

**The European Consensus Proposal for  
Handling Infected Healthcare Workers  
with Hepatitis Viruses B & C  
2003**

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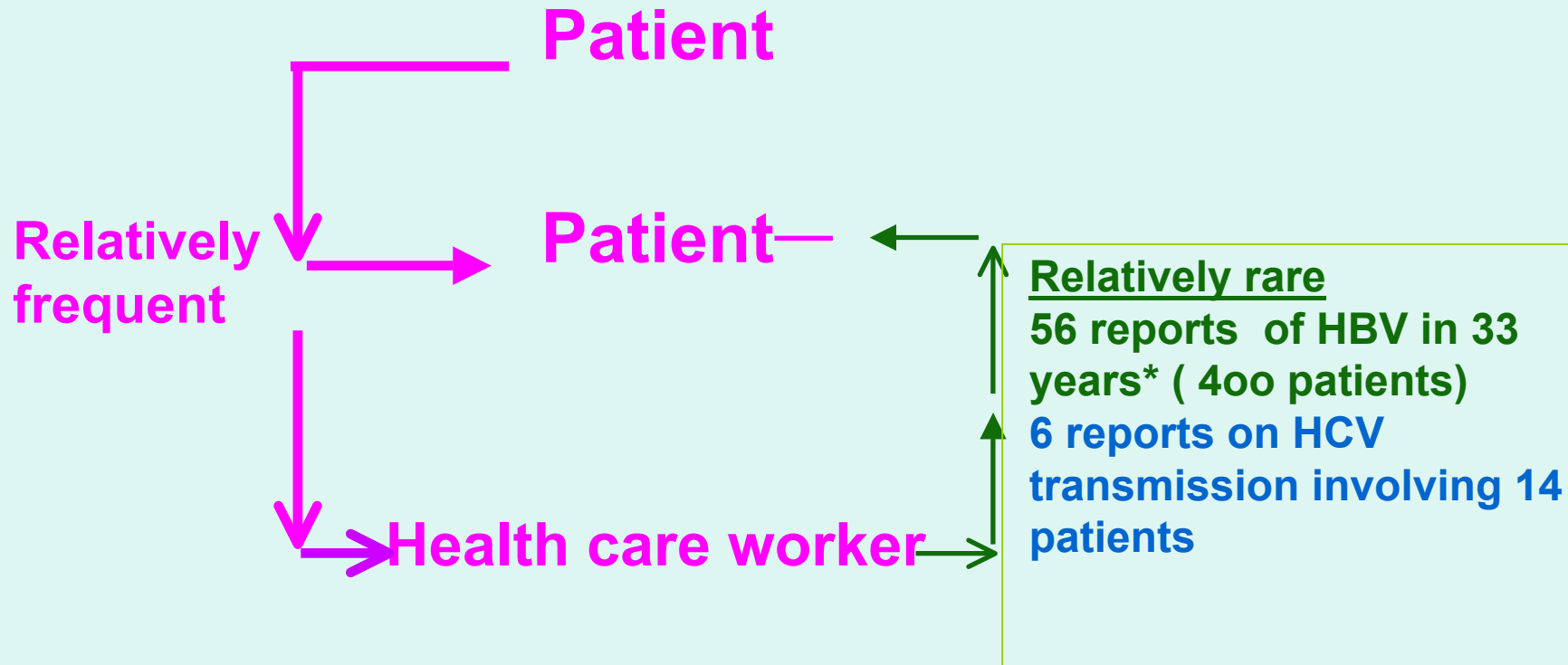
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# Nosocomial HBV In HCWs

## *virus reservoir*



# History

- 45 reports on HBV transmission from HCWs to patients since introduction in 1970s of serologic testing – resulting in 400 infected patients until 1991\* (transmission rates 6-15% in EPPs)
- Between 1991-2003, 11 episodes reported (9/11 from UK, 8/9 with HBeAg(-) pre-core mutants)
- Few Reports on transmission of HCV from infected HCWs to patients
- Question: Do these data reflect the true risk?  
???

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\*Mele et al, *Dig and Liver Dis* 2001, 33:790

# Estimated risk of acquiring viral infection after percutaneous exposure to infected blood\*

- HAV;HEV: very rare
- HBV: 16–67%, (*Variability depending on HBeAg/HBV DNA status*)
- HCV: ~2%
- HIV: 0.3%

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\*Modified according to Gerberding JL. Management of occupational exposures to blood borne viruses. *NEJM* 1995, 332:444.

# The Hepatitis Virus Health Care Worker (HCW) Carrier - Current Status

- Some countries restrict HBeAg+ or HBV-DNA+ HCWs from performing Exposure Prone Procedures (EPP)
- The majority of countries do not restrict practice for HBsAg+/HBeAg– carrier health care workers
- There are no universal clear cut guidelines for practice of HBV or HCV carrier health care workers

# Goal

To reach a consensus statement on the management of healthcare workers (HCW) infected with HBV and HCV

# Potential limitations and concerns re initiation of the survey

- Lack of standardization for HCW epi data collection in individual countries
- Lack of Standardization re viral load assays
- Lack of data on the risk of HBV and HCV transmission from an infected HCW to a patient during EPPs
- Variable attitudes regarding the assessment of an acceptable risk of employing an infected HCW (dependant in part on legal, ethical and professional codes of conduct)
- Concern regarding the effect of opening a debate on the privacy of infected HCWs and on the ability to protect them against discrimination by their employers or patients (i.e.secure compensation and/or retraining and relocation)

# Methods I

- **A questionnaire was devised which requested information on various aspects of HCW management**
- **Experts in blood borne viruses from various countries, mainly in Europe, the US and Israel were than questioned on their national protocols regarding management of the infected healthcare worker**
- **The results and the analysis by the expert committee were than discussed followed by formulation of guidelines and recommendations**
- **The Study was supported by grants from the European Association for the Study of the Liver (EASL) , the British Liver Trust (BLT)**



# Methods II

## Question submitted to experts in 16 countries\*:

- ✓ Estimated sero-prevalence of HBV and HCV in HCWs and the general population
  - ✓ HBV vaccination policies for HCWs
  - ✓ HBV and HCV screening policies for HCWs
  - ✓ Management and restriction of infected HCWs
  - ✓ The lifting of restrictions
  - ✓ Unpublished data on HBV and HCV transmissions to patients
  - ✓ Availability, validation and standardisation of viral load assays for HBV and HCV
-

# Survey

## Countries Participating

- Austria
- Belgium
- France
- Germany
- Greece
- Holland
- Israel
- Italy
- Portugal
- Republic of Ireland
- Sweden
- UK
- US

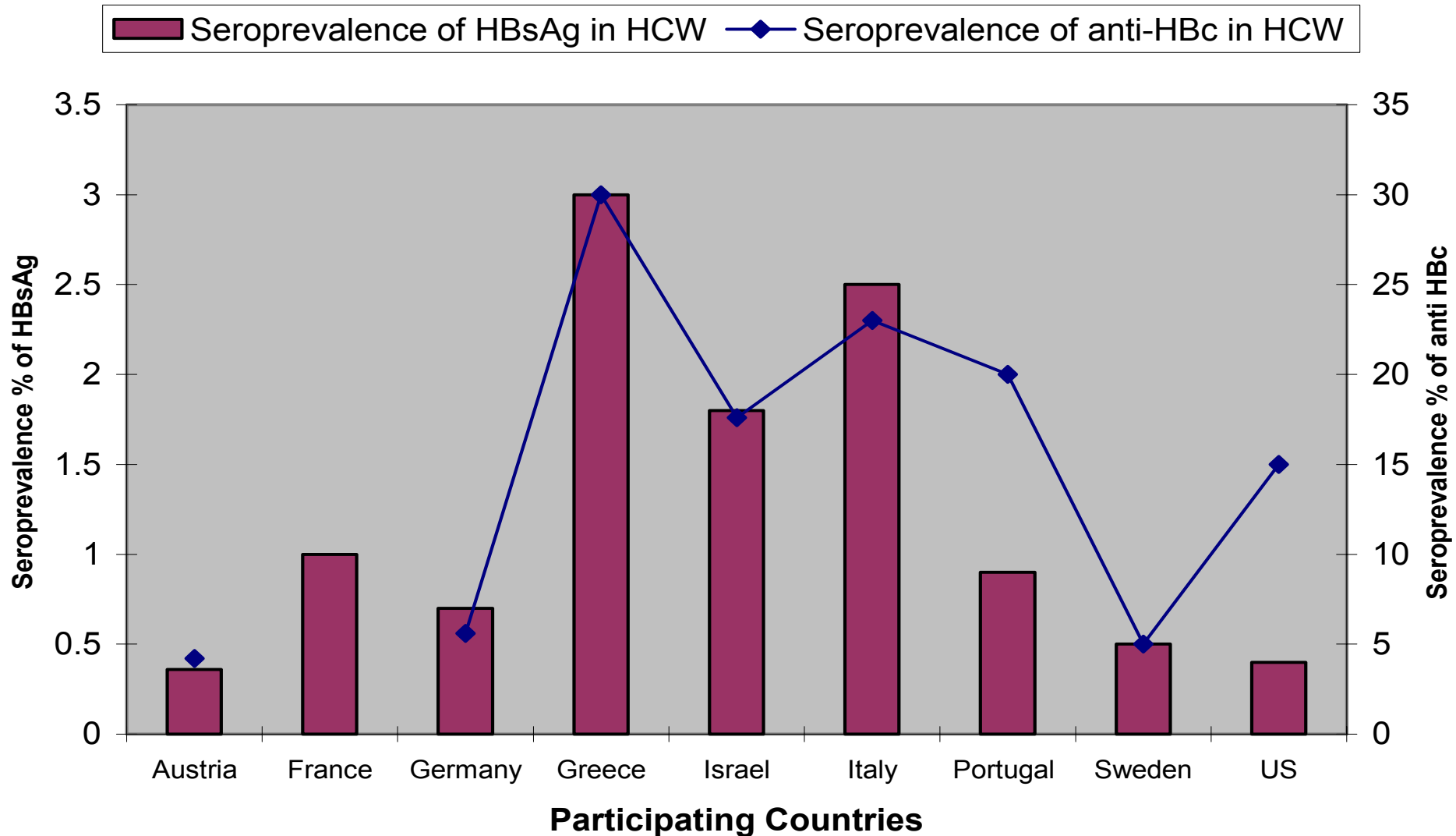
## Countries which did not return questionnaire

- Spain
- Switzerland
- Turkey

# The Infected Healthcare Worker

- Hepatitis B Virus carrier
- Hepatitis C virus carrier

# Seroprevalence of anti-HBc and HBsAg in HCWs



# HBV Transmission from HBeAg-negative HCWs to Patients

<u>Type of Surgeon</u>	<u>Risk Factor</u>	<u>HBV DNA Level</u>	<u>No. Patients Infected</u>
Orthopaedic	EPP	Not published	1
Cardiothoracic	EPP	$1 \times 10^6$ gen equiv/ml	2
General	EPP	$1 \times 10^7$ copies/ml*	1
OB/GYN	EPP	$4.4 \times 10^6$ copies/ml*	1 (? 2 more)
OB/GYN	EPP	$5.5 \times 10^6$ copies/ml*	1
General, urology	EPP	$2.5 \times 10^5$ copies/ml*	1
Orthopaedic	?	$\sim 10^9$ copies/ml	1
General	EPP	$> 2 \times 10^5$ gen equiv/ml	3

\* Retested by Amplicor Monitor and lowest value was  $4 \times 10^4$

# Issues in Prevention of Transmission of Hepatitis Viruses From an Infected HCW to Patients

## Consensus

1. Preventing infection - +++
  2. Identifying infected HCWs ++
  3. Management and restriction of infected HCWs performing EPP +
- 
4. *Removing restriction after successful anti-viral therapy* ???

# 1. Prevention of Nosocomial HBV and HCV Infections

- There is consensus on standard precautions as well as on the need of active immunization against HBV as early as possible in the career of all HCWs and regardless of involvement in EPPs
- There is partial consensus on the approach to non-responders to conventional HBV vaccination
- What about medical students and trainees in health professions? Question was not raised in the survey

# Definitions

Seroprotection: anti-HBs(+) > 10 mIU/ml (UK > 100)

Non-responder: anti-HBs(-) < 2.1 mIU/ml\*

Hypo-responders: anti-HBs (+) 2.1–10 mIU/ml\*\*

Low responder: anti-HBs(+) 11 -100 mIU/ml\*\*

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Seroconversion: anti-HBs (+) > 2.1 mIU/ml

Hyper-responder anti-HBs (+) > 10,000 mIU/ml

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\* after 3+1 or 3+3 doses

\*\* after 3 doses of vaccine



# Approach to the Non-Responder

- ~69% of primary non-responders will develop anti-HBs titers  $>10$  IU/L following a second course of 1-3 injections
- In countries where a pre-S/S vaccine is available, 1-2 booster doses with the more immunogenic vaccine should be encouraged (additional response  $>30\%$ )
- Consider a booster dose in “hypo-responders”<sup>\*</sup> and in HCWs performing EPP if titer of anti-HBs, after 3 doses of vaccine remains  $< 100$  IU/L
- True non-responder HCWs engaged in EPP should be screened for HBV infection at regular intervals (?) and after significant exposure

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***A hyporesponder is defined as a vaccinee who developed an anti-HBs titer between 10-100 IU/L following 3 vaccine doses.***

# Means to Bypass Non-response to Immunization

- Repeated course of vaccination (+++)
  - Try a Pre-S/S Vaccine where available (+)
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## Experimental:

- Intra dermal immunization (+/-)
  - Co-administration of cytokine(s)
  - New adjuvants
  - DNA vaccine
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## 2. Identifying the Infected HCW

- Controversy as to the wisdom of identifying infected HCWs (unless directly involved in a case of HBV or HCV transmission)
- Lack of clear guidelines and legislation
- Despite the above, there was consensus that screening of HCWs as early as possible in their career is recommended giving an opportunity for immunization against HBV.
- In virus carriers it provides an opportunity for important career choices as early as possible

# 3. Management of the Infected HBV Carrier

## Factors which affect decision:

- Performance of EPP
- HBeAg status
- Viral load (quantitative HBV-DNA by PCR)

## Important facts:

- Most HBV transmissions occurred at a viral load  $>10^6$  copies /ml. Transmission unlikely to occur at a viral load of  $10^5$  copies /ml or below
- Seroconversion to anti-HBe may indicate low infectivity and low risk of HBV transmission
- However, 10-30% of anti-HBe+ HBV patients with active liver disease have HBV-DNA levels  $>10^5$ copies/ml

# Viral Load in HBsAg Carriers

- HBV-DNA levels in HBeAg(+) carriers are usually above  $10^5$  copies/ml
- HBV-DNA levels in HBeAg(-) carriers are usually but not always  $<10^5$  copies/m

# Fluctuations in Viral Load in HBsAg Carriers -

- Martinot-Peignoux et al. followed 85 anti-HBe+ carriers with HBV-DNA levels  $<10^5$  copies/ml over a mean period of 3 years (range 0.5-11y). In 96% HBV-DNA levels remained unchanged
- Tedder et al followed 120 anti-HBe+ carriers over a mean period of 6.5y (range 1-18y). In 20/120 (16.6%) a  $\sim 3$  log fluctuation in viral load was observed

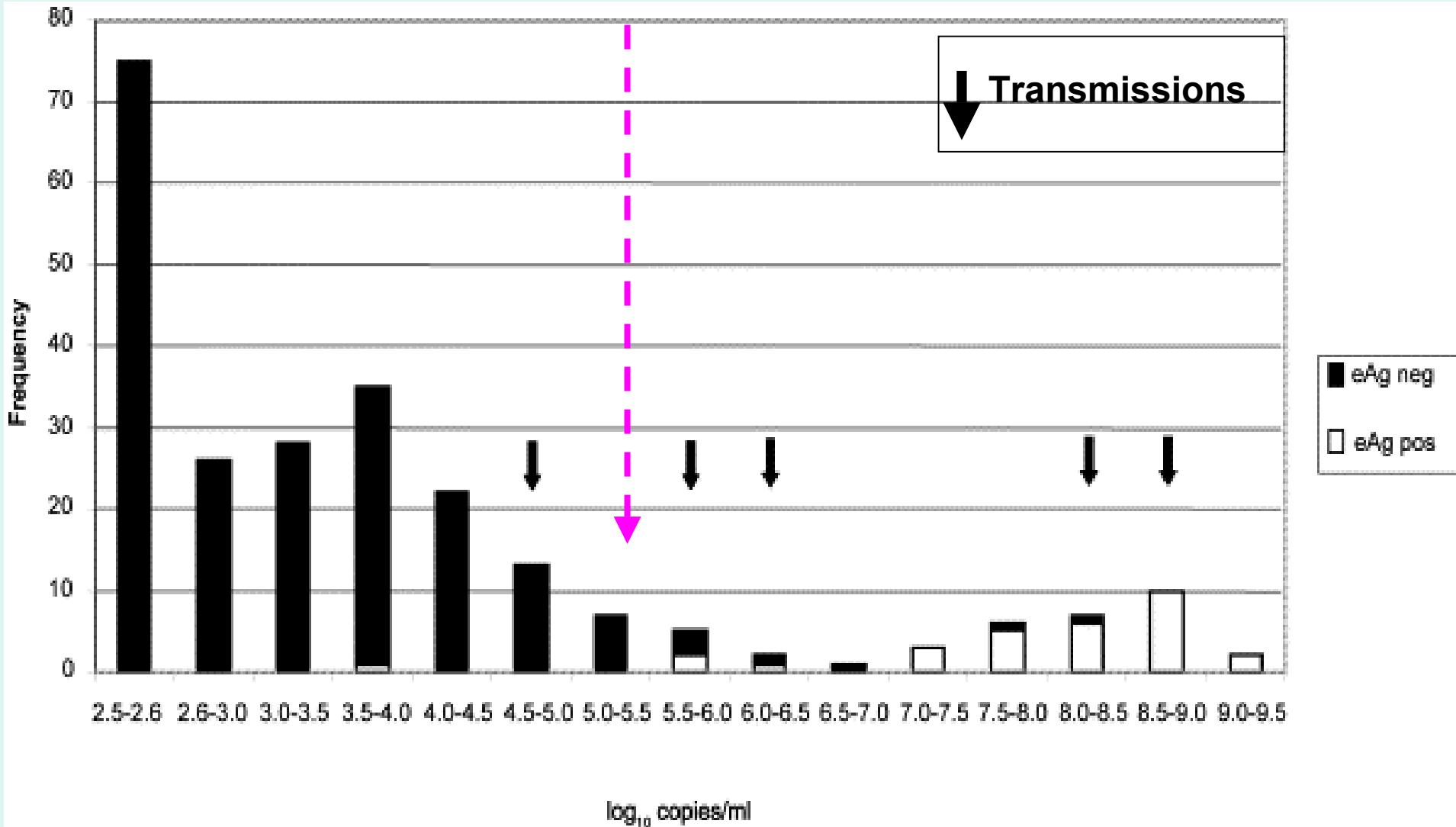
# Range of HBV DNA Levels in HCW (copies/ml)

<u>HBV-DNA</u>	<u>Netherlands</u>	<u>The UK (HBeAg-)*</u>
$\leq 10^3$	1	184
$> 10^3 - 10^4$	2	96
$> 10^4 - 10^5$	6	110
$> 10^5 - 10^6$	3	45
$> 10^6$	5	1
<b>Total</b>	<b>17</b>	<b>436</b>

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*\*In the UK, 7/8 cases of transmission from anti-HBe+ HCW occurred at viral load  $> 10^6$  copies/ml and one at  $2 \times 10^5$  copies/ml*

# Distribution of HBV DNA in 31 HBeAg+ and 211 HBeAg- HBsAg carriers\*





## Changes of HBV DNA levels over time in two anti-HBe (patients closely sampled over 60 and 120 months (

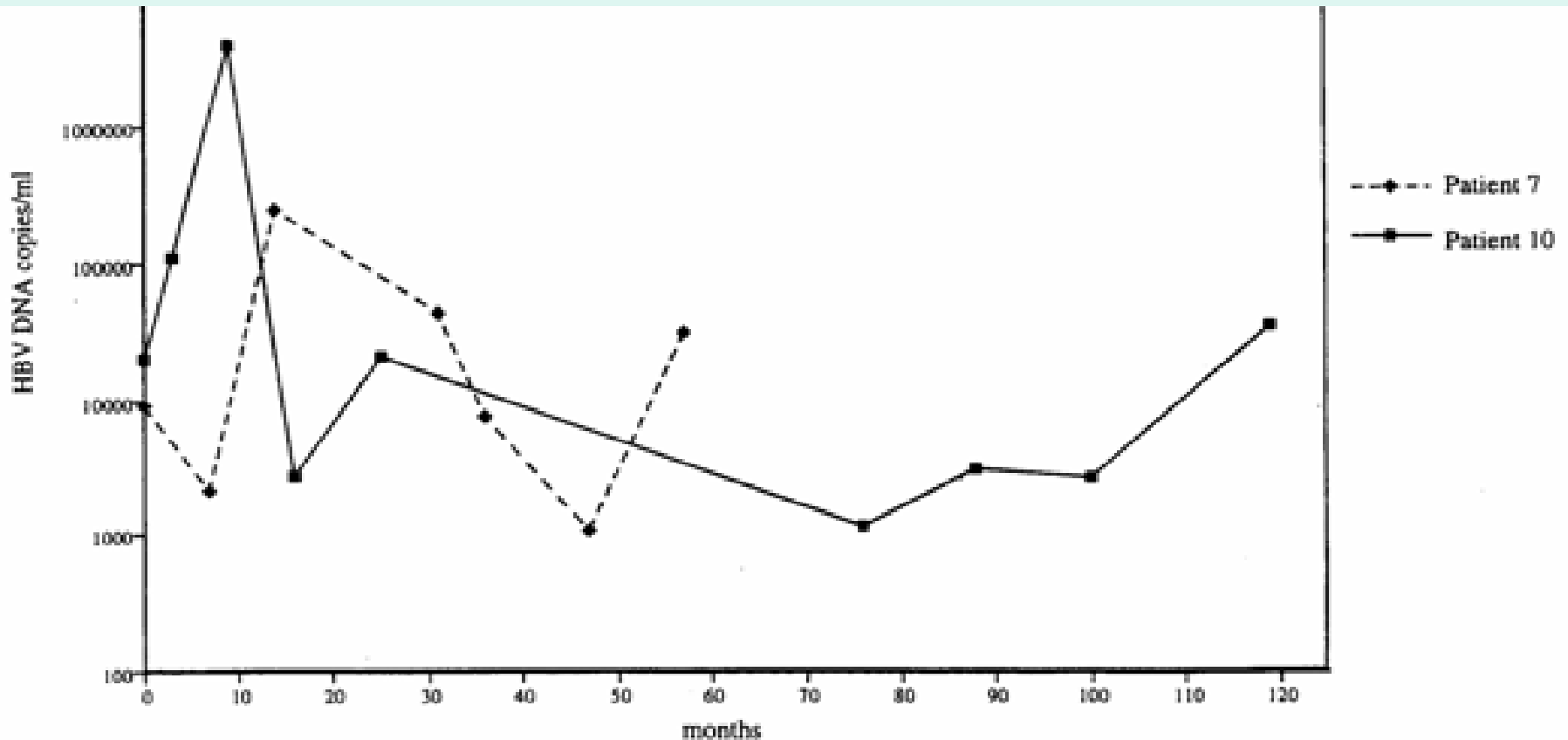


Fig. 5. Changes of HBV DNA levels over time in two patients closely sampled over 60 and 120 months. HBV DNA is expressed as copies per millilitre; follow-up is in months.

# Implications of Stringent Viral Load Threshold on Restrictions of EPP Practice

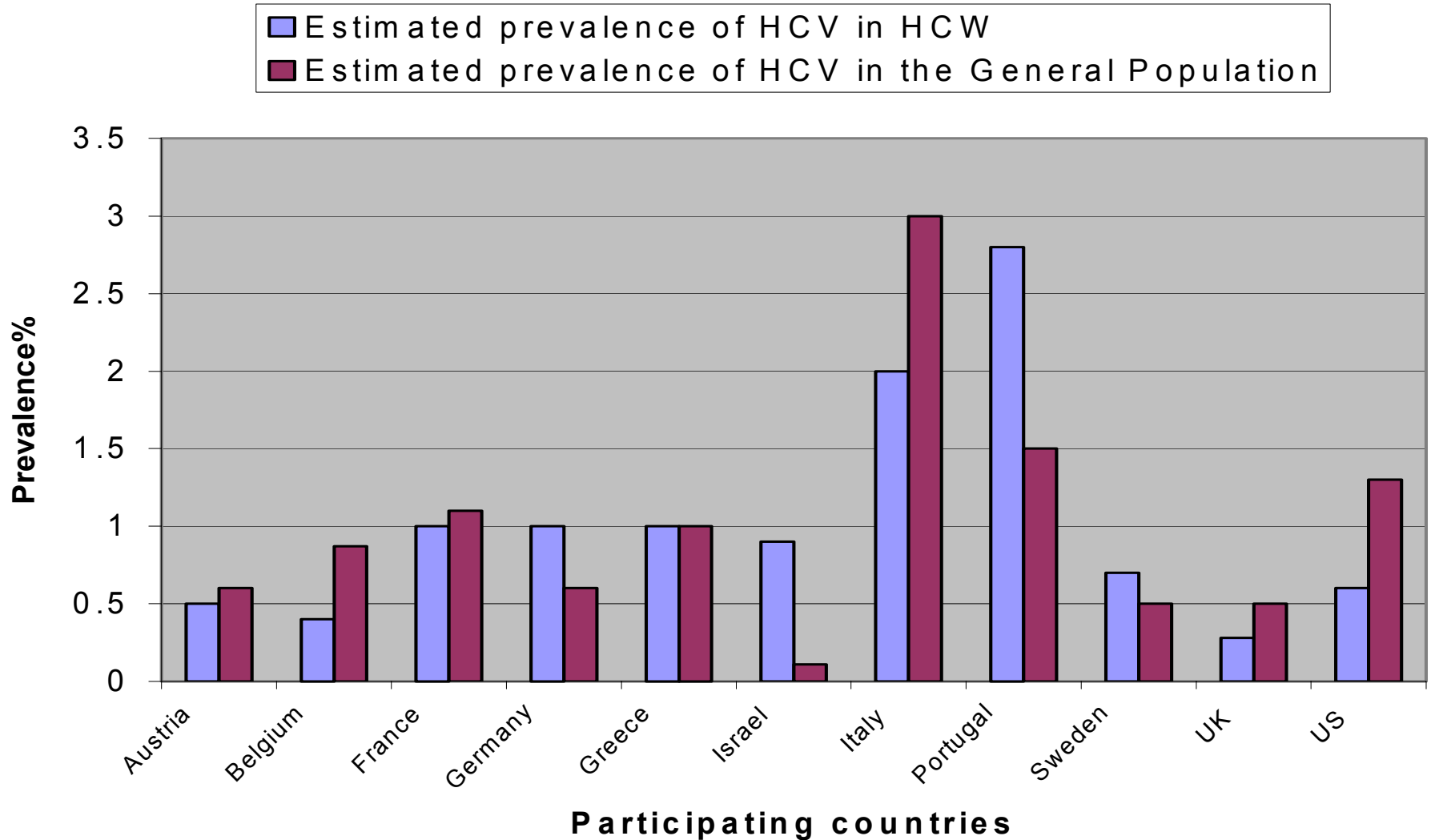
- In the UK cutoff levels of HBV-DNA  $\leq 10^3$  copies/ml lead to restriction of 58% of infected HCW
- In the Netherlands cutoff levels of  $10^3$  copies/ml would lead to EPP Practice restriction of >94% of all infected HCW.  
Therefore the Dutch recommendation was set at cutoff levels  $>10^5$  copies/ml

# Recommendations of the European Consensus Panel

- Each country should define the acceptable risk for HBV transmission from an infected HCW engaged in EPP to patient
- For European countries, the recommended cutoff HBV-DNA level in infected HCW engaged in EPP is  $\leq 10^4$  copies/ml
- The  $\leq 10^4$  copies/ml cutoff level provides a balance between risk of transmission to loss of specialized manpower

# The HCV Infected HCW

# Estimated Prevalence of anti-HCV Among HCW



# Transmission rates of patient look-back studies of non IVDU HCV infected HCWs

HCW	YEAR	NUMBER OF PATIENTS INFECTED	NUMBER OF PATIENT TESTED	TRANSMISSION RATE
Cardiac surgeon	1994	1	278	0.3%
Reconstructive surgeon	1997	0	268	0%
Gynecologist	1993-2000	1	2285	0.04%
Anesthesiology asst.	1998	5	833	0.6%
Orthopedic surgeon	2000	1	229	0.48%

Table 7

Published HCV transmissions from infected HCWs to patients

HCW	Year (country)	Number of patients infected	RNA level	Genotype	Risk factor
Cardiac surgeon	1988–1993 (Spain)	5	$2.2 \times 10^6$ genome equivalents/ml	3	IVDU
Cardiac surgeon	1994 (UK)	1	$10^6$ genome equivalents/ml	4a	EPP
Anaesthesiologist	1994 (US)	1	$3.7 \times 10^6$ genome equivalents/ml	1a	Probable IVDU
Anaesthesiology assistant	1998 (Germany)	5	$1 \times 10^6$ copies/ml	1a	Failure to use standard precautions
Orthopaedic surgeon	2000 (Germany)	1	$1.3 \times 10^6$ IU/ml	2b	EPP
Gynaecologist	2000 (Germany)	1	$2.6 \times 10^5$ IU/ml	1b	EPP
Surgeon <sup>a</sup>	2000–? (UK)	1	/	2b	EPP
Gynaecologist <sup>a</sup>	1978–1999 (UK)	4	/	4	EPP
Member of surgical team <sup>a</sup>	1994–1999 (UK)	2	/	1b	EPP
Cardiac surgeon <sup>a</sup>	1993–1994 (UK)	1	/	?	?
Cardiac surgeon <sup>a</sup>	? (US)	3	/	1b	?
Operating room technician <sup>a</sup>	1991–1992 (US)	40	/	?	IVDU
Anaesthetist	? (Spain)	~217	/	?	IVDU

<sup>a</sup> The investigation into these transmission cases has yet to be published in detail.

# HCV Transmission to HCWs: The Concern

- Most countries do not have a national policy for practice restriction of an HCV infected HCW, unless directly involved in a case of HCV transmission
- The lower risk of transmission (as compared to HBV) is offset by the greater risk of inducing chronic infection in the infected patient
- In most countries, the prevalence of HCV infection in HCWs is similar to the prevalence in the general population.



# Presence of National Guidelines for HCV infected HCWs

## Existing Guidelines

- Belgium
- Germany
- Italy
- UK
- US

## No Guidelines

- Austria
- France
- Greece
- Holland
- Israel
- Portugal
- Republic of Ireland
- Sweden

# HCV Transmission from HCWs to Patients – The Published Evidence

- Overall there appears to be a low risk of transmission
- However, since infection is frequently asymptomatic, the true incidence can not be calculated retrospectively

# Benefits to HCWs of Knowing their HCV Status

- Based on available published data, screening for HCV and restricting infected HCWs is not justified
- It is however recommended that HCWs (including dentists, midwives, nurses etc.) who perform EPP should know their HCV status at the possible earliest stage of their training and before engaging in EPP
- Such a policy enables HCWs to make informed career choices, provides evidence for occupational exposure and would enable infected HCWs to undergo counseling and treatment

# Summary of Recommendations I

- All HCWs should apply standard precautions to every patient!
- All HCWs in contact with body fluids should be vaccinated against HBV and checked for quantitative anti-HBs response within 1-3 month after the final dose
- All HCWs who intend to practice EPP must provide proof of anti-HBs response prior to starting a post (and preferably before starting training) – (Health certificate)
- Non-responders should be given up to additional 3 doses with a conventional HBV vaccine or a third generation PreS/S vaccine where applicable
- Non-responders engaged in EPP must undergo an individual risk assessment with annual testing of anti-HBc and HBsAg
- HCWs who refuse to be vaccinated should confirm that they understand the implications of such an action

# Summary of Recommendations II

- All HBV infected HCWs with HBeAg(+) should not perform EPP
- HBsAg+ HCWs( HBeAg+ or HBeAg-) who wish to practice EPP must be referred to an expert panel and present results of quantitative HBV-DNA testing
- Each country should determine the HBV-DNA cutoff level above which restriction of EPP is mandatory
- The European consensus panel recommended its members a cutoff HBV-DNA level of  $10^4$  genome equivalents/ml

# Summary of Recommendations III

- All HCWs performing EPP should know their HBV and HCV status ,preferably at an early stage of their career
- All HCWs shown to be a source of viral hepatitis transmission to patients should not perform EPP
- No consensus was reached regarding restriction of HCV infected HCWs from EPP
- All infected HCWs (HBV and HCV) should be referred to a hepatologist/gastroenterologist for counseling and potential treatment with anti-viral agents
- All efforts must be made to respect the privacy of infected HCWs

# Referral of HCW to professional counseling

- Hepatology/Infectious disease expert
- A hospital epidemiologist
- A laboratory virologist
- A public health official
- A representative of the HCWs union
- A representative of lay public (optional)

# Counseling for Infected Healthcare Workers

- Establishing viral load
- Clinical evaluation pending antiviral therapy
- Assistance in job relocation if non responsive to treatment
- Importance of confidentiality



# Heterogeneity of Ethical Considerations\*

- There is a complex set of interactions between personal, community, religious, ethnic and cultural values which may vary from country to country
- Differential risk acceptance perception: i.e, we might have 100,000 people who have HCV/HBV or HIV as a result of IVDA but even 10 infected HCWs would be considered excessive by those in the community who do not have HCV (0 tolerance)
- High profile court cases; media and availability of indemnity insurance may influence ethical considerations

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\*Modified according to G. Cooksley

**Impact of Restriction**

**Hypothetical Examples**

# Prevalence of hepatitis C virus in liver transplant surgeons\*

- 117 surgeons at ILTS meeting in Barcelona, 2003
- Anonymous testing for HCV by Elisa III, PCR and genotype
- HCV+ Transplant recipient population 31-40%
- Range of annual transplant number 21-30
- Two surgeons had anti HCV+
- One surgeon was positive for HCV RNA (G1)

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\*Thorburn, AASLD, 2004

# Informed Consent I

*Should disclosure of HBV or HCV seropositivity lead to lifting of restrictions?*

## Arguments for Disclosure

- Allows patient to make an informed choice regarding risk versus expertise of the surgeon and EPP performer
- In the case of an HBV infected HCW, the patient may chose to be vaccinated
- Disclosure has important medico-legal implications for the HCW and his/her employer

# Informed Consent II

*Should disclosure of HBV or HCV seropositivity lead to lifting of restrictions?*

## Arguments Against Disclosure

- Difficulty in educating patients re the real risk and consequences of HBV or HCV infection
- Patients may exaggerate or misinterpret the risk leading to misinformed decision and discrimination of HCWs i.e. based on ethnic origin
- Effect of disclosure on privacy and career of the infected HCW
- Mandatory disclosure of HBV/HCV/HIV status of HCW to patient may lead to a similar requirement on behalf of HCWs wishing to know their patient status prior to performing EPP or refusing to operate on infected patients

**Thank you**

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**\*Journal of Clinical Virology 2003; 27:213**