

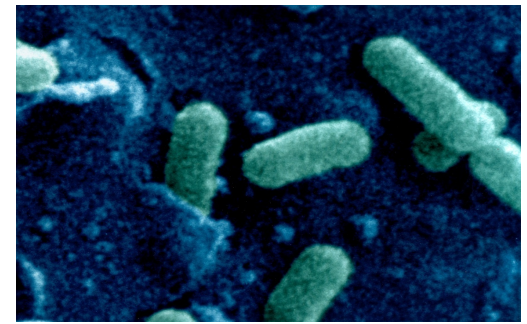
Listériose grossesse



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Listeriosis



Listeria monocytogenes

Gram positive bacillus

Growth at 4°C

B-hemolysis

Ubiquitary distribution

Among the most severe foodborne infections

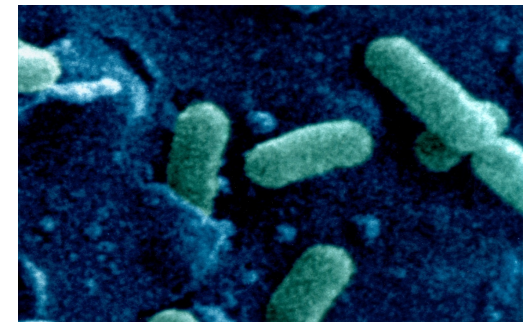
Mandatory reporting

Surveillance systems

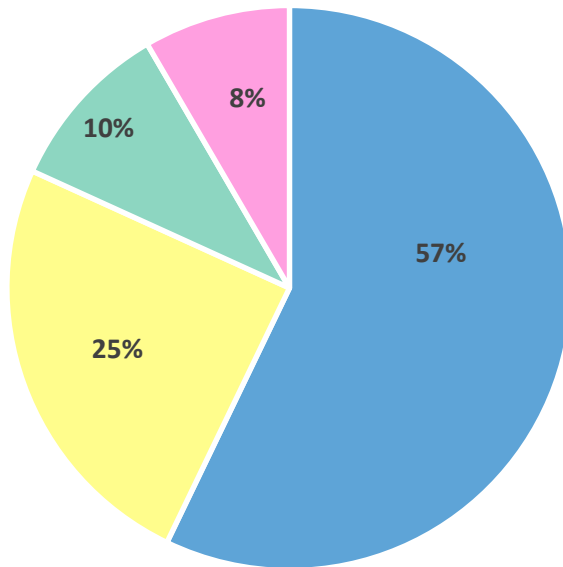
Maternal-neonatal infection

Documentation of Lm in any sample of maternal, fetal or neonatal origin (< 4 weeks)

Listeriosis



Distribution of invasive listeriosis cases in France 2016



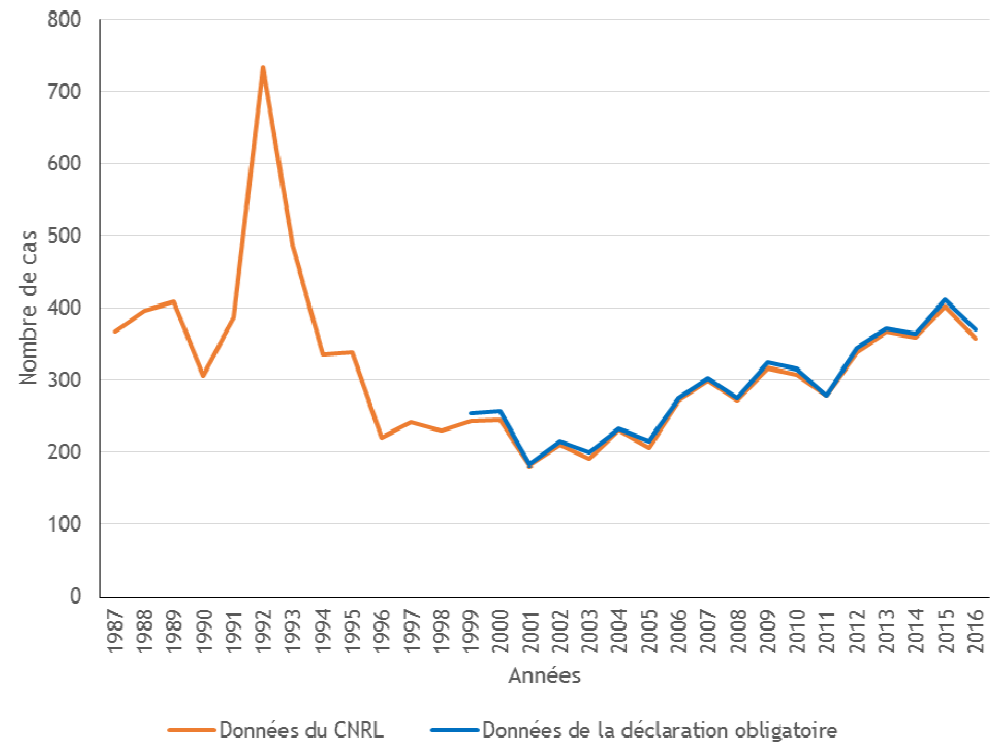
Septicemia , n=204

CNS, n= 88

Other, n=35

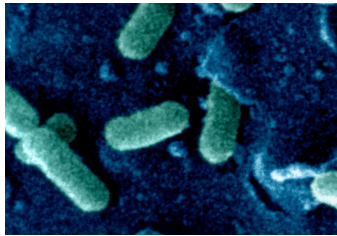
MN, n= 30

Number of cases of invasive listeriosis in France 2016



Incidence 5,6 cas / 10⁶ in 2016

Maternal listeriosis



Listeriosis

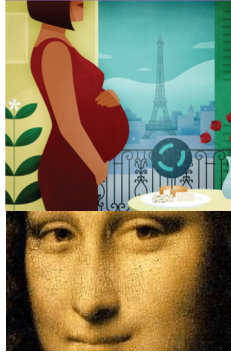
Other
infection



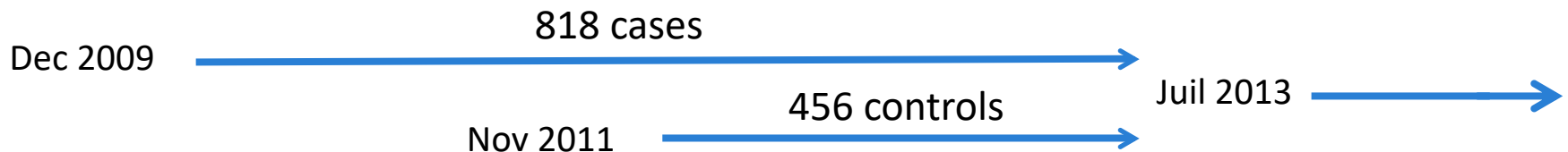
- Ubiquitous distribution and exposure
- Lm does not alter the taste of the food
- New contaminating sources

- **Listeriosis is rare**

MONALISA

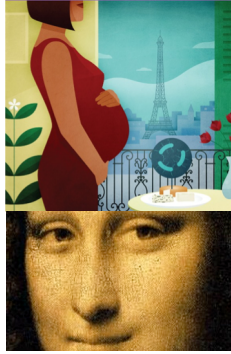


- **M**ulticentric **O**bservational **N**ational **A**nalysis of **L**isteriosis and *Listeria*
- **Prospective case control study**
- **For each patient**
 - Clinical data > 500 items / patient D0 et >M3
 - Isolate and biobank (PBMCs, DNA, serum, plasma)



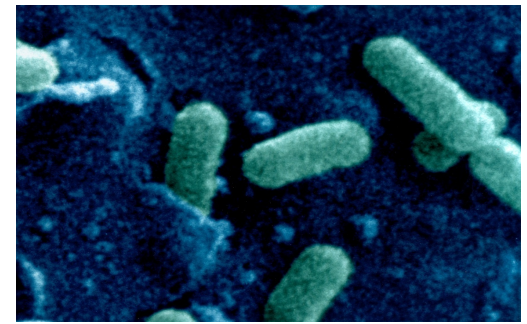
Maternal-neonatal listeriosis

A specific patient profile?



- **No immunosuppression** (92% of cases)
- **Constant food exposure**
 - 100% of cases and controls

Listeriosis



Raw milk dairy products

Meat spreads patés

Ready to eat food

Sprouts (USA 2009)

Cantaloupe (USA 2011)

Caramel apples (Canada 2014)

1980



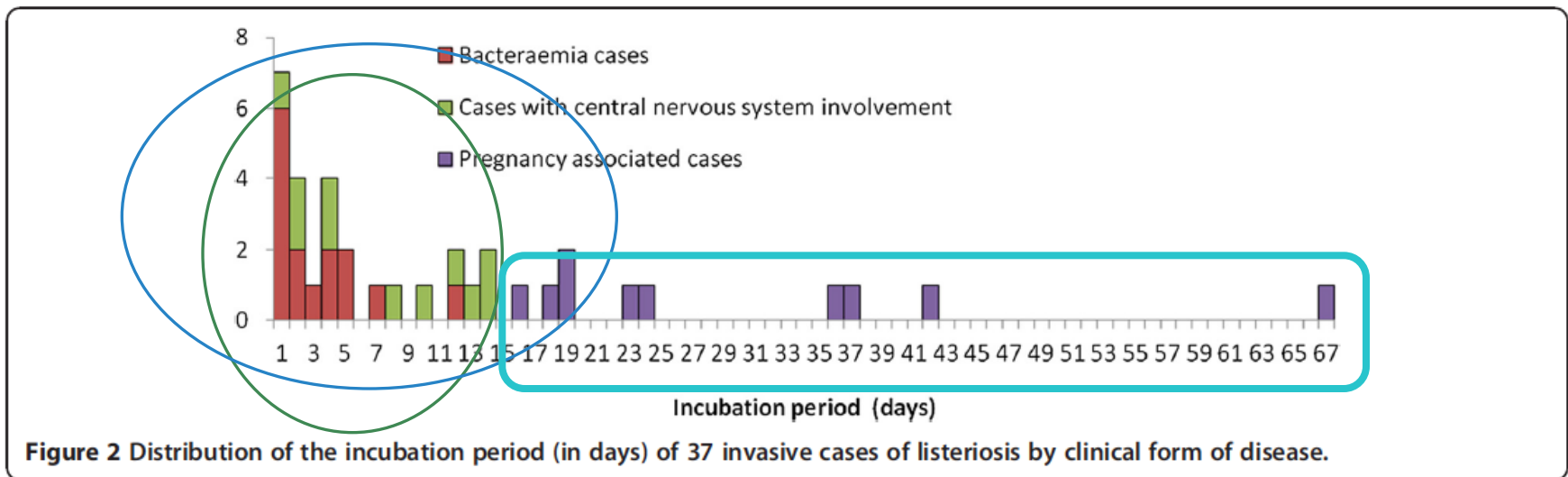
2017



Maternal-neonatal listeriosis

Incubation

Retrospective bibliographic study of 37 listeriosis cases with unique food source identified



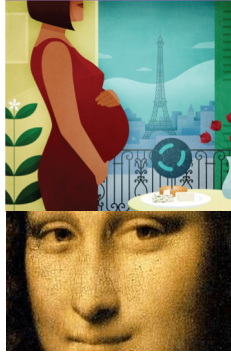
Septicemia :
Median incubation 2d [1-12j]

Maternal listeriosis
Median incubation 27.5d [17-67d]

Central nervous system:
Median incubation 9d [1-14d]

Maternal-neonatal listeriosis

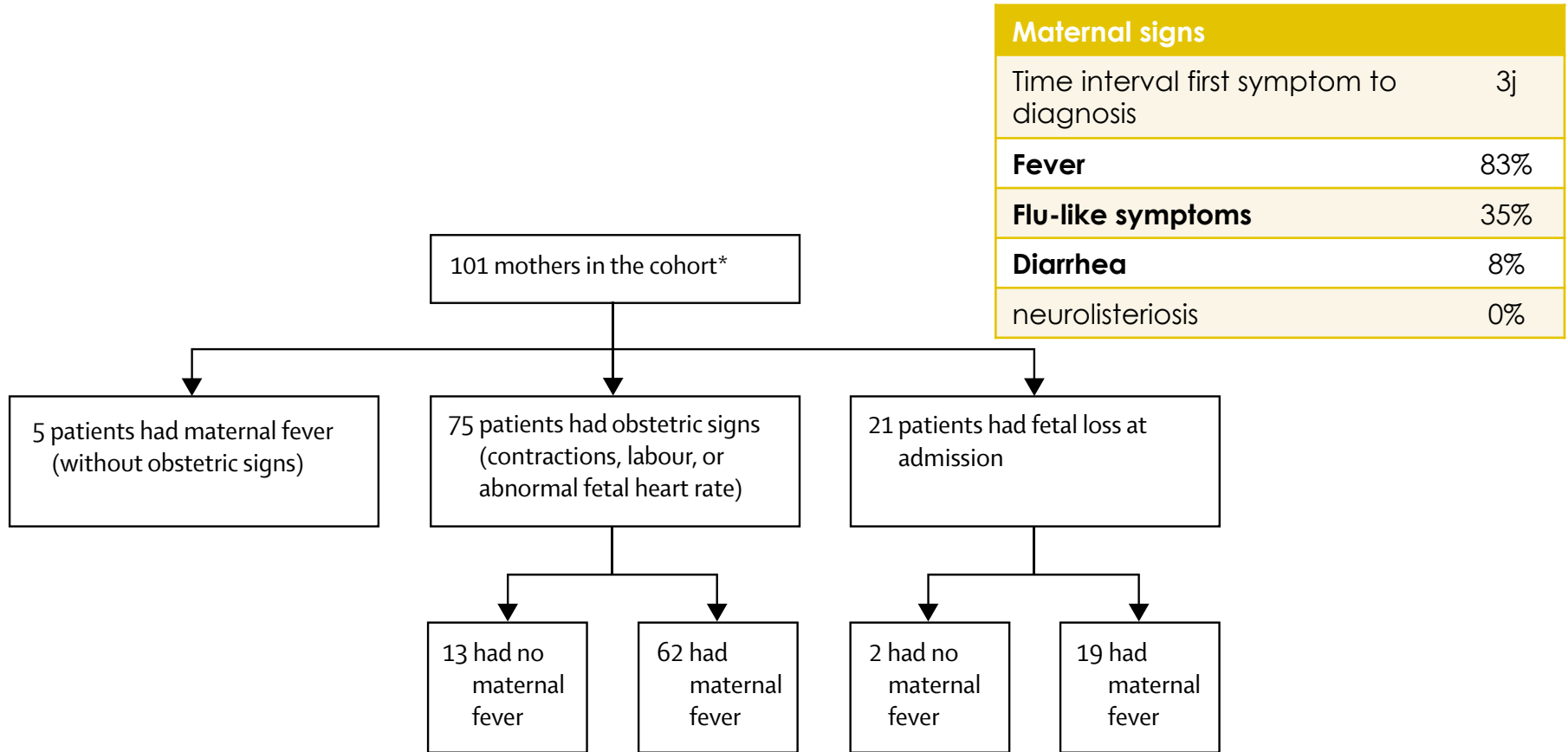
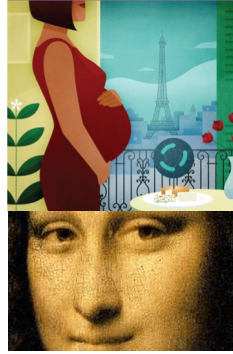
A specific patient profile?



- **No immunosuppression** (92% of cases)
- **Constant food exposure**
 - 100% of cases and controls
- **Over-representation of mothers of African origin**
 - 35/107 (33%) (3x more than expected in the general population)
 - Cf. USA (Mexican minorities) GB (deprived background)
- **Term : mostly 3rd trimester, but not always**
 - T1 n=3, T2 n=28, T3n= 70

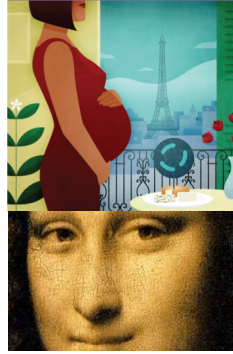
Maternal-neonatal listeriosis

What are the clinical patterns?

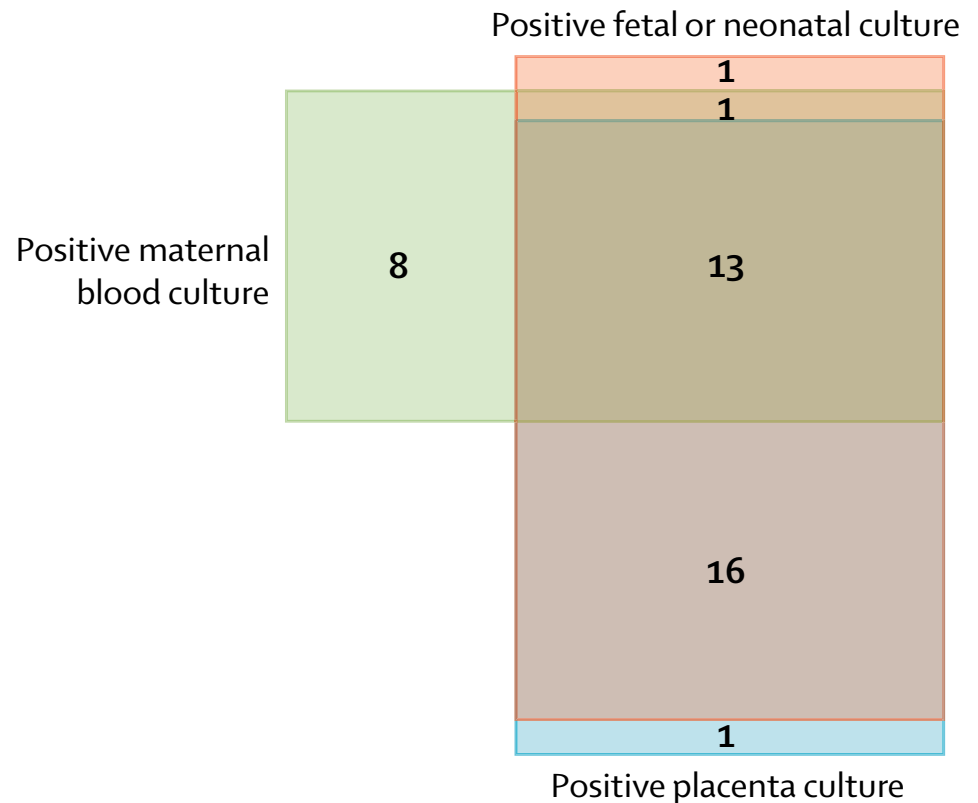


Maternal-neonatal listeriosis

How to diagnose it?



Maternal samples	
Blood	47/85 (55%)
Cervical/vaginal swab	14/54 (26%)
Infant samples	
Placenta	50/64 (78%)
Blood	31/75 (41%)
CSF	10/56 (18%)
Amniotic fluid	8/15 (53%)
Peripheral samples	
Gastric aspirate	52/67 (78%)
Anus	18/26 (69%)
Ear	26/37 (70%)
Pharynx	10/20 (50%)
Other samples†	2/2 (100%)



Maternal-neonatal listeriosis

How to diagnose it?



- **Serological testing is useless whatever the technic**
 - Poor specificity
 - Delayed positivity
- **PCR (hly > 16s)**
 - Validated in the CSF, not in other setting
 - May be valuable, especially in the placenta after preemptive antibiotic treatment

Maternal-neonatal listeriosis

What is the prognosis?



No severe maternal sepsis

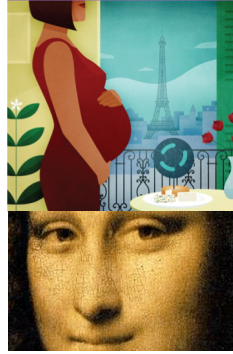
No maternal neurolisteriosis

No maternal death (25-35% in-hospital mortality in CNS and S listeriosis)

But listeriosis remains one of the most severe infections during pregnancy

Maternal-neonatal listeriosis

What is the prognosis?



Outcome	Total cases N=107	T1 [0-14 WG] N=3	T2 [14-28 WG] N=28	T3 [28-41 WG] N=70
Normal	5/107 (5%)	-	11%	3%
Fetal loss	26/107 (24%)	100%	74%	3%
Premature delivery	48/107 (45%)		14%	63%
Abnormal delivery	22/107 (21%)	-	-	31%
Late onset disease	6/107 (6%)	-	-	-

Only 5% of pregnancies face uneventful outcome

80% major complications (fetal loss, EOD, severe prematurity < 32WG)

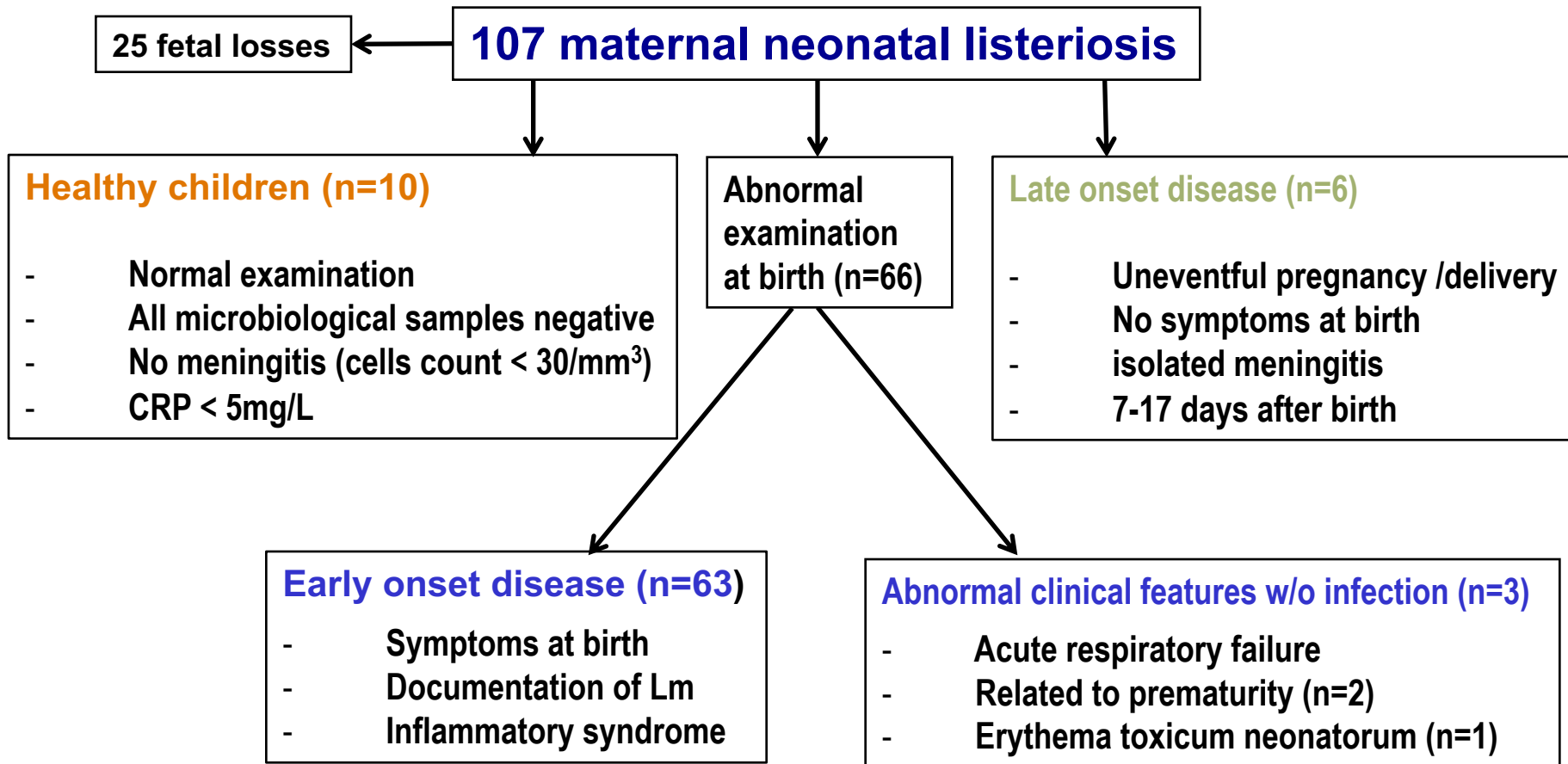
No fetal loss beyond 29 WG

Term at the moment of infection is the main prognostic factor

No fetal loss after 72 hours of adequate management

Maternal-neonatal listeriosis

What is the prognosis?



Maternal-neonatal listeriosis

How to treat?



- **No clinical trial data → low grade recommendations**
- **Intrinsically ineffective molecules**
 - cephalosporins, fosfomicin, oxacillin
- **Few bactericidal drugs**

Maternal-neonatal listeriosis

How to treat?



- Few bactericidal drugs,
- Combination amoxicillin/gentamicin is pivotal
- Some combination are antagonistic (macrolide/ampi)

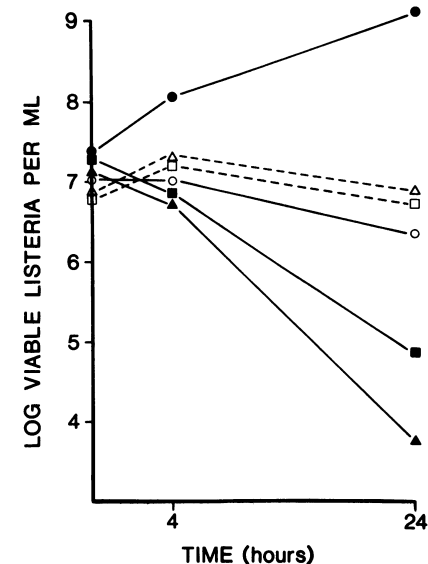
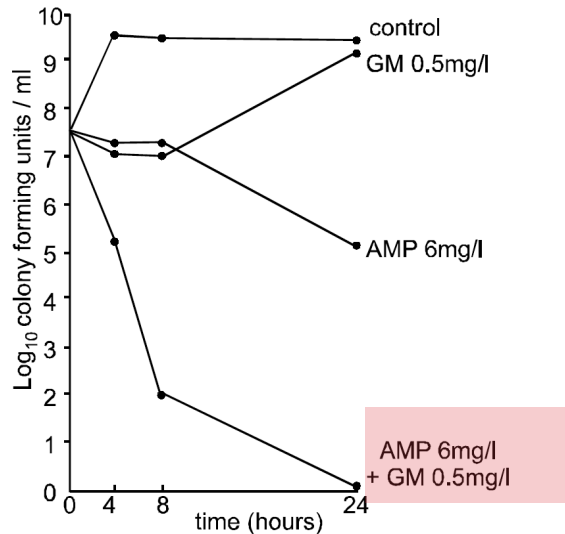
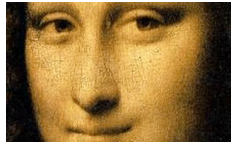


FIG. 1. Effects on *L. monocytogenes* 2 of erythromycin (5 µg/ml), penicillin G (10 µg/ml), and ampicillin (10 µg/ml), alone and in combination. Symbols: ●, control; ○, erythromycin alone; ■, penicillin G alone; ▲, ampicillin alone; △, erythromycin plus ampicillin; □, erythromycin plus penicillin G.

Maternal-neonatal listeriosis

How to treat?



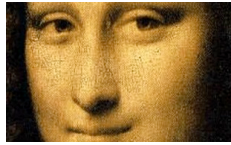
No emergence of resistance in the past 20 years

Interval antimicrobial resistance profile of clinical *L. monocytogenes* isolates^a

Antimicrobial agent	No. (%) of isolates susceptible or resistant during					
	1955–1966		1970–1979		1991–1997	
	Susceptible	Resistant	Susceptible	Resistant	Susceptible	Resistant
Penicillin	17 (94.4)	1 (5.6)	39 (97.5)	1 (2.5)	24 (100)	0
Ampicillin	4 (100)	0	29 (82.9)	6 (17.1)	24 (100)	0
Erythromycin	17 (94.4)	1 (5.6)	41 (100)	0	24 (100)	0
Tetracycline	16 (88.9)	2 (11.1)	22 (100)	0	24 (100)	0
Chloramphenicol	14 (77.8)	4 (22.2)	9 (90)	1 (10)	22 (91.7)	2 (8.3)

Maternal-neonatal listeriosis

How to treat?



- **First line combination : amoxicillin/gentamicin**
- **Second line molecules**

Cotrimoxazole	Teratogenic T1 Hyperbilirubinemia peri-partum
Glycopeptides	Kidney toxicity
Macrolides	Bacteriostatic Does not cross the placenta Antagonism macrolide/ gentamicin

Maternal-neonatal listeriosis

How to treat?



1st line

Septicemic/ MN

Amoxicillin

100mg/kg/d 14-21d

+

Gentamicin

5 mg/kg /d, 3-5 d

Neurolisteriosis

Amoxicillin

200mg/kg/d 21j

+

Gentamicin

5 mg/kg /d 3-5 d

2nd line

Cotrimoxazole

PO : (800/160) : 1 x 2 ou 3/d, 14-21d

+

Gentamicin

5 mg/kg /d 3-5 d

3rd line

Meropenem

IV 2g x 3/d

or

Vancomycin

Loading dose 15mg/kg then
30mg/kg/d , 14-21d

+

Gentamicin

5 mg/kg /d 3-5 d

Documented failure of preemptive treatment in case of maternal fever For the amoxicillin 3g/d 5d regimen
→ amoxicillin > 3g/d > 5d

Traitement post exposition



AVIS DU CONSEIL SUPERIEUR D'HYGIENE PUBLIQUE DE FRANCE (approuvé le 29 juin 1999)

SUR L' OPPORTUNITE D' UNE ANTIBIOPROPHYLAXIE POUR LES PERSONNES AYANT CONSOMME UN ALIMENT CONTAMINE PAR *LISTERIA MONOCYTOGENES*

Considérant :

- qu' il n' y a pas de données dans la littérature qui permettent d' apprécier réellement le risque lié à la consommation d' un aliment contaminé ;
- que les éléments recueillis par le CNR des *Listeria* et les données de l' InVS ont montré que le nombre de cas humains identifiés après différentes alertes alimentaires a toujours été extrêmement faible par rapport au nombre estimé de personnes ayant consommé l' aliment contaminé ;
- qu' il n' y a pas d' exemple, à sa connaissance, de pays recommandant une antibioprofylaxie à la suite de consommation d' aliment contaminé par *Listeria monocytogenes* ;
- qu' en revanche, la recommandation faite aux populations à risque est de consulter un médecin sans délai en cas de fièvre ou syndrome grippal durant les deux mois suivant la consommation d' un aliment contaminé ;

La section des maladies transmissibles du Conseil supérieur d' hygiène publique de France émet l' avis suivant :

En raison de la rareté des cas survenant après consommation d' un aliment qui s' avère *a posteriori* contaminé, de la relative faiblesse du risque tel qu' il apparaît dans l' état actuel des connaissances et de l' absence d' élément scientifique en faveur d' un traitement antibiotique en l' absence de signe clinique, **il n' y a pas lieu de recommander une antibioprofylaxie systématique en cas de consommation d' un aliment contaminé par *Listeria monocytogenes*.**

En revanche une information aux consommateurs est dans ce cas impérative, les invitant notamment à faire preuve de vigilance et à consulter sans délai devant l' apparition de fièvre, isolée ou accompagnée de maux de tête, survenant dans les deux mois qui suivent la consommation de l' aliment contaminé.

CET AVIS NE PEUT ETRE DIFFUSE QUE DANS SON INTEGRALITE SANS SUPPRESSION NI AJOUT