

British HIV Association
BHIVA

**Third Annual BHIVA Conference
for the Management of HIV/Hepatitis Co-infection**

Wednesday 6 October 2010

ONE GREAT GEORGE STREET CONFERENCE CENTRE · LONDON



Third Annual BHIVA Conference for the
Management of HIV / Hepatitis Co-infection

British HIV Association
BHIVA

Dr Janice Main
Imperial College London

Wednesday 6 October 2010, One Great George Street Conference Centre, London

Third Annual BHIVA Conference for the
Management of HIV / Hepatitis Co-infection



Dr Janice Main

Imperial College London

COMPETING INTEREST OF FINANCIAL VALUE \geq £1,000:	
Speaker Name	Statement
Janice Main:	Participated in advisory boards and clinical trials and has given lectures for GlaxoSmithKline, Gilead, Roche, Schering Plough, Boehringer-Ingelheim and Bristol-Myers Squibb.
Date	27 September 2010

Wednesday 6 October 2010, One Great George Street Conference Centre, London

Hepatitis C: what we can do
whilst awaiting new drugs

LOOK AFTER YOUR LIVER!

- Two-hit hypothesis
- Boosting the immune system
- Avoiding the complications of HCV
- Alternative approaches
- Christmas shopping

The trouble with orgies.....

Male age 46 yr

- HIV pos since 2000
- Transferred care May 2006
- Stable HIV
- Tenofovir, lamivudine, nevirapine
- Switched to
- Tenofovir, emtricitabine, nevirapine

Baseline bloods

- CD4 650, HIV <50 copies/ml
- **ALT 2011**
- Investigations?

- HBsAg neg, Anti-HBc -total and IgM neg
- Syphilis EIA pos
- Anti-HAV IgM neg, IgG pos

Anti-HCV pos

- HCV RNA positive
- 4 998 180 IU/mL
- Genotype 3a

ALT levels

Help!

- Prolonged hepatitis
- Very high ALT
- ? Biphasic
- ?compatible with acute HCV
- Reluctant to have PEG/RBV

Reviewed

- Minimal alcohol
- No herbal remedies
- Ibuprofen on occasion
- No ecstasy
- Crystal meth - now and again
- EXAM - nil worrying
- TESTS?

Reviewed

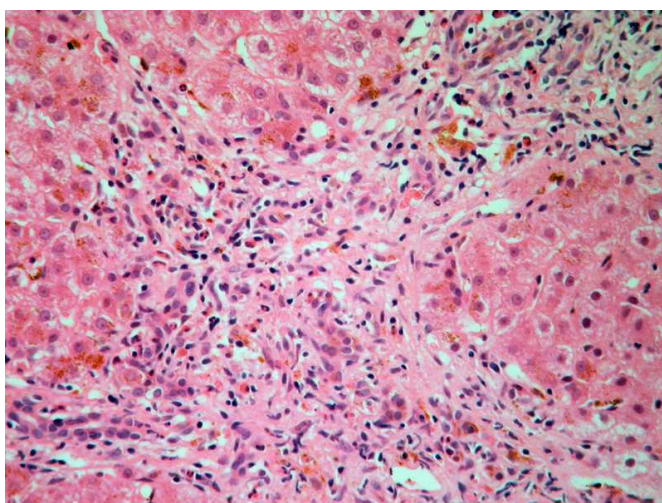
- “Several” diagnostic tests were performed.....

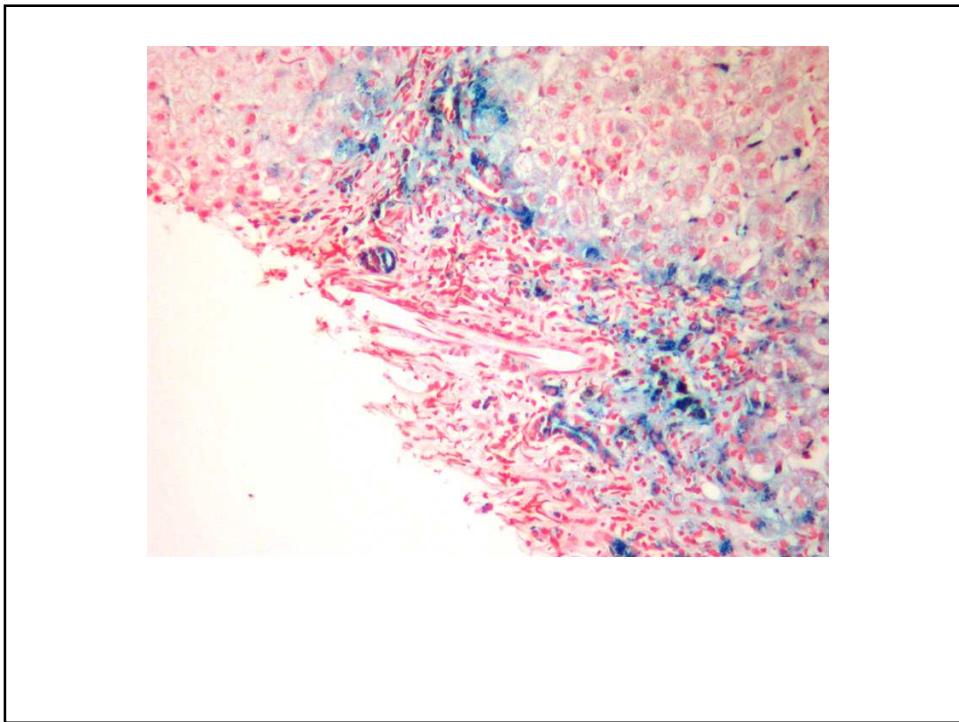
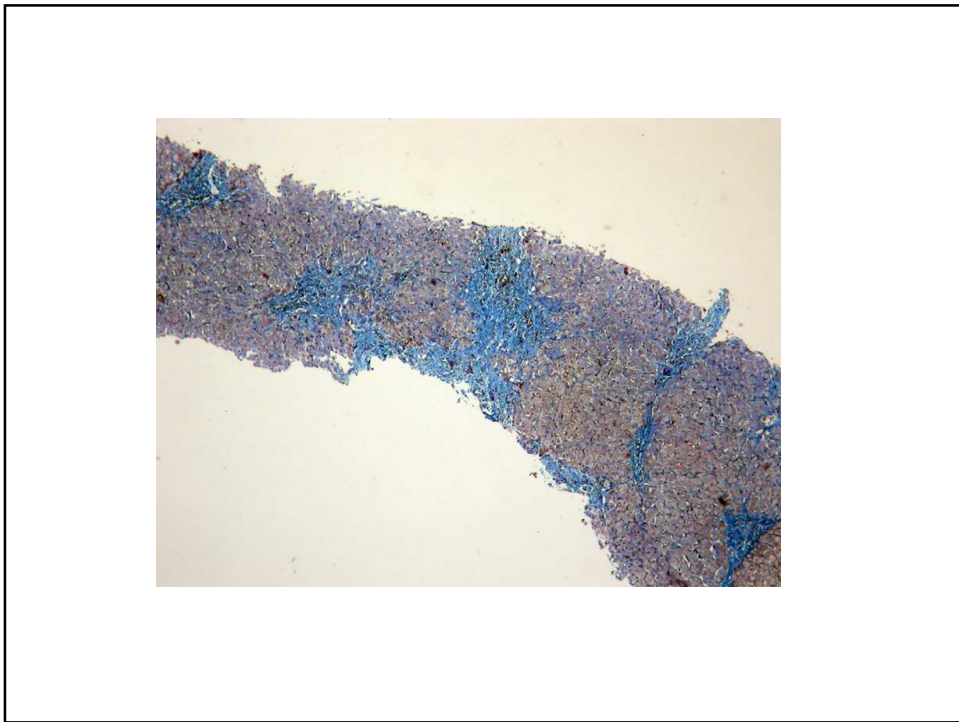
TESTS?

Ferritin

Liver biopsy

Review genotype

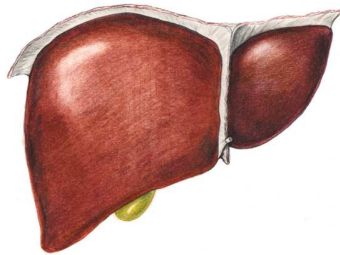




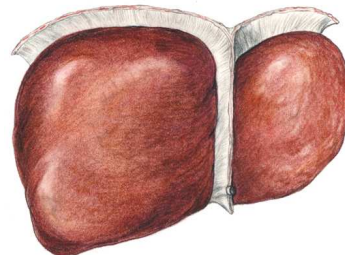
HAEMOCHROMATOSIS CONFIRMED

- YY, HH
- 2 alterations in the HFE gene
- aa 282 can be C (wild type) or Y (penetrant mutation)
- aa 63 can be either H (wild type) or D (suspected mutation with a low penetrance)
- 93% patients are either homozygous for C282Y (YY, HH) or compound heterozygotes (CY, HD)

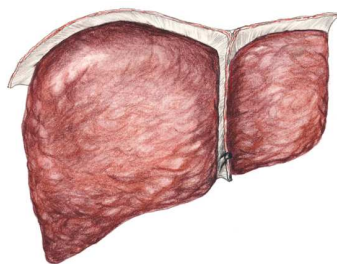
Healthy liver



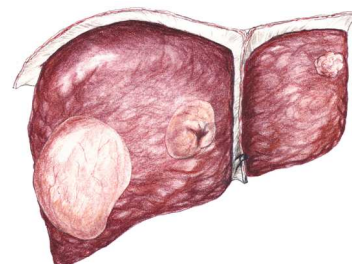
Hepatic fibrosis



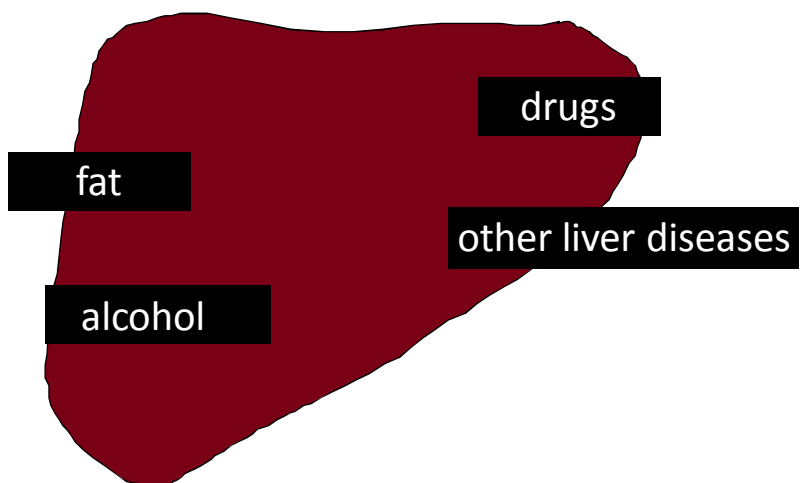
Cirrhosis



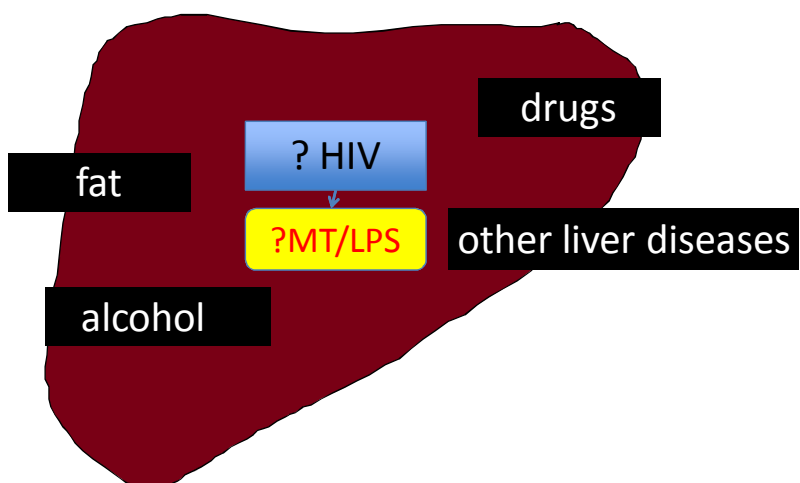
Liver cancer



THE TWO-HIT HYPOTHESIS



THE TWO-HIT HYPOTHESIS



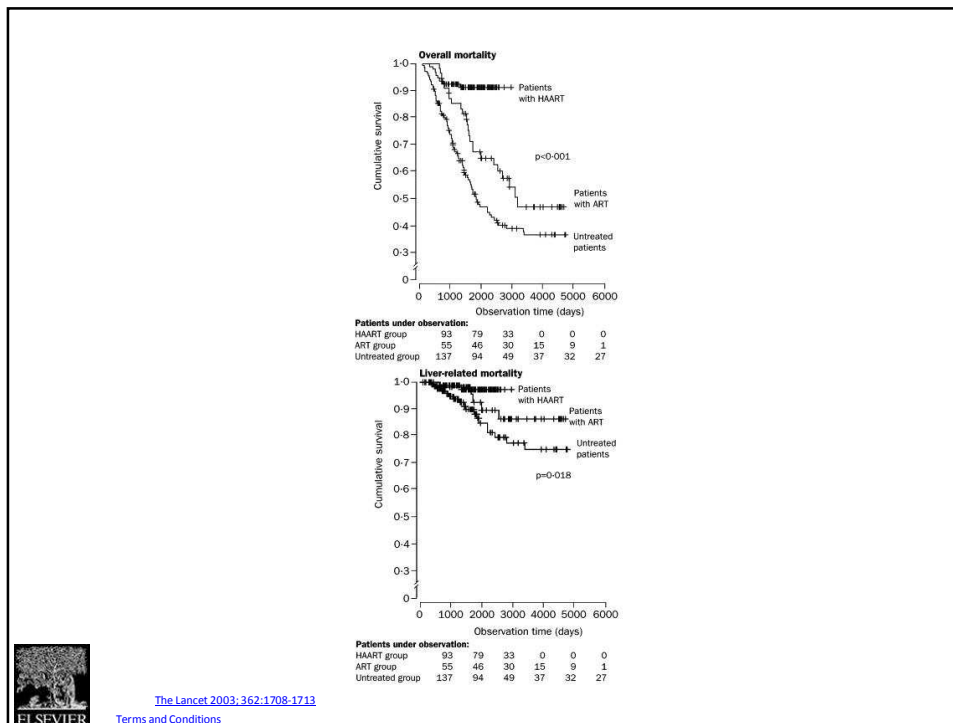
BOOSTING THE IMMUNE SYSTEM

Immunosuppression and hepatitis C

Immune boosting and hepatitis C

EFFECT OF ARV ON LIVER RELATED MORTALITY IN HIV/HCV

- Qurishi et al, 2003
- n = 285, 1990-2002
- HAART (post 1995) 93 patients
- NA only 55
- No treatment 137



TREATING THE HIV

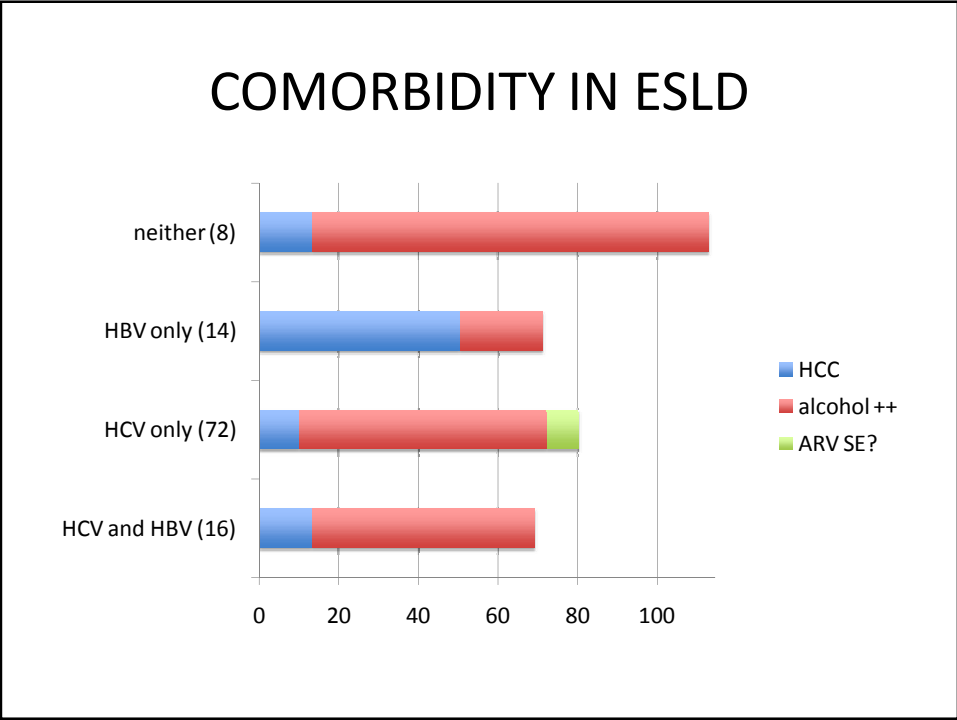
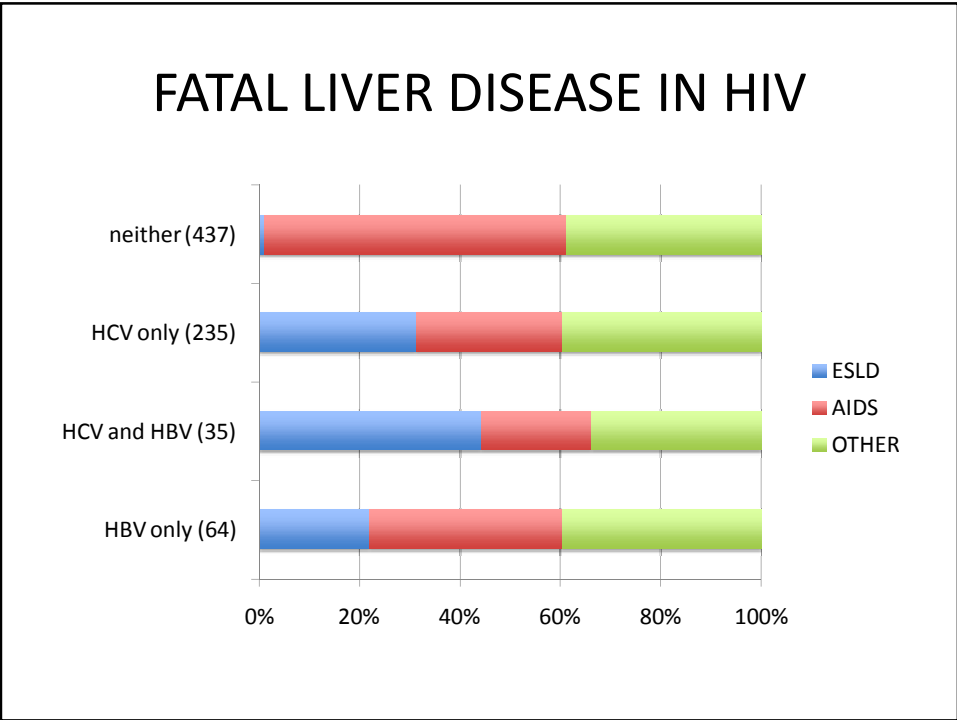
- Slower progression of fibrosis with ARV
- Brau et al, 2006

TREATING THE HIV

- n = 80
- HIV/HCV
- T cell response to HCV core peptides
- Before and after ARV
- Increase in HCV specific immune responses
- In chronic and acute cleared HCV
- Rohrbach et al, 2010

FATAL LIVER DISEASE IN HIV

- Salmon-Ceron et al, 2005
- n = 185 French hospital departments
- All HIV positive deaths in 2000
- n = 822
- HCV 29%
- HBV 8%
- HBV and HCV 4%



LIVER DISEASE AND ALCOHOL

- Excessive alcohol in LD related deaths -59%
- (vs 24% other causes of deaths)
- Excessive alcohol in HCV-LD related deaths -62%
- Excessive alcohol in HBV-LD related deaths -21%

ALCOHOL

- Epidemiology – more high risk behaviour
- Natural history – more rapid progression
- Decreased immune response
- Increased viral replication
- Increased oxidative damage
- NB heavy consumers – excluded from trials

HCV AND ALCOHOL

- n = 2235 patients Poynard et al, 1997
- Rate of fibrosis?
- Age older than 40 years
- Alcohol consumption of 50g or more
- Male sex
- Infection to cirrhosis – median 30 years
- Men infected after 40 years - 13 years
- Non-drinking younger women -42 years

HCV AND ALCOHOL

- n = 2235 patients Poynard et al, 1997
- Rate of fibrosis?
- Age older than 40 years
- Alcohol consumption of 50g or more
- Male sex
- Infection to cirrhosis – median 30 years
- Men infected after 40 years - 13 years
- Non-drinking younger women -42 years

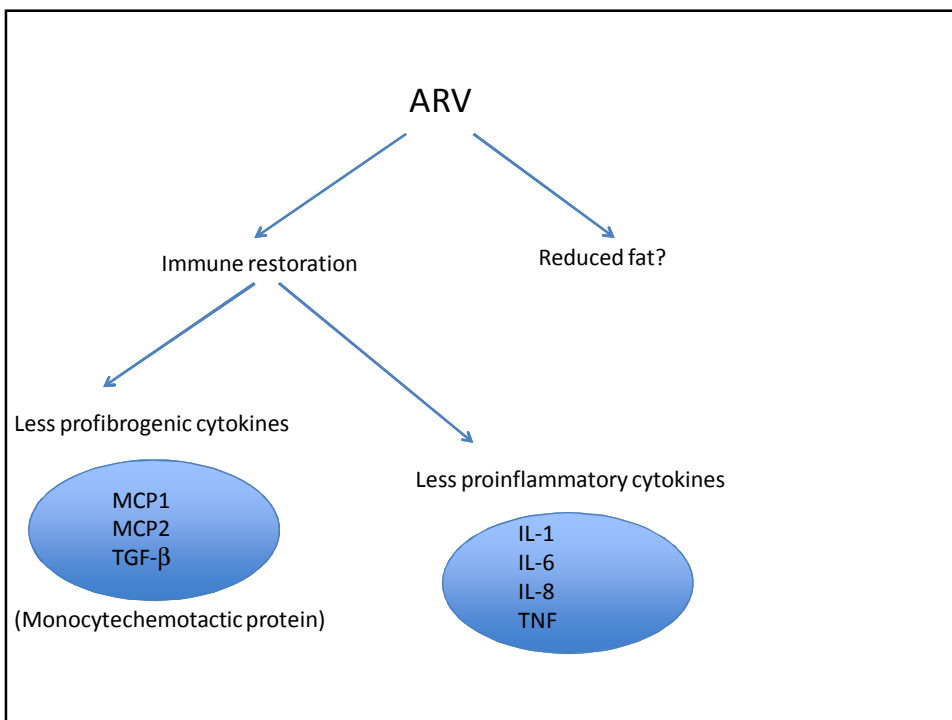
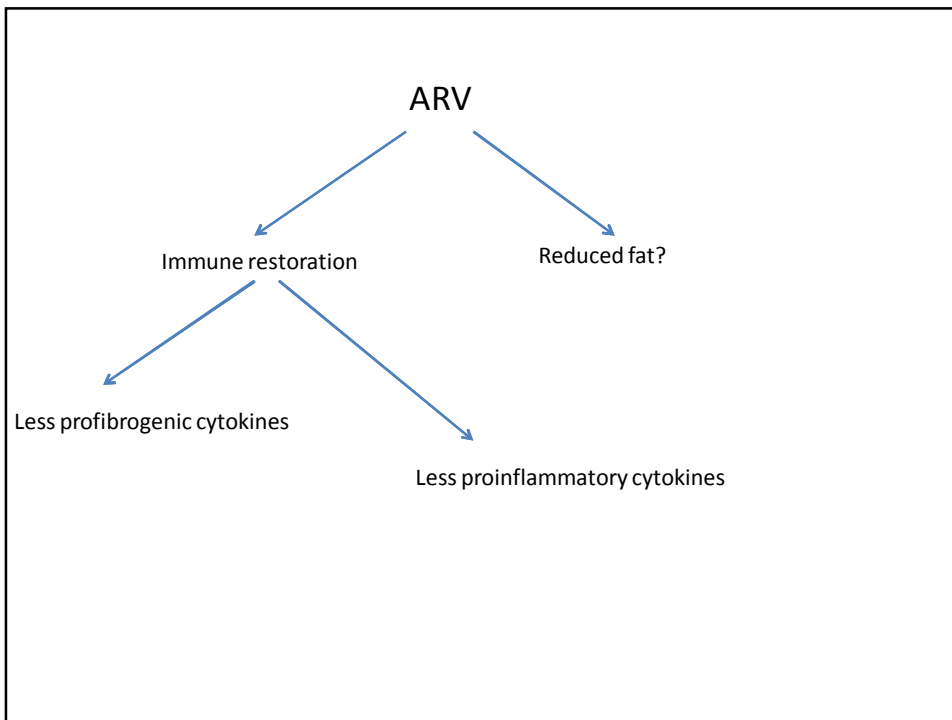
1 unit = 8g

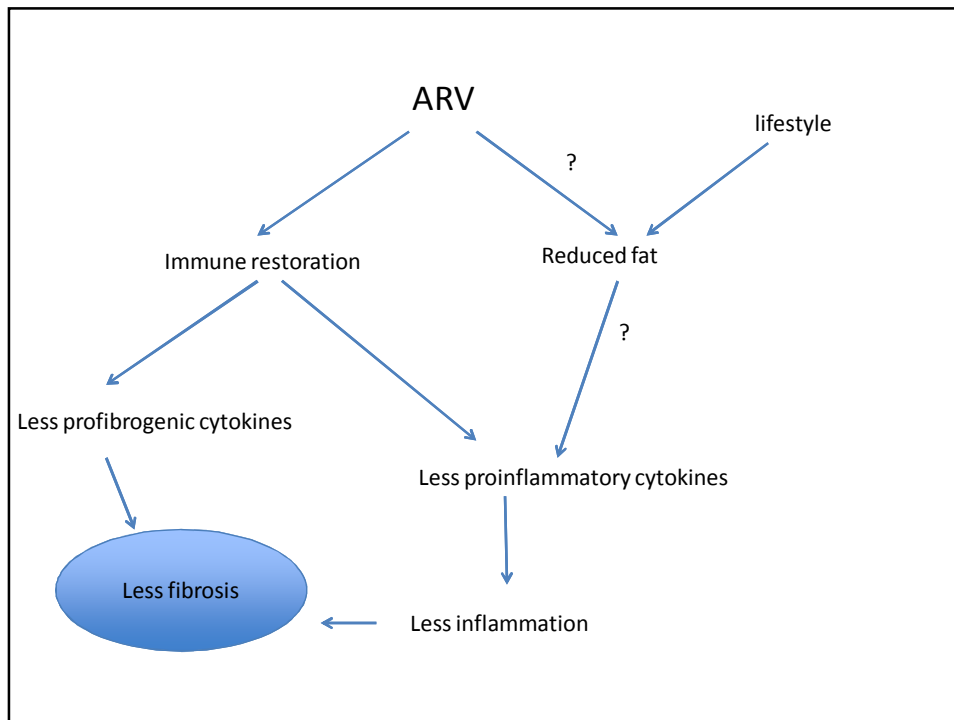
HEPATIC STEATOSIS IN HIV AND HCV

- Non-**alcoholic** fatty liver disease (NAFLD)
- Non-**alcoholic** steatohepatitis (NASH)
- HCV related (genotype 3)
- Metabolic syndrome
- Alcohol
- Drugs
- Other

HEPATIC STEATOSIS IN HIV AND HCV

- ? **Does ARV protect or cause**
- ? **Associated more fibrosis**
- Verma et al, 2008
- n = 66 patients
- Overall prevalence of steatosis 58%
- HAART only 41%
- NRTI only 70%
- Sequential therapy 82%
- NI and steatosis grades
 - independent predictors of advanced fibrosis





NASH TREATMENT (NON-HIV)

N = 31

Intensive lifestyle intervention **veducation** (control)
(2:1 randomisation, 48 weeks, NASH activity score)

Weight loss (%BW) **9.3%**(0.2%)

Achieved goal of 7% weight loss

- Significant improvements in
- Steatosis
- Lobular inflammation
- Ballooning injury
- NAS
- Promrat et al, 2010

PIOGLITAZONE, VITAMIN E OR PLACEBO

- N =247 with NASH
- 96 weeks therapy
- Vitamin E
- significant improvement in NASH vs placebo
- (43% v 19%, P=0.001)
- Pioglitazone
- (34% v 19%, P=0.04)
- Sanyal et al, 2010

PIOGLITAZONE, VITAMIN E OR PLACEBO

- **BUT**
- Other studies > 400IU vitamin E
- Increased risk of death from any cause
- **CONTROVERSIAL!!**
- ? Vitamin E levels (many patients on statins)

DRUGS AND HEPATITIS C

ARV – benefits > risk
other

OTHER DISEASES

INFECTIONS

- other viruses

HAV, HBV, HCV, HDV, HEV, HIV

HAV vaccination

HBV vaccination

OTHER LIVER DISEASES

MONITORING AND SCREENING

Hepatic decompensation

Hepatocellular carcinoma

Screening for varices

Screening for HCC

Monitoring liver function

Prophylaxis for SBP

Liver transplant.....

SMOKING

More fibrosis

Hezode et al, 2003

Dev et al, 2006

More HCC

Hassan et al, 2008

CANNABIS AND LIVER FIBROSIS IN HCV INFECTION

- Cannabinoid receptors type 1 and 2
- CB1 – mainly CNS
- CB2- immune cells
- Receptors upregulated in cirrhosis
- Cannabis use
 - independent predictor of fibrosis (Ishida et al, 2008)
 - association with steatosis (independent of BMI) (Hezode et al, 2008)

CANNABIS IN HCV INFECTION

- What the psychiatrists don't tell you.....

SILYMARIN



SILYMARIN

- Milk thistle
- ? inhibits HCV polymerase
- ? blocks viral entry
- Wagoner et al, 2010

SILYMARIN -? SAFE IN HIV

- N = 21 with HIV-HCV
- Silymarin extract v placebo
- Slight decrease ALT in treatment arm
- Appears safe!

- Carter et al, 2008

CHRISTMAS SHOPPING



