Syphilis et grossesse, Que retenir en 2022?

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The burden of syphilis in pregnancy

- **Congenital syphilis**

Child born from an untreated / bad treated mother

Child with clinical/ biological signs of congenital syphilis

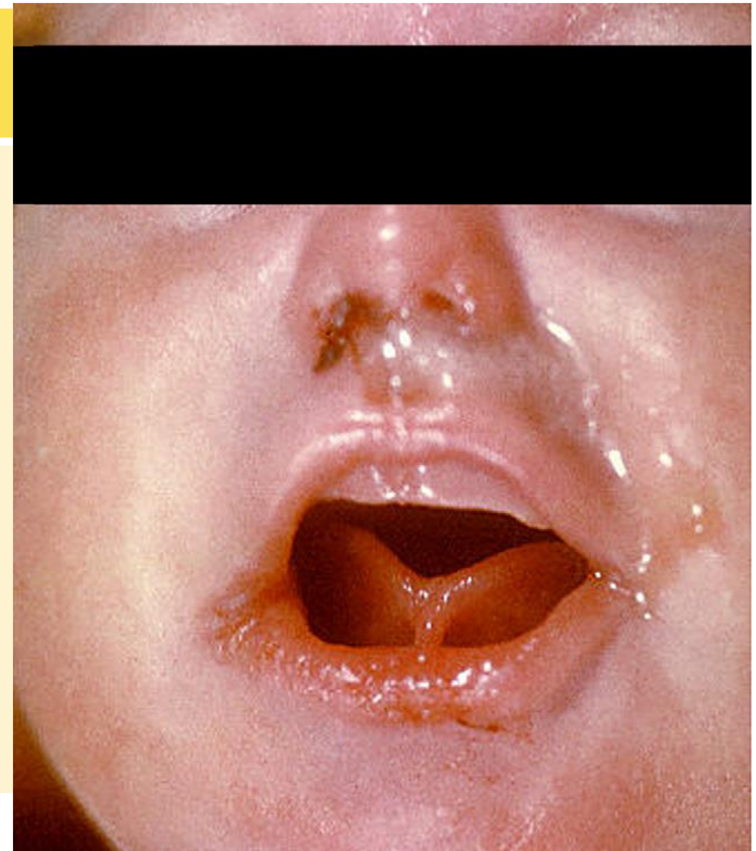
- **Consequences**
  - Fetal loss 40%
  - Premature delivery 20%
  - Congenital infection
    - Early < 2 yrs (1/3)
    - Late < 2 yrs (2/3)

Neonatal mortality 20%
Long term impairment 20%

Newman PlosMed 2013
CDC 2013

Congenital syphilis

Antenatal ultrasound signs	Early Syphilis
Fetal loss Growth restriction Hydrops fetalis Ascites Hepatomegaly Hydrocephaly Brain calcifications	Osteochondritis 61% Hepatomegaly 61-100% Splenomegaly 49% Petechial lesions 41% Other (contagious) skin lesions 35% Meningitis 25% Adenomegaly 32% Jaundice 30% Anemia 30% **Nasal discharge** 22% Nephrotic syndrome 20%



Walker Semin fet Obstet Dis 2008
Charlier LPM 2014

Congenital syphilis

Antenatal ultrasound signs	Early Syphilis	Late Syphilis
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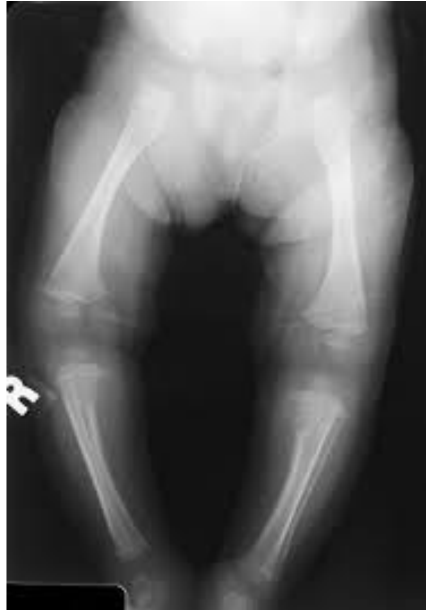
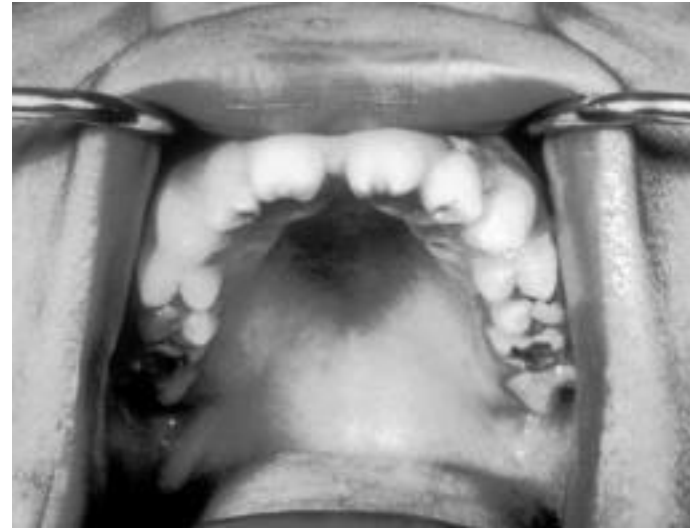
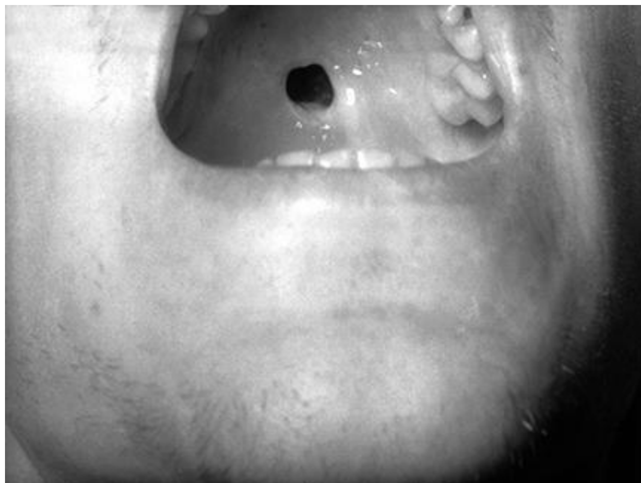
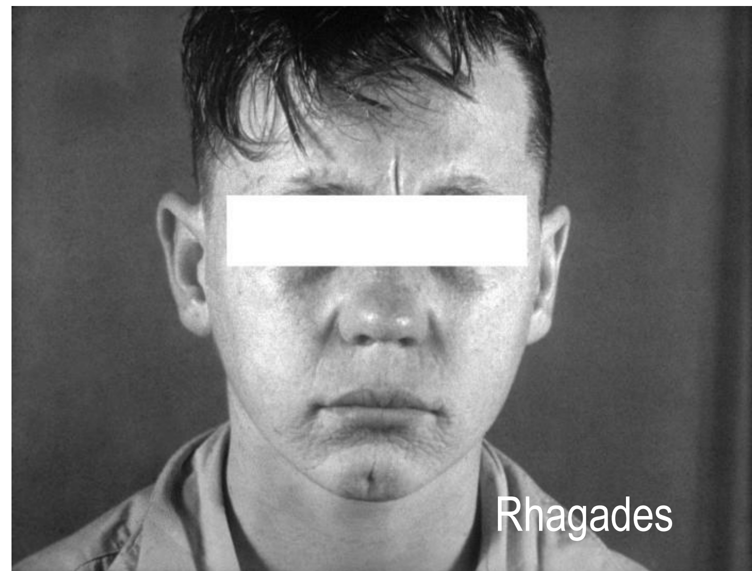
Charlier LPM 2014

Congenital syphilis









CDC

Maternal transmission is linked to 3 parameters

- **Term of pregnancy at infection**
  - **From 16 WG** → Placenta crossing

  Vertical transm. increases with gestational age /decreases in severity
  - **At delivery** → Contact infected maternal genital secretions ++++

- **Stage of infection**

Stage	Rate of transmission
Primary/ Secondary (early)	60-100%
Early latent	40%
Late latent	8-10%

Harter AJOG 1976
Fiumara Clin Obstet Gynecol1975

Maternal transmission is linked to 3 parameters

- **Term of pregnancy at infection**
- **Stage of infection**
- **Maternal treatment**
  - Adequate penicillin based treatment administered before the third trimester and at least > 30d before delivery is the most important parameter

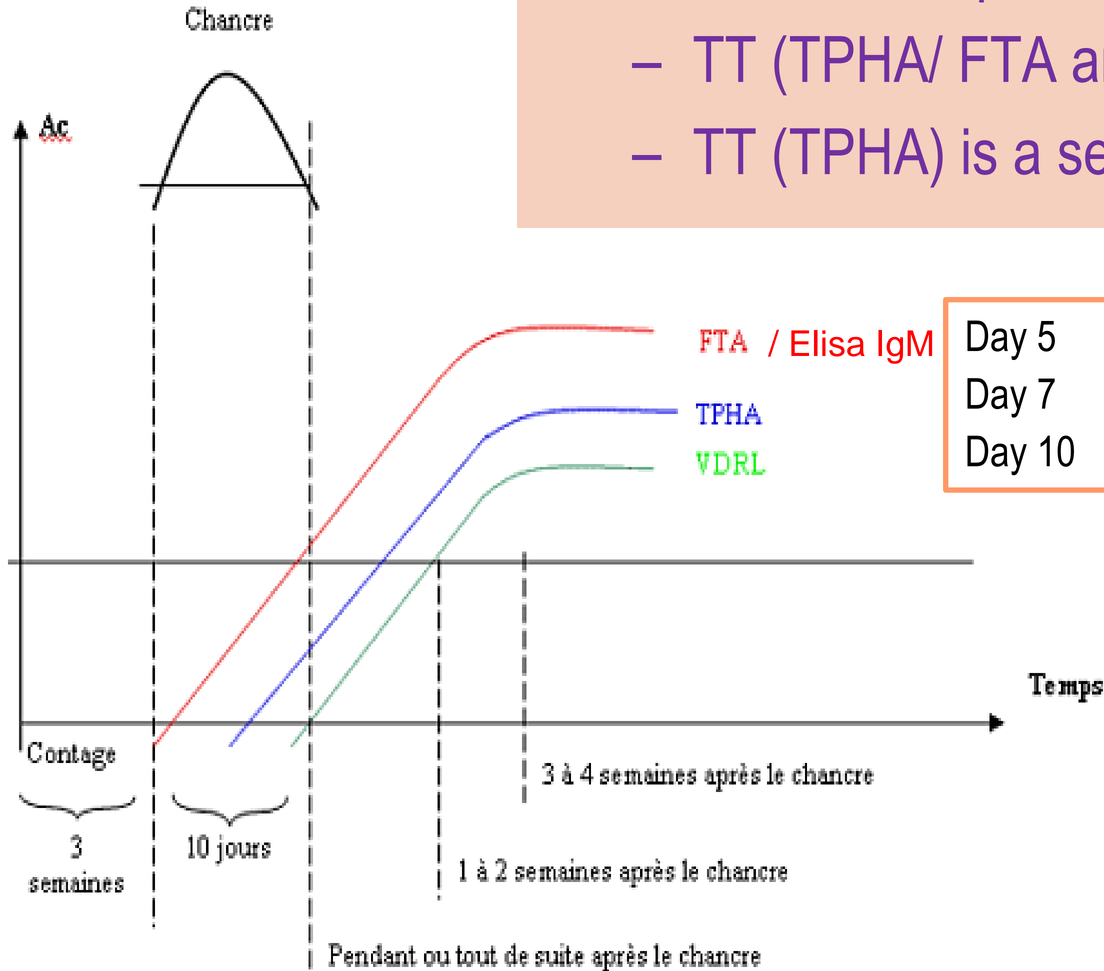
Tableau 2 Facteurs de risque d'atteinte fœtale.
Table 2 Risk factor of fetal effects.

	Absence d'atteinte fœtale (56 cas)	Atteinte fœtale (29 cas)	*p*
< 3 consultations	17 (30,3 %)	16 (55,5 %)	0,025
Absence de traitement	2 (3,6 %)	13 (44,8 %)	0,01
≥ 2 injections Extencilline®	43 (76,8 %)	9 (31 %)	0,001
Délai traitement—accouchement inférieur à un mois	10 (17,8 %)	22 (75,9 %)	0,001
Taux moyen VDRL chez la mère	35	46	NS

Carles JGOBR 2008

Maternal diagnosis which specificities?

- TNT is not specific of *Treponema*
- TT (TPHA/ FTA are not specific of *pallidum sp.*
- TT (TPHA) is a serological scar



Day 5
Day 7
Day 10

Maternal diagnosis : 3 tricks

- **TNT+ , TT (TPPA)- → false positive**

→Double check and check for ACC

- **TNT-, TPPA + → 2 situations**
  - Serological scar : no risk of transmission
  - OR Very early infection

How to distinguish?
→ Past medical history
→ → IgM , repeat testing 2 weeks later

- **Testing repeated at 28WG if**
  - Multiple partners
  - Past history of STI
  - Current STI

Positive treponemic test
→Start treatment immediately in all cases, except if proof of complete adequate previous treatment is available and no risk of new infection
→ Double check (Elisa, IgM, FTA…) and perform TNT

Maternal treatment : 7 points

- Treat ideally before 16 WG, at least before T3
- Penicillin in all cases
- Prevention of Jarisch- Herxheimer in early infections
- Evaluation for other STI
- Evaluate partners
- Evaluate the newborn
- Check for TNT decrease at M3, M6 and M12 + at delivery++

Maternal treatment

- Early infection : < 1yr

→Penicillin 2.4 M units/ week 2 weeks : 2 doses

→Xylocain allowed in pregnancy

- Later infection : > 1yr

→Penicillin 2.4 M units/ week 3 weeks

→NO MISSED DOSE

Pregnant women who miss any dose of therapy must repeat the full course of therapy.

https://www.cdc.gov/std/tg2015/tg-2015-print.pdf

CNR Syphilis

Maternal treatment : penicillin allergy

- **Tolerance induction**

DÉSENSIBILISATION ORALE À LA PÉNICILLINE
(d'après Stark et Sullivan J. Allergy and Clin. Immunol. 1987)
Consentement éclairé signé par le patient

SURVEILLANCE MÉDICALE RÉGULIÈRE ++++

N° dose	Unités administrées	Voie d'administration	Espacement entre les doses	Dose et concentration
1	100 ui	ORALE	15 minutes	1 ml (100 u/ml)
2	200 ui			2 ml
3	400 ui			4 ml
4	800 ui			8 ml
5	1 600 ui			1,6 ml (1 000 u/ml)
6	3 200 ui			3,2 ml
7	6 400 ui			6,4 ml
8	12 800 ui			12,8 ml
9	25 000 ui			2,5 ml (10 000 u/ml)
10	50 000 ui			5 ml
11	100 000 ui			1 ml (100 000 u/ml)
12	200 000 ui			2 ml
13	400 000 ui			4 ml
14	200 000 ui	SC	15 minutes	
15	400 000 ui			
16	800 000 ui			
17	1 000 000 ui	IM	15 minutes	
18	Dose thérapeutique	IV	Chronologie habituelle sans jamais espacer plus de 8 heures les doses délivrées	

Voie veineuse impérative - Chariot de réanimation à proximité
adrénaline, corticoïde injectable, antihistaminique disponibles

Faire préparer par la pharmacie de l'hôpital les dilutions de pénicilline de 100 000 ui/ml à 100 ui/ml à partir de la phénoxyméthylpénicilline (Oracilline suspension 1 000 000 ui/10 ml).
Passer à la péni G (flacons à 1 000 000 ui) pour les injections.

Neonatal evaluation : 3 situations

→**Clinical evaluation + paired serum TNT mother / child**

- Situations requiring maximal evaluation and antibiotic treatment
- Situations with minimal risk
- Situation without risk: no further evaluation/ NN treatment

Adapted from CDC

and from GH centre / CNR procedure

Maximal evaluation and treatment

WHO?

- **PCR positive on any infant sample**

(CSF/ nasal discharge, skin, blood, placenta…)

- **TNT NN/mother > 4**
- **IgM NN positive**
- **TNT NN positive and**
  - Clinical signs in NN OR
  - Maternal treatment not performed or not adequate (not penicillin, to late (< 4 wks before delivery), no serological response)

Maximal evaluation and treatment

WHAT?

- CBC
- Liver tests
- CSF examination (PCR, VDRL, IgM)
- Long bones radiographs
- (Brain imaging, ophtalmologist evaluation)

- Penicillin IV 150,000 U/kg/d (25,000 U/Kg x 6/d)
- For 10 -14d (14 d in neurosyphilis)

No risk

WHO?

- **TNT NN negative and**
  - No clinical signs in NN
  - Maternal treatment performed and adequate (penicillin, < 16 WG, good serological response)

WHAT?

- **No further evaluation**
- **No treatment**
- **No serological monitoring**

Minimal risk

WHO?

- **TNT NN positive and**
  - VDRL NN/mother < 4
  - No clinical signs in NN
  - Maternal treatment performed and adequate (penicillin, >4 wks before delivery, good serological response)

WHAT?

- **No further evaluation**
- **Penicillin IM 50,000 U /kg single dose**
- **Serological monitoring**

RISQUE	MAX	NUL	MINIMAL
Clin	**Signes cliniques**	Examen normal	Examen normal
Traitement mat	**AUCUN OU** **MAUVAIS OU** **< 1mois avant acc**	Complet < 16 SA	COMPLET > 1 MOIS
TNT BB	+	-	**+**
TNT BB/maman	**>4**	O	<4
IgM BB	+	-	-
PCR BB	+	-	-
CAT	Rx/PL/bio **PENI G 10-14j** **150.000U/kg/j**	**RIEN**	**1 IM Extencilline** **50.000 U/kg 1 fois**
Surveillance	Séro 2 ans	**RIEN**	OUI

Congenital syphilis

- **Subsequent evaluation by the pediatrician**
  - Clinical / 3 months for 2 years
  - Serological testing at M3 M6 M12
  - VDRL negative at M6, TPHA negative at M12

- **Management of Treponema exposure at delivery**
  - All staff in contact with the infant < 24 hrs of treatment
  - Skin / mucosal contact with infections lesions (nasal discharge, skin or mucosal infected lesions)
  - Penicillin 2.4M U 1 dose
  - Clinical evaluation W2 + Serology M1,M3,M6 and M12

Syphilis and breastfeeding

- No transmission through the milk
- Transmission possible in case of lesion on the nipple
- Penicillin is not contra-indicated during lactation