

# **FOIE ET ADDICTION**

cours présenté le 4 octobre 2001 à Genève  
lors de la journée COROMA 2001  
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Chef de service de la Division de gastroentérologie  
et d'hépatologie des Hôpitaux universitaires de Genève.

A dark, starry night sky with a bright yellow star in the center. The text "Le foie et..." is written in white, sans-serif font in the upper left quadrant.

Le foie et...

l'addiction...

Antoine Hadengue, Genève, 4 octobre 2001

Mal. Alc. du foie

Hépatite C

Le foie et ... et plus  
l'addiction

Hépatite toxique

Transplantation

Le foie et  
l'addiction

Hépatite C

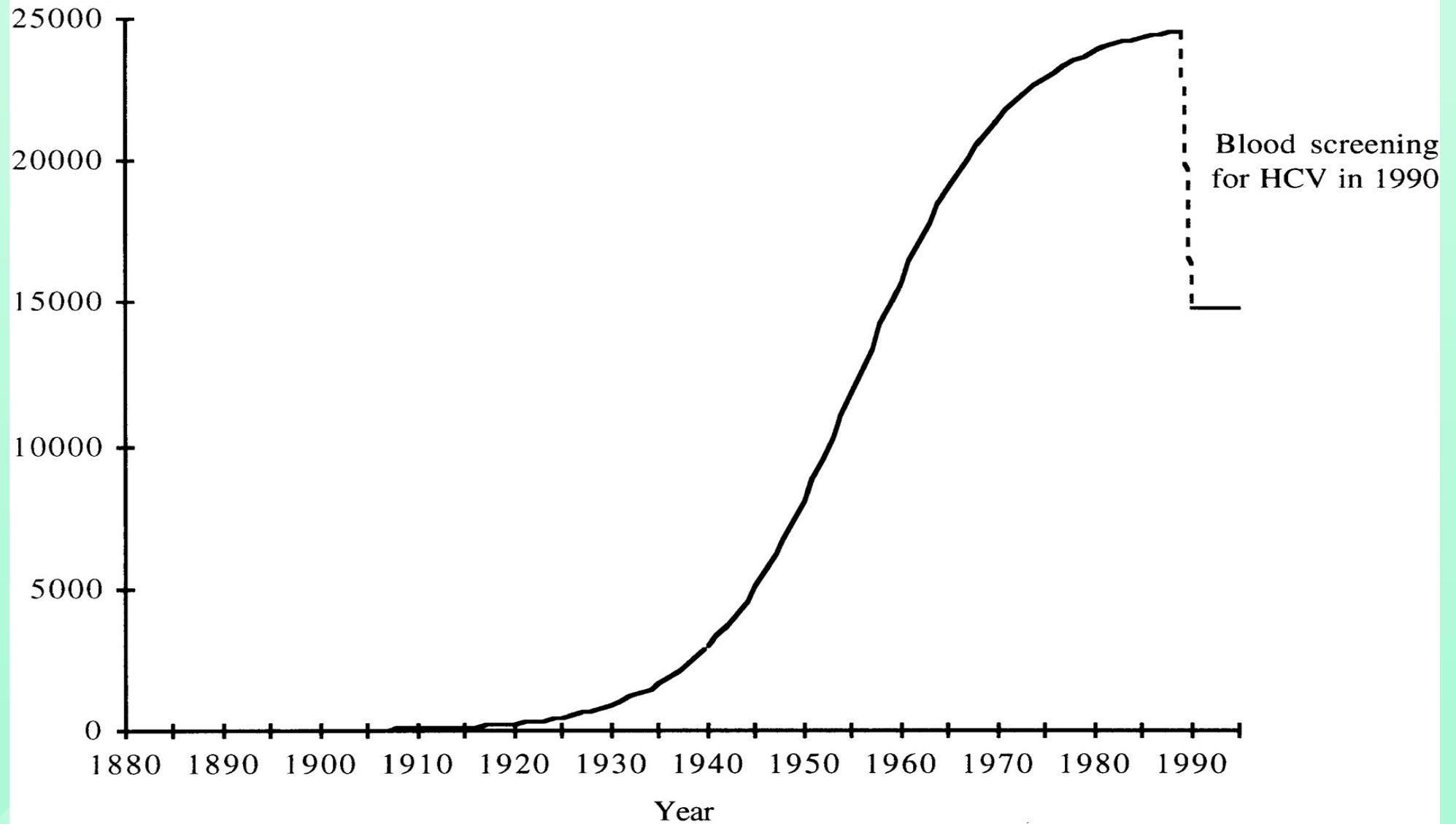
Epidémiologie

Co-infections

Traitement

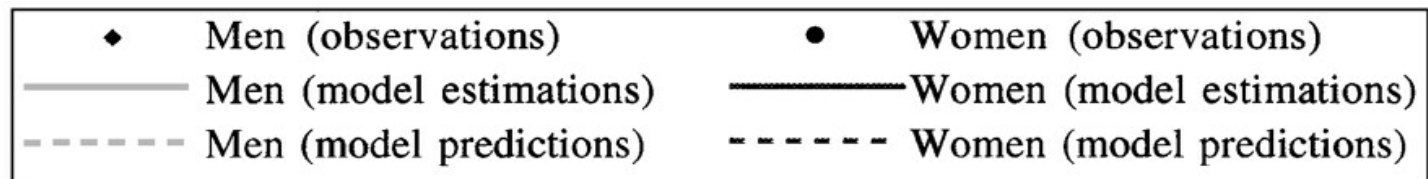
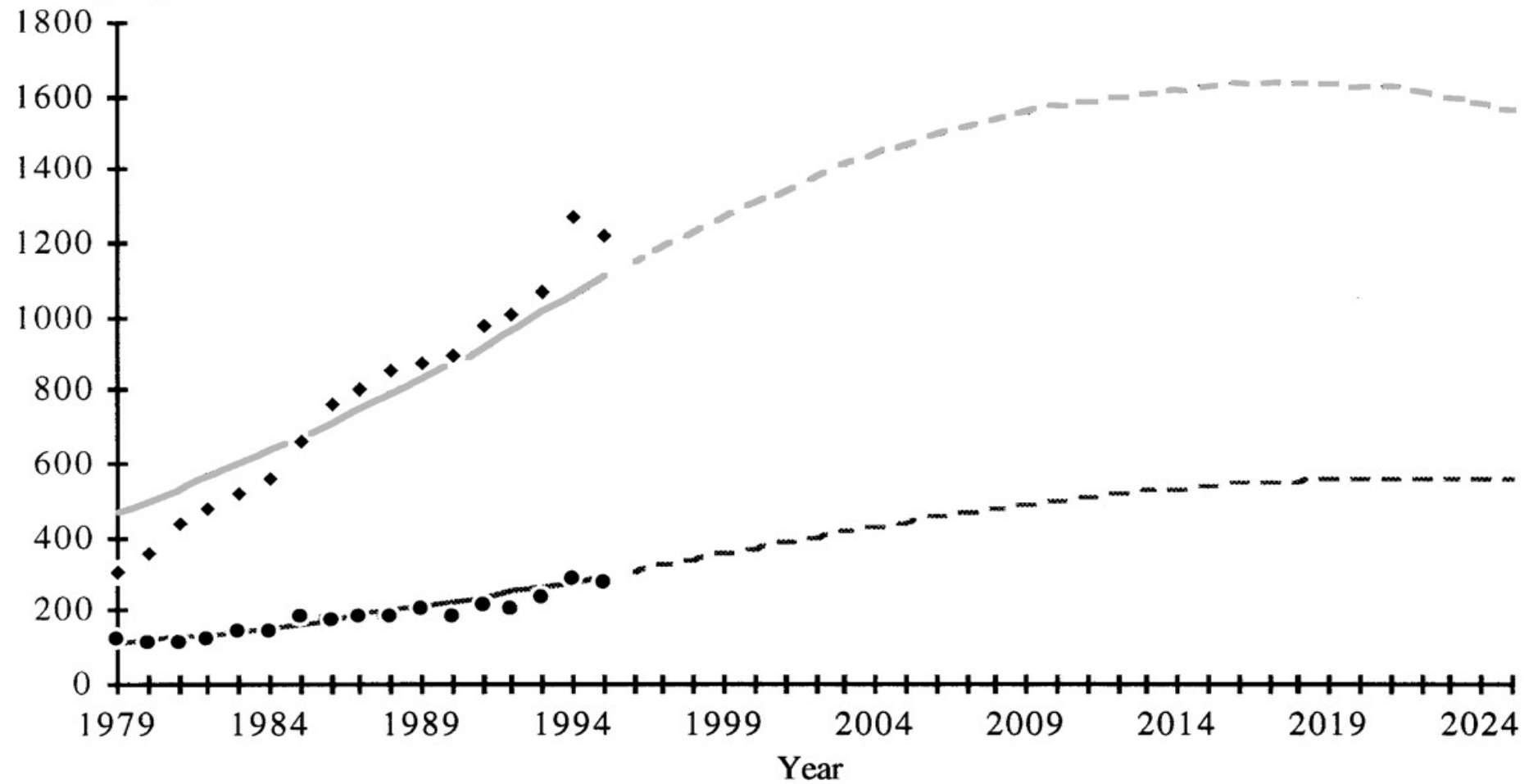
Tabac...

HCV incidence  
by year



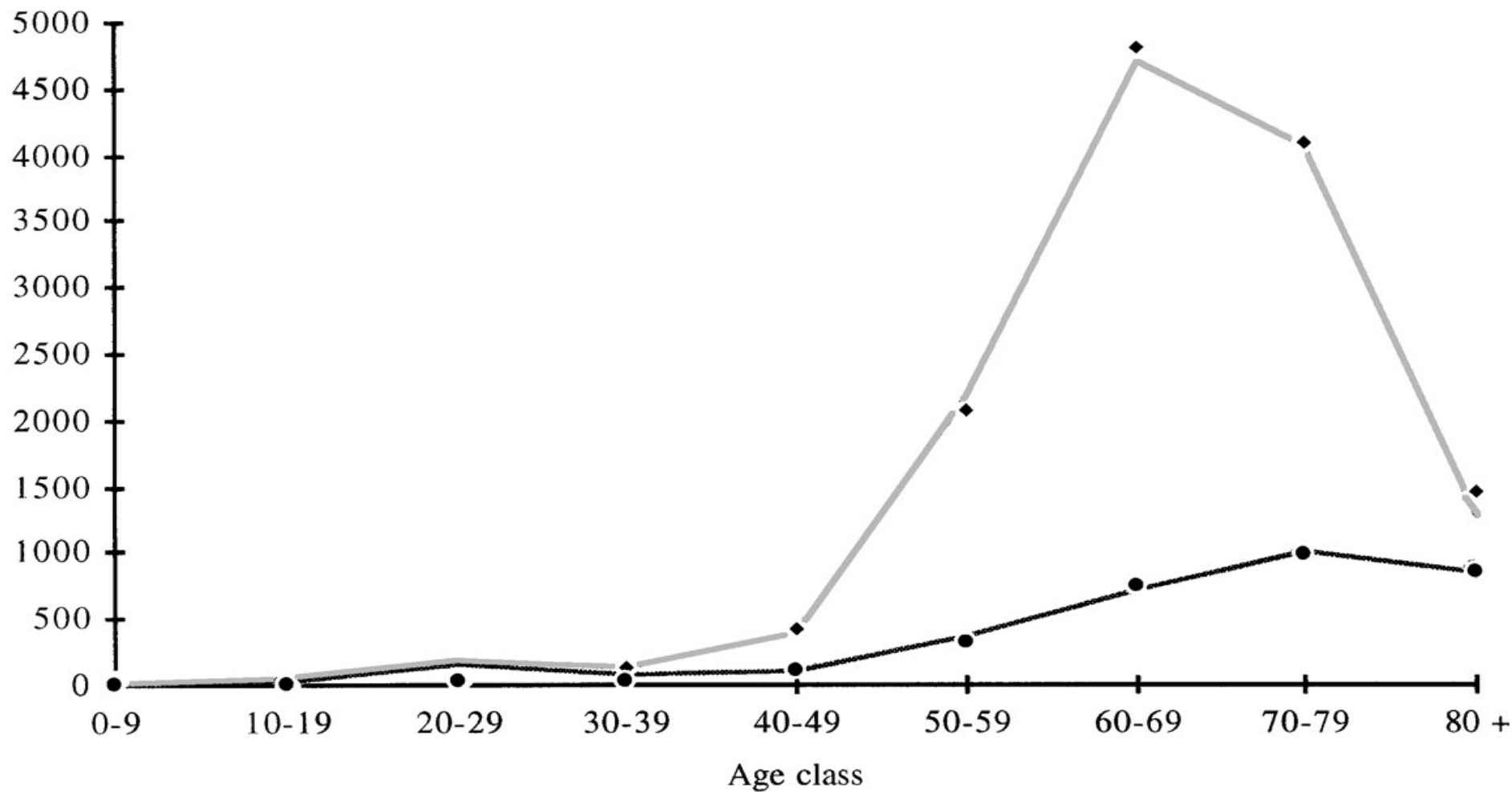
**A****HCC deaths  
attributable to HCV**

per year



# B

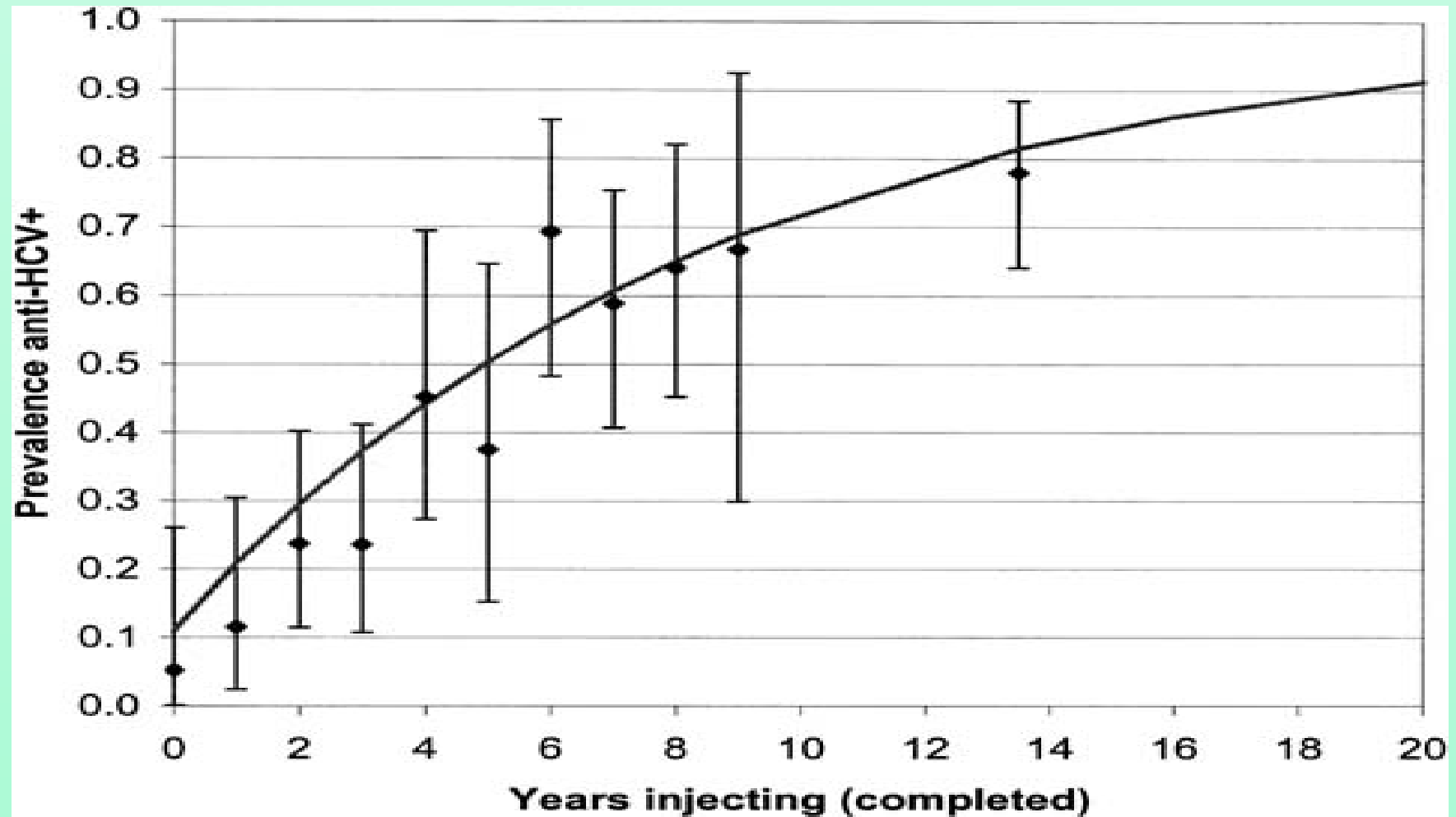
HCC deaths  
attributable to HCV  
per age class



Hepatitis C among IV drug users:  
87% in 306 methadone maintenance program...

- ➔ Awareness: 2/3 of those reporting seronegativity had anti-HCV antibodies
- ➔ Perceived risk: half of those positive thought it could induce cirrhosis
- ➔ Willingness to receive treatment: 53% would definitively or probably use IFN

Observed prevalence (95% CI) of anti-HCV in IV drug users  
and predicted prevalence assuming 11% ppy incidence (—)



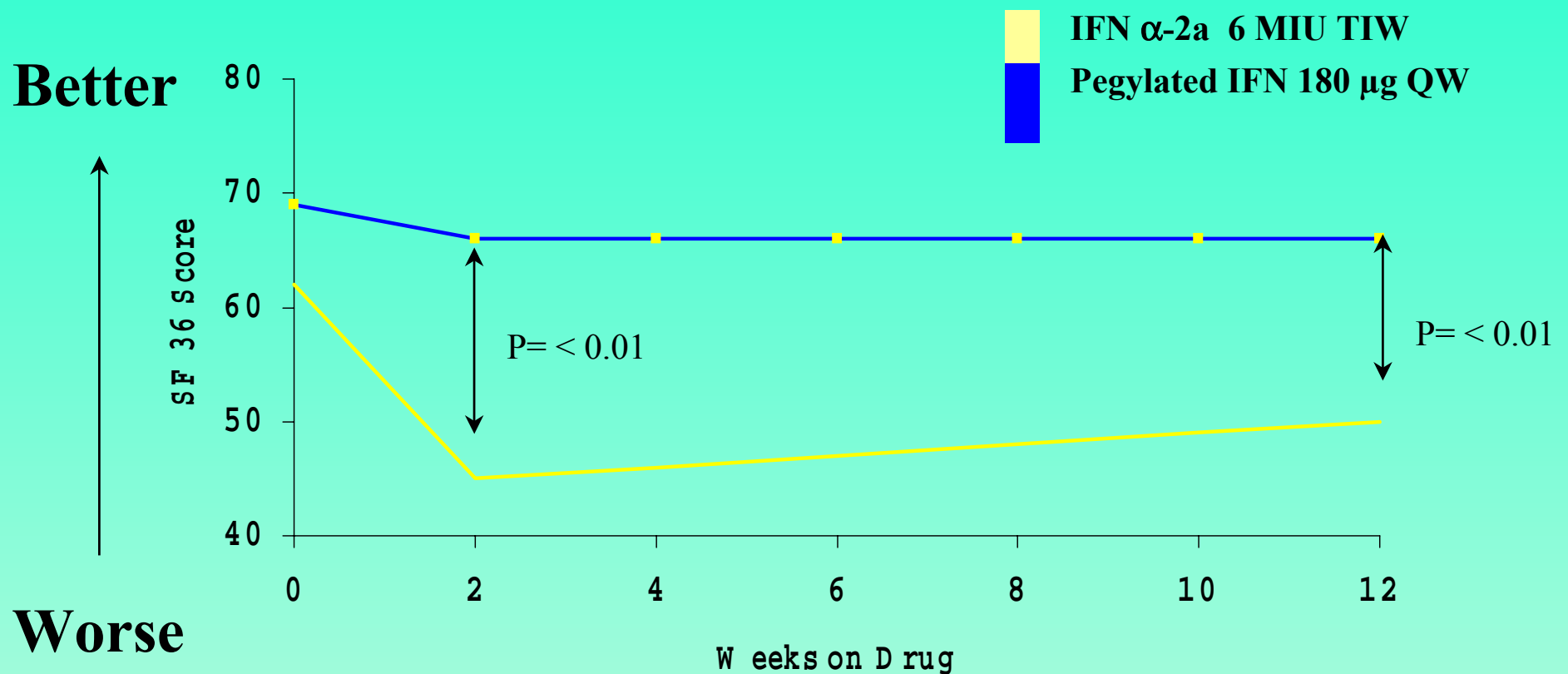
*JA Hahn et al Hepatology 2001;34:180-7*

## Multivariate Analysis of Factors Associated With Anti-HCV (n = 308)

➔ Age / Duration of IVDA	1.21	<.01
➔ Initiation by a sexual partner	<u>4.06</u>	<.01
➔ Injected daily in the past month	<u>3.85</u>	<.01
➔ Ever borrowed a needle	<u>2.56</u>	.02
➔ Cleaned needle with bleach	<u>0.50</u>	.06
➔ Snorted/smoked cocaine or other	.02	<u>0.48</u>
➔ Inj. by someone else in past 30 days	.05	<u>0.50</u>

*JA Hahn et al Hepatology 2001;34:180-7*

# Quality of Life during IFN treatment



Roche International, Data on file

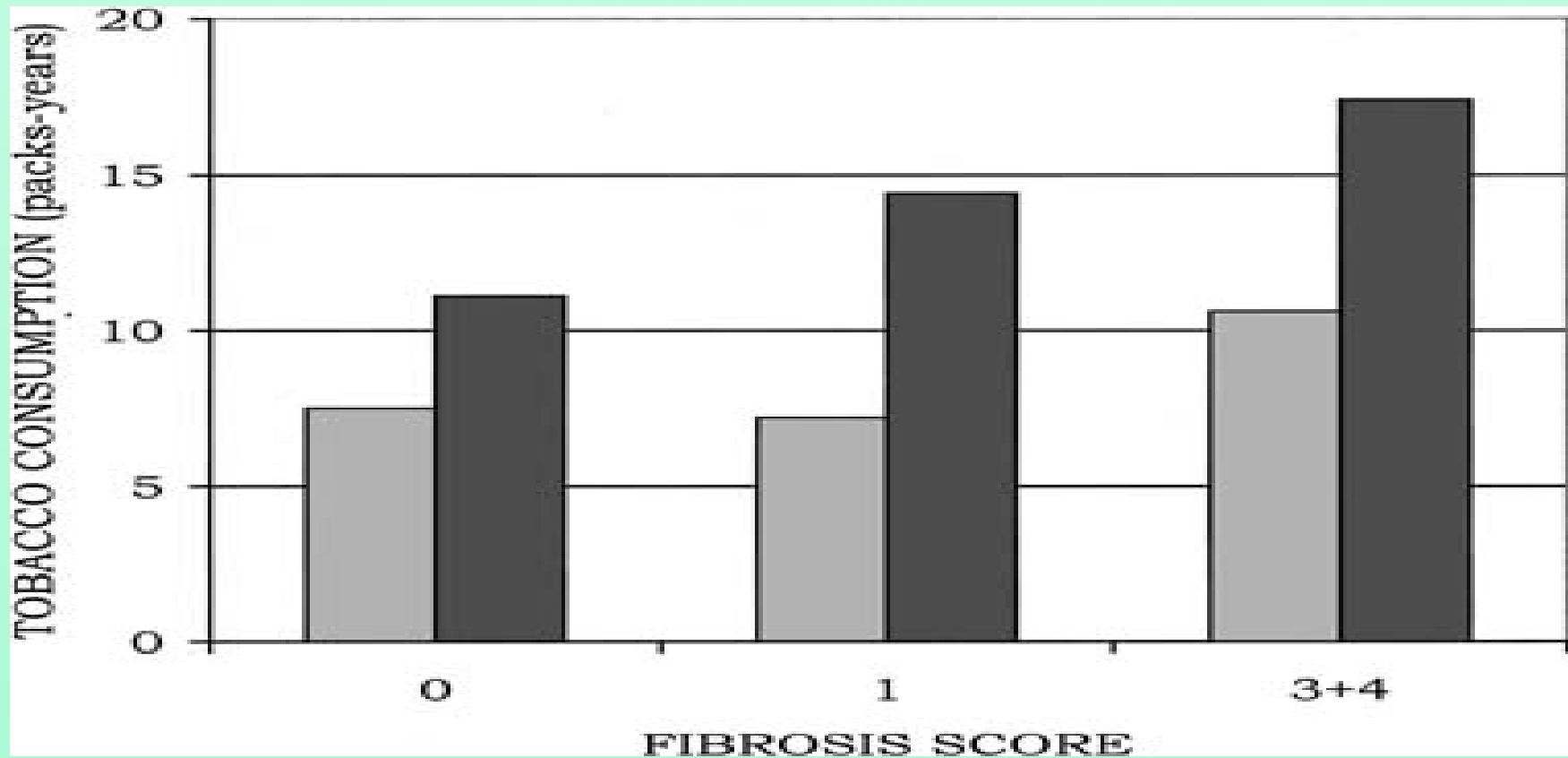
Psychosis in a methadone-substituted patient  
during IFN- $\alpha$  treatment of hep C

*Schafer et al Addiction 2000;95:1101-4*

Suicide as a complication of  
IFN- $\alpha$  treatment of hep C

*Reichen et al J Hepatol 1996*

Tobacco consumption increases with fibrosis  
in 310 patients with chronic hepatitis C  
(whatever the drinking status)

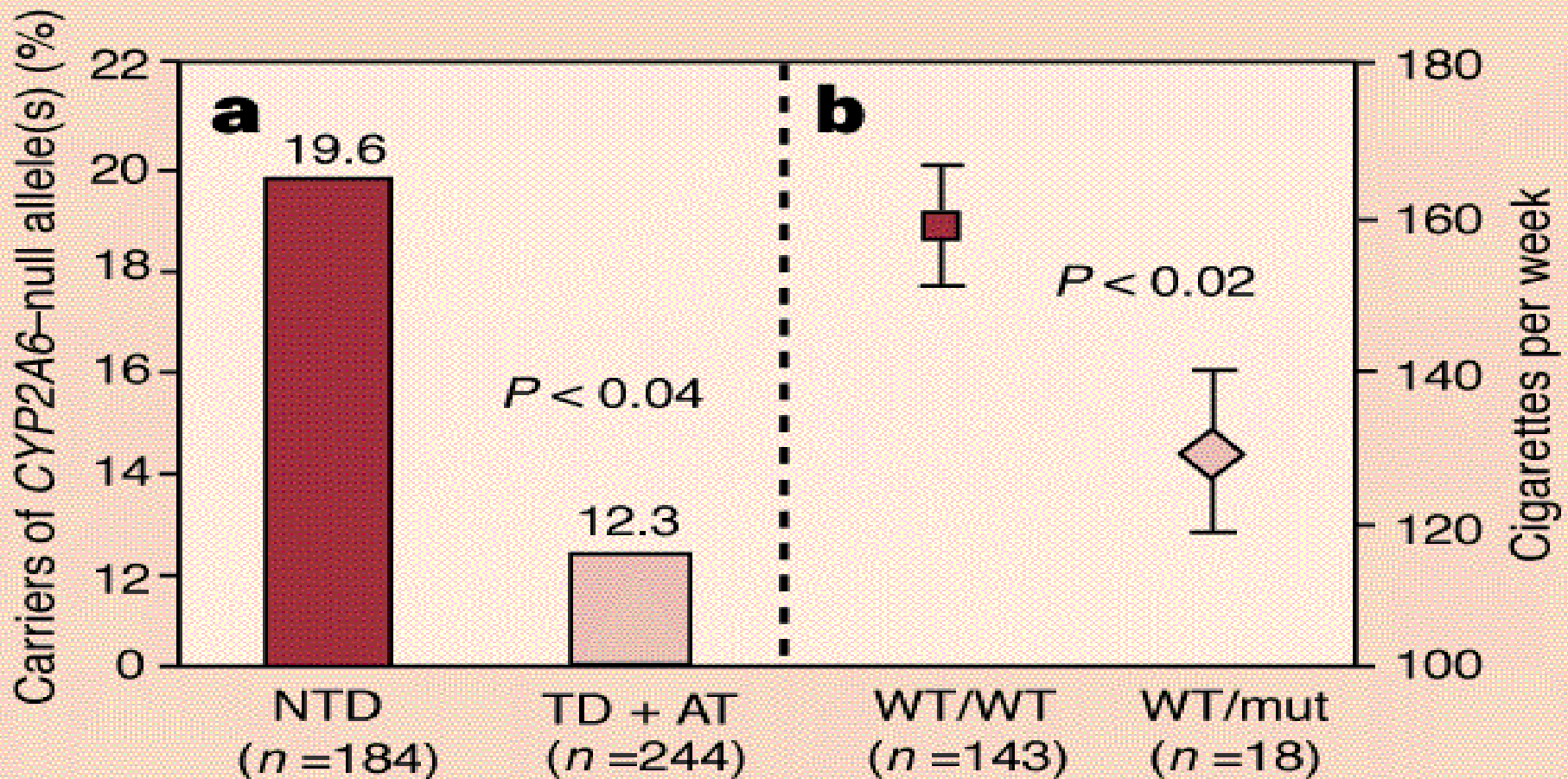


F. Pessione et al Hepatology 2001;34:121-5

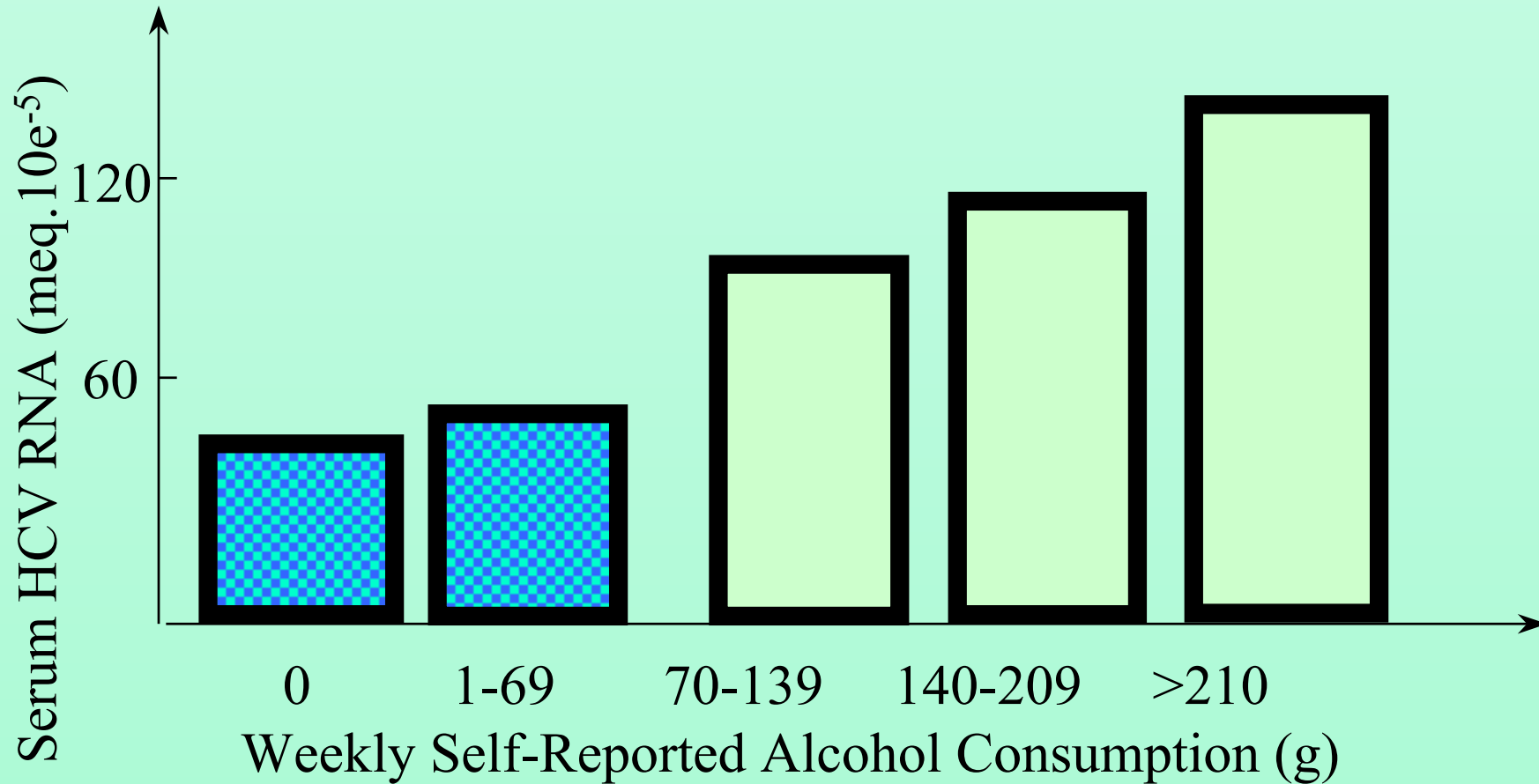
# Effect of *CYP2A6* alleles on tobacco dependence

(NTD: never tobacco-dependant TD + AD tobacco + alcohol dependant)

Pianezza et al Nature 1998



# Effect of Alcohol consumption on serum HCV-RNA



Pessione et al. Hepatology 1998;27:1717

# Hepatitis C

## Odds ratio for presence of cirrhosis

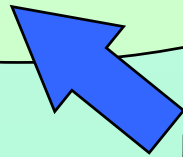
- ◆ Age Risk x 3.44 per 10 years
- ◆ Alcohol Risk x 1.14 per 100 Kg

Mal. Alc. du foie

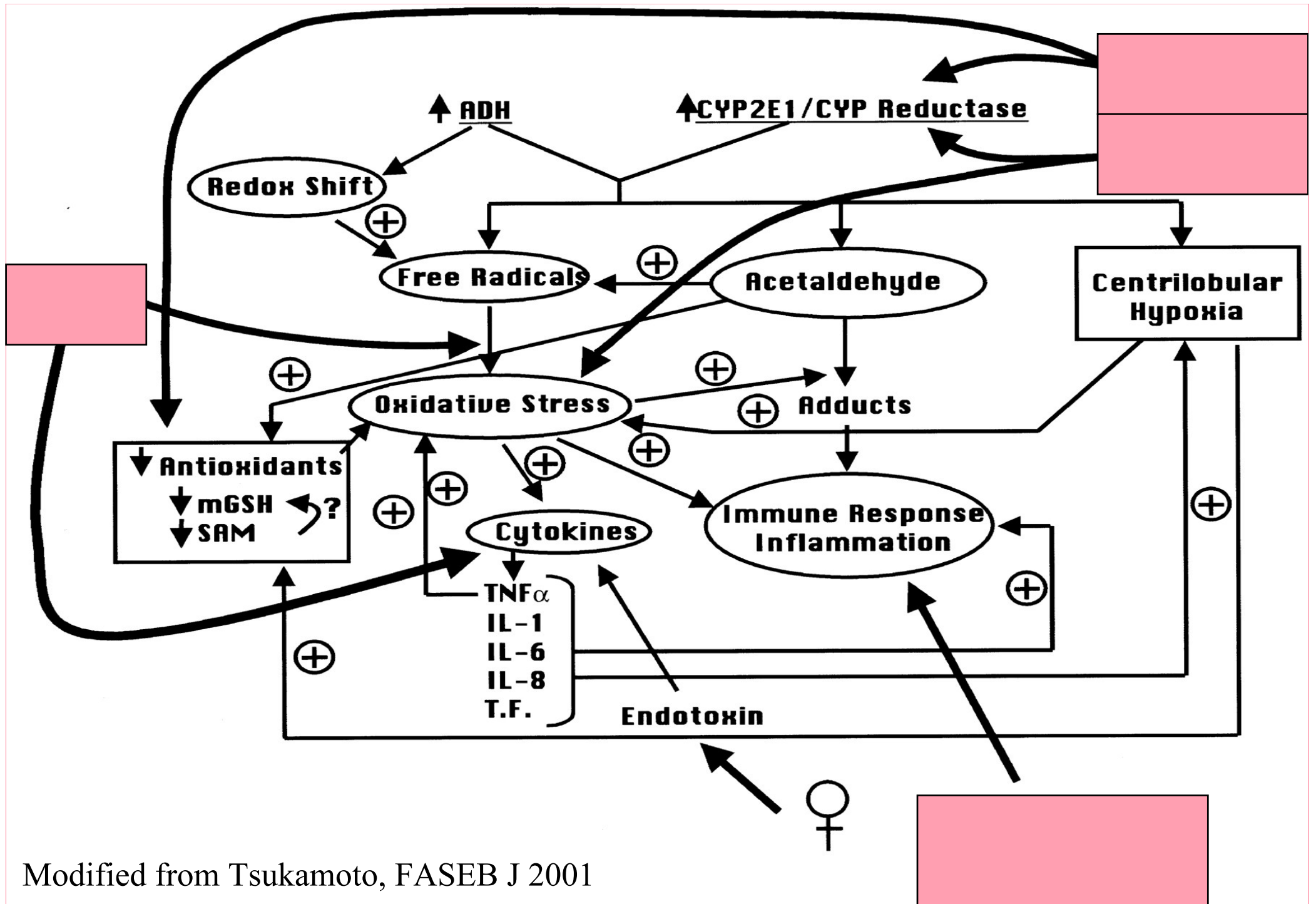
Interactions avec HCV

Interactions avec HFE

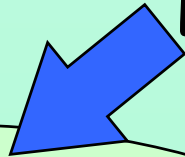
Prédispo. Génétique...



Le foie et  
l'addiction



# Le foie et l'addiction



## Hépatites toxiques

Ecstasy

Cocaine

Carbamazepine

...

# Ecstasy, a common cause of severe acute hepatotoxicity

Liver unit, Barcelona (62 cases of ALF / 3 years)

- Ecstasy= 31% of cases of drug hepatotoxicity
- 2nd most common cause of liver failure < 25 years

Cave : Hepatitis Onset: 2-60 days after use!

# Métabolisme de l'ecstasy (MDMA)

Methamphétamine

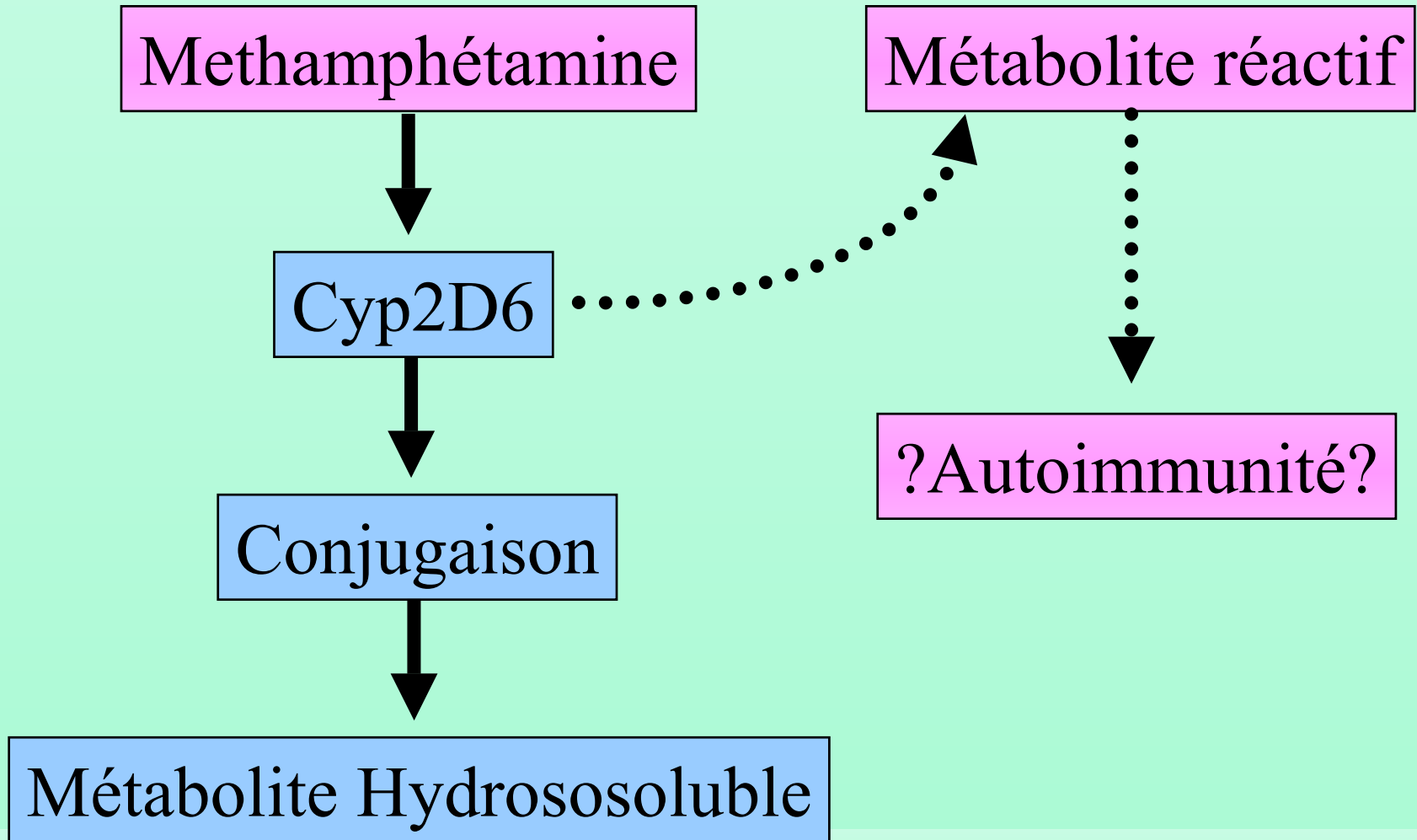
Métabolite réactif

Cyp2D6

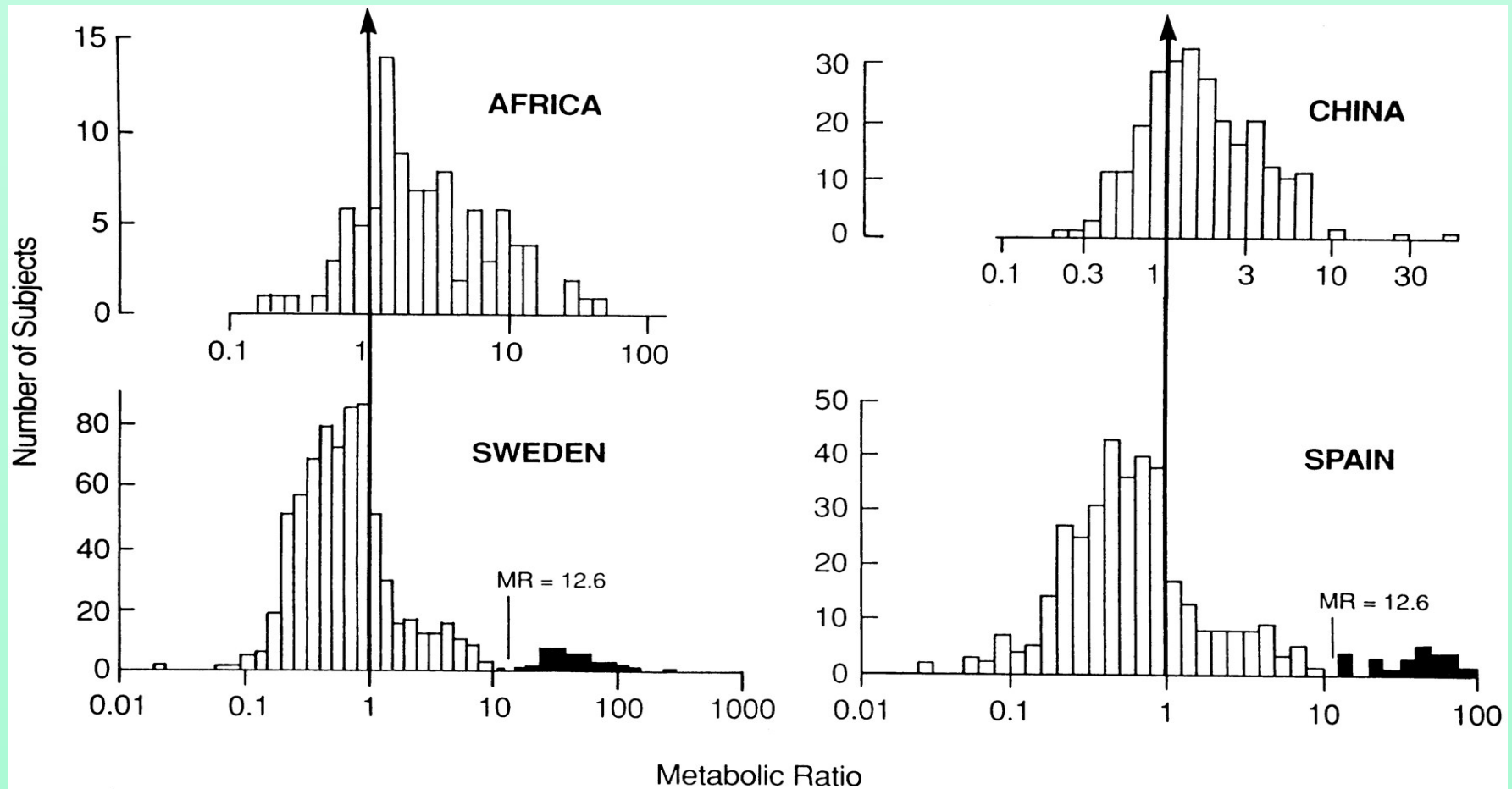
Conjugaison

Métabolite Hydrososoluble

?Autoimmunité?



# Polymorphisme génétique: *CYP2D6* dans 4 populations humaines



## Cocaine-induced acute hepatitis

2 mechanisms

- toxic centrilobular (heat shock)
- immune-mediated

Possible in exclusive sniffers

Mal. Alc. du foie

Hépatite C

Le foie et  
l'addiction

Hépatites toxiques

Addiction et  
transplantation

# Criteria for placement of adults on the liver waiting list: alcohol

Non-disease specific

1 Year expected mortality > 50%

**Disease specific**

**Alcoholic relapse rate**

**Rate of 'harmful drinking'**

**Rate of compliance to therapy**

Region/Time dependent

'All criteria open to accommodate advances in the field'

*Lucey et al. Liver Transpl Surg 1998*

## Alcohol relapse rate after LT

Abstinence < 6 months

Relapse: 50-70%

Harmful drinking : 10-20 %

Abstinence > 6 months

Relapse: 20-30%

Harmful drinking : 3-10 %

**'A relapse risk model...may be more adequate than duration of sobriety to predict patients who are most likely to benefit from LT'**

*Yates et al. Alcohol Clin Exp Res 1998*

## Assessing priorities for donor liver grafts: survey of public and clinicians

General  
population

Family  
doctors

Gastro-  
enterologists

1	<b>Age</b>	<b>Outcome</b>	<b>Outcome</b>
2	<b>Outcome</b>	<b>Age</b>	<b>Work status</b>
3	<b>Time on waiting list</b>	<b>Work after OLT</b>	<b>Non-alcoholic</b>

*Neuberger et al. BMJ 1998*

# Transplantation d'organes

## Facteurs psychosociaux associés au succès

- ➔ Alcool : sevrage de plus de six mois
- ➔ Absence de dépression préopératoire
- ➔ Soutien sociofamilial
- ➔ Absence de déni

# Transplantation hépatique

## Complications psychiatriques

- ➔ Incidence : 15-20%
  - ! Corticothérapie
  - ! Ciclosporine / tacrolimus
- ➔ Anxiété / Dépression
  - Régression, agitation, irritabilité, sommeil
  - Aggressivité vis-à-vis de l'équipe soignante
  - Non observance
- ➔ Episodes délirants / maniaques
- ➔ Syndrome de stress post-traumatique

# Transplantation d'organes

## Grefe anatomique et 'greffe psychologique'

### ➔ Angoisse

- De mort
- De castration
- De perte et de séparation
- De 'l'inquiétante étrangeté'
- De perdre sa place dans la famille

# Transplantation d'organes

## Greffe anatomique et 'greffe psychologique'

### ➔ **Deuil (/ déni)**

Du fantasme de toute-puissance infantile

Du foie mort

Du donneur

### ➔ **Intégration psychique du greffon ('accorporation')**

Réinvestir une image corporelle positive

Incorporation / Introjection / Identification

**Liver Transplantation and Opioid Dependence**  
**Monika Koch and Peter Banys, JAMA. 2001;285:1056-1058**

**Table 1. Eligibility Criteria for Minimum Abstinence Requirements (n = 87 Programs)**

Type of Substance Used	No. (%) of Liver Transplantation Programs				
	Not Answered or Not Applicable	Individually Assessed and No Routine Minimum	Minimum Duration of Abstinence Required, mo*		
			≤3	6	≥12
Alcohol	0	4 (5)	6 (7)	76 (87)	1 (1)
Illicit opiates	3 (3)	8 (9)	4 (5)	65 (75)	7 (8)
Other illicit drugs	2 (2)	9 (10)	8 (9)	63 (72)	5 (6)

\*Includes individual assessment with routine minimum requirement of applicable months.

**Liver Transplantation and Opioid Dependence (n=213)**  
**Monika Koch and Peter Banys, JAMA. 2001;285:1056-1058**

**Table 3. Posttransplantation Problems With Methadone Maintenance Treatment (MMT)\***

<b>Problems in 39 Programs</b>	<b>No. of Programs</b>	<b>No. of Patients†</b>
Relapse to illicit opiates	6	16
Noncompliance with immunosuppressive medication	6	41
Difficulties with postoperative pain management	3	18
Requests for higher dose methadone	1	2
Lack of social support	1	20
No problems	26	116

Foie et addiction ... et encore...

amyloidosis des "skin poppers"

polyarterite noueuse

endocardite bacterienne

disulfiram

"Talc liver" ...