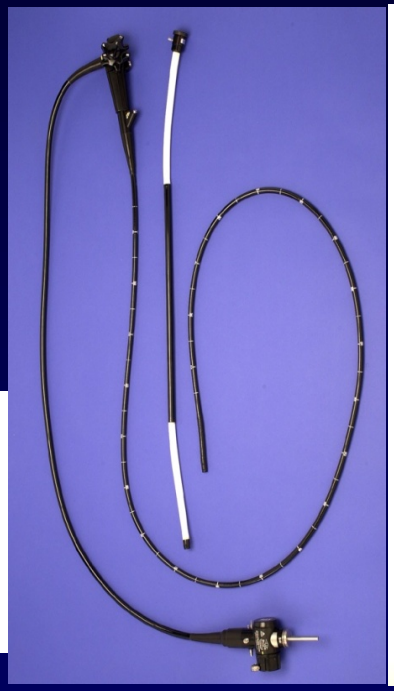
Dr David Rowbotham

Newcastle University

King's College Hospital NHS
NHS Foundation Trust

The Leeds Teaching Hospitals NHS
NHS Trust

AUCKLAND DISTRICT HEALTH BOARD
Te Toka Tumai



Queen Elizabeth Hospital NHS
NHS Trust

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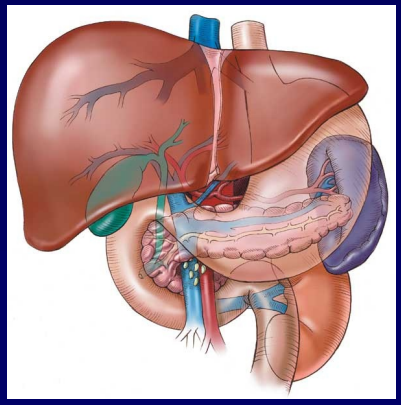

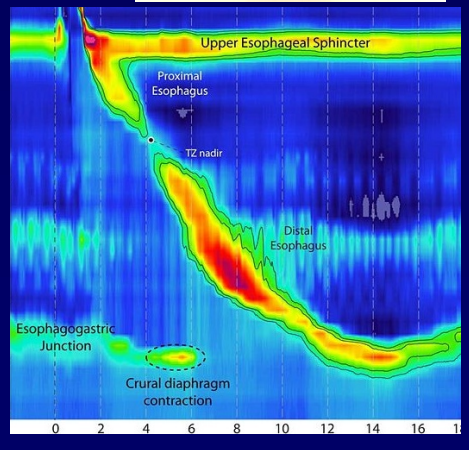

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Digestive Diseases & Endoscopy

Nurses Update
June 2010

Chronic Hepatitis
HBV / HCV

David Rowbotham

Clinical Director & Consultant Gastroenterologist

Dept of Gastroenterology & Hepatology

Auckland City Hospital

AUCKLAND DISTRICT HEALTH BOARD
Te Toka Tumai

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FRANK'S INVOLUNTARY EXCLAMATION OF SURPRISE WAS ABOUT TO HAVE GRAVE CONSEQUENCES.

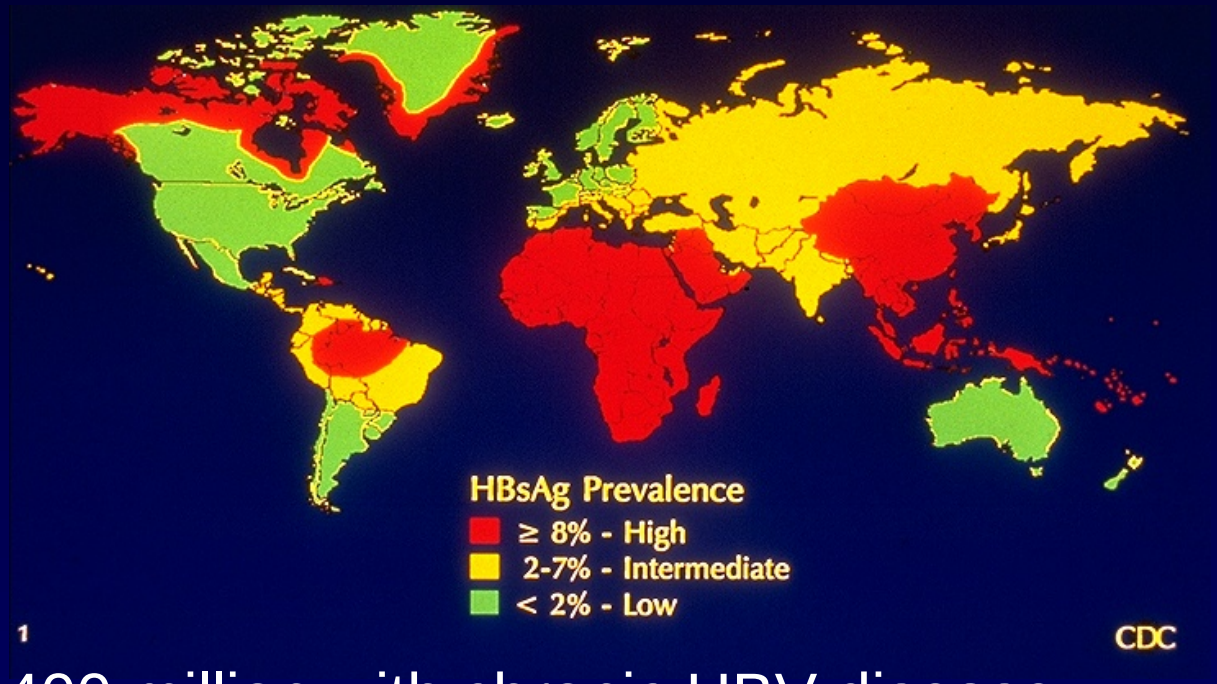
Chronic Hepatitis B and C

Both are silent killers

Both are potentially treatable / curable

- Background
- How to diagnose them
- Who do you need to refer on?
- How can they be treated?

Prevalence of chronic HBV infection



- 300 - 400 million with chronic HBV disease
- 25 - 40% of chronic HBV die from cirrhosis or hepatoma
  - > 300,000 cases/year of HBV-related HCC
  - HBV second most important carcinogen behind tobacco

World Health Organization. Fact sheet. Available at: http://www.who.int

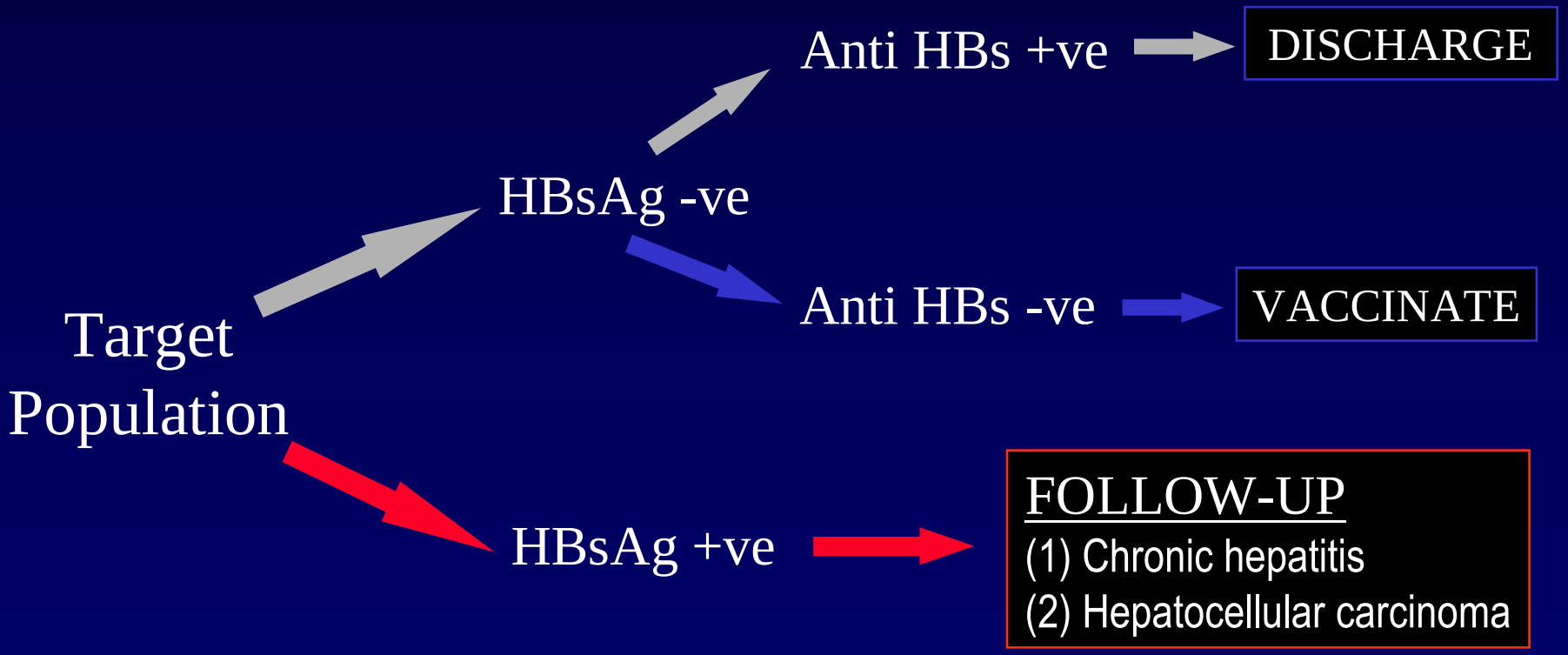
Center for Disease Control. Fact sheet. Available at: http://www.cdc.gov

Lai CL *et al., Lancet* 2003;**362:**2089-2094

NZ HBV Screening Programme

(1999-2002)

All Maori, Pacific Island, Asian persons >15 yrs



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HBV transmission

- Perinatal / vertical (95%)
- IVDU (high-risk)
- Horizontal
  - Sexual contact
  - Saliva
  - Any bodily fluid

- High endemicity populations: most transmission is perinatal or early childhood contact

Diagnosing chronic HBV

Simple

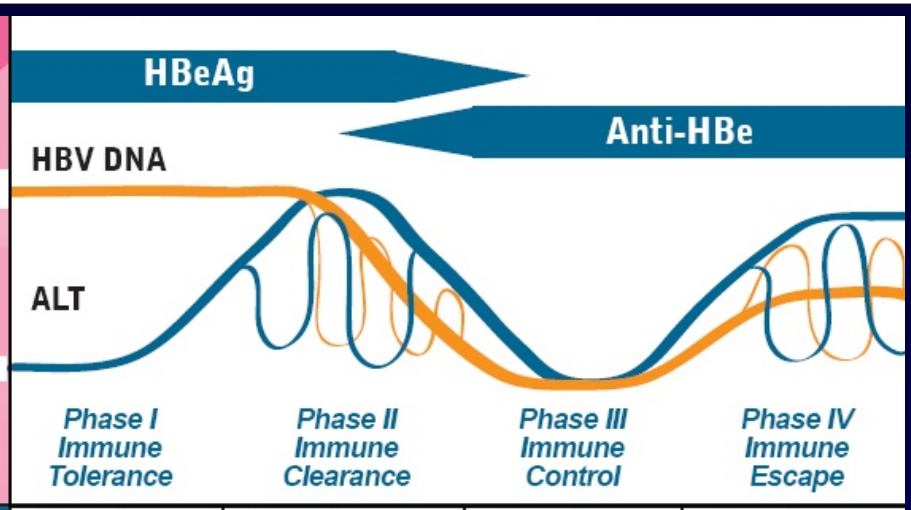
- Risk factors/Ethnicity
- Abnormal LFTs

→ do the test ...

- HBsAg +ve for ≥ 6 months = Chronic HBV

Assessing chronic HBV

GESA Gastroenterological Society of Australia
Australian Liver Association



	Phase I Immune Tolerance	Phase II Immune Clearance	Phase III Immune Control	Phase IV Immune Escape
HBsAg	> 6 months	> 6 months	> 6 months	> 6 months
HBeAg	+	+	–	–
Anti-HBe	–	Spontaneous seroconversion to anti-HBe may occur	+	+
ALT	Persistently normal	Persistently or intermittently elevated	Persistently normal	Persistently or intermittently elevated
HBV DNA	≥ 20,000 IU / mL	Persistently or intermittently ≥ 20,000 IU / mL	< 2000 IU / mL	Persistently or intermittently ≥ 2,000 IU / mL
Liver Histology	Minimal or mild hepatitis Usually no fibrosis	Inflamation score ≥ 4 Fibrosis: + / -	Inflammation score < 4 Fibrosis: + / -	Inflammation score ≥ 4 Fibrosis: +

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So who should you refer?

- Chronic HBV with:
  - Persistently raised ALT (HBeAg +/-)
  - Fluctuating LFTs (HBeAg +/-)
  - HBeAg –ve but high viral load (HBV DNA)
  - Rising AFP
  - Suspicion of cirrhosis/advanced liver disease
- Immunotolerant patients with higher risk factors
  - Male / >30 yrs / HBeAg +ve (even if normal ALT)
- Anyone you are concerned about ... that will turn up!

Goals of treatment

- Suppress HBV replication
  - Achieve HBeAg seroconversion
    - *on treatment*
    - *off treatment*
- Prevent cirrhosis
- Prevent need for liver transplant
- Prevent death

Goals of treatment:
2 distinct patient populations

HBeAg positive (wild type)

- Loss of HBeAg +/- seroconversion
- Durable suppression of HBV DNA (low/undetectable)
- Stop Rx after seroconversion (80% sustained response)

HBeAg negative (precore / core promoter mutants)

- HBeAg seroconversion is not an endpoint
- Durable suppression of HBV DNA (low/undetectable)
- Usually long term Rx (relapse common if stop treatment)

Treatment options

Previously ...

- Lamivudine (YMDD)
- Adefovir (less resistance; occ renal toxicity)
- Standard interferon

Treatment options (2009)

- 1 April

  Pegylated INF 2$^{\alpha}$

- 1 August

  Entecavir (1° therapy)

- 1 December

  Tenofovir (add-on therapy)

Treatment options (1 April 2009)

- Pegylated INF 2^{α}

  Chronic Hep B (HBsAg +ve > 6/12)
  Rx naïve
  HBeAg +ve or viral load/significant fibrosis

  Weekly SC injection
  48 weeks fixed course (continuing benefits)

  Renal impairment / thrombocytopenia

Treatment options (1 August 2009)

- Entecavir

  Chronic Hep B (HBsAg +ve > 6/12)

  Nucleoside analogue Rx naïve (Lamivudine)

  HBeAg +ve or viral load/significant fibrosis

  Continue 6/12 after HBeAg seroconversion

  Continue 12/12 after seroconversion if advanced fibrosis or cirrhosis

Treatment options (1 December 2009)

- Tenofovir

  Chronic Hep B (HBsAg +ve > 6/12)

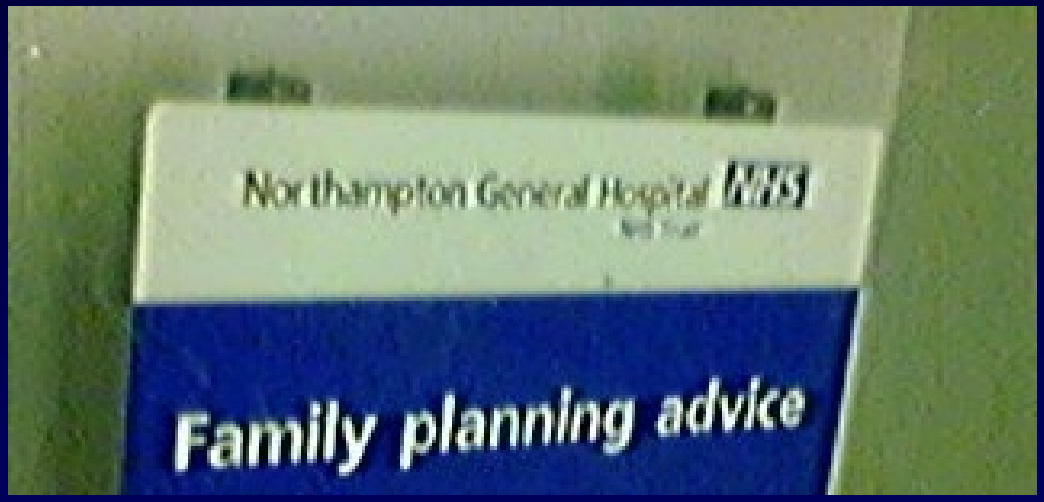
  Previous Rx (Lamivudine, Adefovir, Entecavir)

  HBeAg +ve or viral load/significant fibrosis

  Continue 6/12 after HBeAg seroconversion

  Renal impairment

Not all advice is good ...



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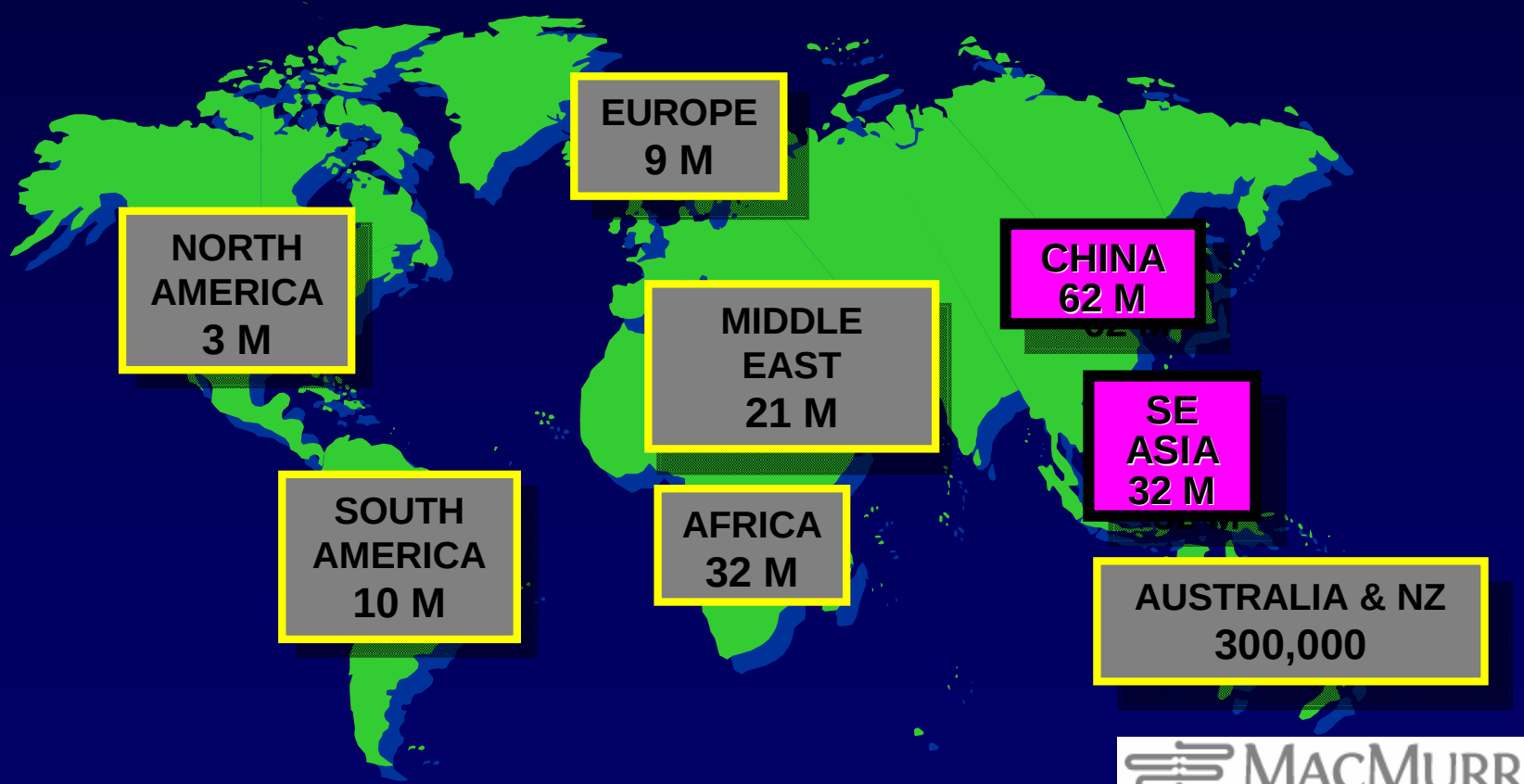
Not all advice is good ...

Epidemiology of HCV
Global Epidemic

- 180 M infected worldwide
- 3-4 M new cases/year



Weekly Epidemiological Record. N° 49, 10 December 1999, WHO

HCV Transmission: Risk factors

- Blood products (pre-1992)
  - Transfusion
  - Haemophiliacs
- IV drug users
- Individuals from endemic countries

- Tattoos
  - Unsterilised needles
  - Shared ink
- Incarceration (>20% prevalence)

- Maternal transmission (<2%)
- Sexual contact?
- Note: Up to 30% of infected individuals spontaneously clear HCV

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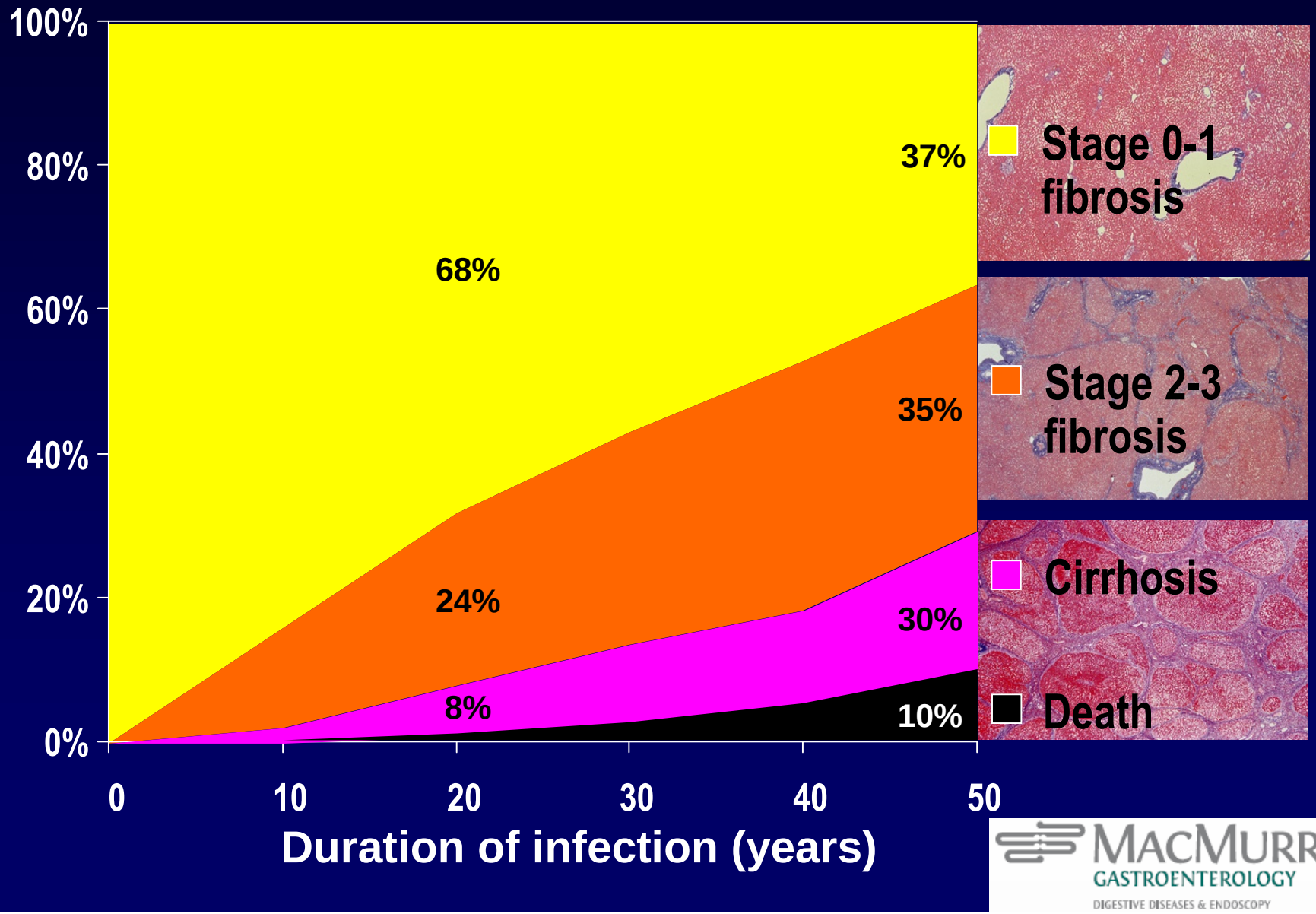
Natural history of chronic hepatitis C



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How to diagnose chronic HCV

- Think about it!
- At risk groups (includes the 60's)
- ALT not helpful or relevant

- Anti HCV Ab: Highly sensitive
  Good as initial screen
  - Caution: may take some months to become positive after acute infection

- HCV RNA (PCR): To confirm current infection

- HCV genotype useful to guide Rx

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Who do you need to refer?

Chronic hepatitis C

- HCV RNA +ve
- Desire to get rid of the virus
- (Not actively IVDU)
- Don’t rely on ALT

Acute hepatitis C

- Refer all cases

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A word on liver biopsy ...

The usual question ...

- Will I need one?
- Not any more!

- *Fibroscan* validated in chronic HCV

- Not useful if ascites, too fat, acute inflammation

HCV Treatment
Pegasys® PEG-IFN 2α + Ribavirin

Genotype 2 or 3	Genotype 1 or 4
24 weeks PEG-IFN + Ribavirin	48 weeks PEG-IFN + Ribavirin

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HCV Treatment
Pegasys PEG-IFN 2α + Ribavirin

Genotype 2 or 3	Genotype 1 or 4
24 weeks PEG-IFN + Ribavirin	48 weeks PEG-IFN + Ribavirin
Up to 85% cure	***Up to 55% cure***

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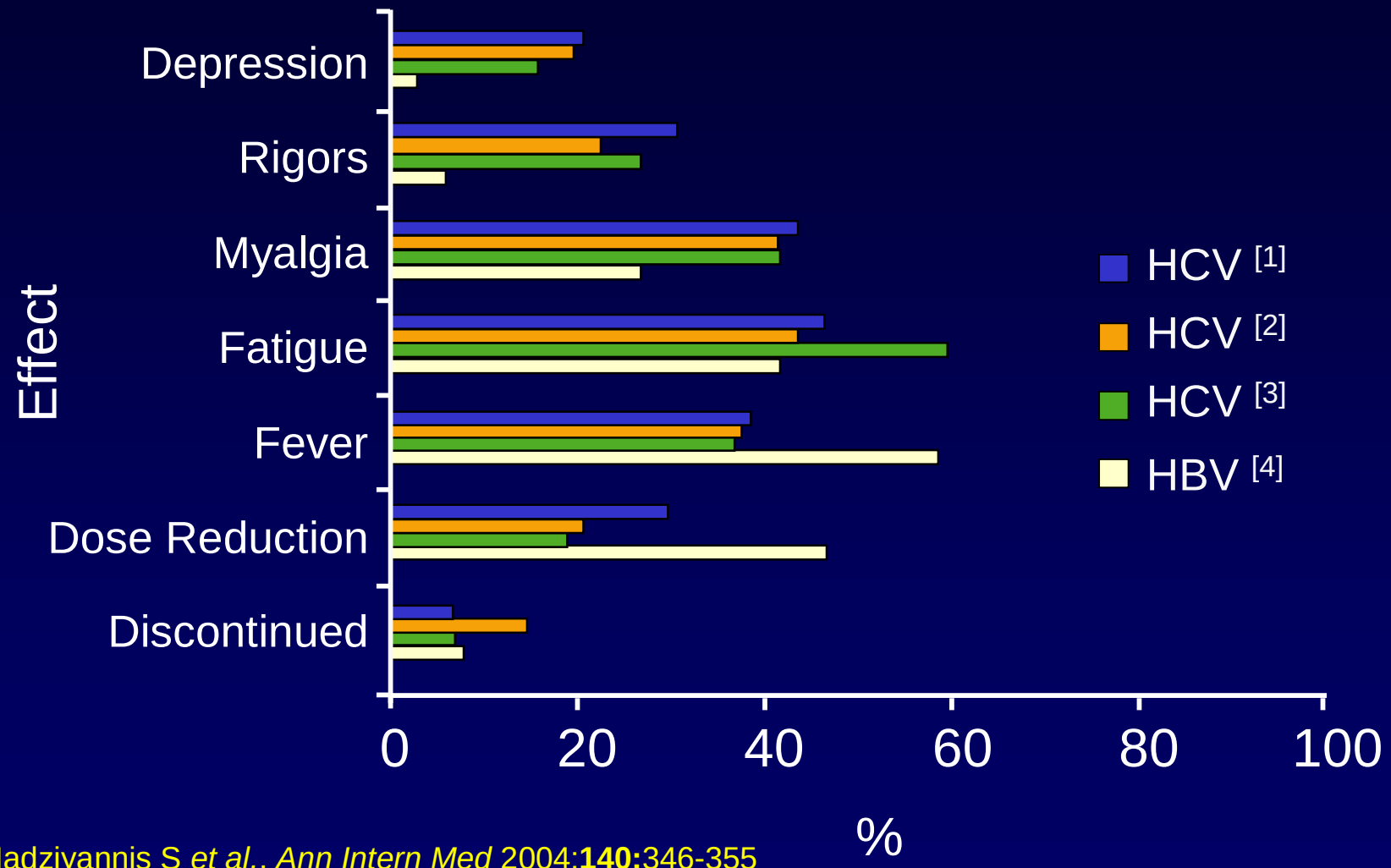
Adverse effects of PEG-IFN



1. Hadziyannis S *et al.*, *Ann Intern Med* 2004;**140:**346-355
2. Fried M *et al.*, *NEJM* 2002;**347:**975-982.
3. Zeuzem S *et al.*, *Gastroenterol* 2004;**127:**1724-1732
4. Marcellin P *et al.*, *NEJM* 2004;**351:**1206-1217

Take home messages

Hepatitis B

- Refer all patients with active disease
- Don’t be fooled by HBeAg negative
  - Look for raised ALT or DNA levels
- Viral suppression improves long-term outcome
  - Prevent cirrhosis, hepatoma, liver failure

Take home messages

Hepatitis C

- Refer all patients with HCV (IVDU)
- Cure rates up to 85% for genotypes 2/3
  - ~ 50% for genotype 1
- New treatments available via clinical trials

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The only comprehensive digestive disease centre in Auckland

Consultations in a team environment
- 5 Gastroenterologists
- 1 Hepatologist
- 2 Upper GI & 1 Colorectal Surgeons

Dietitian
Health Psychologist
Clinical Nurse Specialists

The only place with full diagnostic and therapeutic services

Full endoscopy services
Capsule endoscopy
High resolution Impedance Manometry
24 hr pH/Impedance
BRAVO
CT colonography

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