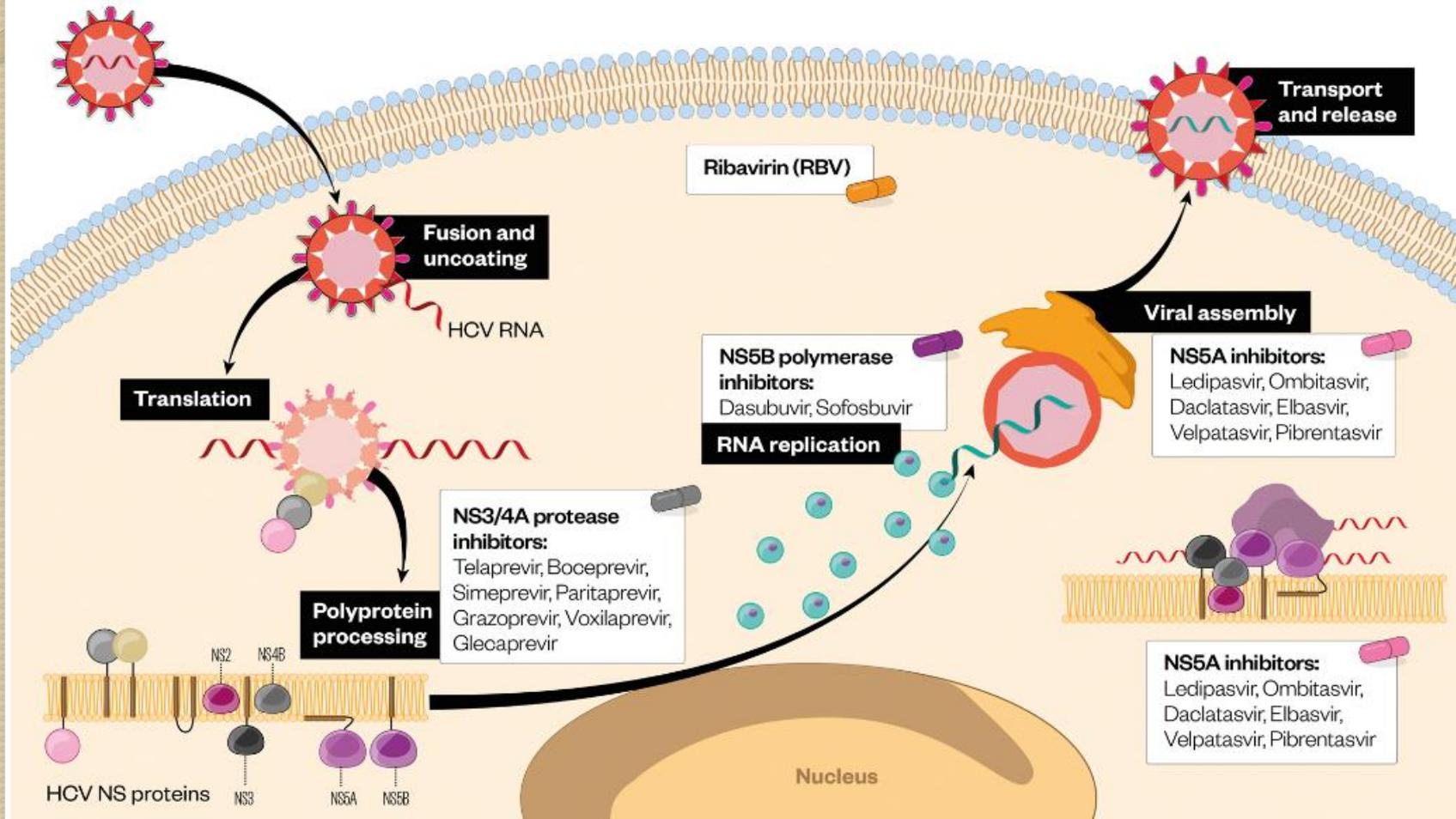
# Problems with Interferon

- Systemic, flu-like symptoms.
- Almost universal fatigue.
- Depression in up to 40% of patient.
- Cytopenias: anaemia, platelets, neutrophils.
- Rashes.

## **Rarer side-effects**

- Activation of autoimmune phenomena (e.g. rheumatoid arthritis)
- Hypothyroidism.
- Alopecia.
- Anorexia and weight loss.
- Loss of libido and impotence.

# Hepatitis C Lifecycle and DAA targets



# The new regimens...

- Sofosbuvir / ledipasvir (Harvoni)
  - Sofosbuvir / velpatasvir (Epclusa)
  - Elbasvir / grazoprevir (Zepatier)
  - Glecaprevir / pibrentasvir (Maviret)
  - Sofosbuvir / velpatasvir / voxilaprevir (Vosevi)
- 
- Sometimes with ribavirin
  - Range of treatment lengths (8-16 weeks)

# Patient Journey



# Which treatment?

- Genotype
- Previous treatment
- Degree of cirrhosis
- Drug Interactions
- Cost of treatment.....

# Common Drug Interactions

- Antipsychotics
- Antiepileptics
- Anticoagulants
- PPIs
- Statins
- HIV medications

# Hepatitis Drug Interactions


HEP Drug Interactions


UNIVERSITY OF LIVERPOOL

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HEP iChart app users - please update to the newest version to ensure up-to-date information

## Interaction Checker

Access our free, comprehensive and user-friendly drug interaction charts

### Educational Videos

A series of mini-lectures on topics including pharmacology, hepatitis and drug-drug interactions

### Prescribing Resources

Interaction tables, treatment selectors, clinical prescribing resources, and pharmacokinetic fact sheets

### Twitter

 [@hepinteractions](#)  
 Follow us on Twitter for interaction news and for the latest additions and changes to the website

### Mobile Apps

 Available on the App Store
  Google play

### HIV Website


HIV Drug Interactions

### Cancer Website


Cancer Drug Interactions

Cookies help us deliver our services. By using our services, you agree to our use of cookies. [OK](#) [Learn more](#)

- <https://www.hep-druginteractions.org/>

# Delivery Of Care

- Operational Delivery Networks.
- Bristol and Severn Hep C ODN – hub and spoke model.
  - Bristol, Gloucester, Bath, Yeovil.
- Out-reach services:
  - Bristol Drugs Project
  - Homeless Health Service Bristol
  - Addaction Drug Service Weston-Super-Mare
  - South Bristol Community Hospital
  - Local prisons
  - Trowbridge clinic

# Delivery Of Care

- MDT meetings
  - Once a week at the hub.
  - Fortnightly dial in from the spoke centres.
  - Consultant, specialist pharmacist, specialist nurses, co-ordinator.
- Blueteq
  - Electronic approval from NHS England.
  - Funding agreement.

# What's holding us back?

- Undiagnosed
  - Increase testing and awareness of new drugs.
  - Promotional events – national and local.
- DNA
  - Supervised consumption.
  - Peer support.
  - Incentivisation.
- Re-infection
  - Risk/harm reduction methods.
- Prescribers
  - Pharmacist Independent Prescribers.

# What Community Pharmacy Can Do To Help

- Spread the message about simple treatments!
- Encourage testing.
- Self referral.
- Incentivisation scheme.

# Incentivisation Scheme

## Do you know someone who has hepatitis C?

If the answer to this question was 'yes', you could *potentially* receive £40 per patient you 'refer' by bringing them to your next session - please read below:

The BRI is starting a scheme where if you bring someone who has hep C to your appointment, they will receive support from our friendly hep C team to be treated.

If your friend starts treatment, **both** of you will receive vouchers for £20 at their second appointment into treatment (see overleaf for details on where these vouchers can be spent).

At your friends final appointment (12 weeks after finishing treatment) you will **both** get another £20 voucher.

You will be given the voucher by your hep C Nurse - a form will need to be completed, and vouchers will only be issued to the referring patient, and the new patient, i.e. not available for collection by a third party.

# ODN Website

[www.uhbristol.nhs.uk/hepc](http://www.uhbristol.nhs.uk/hepc)

# Self-referral

## Support, testing and how to refer

It is possible to obtain a test from your GP, one of the drug and alcohol agencies (linked below), or alternatively you could complete and submit the form below and we will make contact with you to discuss any queries around treatment with a view to making appropriate arrangements for testing in a one of the venues appropriate to you. A test can take as little as a minute for a finger prick test, to 5-10 minutes for a blood test. The outcome could be known within a couple of weeks.

Tests are primarily via blood test within GP and hospital settings, and within prisons and drug and alcohol settings a fingerprint test will be offered.

If you already have a positive outcome from a previous test but have not yet enrolled for treatment, please do use the form below to self refer direct onto treatment.

Contact

Name

Date of birth

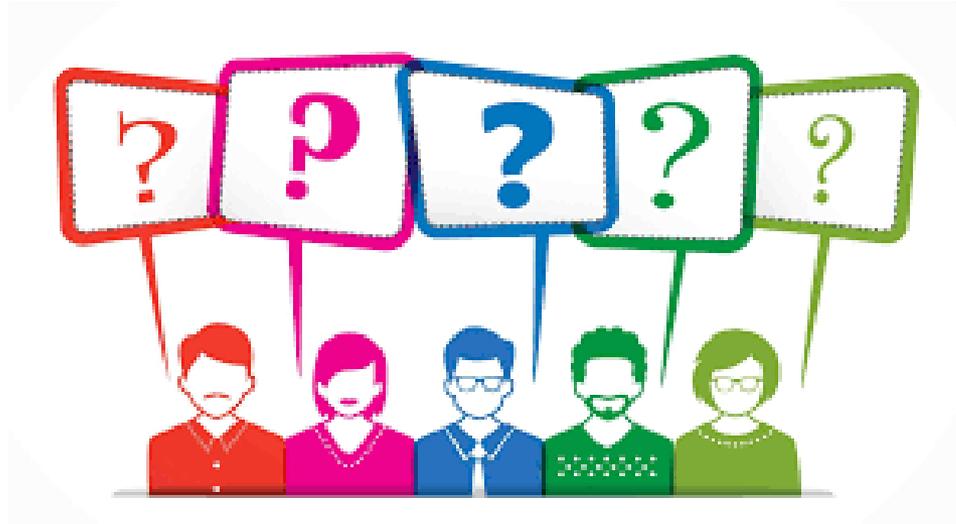
Address

Email

Telephone

Message

# Any Questions?



For further information please contact Janki Jethwa  
[Janki.jethwa@uhbristol.nhs.uk](mailto:Janki.jethwa@uhbristol.nhs.uk)

# Main References and Further Reading

- [https://www.youtube.com/channel/UCNI0qOojpkhsUtaQ4\\_2NUhQ](https://www.youtube.com/channel/UCNI0qOojpkhsUtaQ4_2NUhQ) Osmosis, Youtube
- <http://apps.who.int/iris/bitstream/handle/10665/255016/9789241565455-eng.pdf;jsessionid=041E02C2246609AED5494CC6C79DC7D3?sequence=1> WHO Global Hepatitis Report, 2017
- [https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\\_data/file/732469/HCV\\_IN\\_THE\\_UK\\_2018\\_UK.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/732469/HCV_IN_THE_UK_2018_UK.pdf) PHE Hepatitis C Report, 2018
- <http://www.hepctrust.org.uk/> The Hepatitis C Trust
- <https://www.britishlivertrust.org.uk/> The British Liver Trust
- <https://www.hep-druginteractions.org/> Hepatitis Drug Interactions