CASE 2

- Pr Nicolas Dupin
- Dr Françoise Plantier
- Hôpital Tarnier Cochin
• Man 57 y o
• Mucous patches and ulcerations of the oral cavity
Secondary syphilis
• Treponema pallidum and syphilis have one of the richest recorded histories known to humankind

• There are Biblical and old Chinese writings consistent with late Syphilis

• Syphilis (Morbus gallicus, lues venerea) have been recognised in late 15th century

• The first book dealing with syphilis, » In Pustulis Malas Morbum quem Malum de Francia vulgus appellat, que sunt de genere Formicarum » was published by Konrad Schelling in 1495
• Following its diminishing incidence over the past 3 centuries spontaneously and under penicillin therapy rates are again increasing

• It is highly infectious (risk of transmission 30 to 51%)

• Association with other STDs such as HIV increases the prevalence and complexity of the disease and syphilis increases the risk of acquiring HIV infection
• In the first 50 years of Syphilis in Europe the lesions described (Fracastoro, Ulrich von Hutten) were much more severe than today and death rate was around 20 to 40%. (co-infection? true virulence?)

• All historical accounts emphasize the spontaneous diminution in the virulence of syphilitic infection to the level that we recognize today
• In France we still classify Syphilis in 3 stages (primary, secondary and tertiary)
• In international litterature there are 2 stages:
  - early syphilis is less than one year’s infection
  - And late syphilis more than one year’s duration
• **Primary syphilis**

• primary lesion or chancre at the site of infection 3 weeks after the inoculation.

• Chancre is usually found on genital or perianal skin (5\% extra genital). Multiple or extensive chancre are sometimes present in HIV patients.

• It is an indolent and indurated ulceration, associated with enlarged lymphadenopathy spontaneously healing in one to two weeks.

• Treponemes can be identified directly by dark ground microscopy of the exsudates.
Secondary syphilis

- About one third of untreated primary lesions will develop into secondary syphilis
- Secondary cutaneous lesions (syphilids) are highly infectious
- Present 6-8 weeks after the chancre
- Develop insidiously (up to 80% of patients) during two years
- May mimic any skin disorder
Secondary syphilis

- Rashes are associated with widespread lymphadenopathy (50-85%)
- And more or less associated with general symptoms: fever, headache, arthralgias, weight loss, hepatitis, glomerulonephritis,
- With sometimes neurological manifestations: uveitis, retinitis,
• **macular rash** on the trunk: pale pink, flat spots usually 4 to 8 mm in diameter.

• often confused with viral exanthems or drug eruption
• Papular lesions:
  • small, distinct, localized elevations of skin
  • Varies in color
  • May appear on any part of the body, including flexor surfaces of the limbs, palms of hands and sole of foot, forehead..
  • In the genital areas, the groin, and the axilla, they may appear in the form of condylomas.
• Lesions can be very polymorphous: syphilis is the great simulator:
• Psoriasiform, pustular, lichenoid, annular, erosive, acneiform, condylomata, necrotic, vesiculous..
• Patchy alopecia
Clinical microbiological review 2005 18 105-16
Tertiary syphilis

- Secondary syphilis is followed by a latent phase and either seronegativity and cure
- either persistant seropositivity without lesions
- either tertiary lesions, many years after initial infection
- Cardiovascular, neurological manifestations (tabes..)
- Skin: nodular, chronic gummatous ulcer..
• **Histopathogy**

• Macular lesions: normal epidermis, Endothelial swelling and perivascular inflammatory infiltrate+ few plasmocytes

• Papular lesion: parakeratosis, spongiosis, acanthosis, exocytosis, thick walled blood vessels, endothelial swelling, superficial and deep perivascular infiltrate+/-band like distribution, numerous plasma cells
there is a considerable variation in the histopathological pattern:

- Plasma cells absent or scarce
- Infiltrate predominantly lymphocytic CD8+, with histiocytes, granulomas
- Neutrophilic vascular reaction (early lesions) heavy sweet’s syndrome-like neutrophilic infiltrate
- Dermal infiltrate may be heavy and diffuse pseudo lymphomatous, granulomatous
• The infiltrate may involve hair follicles, sweat glands, ..., follicular pustules can be seen
• Spirochetes can be detected by the silver stain technique
  but: a marked background artifacts
  a variable detection rate ranging from 33 to 71%
  not specific to T. pallidum
  (difficult to detect lesions in nontreponemal spirochete contaminated areas (i.e., oral mucosa))
New tool for diagnosis: immunohistochemistry

immunohistochemistry directed against T. pallidum improved both the sensitivity and specificity

Diagnosis of secondary syphilis is sometimes difficult

false negative serology can be observed in the setting of HIV infection
• T. pallidum appears to be mainly located in the epidermis and in the upper dermis areas.
• The strong epidermal homing of T. pallidum is obvious in early syphilis
• In the epidermis, the quantity of *T. pallidum* varied with only a few bacteria to a large number in the basal layer.
In the dermis, T. pallidum is present in the perivascular area in the superficial dermis and inside capillary vessel. T. pallidum is capable of attaching to vascular endothelium, passing through the endothelial cell layer by moving between the junctions of cells.
In the dermis, *T. pallidum* can be found surrounding the pilary infundibulum and in the arector pili muscles in the deep dermis.
• IHC has a good sensitivity (91%)
• false positives are described for other spirochetal infections or borreliosis (not found in the study of M. Buffet)
