

# *Caractéristiques et variations régionales des endocardites infectieuses (EI) à streptocoques du groupe D (SGD) en France*

E. Giannitsioti, C. Chirouze, A. Bouvet, I. Béguinot,  
F. Delahaye, J.L. Mainardi, M. Celard,  
L. Mihaila-Amrouche, V. Le Moing, et B. Hoen,  
pour le groupe de travail de l'AEPEI



# Nouvelle classification

---

## Le complexe *Streptococcus bovis/Streptococcus equinus*

---

Ancienne dénomination	Nouvelle dénomination	Synonyme
<i>S. bovis</i> biotype I	<i>S. gallolyticus</i> subsp. <i>gallolyticus</i>	<i>S. caprinus</i>
<i>S. bovis</i> biotype II.2	<i>S. gallolyticus</i> subsp. <i>pasteurianus</i>	<i>S. pasteurianus</i>
<i>S. bovis</i> biotype II.1	<i>S. infantarius</i> subsp. <i>infantarius</i> ou subsp. <i>coli</i>	<i>S. lutetiensis</i>

---

*Données récentes sur  
l'épidémiologie des EI à SGD*



# Profile of IE in France



- 2 prospective surveys conducted by the Association pour l'Etude et la Prévention de l'Endocardite Infectieuse (AEPEI) study group
  - ◊ Characteristics of infective endocarditis in France in 1991. A 1-year survey.  
*F. Delahaye et al, Eur Heart J 1995;16:394-401*
  - ◊ Changing Profile of Infective Endocarditis Results of a One-Year Survey in France.  
*B. Hoen et al. JAMA 2002;288:75-81*

# Distribution of microorganisms

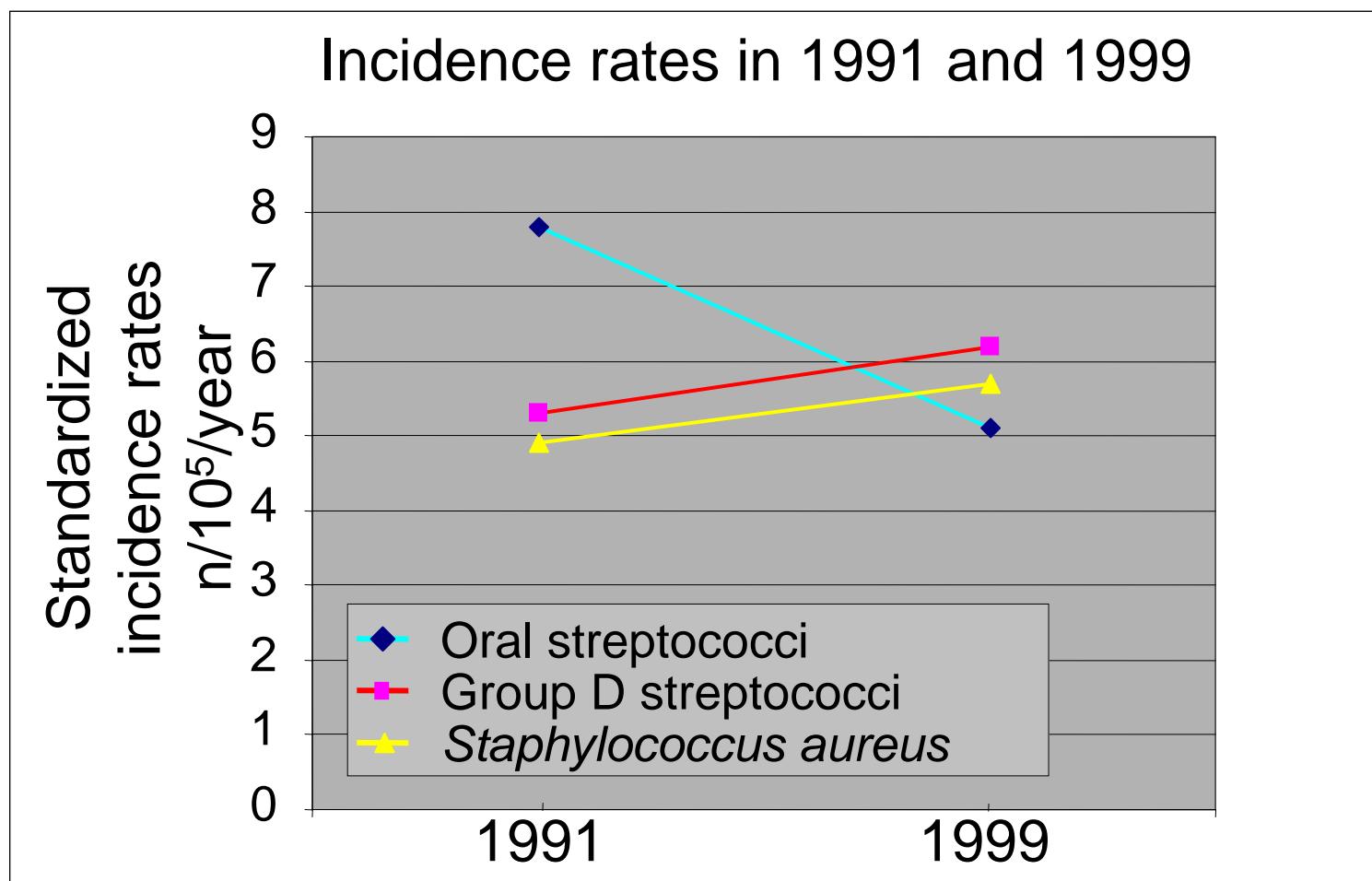
<i>Streptococcaceae</i>	225	58%
Oral streptococci	68	17%
Group D streptococci	98	25% 
<i>S. gallolyticus</i> (51)		
<i>S. infantarius</i> (6)		
<i>S. bovis</i> biotype II.2 (4)		
Not further identified (37)		
Pyogenic streptococci	22	6%
Enterococci	29	7%
Other <i>Streptococcaceae</i>	8	2%
<i>Staphylococcaceae</i>	115	29%
<i>Staphylococcus aureus</i>	90	23%
Coagulase-negative staphylococci	25	6%
Other microorganisms	18	5%
≥ 2 microorganisms	13	3%
No microorganism identified	19	5%

## From 1991 to 1999: some trends

- No known valvular disease      33%      47%
- Identified microorganism      92%      95%
- *Streptococcus bovis*                  13%      25%
- Staphylococci                            23%      29%
- Surgical Rx                              30%      49%
- Lethality (hospital stay)            21%      17%

# Changes in France

Comparison of results from 2 nationwide surveys in France

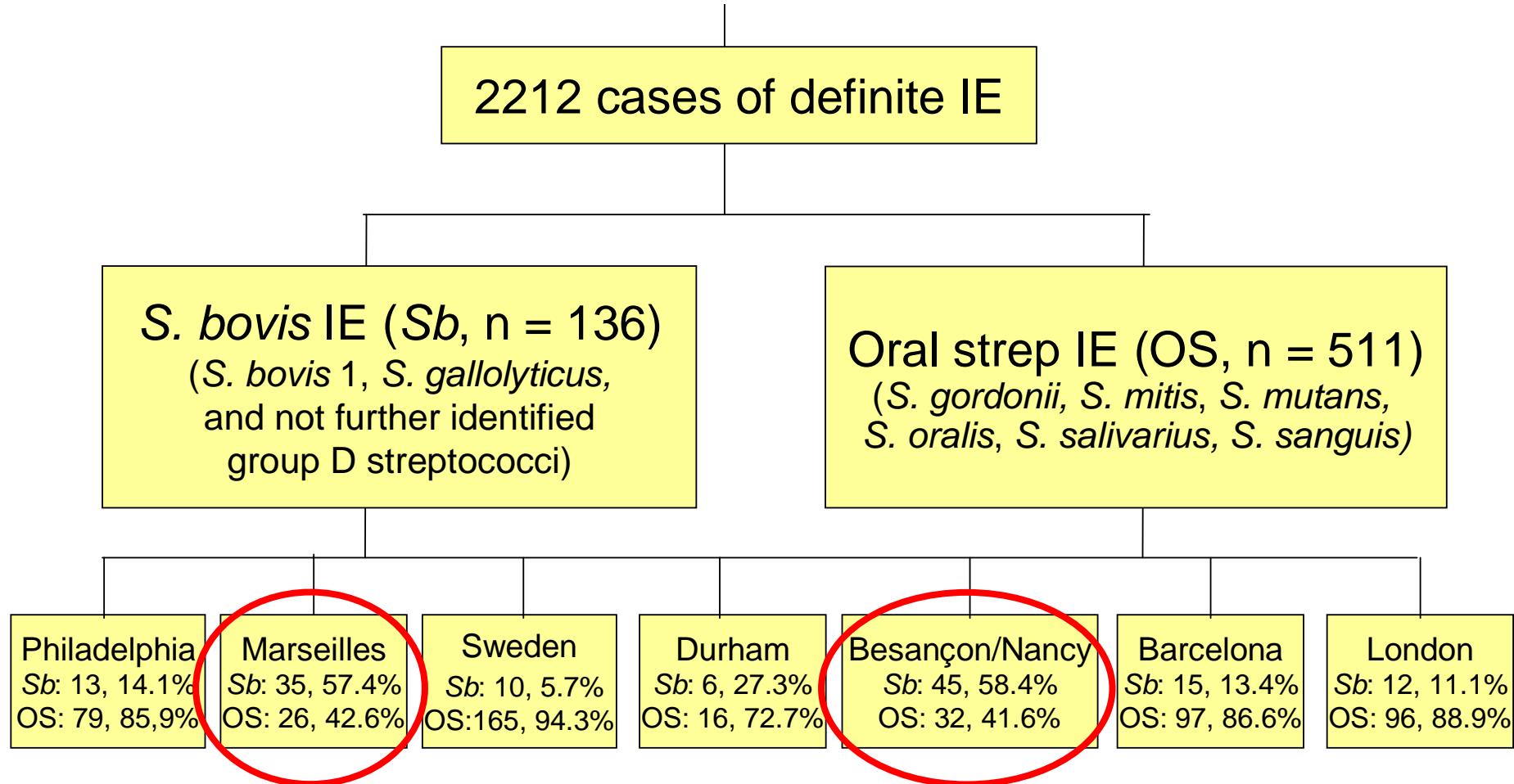


after Hoen et al. JAMA 2002

# IE one-year French surveys : 1999 vs. 1991



# Emergence of endocarditis due to group D streptococci: findings derived from ICE-MD



Characteristic	Oral streptococcal IE (n=511)	<i>S. bovis</i> IE (n=136)	P value
Age (years), mean ± SD	54.7 ± 18.2	62.9 ± 16.4	<0.00001
Males, no. (%)	354 (69.3)	99 (72.8)	0.46
Period of admission, no. (%) <sup>a</sup>			0.0007
Early decade (1979–1989)	131 (25.7)	16 (12.2)	
Late decade (1990–1999)	379 (74.3)	115 (87.8)	
Geographical origin, no. (%)			<0.00001
France	58 (11.4)	80 (58.8)	
Rest of Europe	358 (70.0)	37 (27.2)	
USA	95 (18.6)	19 (14.0)	
Diabetes, no. (%)	25 (4.9)	13 (9.6)	0.06
Intravenous drug use, no. (%)	33 (6.5)	0	0.0006
Any comorbidity, no. (%)	84 (16.4)	41 (30.1)	0.0003
Congenital heart disease, no. (%)	75 (14.7)	9 (6.6)	0.01
Mitral valve prolapse, no. (%) <sup>b</sup>	36 (11.4)	4 (4.5)	0.07
Prior valve surgery, no. (%)	61 (11.9)	29 (21.3)	0.008
Prosthetic valve, no. (%)	59 (11.5)	27 (19.9)	0.02
Fever >38°C, no. (%) <sup>c</sup>	270 (69.2)	65 (79.3)	0.08
New regurgitation murmur, no. (%)	86 (16.8)	37 (27.2)	0.009
Cardiac failure, no. (%)	156 (30.5)	49 (36.0)	0.25
Multiple-valve involvement, no. (%)	28 (5.5)	19 (14.0)	0.002
Any embolic event, no. (%)	133 (26.0)	35 (25.7)	1.0
Stroke, no. (%)	47 (9.2)	16 (11.8)	0.42
Visible vegetation, no. (%)	352 (68.9)	97 (71.3)	0.60
Intracardiac abscess, no. (%)	41 (8.0)	7 (5.1)	0.36
Surgical treatment, no. (%)	180 (35.2)	44 (32.4)	0.55
In-hospital death, no. (%)	53 (10.4)	17 (12.5)	0.53

# Regional variations in streptococcal/enterococcal IE within the ICE-PCS (1779 cases of definite IE)

- 621 (34.9%) were streptococcal/enterococcal IE
  - 319 (51.4%) oral streptococcal IE
  - 188 (30.3%) enterococcal IE
  - 114 (18.3%) group D streptococcal IE
- Four geographical regions were considered
  - North America (NA), South America (SA), Australia/New Zealand (A/NZ), and Europe/Middle East (E/ME).

	NA (n=109)	SA (n=65)	A/NZ (n=132)	E/ME (n=315)	p value
Oral strep	46 (42.2)	<b>40 (61.5)</b>	<b>84 (63.6)</b>	149 (47.3)	<0.001
Enterococcal	<b>57 (52.3)</b>	16 (24.6)	38 (28.8)	77 (24.4)	
Group D strep	6 (5.5)	9 (13.8)	10 (7.6)	<b>89 (28.3)</b>	

## *S. bovis* endocarditis and its association with chronic liver disease: an underestimated risk factor

	Non-Sb n = 169	Sb n = 30	P value
Age, years (m ± SD)	46.0 ± 17.0	58.6 ± 12.4	<0.001
Bivalvular IE (n (%))	13 (7.8)	13 (43.3)	<0.001
Embolism (n (%))	68 (40.0)	22 (73.3)	0.002
Diskitis (n (%))	1 (0.6)	7 (23.3)	<0.001
Liver disease (n (%))	26 (15.4)	17 (56.7)	<0.001

- 45% of the patients had a colonic tumors
- 17 patients with chronic liver disease
  - 14 HCV/HBV, 2 alcohol, 1 unknown

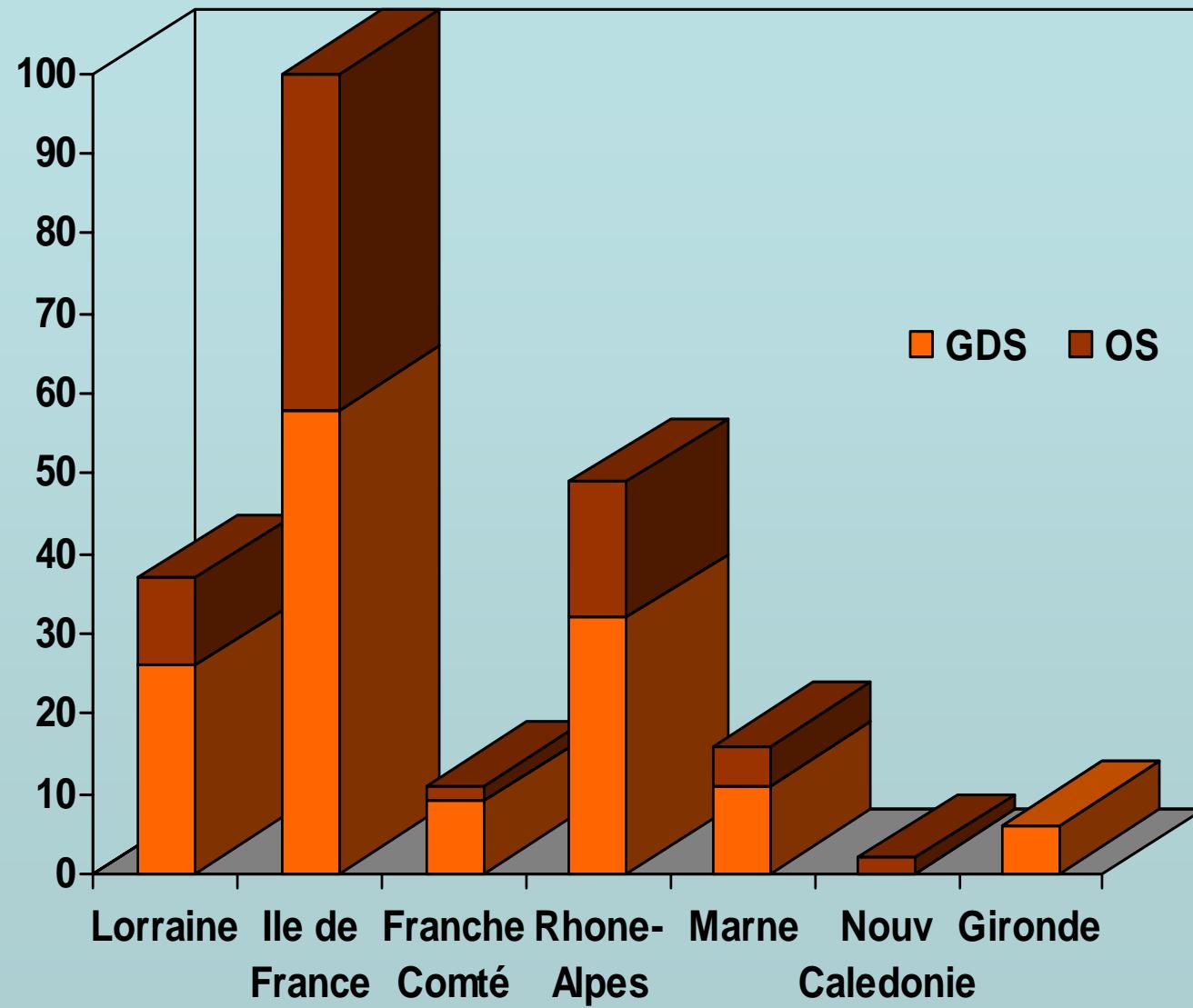
# Characteristics and regional variations of IE due to group D streptococci in France

	GDS IE N=142	OS IE N=79	P
Age (mean ± SD)	62.7 ± 13.3	56.6 ± 16.1	0.01
Rural residence, n(%)	44 (31.0)	12 (15.2)	0.001
Prior valvulopathy, n(%)	48 (33.8)	53 (67.1)	<0.0001
Diabetes mellitus, n(%)	23 (16.2)	1 (1.3)	0.006
Cirrhosis, n(%)	12 (8.5)	2 (2.5)	0.08
Colon disease, n(%)	71 (50.0)	9 (11.4)	<0.0001

# Characteristics and regional variations of IE due to group D streptococci in France

	<b>GDS IE N=142</b>	<b>OS IE N=79</b>	<b>P</b>
<b>BMI (mean ± SD)</b>	24.2 (4.8)	24.3 (3.9)	0.8
<b>Cardiac failure, n(%)</b>	41 (19.0) <sup>7</sup>	16 (15.2)	0.1
<b>Vasc. phenomena<sup>4</sup>, n(%)</b>	55 (38.7)	28 (35.4)	0.6
<b>Embolism<sup>5</sup>, n(%)</b>	47 (33.1)	25 (31.6)	0.8
<b>Immun. phenomena<sup>6</sup>, n(%)</b>	36 (25.4)	25 (31.6)	0.3
<b>Surgical treatment, n(%)</b>	73 (51.4)	46 (58.2)	0.6
<b>Hospital mortality, n(%)</b>	18 (12.7)	5 (6.3)	0.1

## Regional variations of GDS & OS IE in France



# Molecular epidemiology of *Streptococcus bovis* causing endocarditis in Italian patients

- 25 *S. bovis* isolates responsible for endocarditis and bacteremia in Italian patients
  - *S. bovis* I n = 20
  - *S. bovis* II n = 5
- PFGE analysis
  - 22 different migration profiles (similarity < 87%).
  - 3 strains with identical PFGE in 2 different patients.
- The increase of *S. bovis* endocarditis in Napoli area is likely to result from the selection of sporadic endemic clones from the endogenous intestinal flora.

# Epidémiologie des IE à SGD

- Augmentation récente de son incidence
  - Dans certains pays seulement
  - Vraisemblablement non liée à une diffusion clonale
- Caractéristiques cliniques
  - Patients âgés
  - Risque augmenté en cas de tumeur chronique et d'hépatopathie chronique
  - Patients souvent sans valvulopathie préalable
  - Atteinte multivalvulaire et spondylodiscite fréquentes.
- Rôle de la ruralité ?
  - Alimentation, agents environnementaux ?

Endocardite infectieuse  
*Streptococcus bovis*,  
et cancer colique

ou

le cancer colique,  
une maladie infectieuse ?

# Le début de l'histoire

- Association of *Streptococcus bovis* with carcinoma of the colon
  - Klein, N Engl J Med 1977
- *Streptococcus bovis* septicemia and carcinoma of the colon
  - Klein, Ann Intern Med 1979
- *Streptococcus bovis* bacteraemia requires rigorous exclusion of colonic neoplasia and endocarditis
  - Beeching, Quarterly J Med 1985

# Tumors of the colon increase the risk of developing *Streptococcus bovis* endocarditis a case - control study

	RR	95% CI
No tumor	1	-
Any colorectal tumor	3.6	1.4 - 9.4
Adenoma	3.4	1.2 - 9.2
Adenocarcinoma	5.7	0.9 - 48.5

# Bacteria and cancer

Bacteria

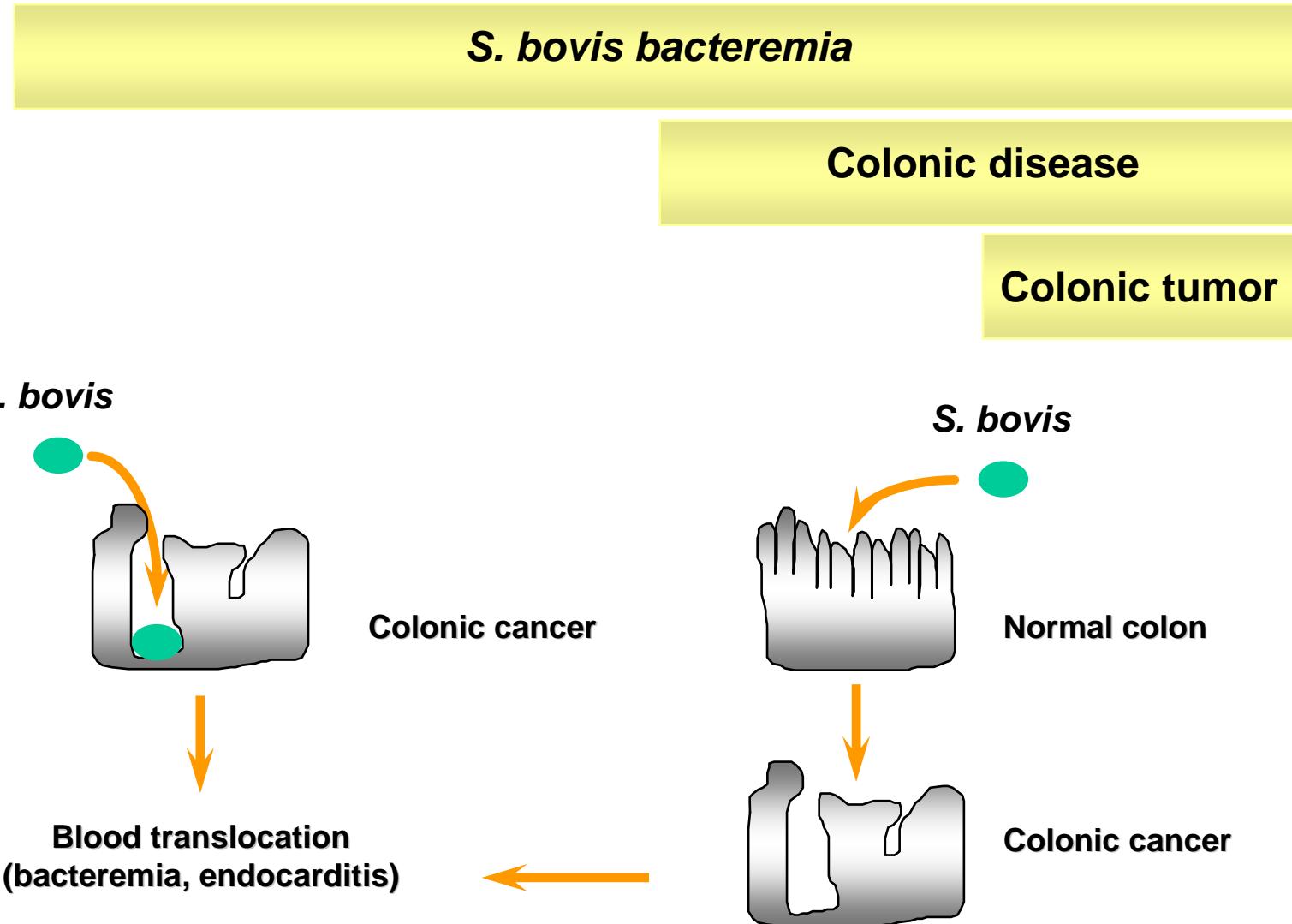
*Helicobacter pylori*  
*Salmonella Typhi*  
*Citrobacter rodentium*

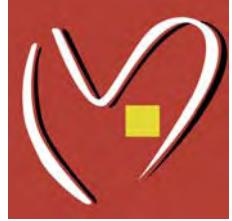
**chronic infection**

**chronic inflammation**

**CANCER**

# *Streptococcus bovis* and colonic cancer





# Remerciements

## Coordinateurs régionaux

### Franche-Comté

Y. BERNARD  
F. DUCHENE  
B. HOEN  
P. PLESIAT

### Lorraine

F. ALLA  
N. DANCHIN  
T. DOCO-LECOMPTE  
C. SUTY-SELTON  
M. WEBER

### Marne

I. BEGUINOT  
P. NAZEYROLLAS  
V. VERNET

### N-Calédonie

B. GARIN  
F. LACASSIN  
J. ROBERT

### Paris

A. ANDREMONT  
E. GARBAZ  
V. GOULET  
V. LE MOING  
C. LEPORT  
J.L. MAINARDI

### Rhône-Alpes

C. CHIDIAC  
F. DELAHAYE  
J. ETIENNE  
F. VANDENESCH

## Soutien des sociétés savantes :

SPILF	SFC
SNFMI	SFCTCV
SRLF	SFG
SFAR	

## Financement

PHRC 1997, CHU de Besançon  
Aventis, Beecham, FFC