HBV and HCV infection in health-care workers

Y.Yazdanpanah
Service Universitaire des Maladies Infectieuses et du Voyageur
C.H. Tourcoing, Faculté de Médecine de Lille
CNRS U362, Lille, France

Hepatitis C Virus

HCV transmission in the health care setting

- patient to provider
- patient to patient
- provider to patient

HCV transmission in the health care setting

patient to provider
patient to patient
provider to patient

Patient to provider

HCV transmission: patient to provider

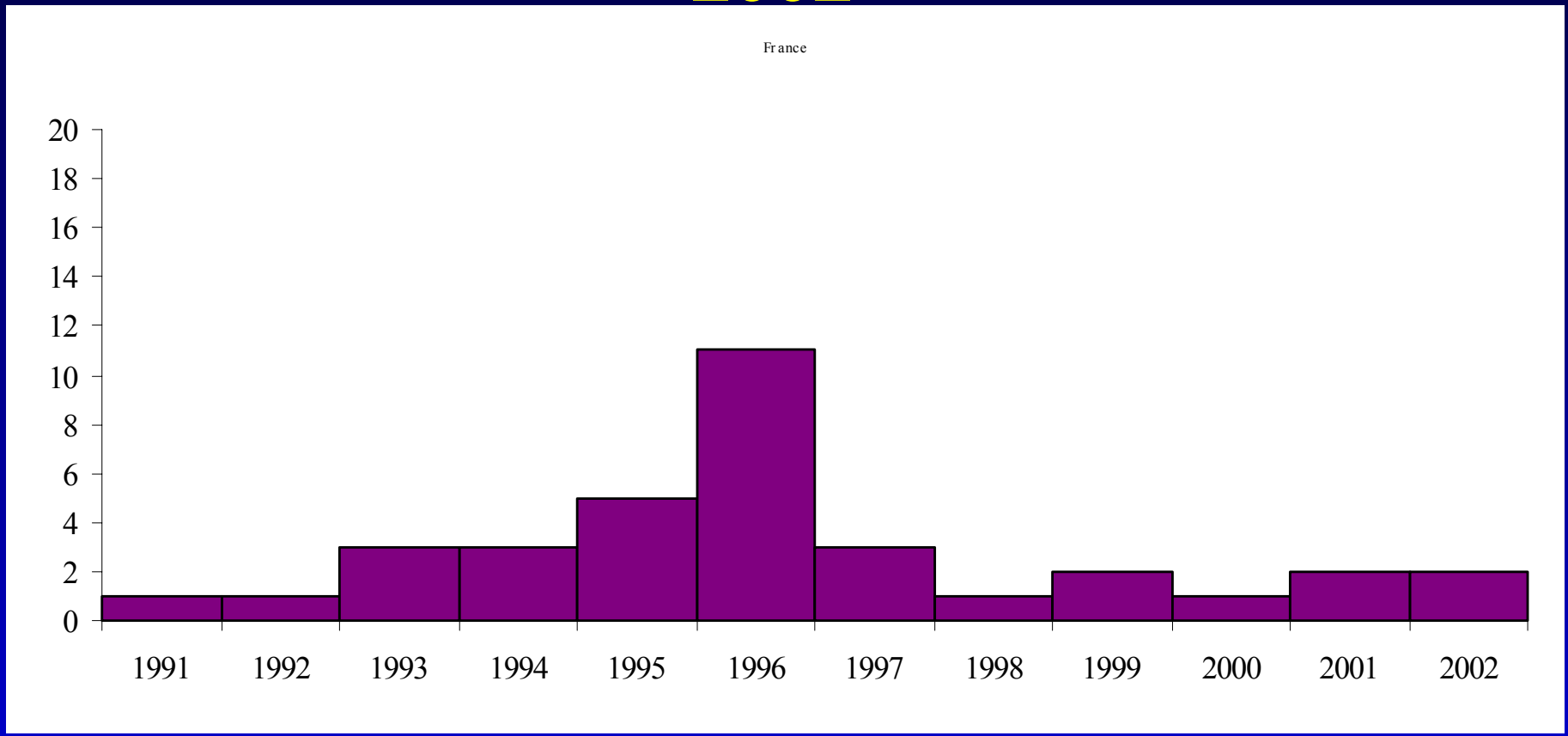
- **Evidence from case reports**
  - Percutaneous exposure to infected patients' blood: multiple case reports
  - Splashes of blood onto health care workers' (HCW) mucous membranes: few case reports
    - » **Rosen.**1997. Acquisition of hepatitis C by a conjunctival splash. Am. J Infect. Control **25:**242–247.
    - » **Sartori et al.** 1993. Transmission of hepatitis C via blood

French national surveillance systems for occuptionally HCV infection (InVS)

- **Data retrospectively collected up to 1998**
- **Data prospectively collected from 1998**

- Confirmed case definition = HCWs who had:
  - Documented occupational exposure to blood or infectious body fluids from an anti-HCV antibodies positive source
  - Anti-HCV negative at the time of exposure
  - HCV seroconversion temporally associated with the exposure

Confirmed cases of transmission in France per year of exposure: 1991-2002



HCV transmission: patient to provider

- **The risk of HCV transmission**
  - **Cohort studies:**
    - » **Cooper et al.** 1992. Infect. Control Hosp. Epidemiol.
    - » **Di Nardo et al.** 1994 Infection.
    - » **Gerberding** 1994. J. Infect. Dis.
    - » **Lanphear et al.** 1994. Infect. Control Hosp. Epidemiol.
  - **Mathematical models:**
    - » **Petrosillo et al.** 1995 Am J Infect Control
    - » **Pietrabissa et al**. 1997 World J Surg
    - » **Hung Kuo et al.** 1999 Ann Thorac Surg
    - » **Yazdanpanah et al**. 1999 J Hepatol

Conflicting results on the risk of HCV transmission

Infection rates among HCV-Exposed HCWs (adapted from Jagger et al. JAMA 2002)

Author	Year	Country	Cases Exposed	Infection n	Infections Rate (%)	95% Confidence intervals
Hernandez	1992	Spain	81	0	0	0.0- 4.4
Zuckerman	1994	U.K.	24	0	0	0.0-14.2
Hasan	1999	Kuwait	24	0	0	0.0-14.2
Baldo	2002	Italy	68	0	0	0.0- 5.3
Evans	2002	U.K.	439	1	0.2	0.0- 1.3
Monge	1995	Spain	603	2	0.3	0.0- 1.2
Kidouchi	1999	Japan	4 836	15	0.3	0.1- 0.5
Petrosillo	2001	Italy	4 292	19	0.4	0.2- 0.6
Serra	1998	Spain	443	3	0.7	0.1- 2.0
Takagi	1998	Japan	250	4	1.6	0.4- 4.0
Sodeyama	1993	Japan	90	2	2.2	0.2- 7.8
Arai	1996	Japan	56	3	5.4	1.1-14.9
Lanphear	1994	U.S.A.	50	3	6.0	1.2-16.5
Mitsui	1992	Japan	68	7	10.3	3.0-17.5
Total			**11 324**	**59**	**0.5**	**0.4- 0.7**

Factors influencing infectivity?

Prevention and management of occupational exposure to HCV

Management of exposure to HCV

- Prophylaxis for HCV: not available
- Treatment of acute HCV infection: PegIFN +/-Ribavirin
  - Treatment of acute HCV infection more effective than early treatment of chronic HCV?

Management of exposure : if exposure to an HCV positive source

French recommendations*	European recommendations**	US recommendations***
Baseline, month 1,3,6: Anti-HCV antibodies ALT activity *If ALT level increased:* *Qualitative HCV-RNA*	Baseline, month 1,(3),6: Anti-HCV antibodies Baseline, month 1,2,3,4: ALT activity *If ALT level increased:* *Qualitative HCV-RNA*	Baseline, months 4-6: Anti-HCV antibodies ALT activity 4–6 weeks : Qualitative HCV-RNA (if earlier diagnosis of HCV is desired)

*CIRCULAIRE DGS-VS2/DH-EO2 n° 99/680 DU 8 décembre 1999

**http://europa.eu.int/comm/health/ph_projects/2000/com_diseases/fp_commdis_2000_frep_10_en.pdf, 2002

***U.S. Public Health Service Guidelines, MMWR, 2001

Risk factors for HCV transmission after occupational exposure in health care workers (HCWs): a European case-control study (ANRS)

Y.Yazdanpanah, G.De Carli, B.Migueres, F.Lot, M.Campins, C.Colombo, T.Thomas, S.Deuffic, A.Tarantola, D.Abiteboul, P.Deny, S.Pol, J.C.Desenclos V. Puro, E.Bouvet.

GERES, Paris, France ; Istituto Nazionale per le Malattie Infettive, Rome, Italy ; InVS, Saint-Maurice , France ; Hospital Vall d'Hebron, Barcelona, Spain; Div.Infect Dis and Hospital Epidemiol, Zurich, Switzerland; HIV & STI Div CDSC, London, UK

Cases and controls enrolled

	France	Italy	U.K.	Spain	Switz	Total
Cases	35	16	3	4	2	60
Controls	110	64	9	12	9	204

Characteristics of injuries sustained and information on source patients by case patients and matched controls

	Cases (n =60)	Controls (n = 204)
Body material		
Blood	**98.3%**	**93.1%**
Other	**1.7%**	**5.9%**
Viral load (source)*		
PCR +	**100.0%**	**85.0%**
PCR -	**0.0%**	**15.0%**
Exposure		
Percutaneous	**100.0%**	**83.8%**
Other	**0.0%**	**15.7%**

*cases = 37, controls =61

Risk factors for HCV transmission after percutaneous exposure to HCV: multivariate analysis*

	Cases (n =60)	Controls (n = 204)	OR	95%CI
Device				
Hollowbore needle in vein or artery	**80.0%**	**38.2%**	**22.9**	**4.7- 105.1**
Hollowbore needle	**15.0%**	**22.1%**	**10.6**	**0.9- 128.4**
Other sharp objects	**5.0%**	**23.5%**	**1.0**	
Severity				
Deep	**58.5%**	**17.2%**	**88.3**	**10.5-743.7**
Moderate	**36.2%**	**34.0%**	**33.3**	**4.2-261.1**
Superficial	**5.3%**	**31.9%**	**1.0**	
Gender				
Male	**30.5%**	**19.6%**	**3.4**	**1.1- 9.9**

*information on the source patient not included

Impact of source patient viral load on HCV transmission - univariate analysis

	Cases (n =60)	Controls (n = 204)	OR	95%CI
HCV viral load				
<= 4 log_{10} cop/mL	8.3%	40.7%	**1.0**	
4< <=6 log_{10} cop/mL	41.7%	37.0%	**5.5**	0.6-55.5
> 6 log_{10} cop/mL	50.0%	22.2%	**11.0**	1.1-114.1

*cases = 12, controls =27

Factors influencing infectivity and risk factors for acquiring HCV infection among HCWs:

Management of occupational exposure to HCV

- Severity of the injury
- Device involved
- Source patient qualitative and quantitative HCV RNA

Low risk exposures : follow-up based on anti-HCV antibodies

High risk exposures : follow-up based on ALT monitoring or HCV RNA testing

Provider to patient

Not cross-contaminations.

HCV transmission: provider to patient

- **Evidence from case reports and clusters cases:**
  - **Public Health Laboratory Service.** 1995. Commun. Dis. Rep. Wkly.
  - **Esteban et al.** 1996. N. Engl. J. Med.
  - **Public Health Laboratory Service.** 1999. Commun. Dis. Rep. Wkly.
  - **Ross et al.** 2000. N. Engl. J. Med.
  - **Ross et al.** 2002. J. Med. Virol.

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	2.2×10^6 genome equivalents/ml	3	IVDU
Cardiac surgeon	1994 (UK)	1	10^6 genome equivalents/ml	4a	EPP
Anaesthesiologist	1994 (US)	1	3.7×10^6 genome equivalents/ml	1a	Probable IVDU
Anaesthesiology assistant	1998 (Germany)	5	1×10^6 copies/ml	1a	Failure to use standard precautions
Orthopaedic surgeon	2000 (Germany)	1	1.3×10^6 IU/ml	2b	EPP
Gynaecologist	2000 (Germany)	1	2.6×10^5 IU/ml	1b	EPP
Surgeon[a]	2000–? (UK)	1	/	2b	EPP
Gynaecologist[a]	1978–1999 (UK)	4	/	4	EPP
Member of surgical team[a]	1994–1999 (UK)	2	/	1b	EPP
Cardiac surgeon[a]	1993–1994 (UK)	1	/	?	?
Cardiac surgeon[a]	? (US)	3	/	1b	?
Operating room technician[a]	1991–1992 (US)	40	/	?	IVDU
Anaesthetist	? (Spain)	~217	/	?	IVDU

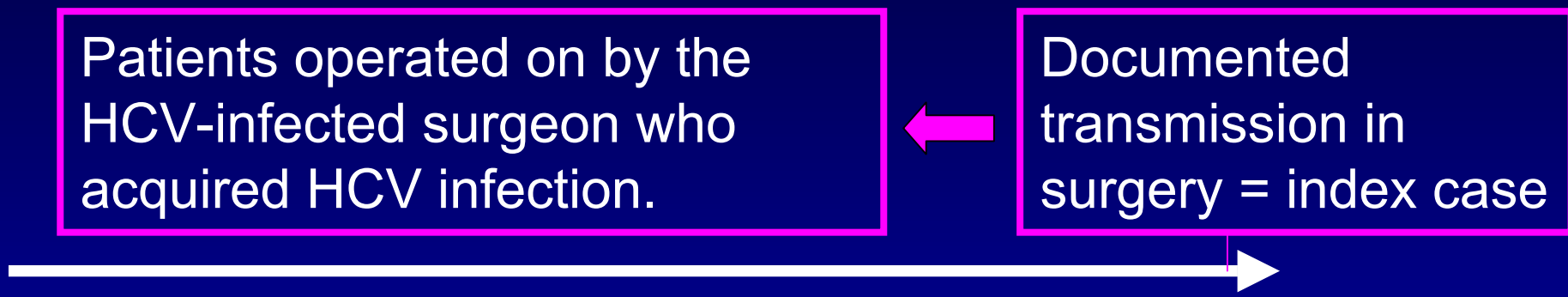
[a] The investigation into these transmission cases has yet to be published in detail.

Gunson et al. J Clin Virol 2003

HCV transmission: provider to patient

- **The risk of HCV transmission**
  - **Look-back studies:**
    - **Esteban et al.** 1996. N. Engl. J. Med.
    - **Public Health Laboratory Service. 2000**. Commun. Dis. Rep. Wkly
    - **Pugliese et al.** 2000. Infect. Control Hosp. Epidemiol.
    - **Ross et al. 2002** Arch. Intern. Med.
  - **Mathematical models:**
    - **Ross et al. 2000** Arch. Intern. Med.

Look-back studies



- Proportion of operated patients who acquired HCV: 0.13% - 0.18% (up to 7 years; in one case 22 years before the index case transmission)
- Limitation: look back studies only if index cases
- Proprtion of patients operated on by an HCV-infected surgeon who acquire HCV infection: **0 to 0.18%**

Mathematical models

Pr [transmission from infected medical staff to patients]

=

Pr [percutaneous injury]

X

Pr [patient to provider blood exposure]

X

Pr [transmission after exposure to infected blood]

Risk of HCV transmission: an infecetd surgeon to one patient

Ross et al. Arch Intern Med 2000

2.3%

27.0%

1.0%

2.2%

9.2%

Mathematical models: risk of HCV transmission from an infecetd surgeon to one patient Ross et al. Arch Intern Med 2000

Pr [VHC Transmission after exposure to infected blood]	Pr [Transmission-an infecetd surgeon to one patient]	
	In one year	In 30 years
1.0%	3.1%	60.6%
2.2%	6.8%	87.8%
9.2%	24.8%	100.0%

Face validity?
Look-back studies: 0 to 0.18%

Mathematical models

Pr [transmission from infected medical staff to patients]

=

Pr [percutaneous injury]

X

Pr [patient to provider blood exposure]

X

Pr [transmission after exposure to infected blood]

Risk of HCV transmission: an infecetd surgeon to one patient

Ross et al. Arch Intern Med 2000

2.3%

27.0%

1.0%

2.2%

9.2%

Management of infected HCWs

Pr [transmission from infected medical staff to patients]

=

Pr [percutaneous injury] ← **Technique changes and safer needle devices**

X

Pr [patient to provider blood exposure] ← **Protective barriers: double gloving +++**

X

Pr [transmission after exposure to infected blood] ← **HCW to be referred to a hepatologist for treatment**

Liberté • Égalité • Fraternité
RÉPUBLIQUE FRANÇAISE

MINISTERE DE LA SANTE, DE LA FAMILLE
ET DES PERSONNES HANDICAPEES

DIRECTION GENERALE DE LA SANTE

AVIS DU CONSEIL SUPÉRIEUR D'HYGIÈNE PUBLIQUE DE FRANCE
SECTION MALADIES TRANSMISSIBLES
Relatif à la prévention de la transmission du virus de l'hépatite virale C (VHC)
aux patients par les professionnels de santé

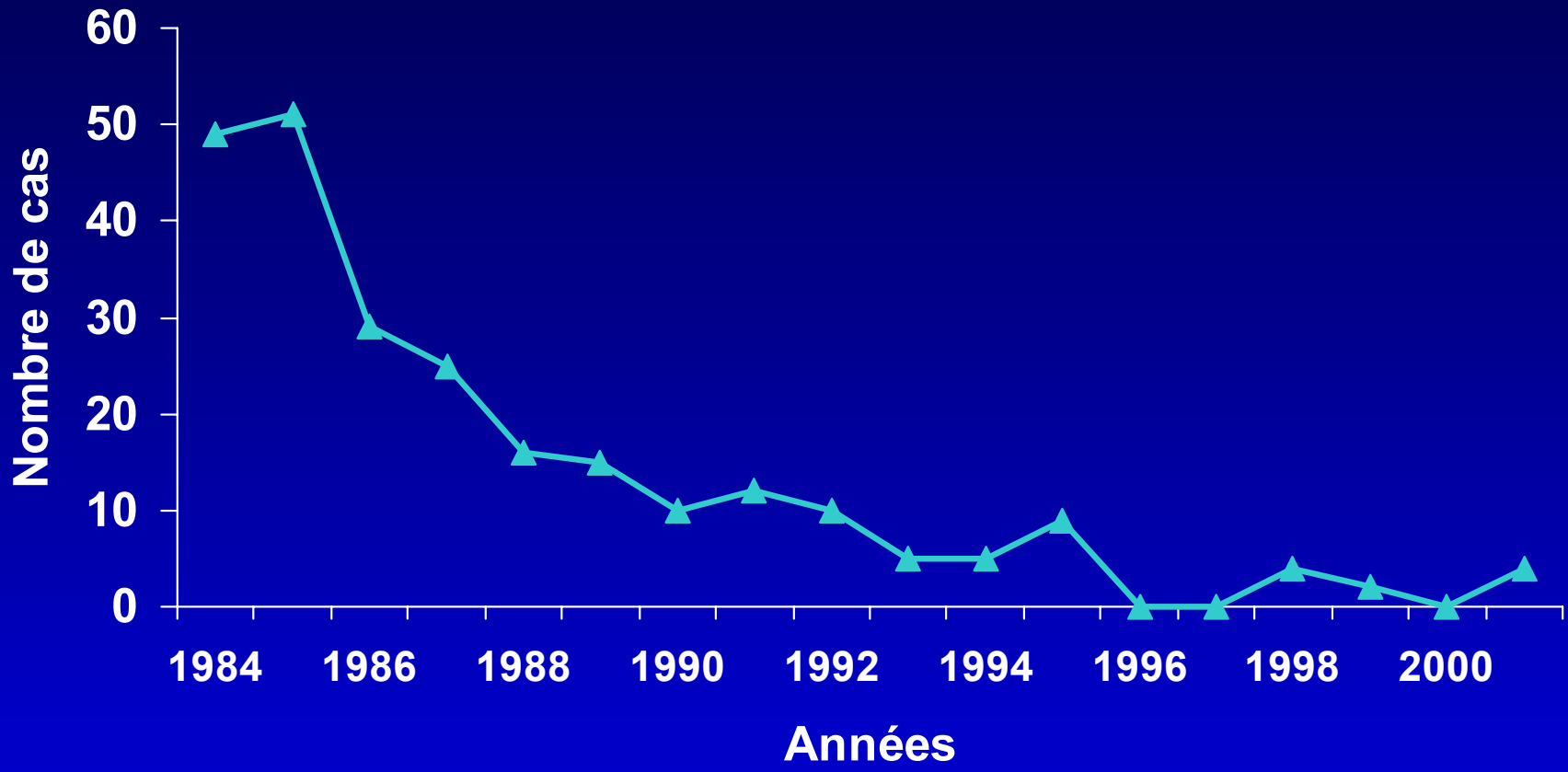
(séance du 26 septembre 2003)

"En cas de sérologie positive et d'infection chronique confirmée par la positivité de la recherche de l'ARN viral dans le sérum,

- ces professionnels devraient consulter un spécialiste afin de définir les modalités d'une éventuelle prise en charge thérapeutique,
- si un éventuel traitement ne permettait pas d'obtenir une éradication du virus, ces professionnels de santé devraient entrer en contact avec une **commission spécifique,** commission dont le rôle serait de **les conseiller afin d'adapter leurs pratiques** à leur situation virologique et **de discuter d'un éventuel reclassement professionnel**."

Hepatitis B Virus

Distribution of occupationnaly acquired cases of hepatitis B per year of declaration– Paris public hospitals: 1984-2001



Source: Drs Abiteboul et Benketira, Médecine du travail, médecine de contrôle AP-HP

Prevention of HBV infection in the HCW

- Standard precautions
- HBV vaccination
  - Non-responders (5-10%)
  - Vaccination coverage

*Non-responders: anti-HBs levels B <10 after 6 doses of HBV vaccine

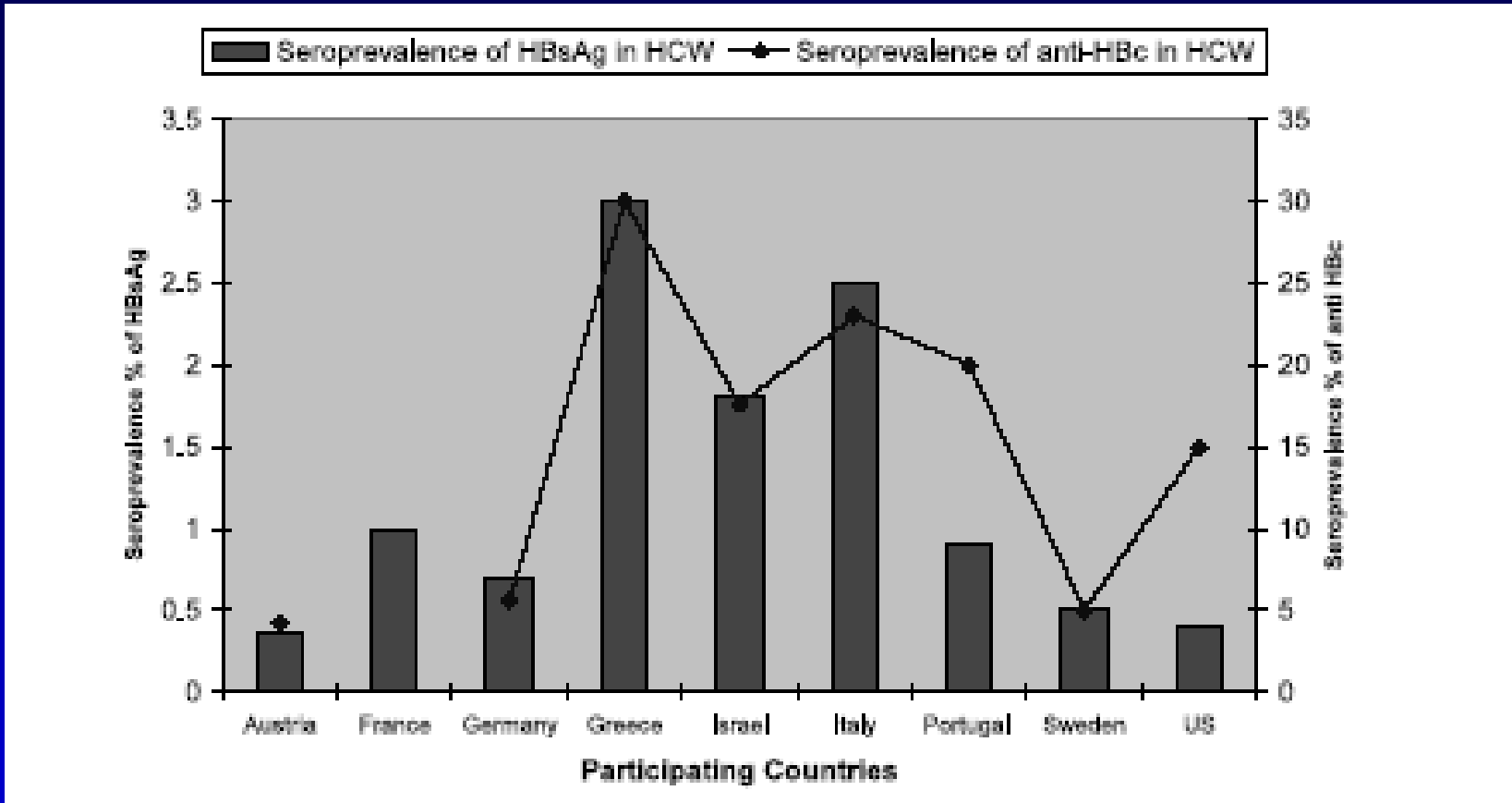
Vaccination coverage

- HCWs in Paris public hospitals (AP-HP):
  - 1990: 72%
  - 1993: 91%
- Surgeons in France
  - 1997: 79%

Denis et al. Med Mal Infect 2004
GERES 1997

Management of infected HCWs

The seroprevalence of HBsAg and anti-HBc in HCW



Gunson et al. J Clin Virol 2003

Liberté • Égalité • Fraternité
RÉPUBLIQUE FRANÇAISE

MINISTERE DE LA SANTE, DE LA FAMILLE
ET DES PERSONNES HANDICAPEES

DIRECTION GENERALE DE LA SANTE

AVIS DU CONSEIL SUPÉRIEUR D'HYGIÈNE PUBLIQUE DE FRANCE
SECTION MALADIES TRANSMISSIBLES
Relatif à la prévention de la transmission du virus de l'hépatite virale B (VHB) aux patients par les professionnels de santé
(séances du 27 juin et du 7 novembre 2003)

- La présence de signes d'infectiosité implique que les gestes associés à un haut risque de transmission ("*exposure prone procedures*“) ne peuvent être autorisés.
  - (i) la détection de l'antigène HBe dans le sérum;
  - (ii) si l'antigène HBe est indétectable, une concentration de l'ADN du VHB dans le sérum supérieure à un seuil de référence
- Les possibilités de traitement par les antiviraux et la réponse à ces traitements doivent également être prises en compte dans l'évaluation

Management of HBV infected HCWs

- Lifting the restrictions on the HBV infected HCWs
  - Three approved antiviral agents for the treatment of chronic HBV: interferon, lamivudine, adefovir (+ tenofovir and emtricitabine in HIV infected patients)
  - Two antiviral agents likely to become available in the future: entecavir, telbivudine

To consider allowing HCWs on long-term mono-therapy, with successful suppression of HBV DNA, to return to performing invasive procedures?

Back-up slides

Study Design – Study Population

- A matched case-control study
  - Cases = HCWs who had:
    - Documented occupational exposure to HCV-infected body materials
    - HCV seroconversion temporally associated with the seroconversion
    - No other reported concurrent exposure to HCV
  - Controls = HCWs who had:
    - Documented occupational exposure to HCV-infected body materials
    - HCV negative at exposure and at least 6 months later

Identification of case patients and controls

- Cases identified through reports to national or regional surveillance systems for occuptionally HCV infection
  - In France, Italy, Spain, Switzerland, United Kingdom
  - From 01/1993 to 12/2002.
- Controls identified by physicians in charge of surveillance of occupational infections matched to cases for:
  - Center
  - Time period

Exposure prone procedures

- Digital palpation of a needle tip in a body cavity
- Simultaneous presence of the HCW's fingers and a needle or other sharp instrument in a poorly visualized or highly confined anatomic site.

Screening of HCWs with hepatitis C?

Liberté • Égalité • Fraternité
RÉPUBLIQUE FRANÇAISE

MINISTERE DE LA SANTE, DE LA FAMILLE
ET DES PERSONNES HANDICAPEES

DIRECTION GENERALE DE LA SANTE

AVIS DU CONSEIL SUPÉRIEUR D'HYGIÈNE PUBLIQUE DE FRANCE
SECTION MALADIES TRANSMISSIBLES
Relatif à la prévention de la transmission du virus de l'hépatite virale C (VHC) aux patients par les professionnels de santé

(séance du 26 septembre 2003)

. Afin qu'ils puissent mettre en œuvre tous les moyens leur permettant d'éviter une transmission du virus à leurs patients en cas de positivité et afin d'éviter de voir leur responsabilité civile ou pénale engagée, les professionnels de santé en exercice devraient connaître leur sérologie vis-à-vis du VHC.