Dr Edward Coughlan

Clinical Director

Christchurch Sexual Health,Christchurch

Saturday, August 13, 2016

(Room 9)

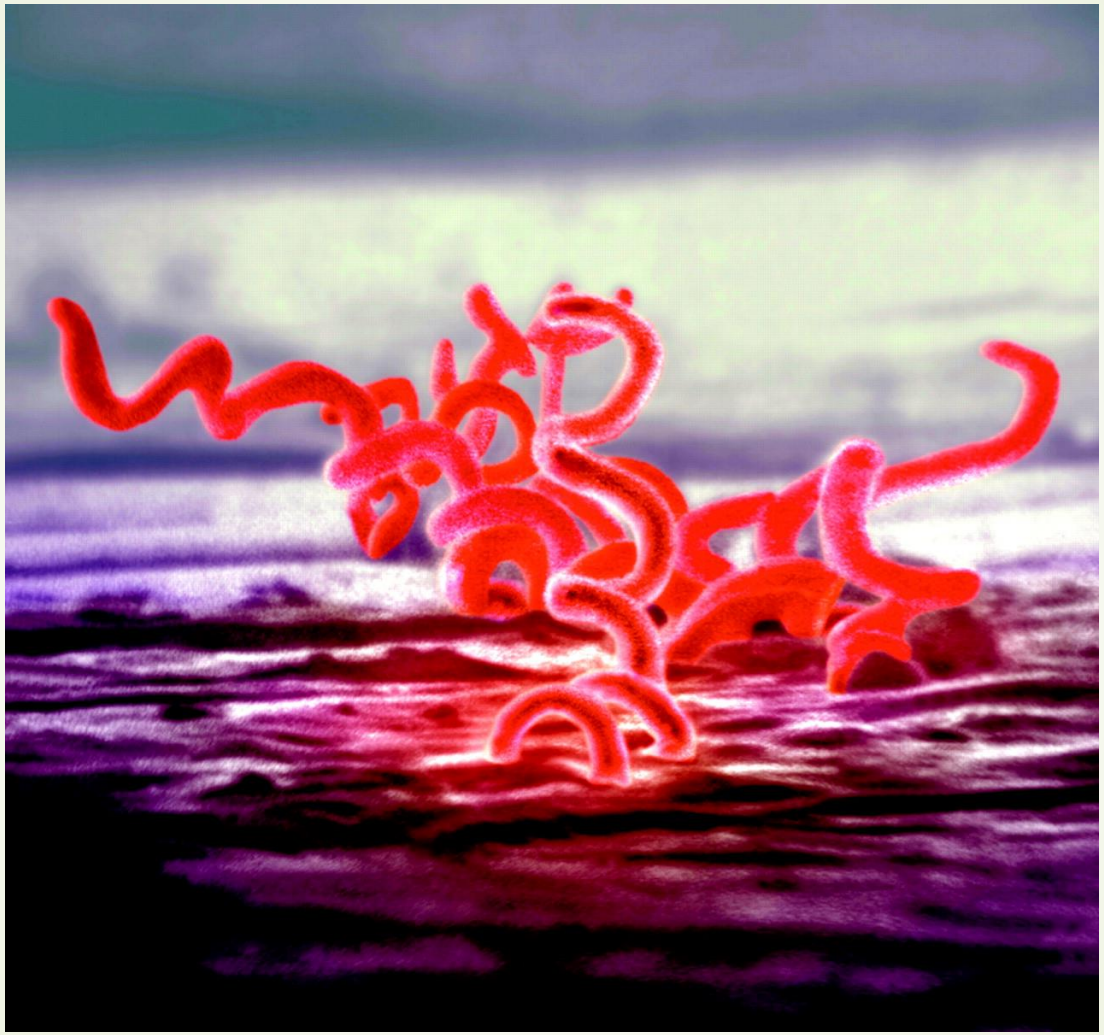
8:30 - 9:25 WS #69: The Dreaded Syphilis Strikes Again

9:35 - 10:30 WS #79: The Dreaded Syphilis Strikes Again (Repeated)

Christchurch Sexual Health
314 Riccarton Road

Dr Edward Coughlan
Clinical Director

Fig 1 Treponema pallidum.



French P BMJ 2007;334:143-147

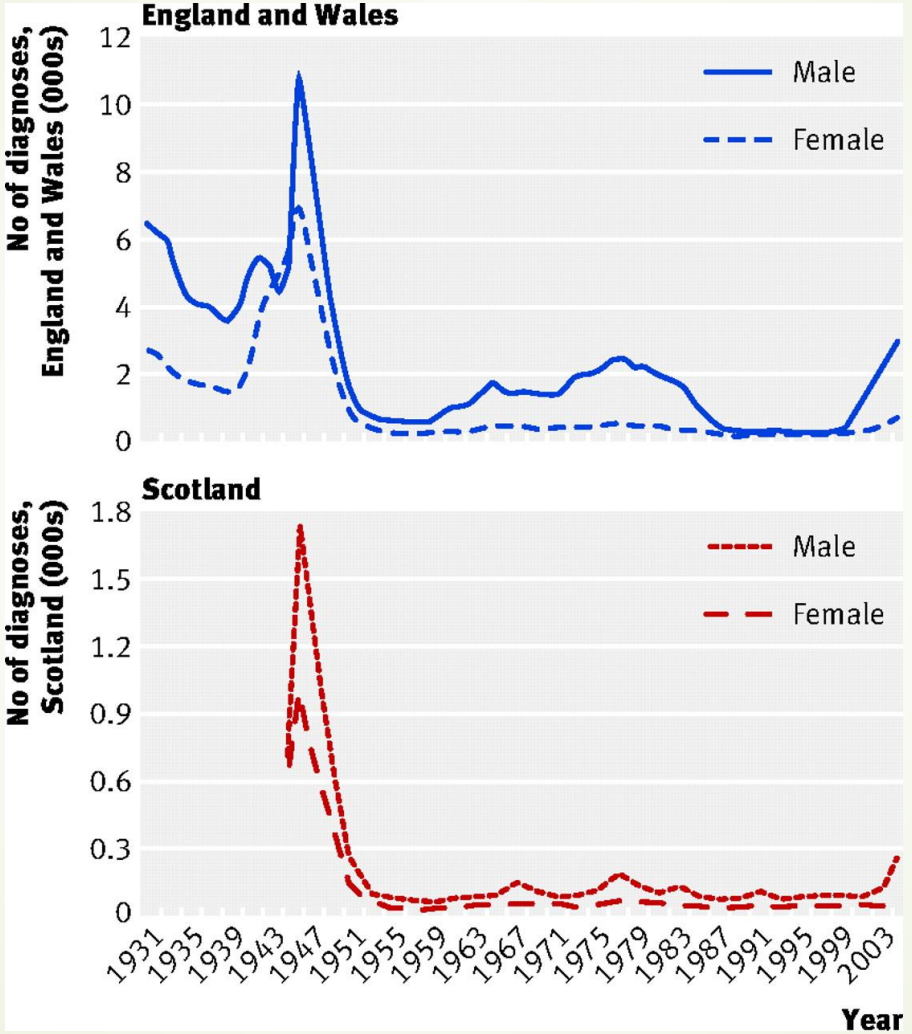
BMJ

20/1/42 → 27/2/42

Genito-Urinary Department

Age	Lab. Reports: Smears	Lab. Reports: Wass.	M. or S.	Gonorrhoea	Syphilis	Congenital	Chancroid	Treatment
Urgo.	+	—	S	/				Discharged July 1942. Cured
22	+	—	S	/				
7½	+	—	S	/	—			Gone to Burnham Camp.
12	+	—	M	/				Gone to Wellington
50	—	++	M.	—	++			" FEMALE
8	+	—	S	/	—			Discharged Aug 1942. Cured.
9	+	—	S	/	—			Transferred to Dun. July. 1942.
5	+	—	S	/	—			Discharged July 1942. Cured
2	+	—	M	/	—			
6½	?		S.					No. V.D.
7	?		S.					No. V.D.
20			S	/				(Negative serology) Primary Male
38			M					Balanitis
25		—	S		/			Primary Chancre B/P Call found
21	+		S	/				
23	+		S	/				
2		—	S					N.V.D
15			M					N.V.D
39	+		S	/				
54			S		/			"
21		++	S		/			Secondary Condylomata B/P Call
26		++	S		/			Late Primary Cleared from
17	+		S	/				
27	+		S	/				
21	+		S	/				
12	—		S	/				from Wellington
27	+		S	/				from Dunedin
27	+	?	S	/				
27	+	—	M	/	—			

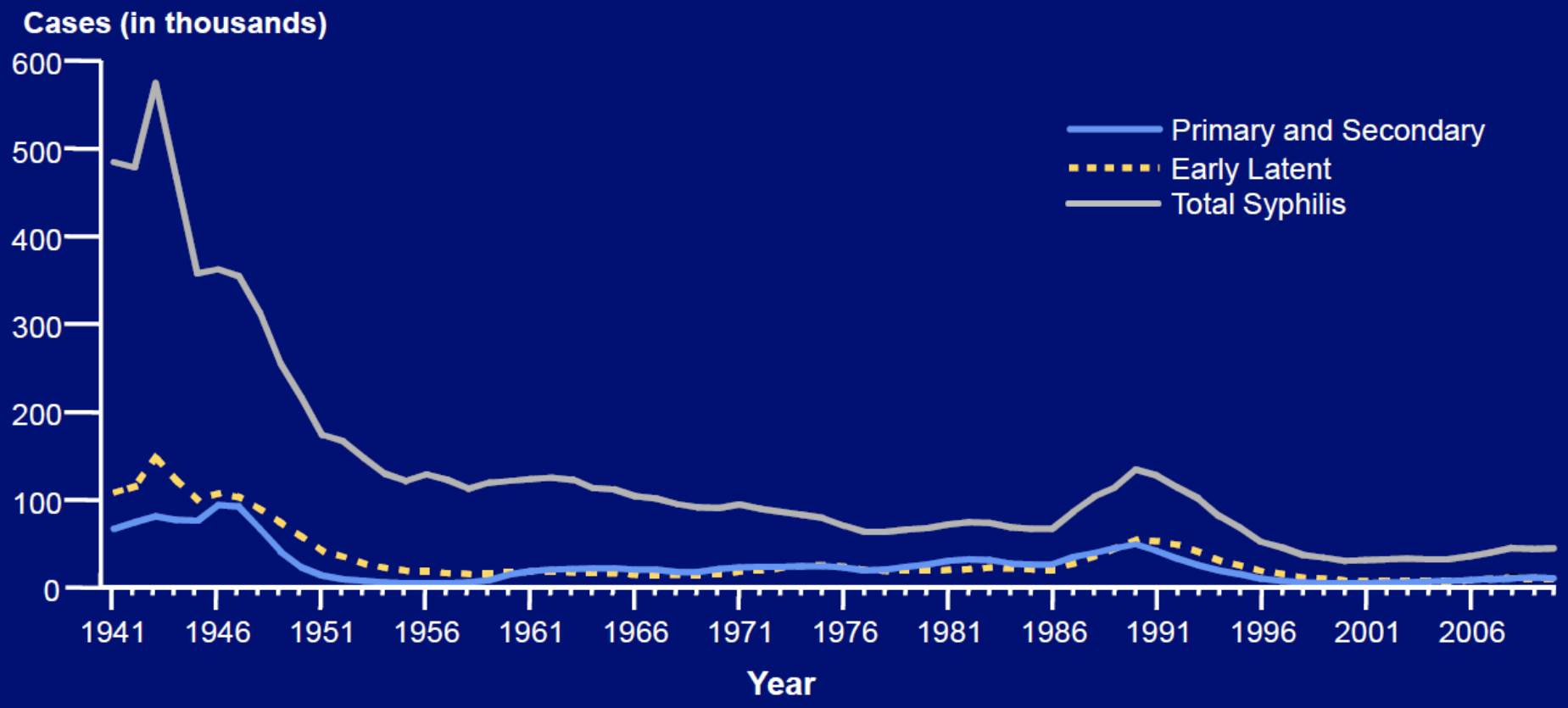
Fig 2 Numbers of diagnoses of syphilis (primary, secondary, and early latent), by sex, recorded in genitourinary medicine clinics in England, Wales, and Scotland (equivalent Scottish data not available before 1945).



French P BMJ 2007;334:143-147

BMJ

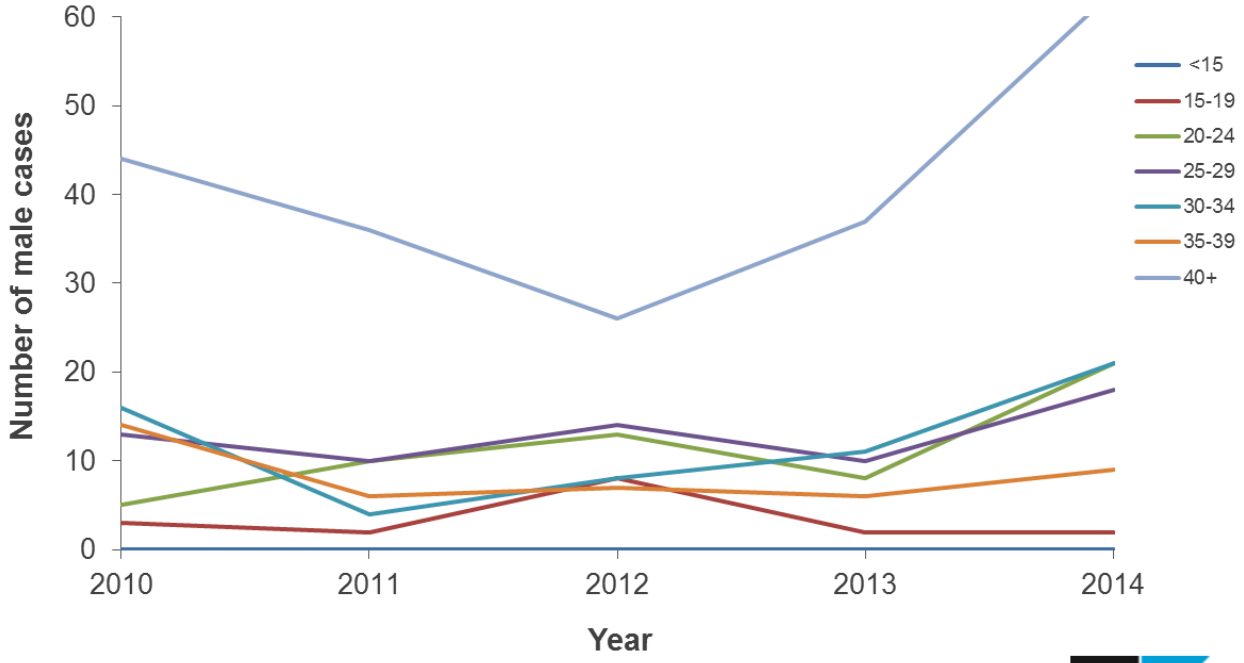
Syphilis—Reported Cases by Stage of Infection, United States, 1941–2010



ESR 2014 report

- Number of cases of early Syphilis Increasednotably between 2013 and 2014
- 85 to 141 cases
- Predominantly male 95.7%
- Of those mostly MSM
- Mostly Auckland and Canterbury

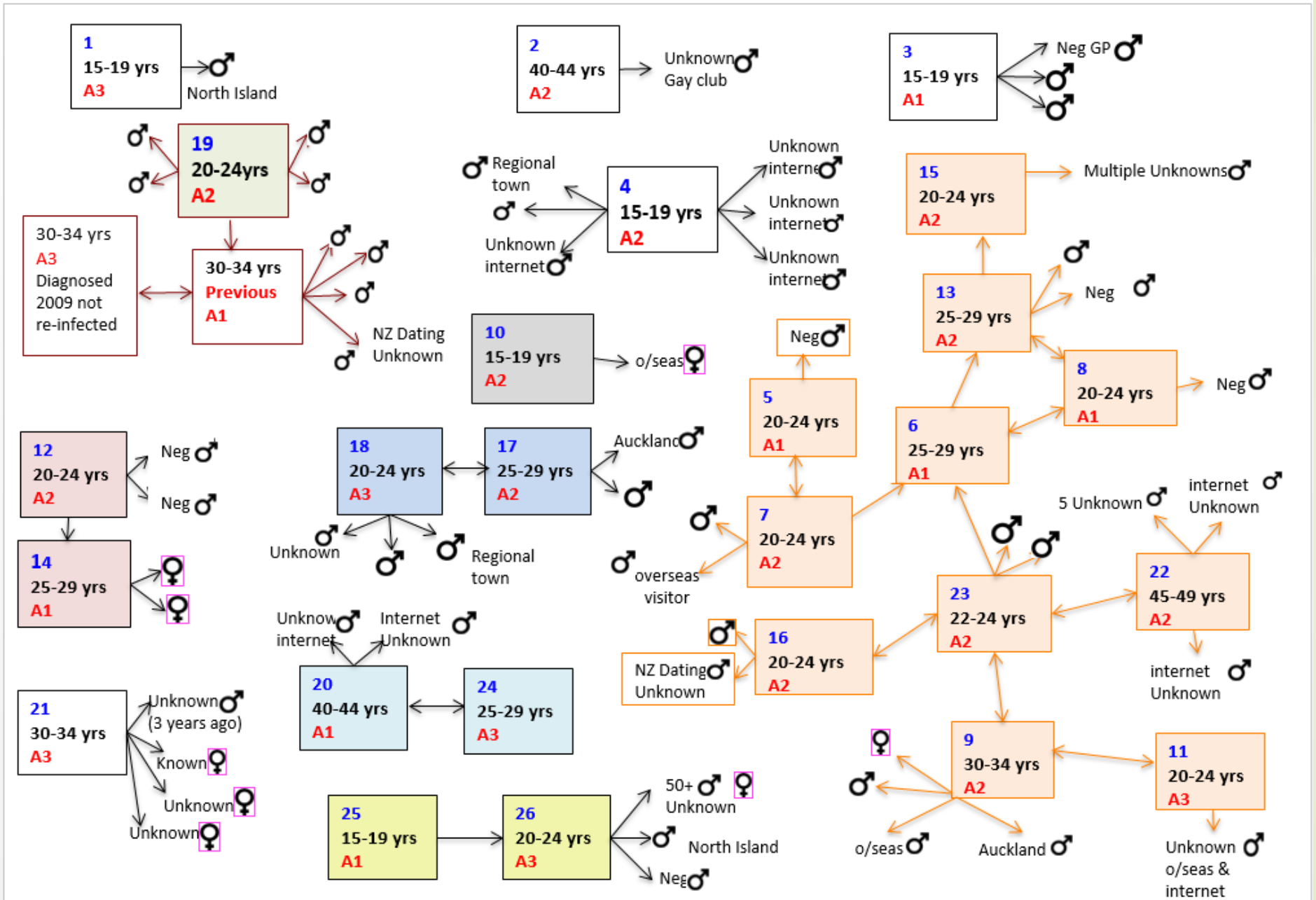
Number of infectious syphilis cases in SHCs in males by age group, 2010–2014



Source: Sexually Transmitted Infections in New Zealand: Annual Surveillance Report 2014, available from www.esr.cri.nz

The rise of Syphilis in Christchurch

- The infectious syphilis outbreak in Christchurch continues
  - 2011 – 8 cases all male
    median age 42yrs
  - 2012 – 26 cases all male
    median age 24yrs



Arrow direction = who named who as a contact with double arrow indicating they named each other/
ESR codes: A1=Primary, A2=Secondary, A3 =latent syphilis / /unknown=no first or surname given/♂ = named but untraceable/♂ neg = named and tested

Year	Total	(MSM)	(MSMSW)	(MSW)	(WSM)	Con-current infection				
						HIV	HSV	HPV	Chlamydia	GC
2011	8	6	1	1	0	2			1	
2012	26	22	2	2	0	2	1	1	10	
2013	18	15	1	2	0	3			2	1
2014	28	22	3	1	2	2			4	1
2015	26	20	2	1	3		3	2	9	3
2016										
2017										

SEXUAL HEALTH

Syphilis 'back with a vengeance'

Homosexual hookups easy with iPhone apps

Alarming trend

"People can access sexual partners with the greatest freedom they have ever had now.

"It is very important for us to realise that, despite our advances in technology, these diseases are still prevalent in our community.

Infectious syphilis cases in Christchurch

WHAT IS SYPHILIS?

Syphilis: The Facts

On this Page

What is syphilis?

Syphilis is a sexually transmitted infection caused by a bacteria (bug) called *treponema pallidum*. This bacteria enters the body through tiny breaks in the skin, mainly in the anal area, genital area, or the mouth.

Important! There has been a sudden increase in syphilis in New Zealand in the last few years. Initially it was mostly seen in homosexual men but is now occurring in heterosexual men and women. It is very important to get checked out if you have any new genital sores or if you think you may be at risk.

Minister of Health's visit to CDHB Sexual Health Centre

Tony Ryall, Minister of Health, made a special visit to the CDHB Sexual Health Centre on Thursday following interest from a recent story in The Press.

The purpose of the Minister's visit was an opportunity for him to hear about emerging health issues in Canterbury.

Dr Coughlan says the team were very grateful to the Minister for taking the time to meet them and hear about some of the issues facing our communities.

"Minister Ryall showed a lot of interest in what the team had to say and seemed very impressed with our enthusiasm and commitment in providing an excellent service to the people of Canterbury," Dr Coughlan says.

"It was a really positive meeting. We believe Sexual Health often goes under the radar, as there is still a lot of stigma associated with it. Having the Minister come and listen to what we think needs to be done to improve health outcomes was incredibly encouraging and we look forward to seeing what comes out of it."

Hnr Tony Ryall, Health Minister, Cathie Parkes, Sexual Health Centre Charge Nurse Manager, Dr Edward Coughlan, Sexual Health Centre Clinical Director, Dr Heather Young, Sexual Health Centre Physician, Margaret Knowles receptionist , Dr Ramon Pink, Canterbury Medical Officer of Health, Maureen Coshall , Sexual Health Centre Nurse Specialist, Sue Teague, Sexual Health Centre Service Manager

Syphilis

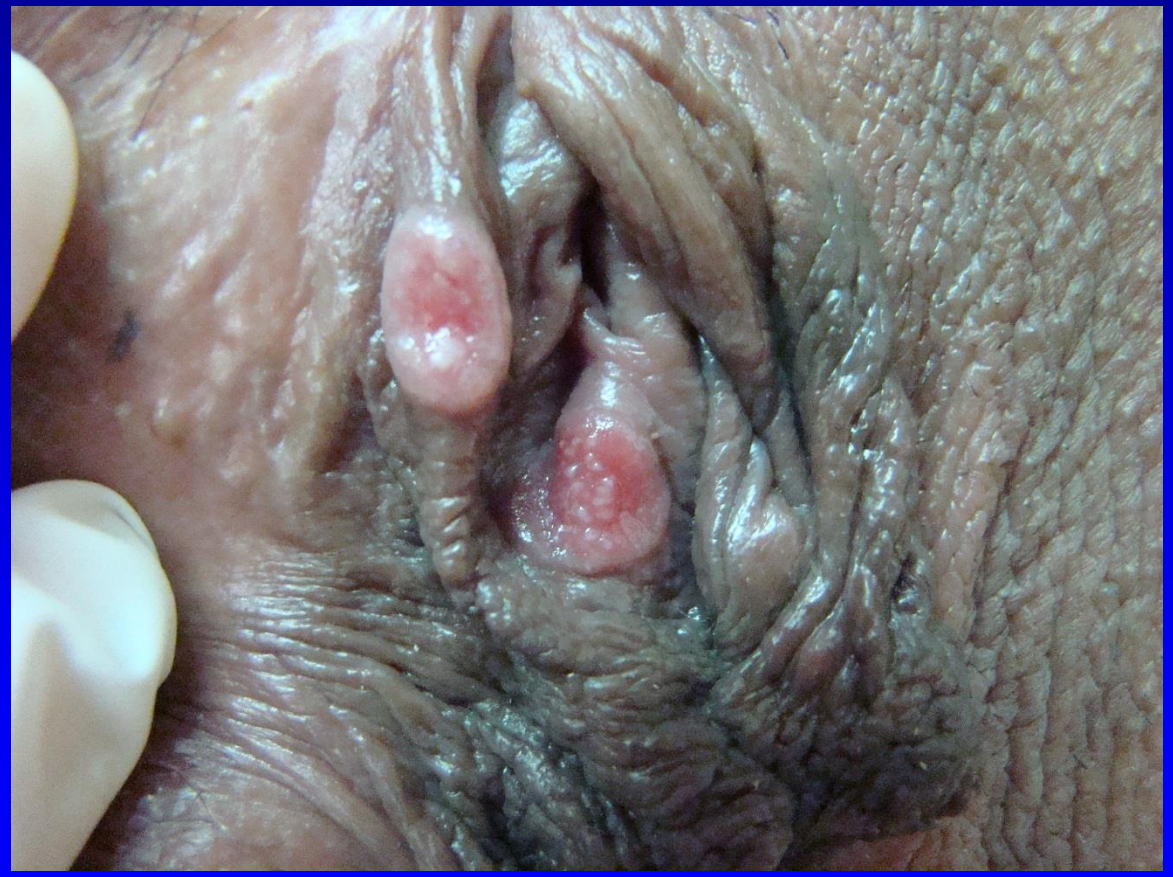
- Order - Spirochaetales
  - Genus:
    - *Treponema*
    - *Borrelia*
    - *Leptospira*

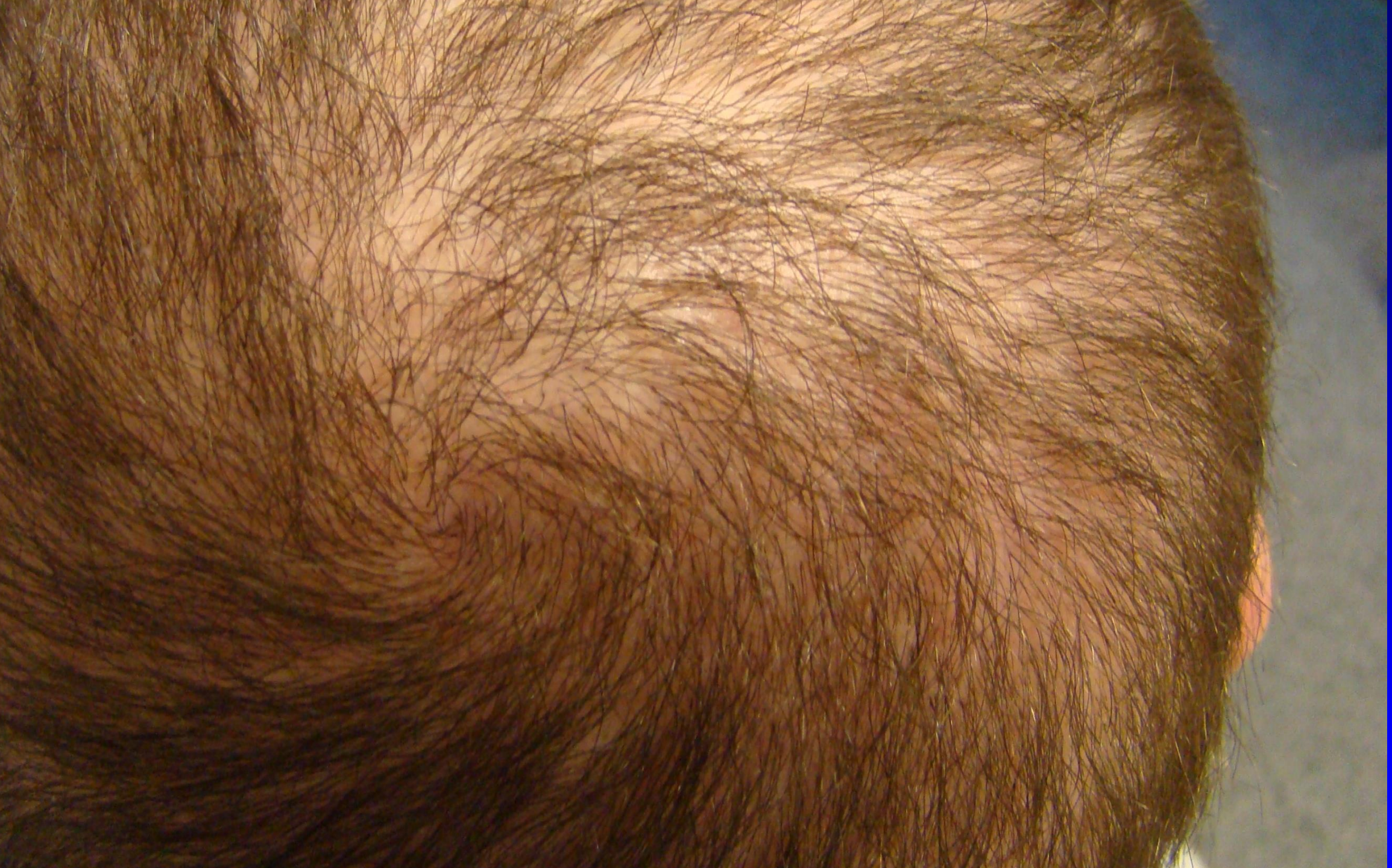
Treponema Species

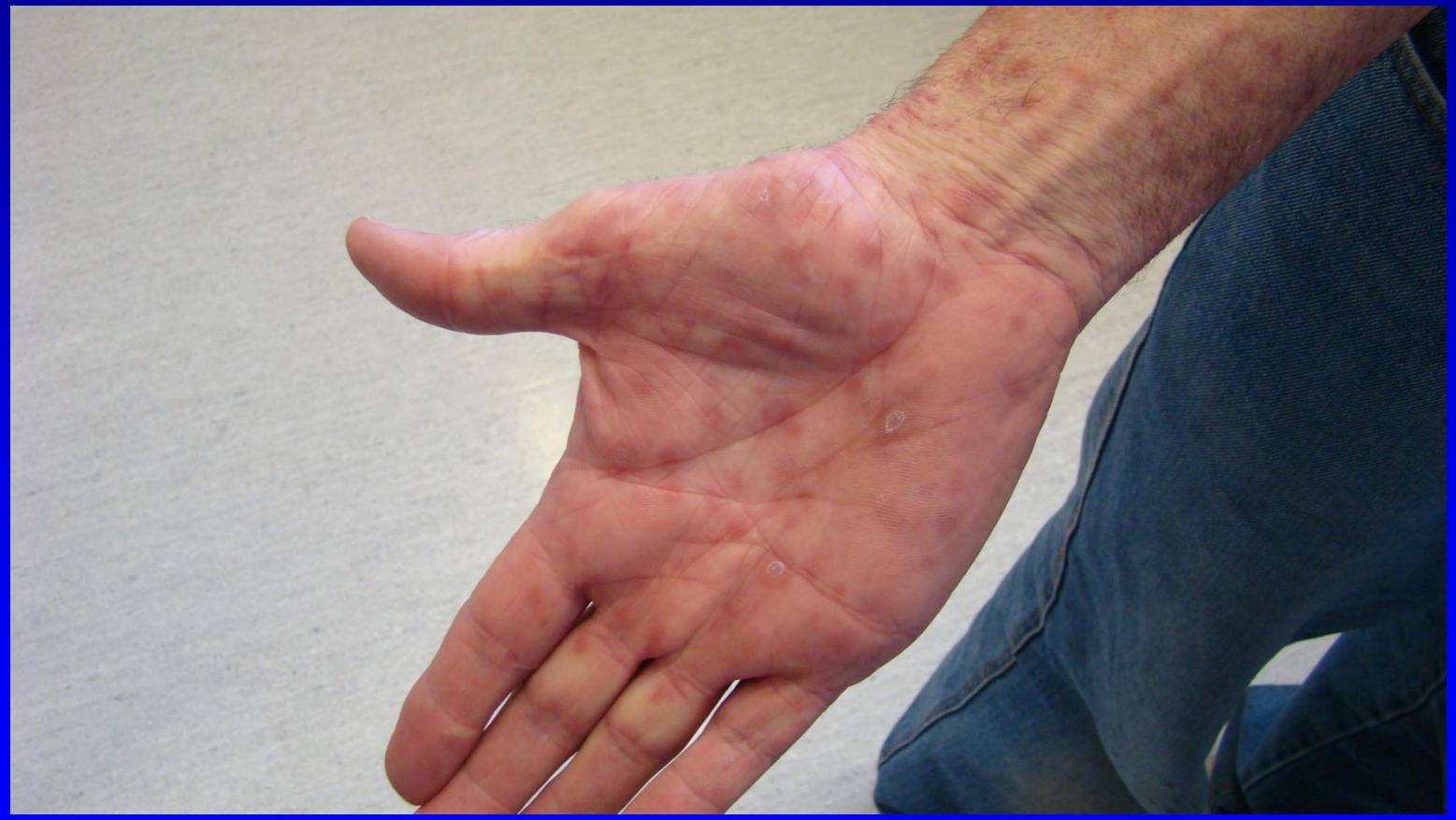
- Treponema pallidum subspecies pallidum
  - Venereal Syphilis
- Treponema pallidum subspecies pertenue
  - Yaws
- Treponema pallidum subspecies endemicum
  - endemic syphilis
- Treponema pallidum subspecies carateum
  - Pinta

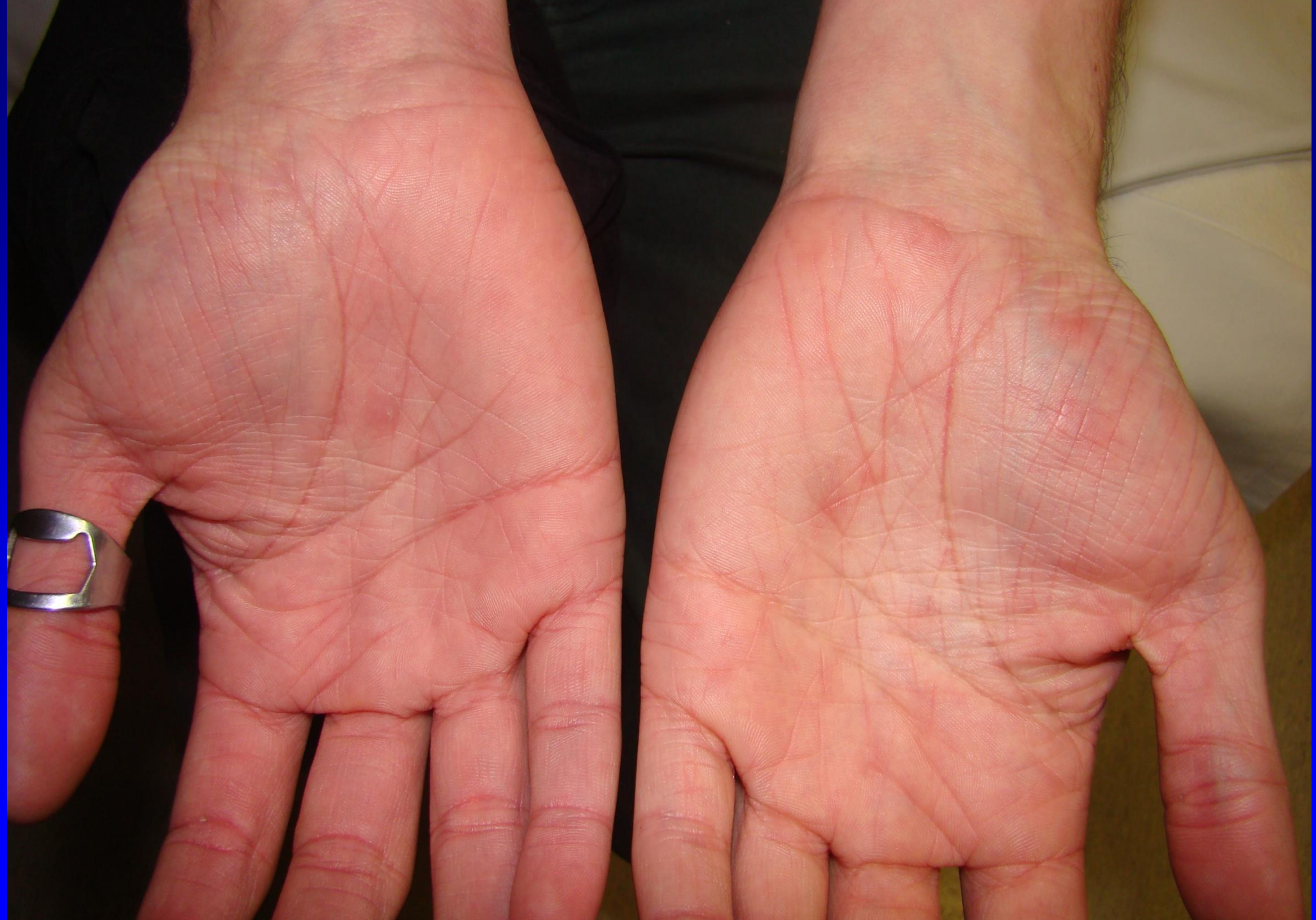
Clinical Features

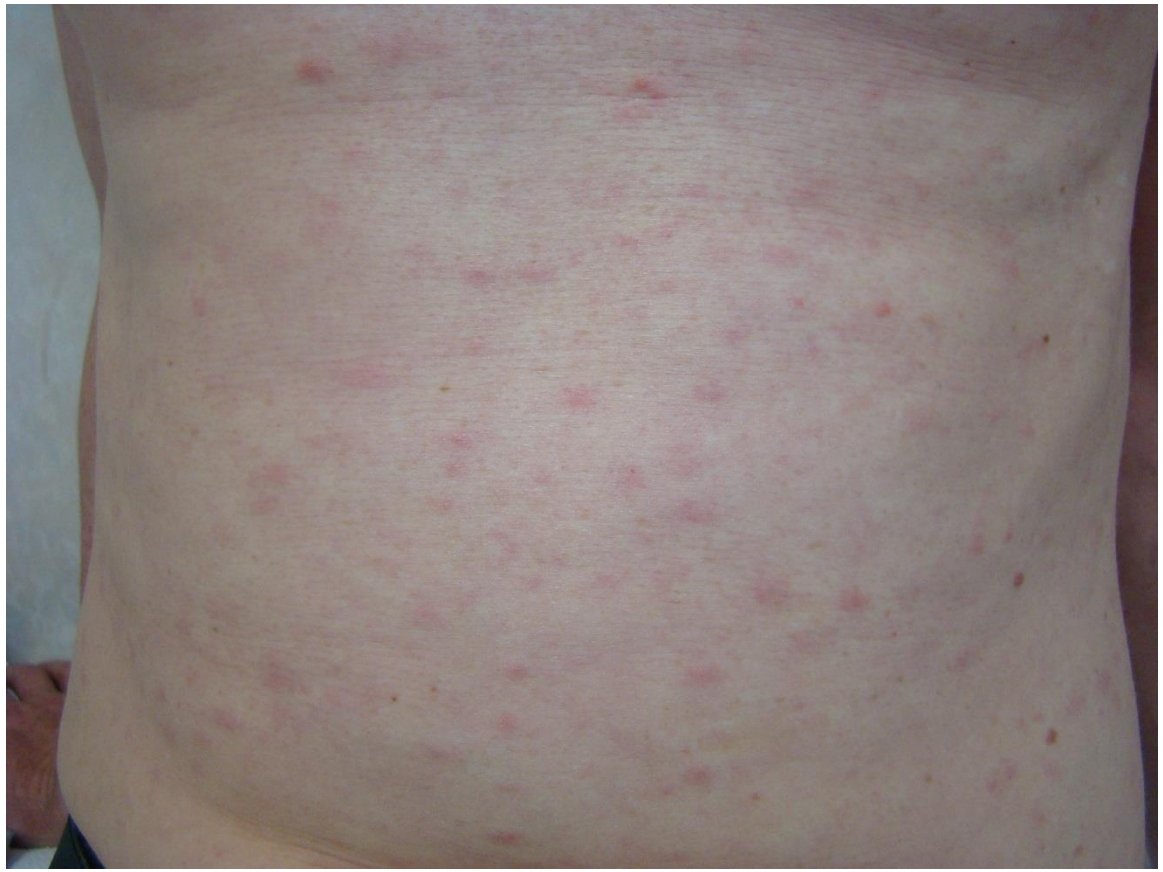
- Primary
  - Incubation period 2 -3 weeks (range 9 to 90 days)
- Secondary
  - Incubation period 6 -12 weeks (range 1 to 6 months)

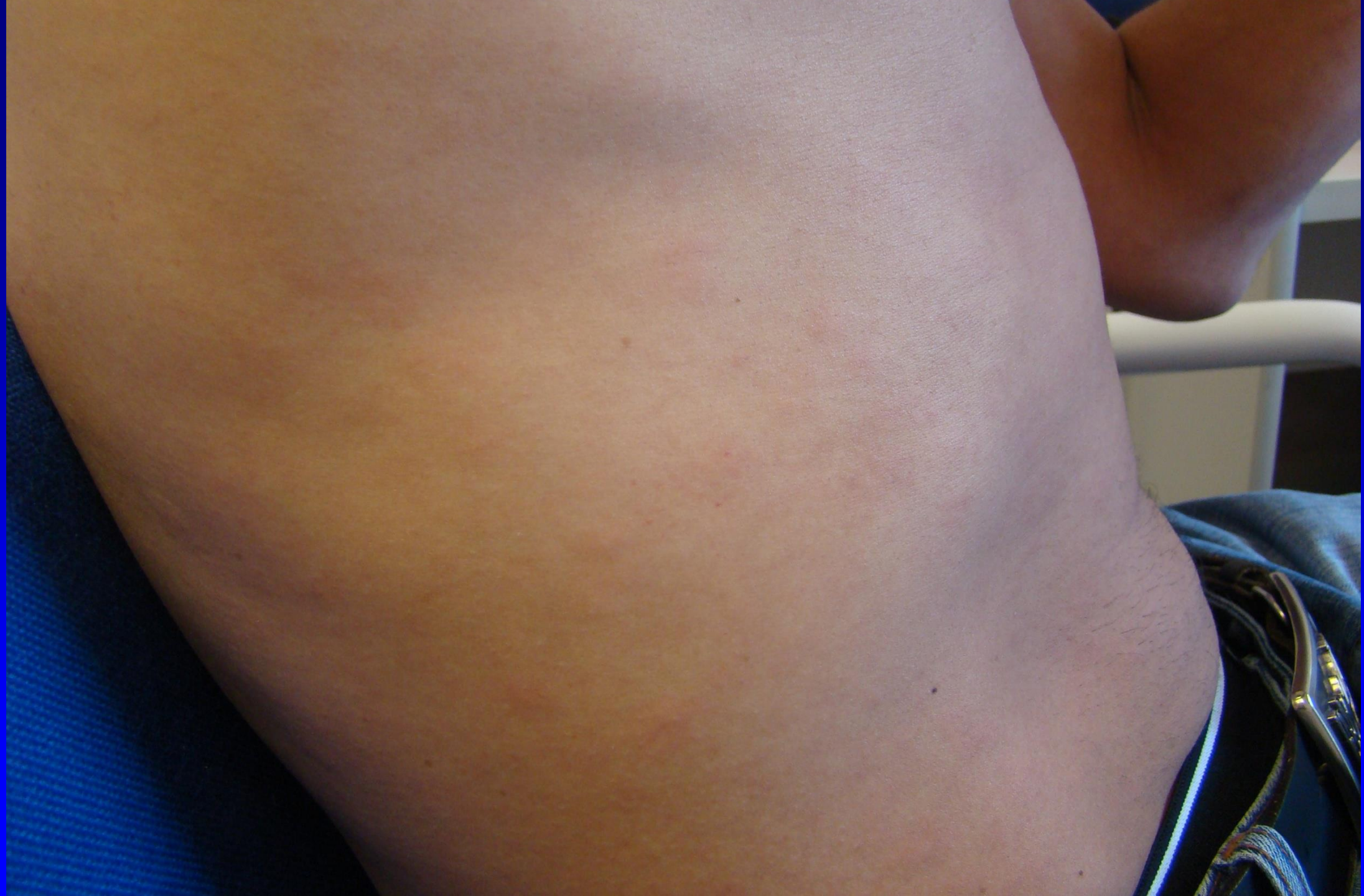


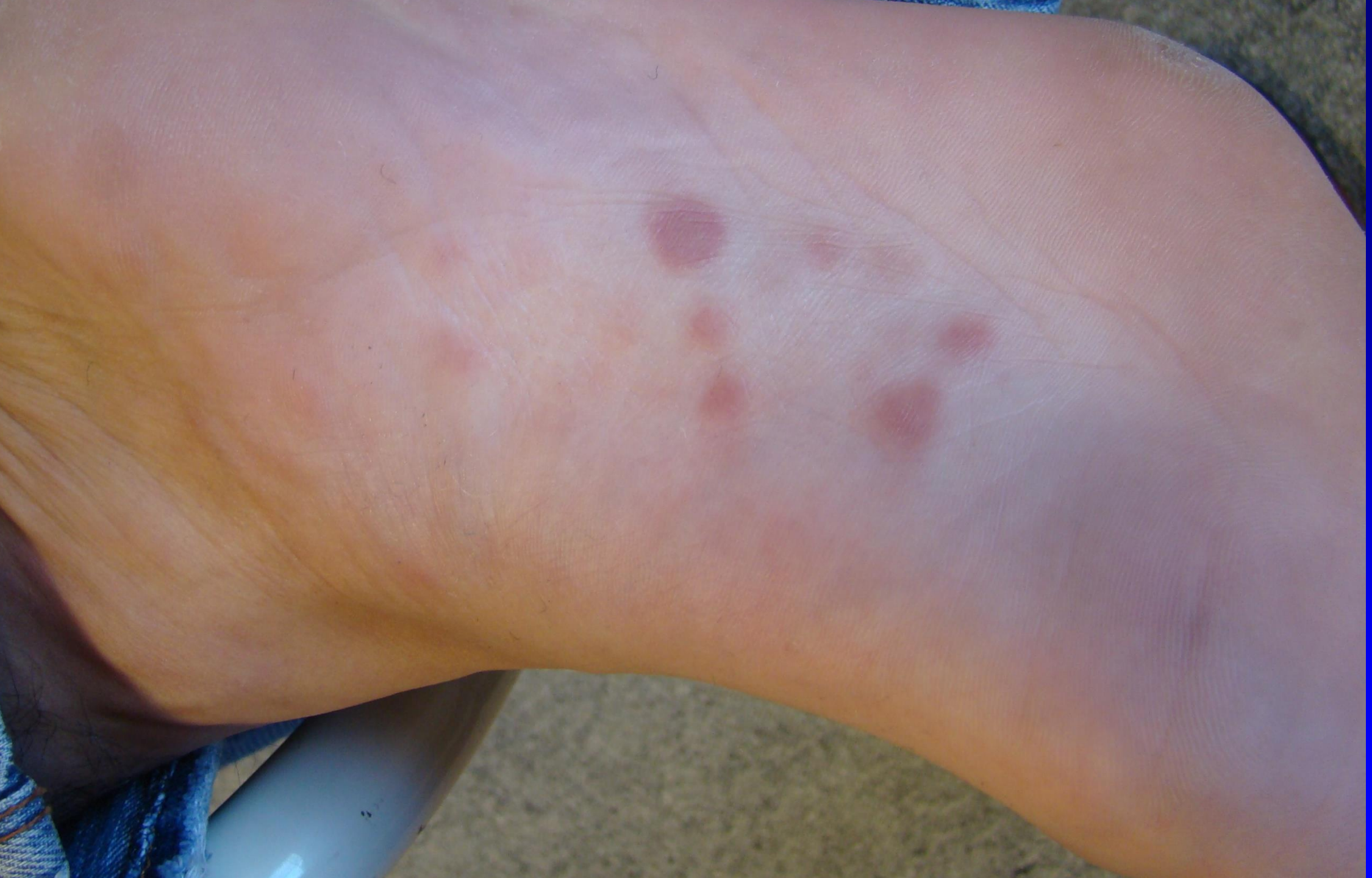


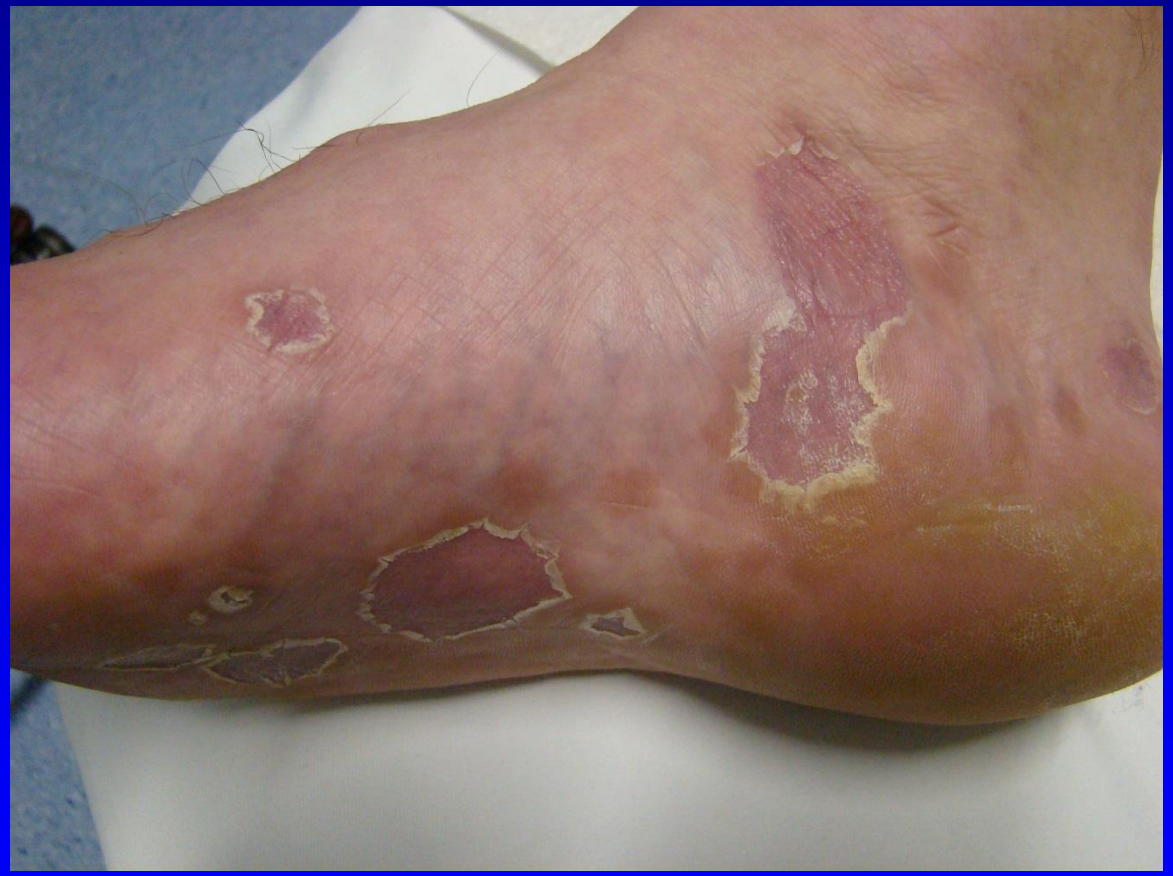






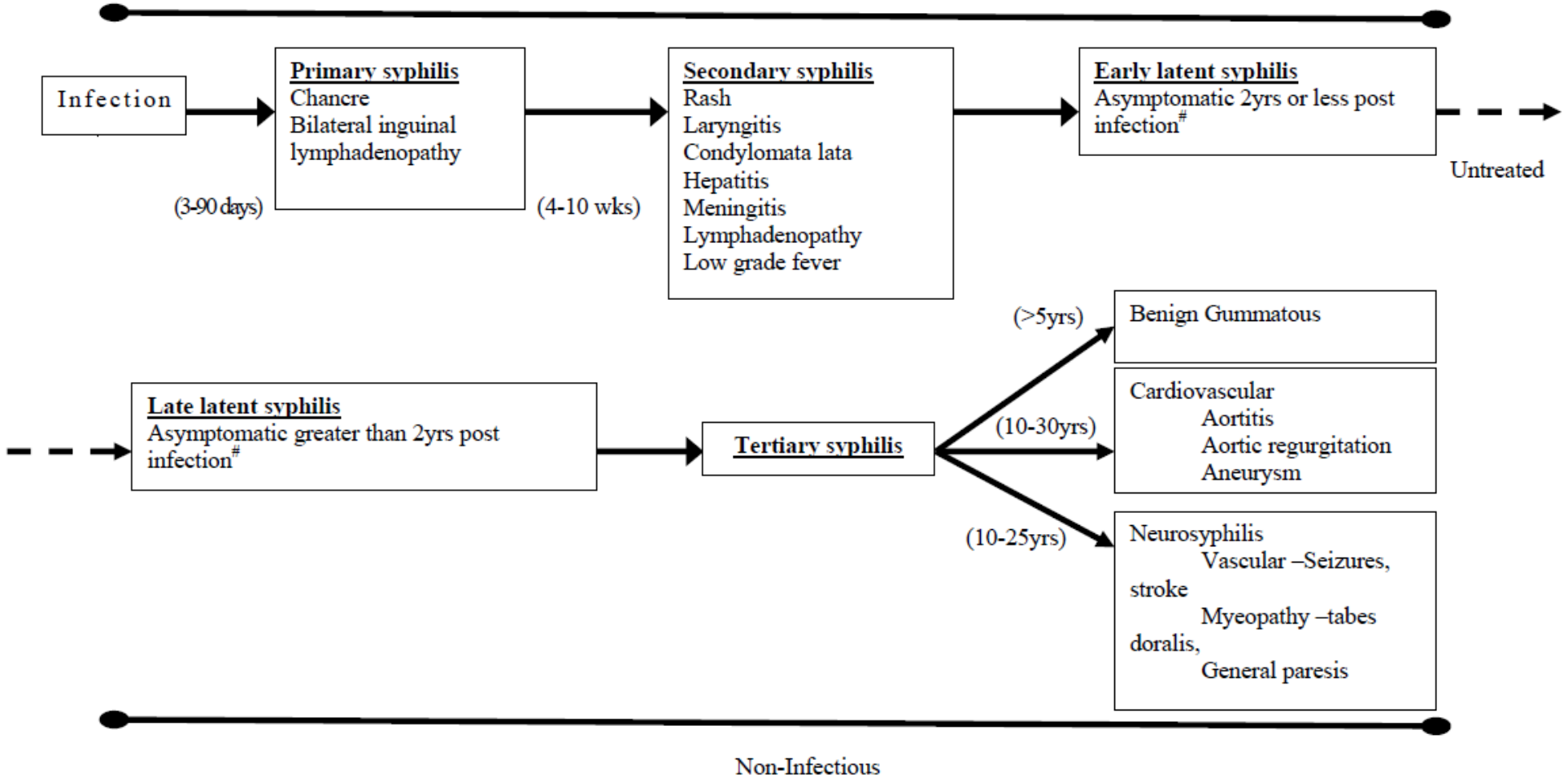






- Early Latent
  - Asymptomatic
  - <2 years duration (US 1 year)
- Late Latent
  - Asymptomatic
  - .2 years duration

- Tertiary
  - Cardiovascular : 10 to 30 years after initial involvement ,aortitis is most common manifestation
  - Neurosyphilis
    - Asymptomtic,meningeal,meningovascular,parenchymatous
  - Gummatous
- Congenital syphilis



1yr or greater in US and European guidelines [10, 11]

Fig. (1). Stages of Syphilis.

Natural History

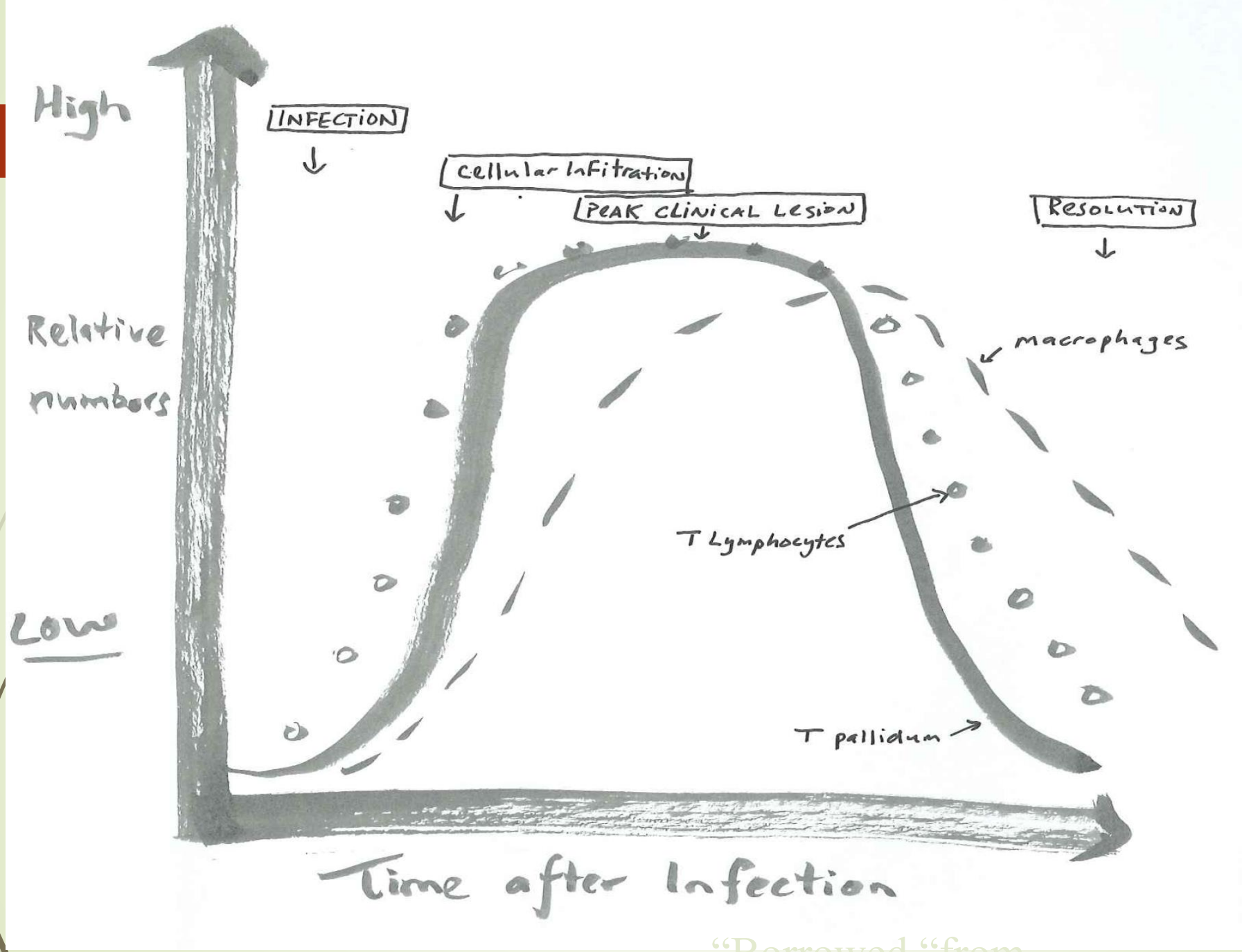
- Descriptions of untreated syphilis described in 2 two large prospective study and one retrospective
  - Oslo Study
  - Tuskagee Study
  - Rosahn study

Oslo study

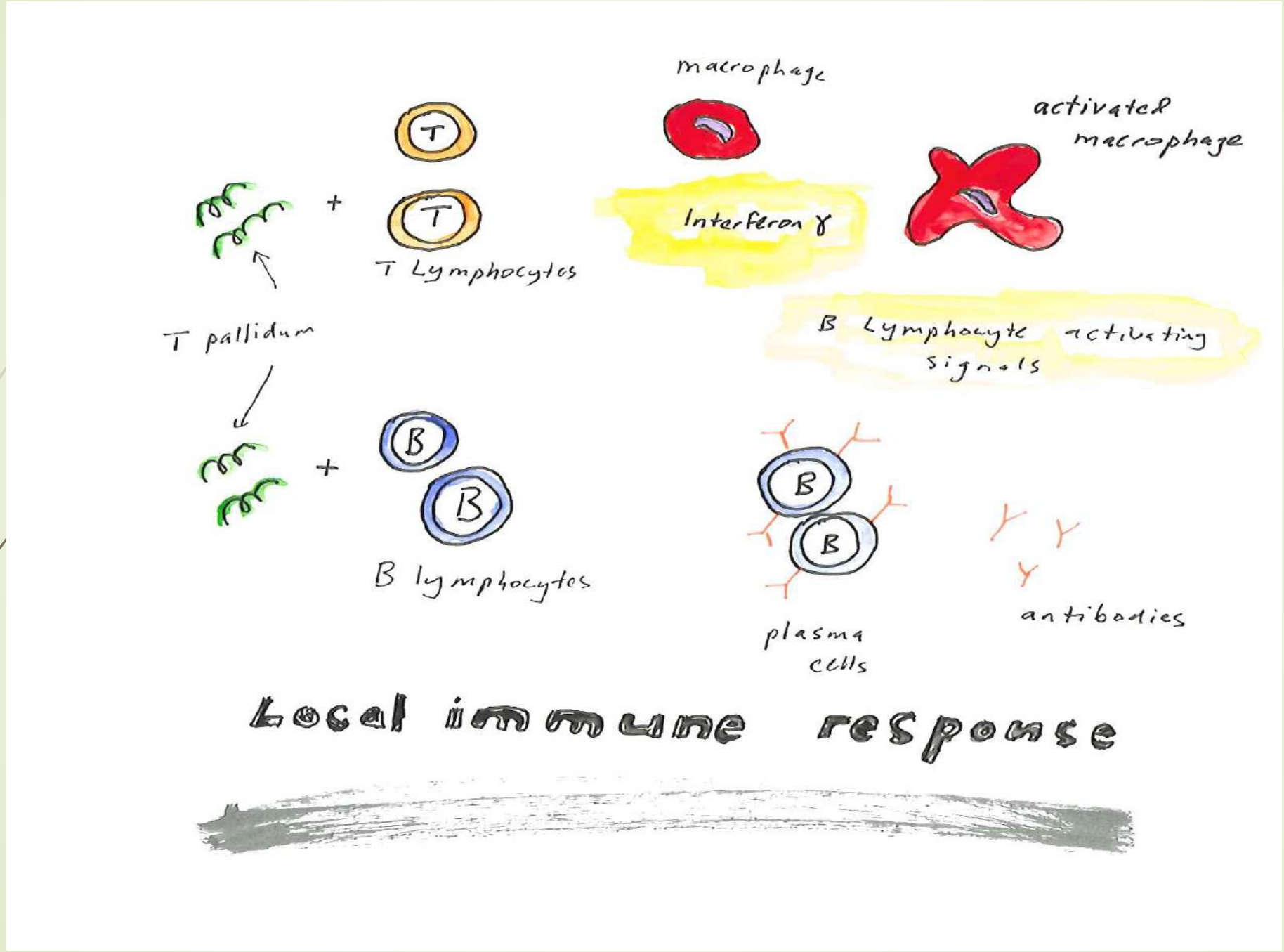
- Started in 1891 by Boeck
- 1978 patients
- After 20 years continued by Brusgaard
- Between 1949 and 1951 Gjiestland reviewed 1404 of the original 1978 patients
- Large review of data in 1964 by Clark and Danbolt
  - Clark,Danbolt 1964 Med Clin North America 48: 613-623

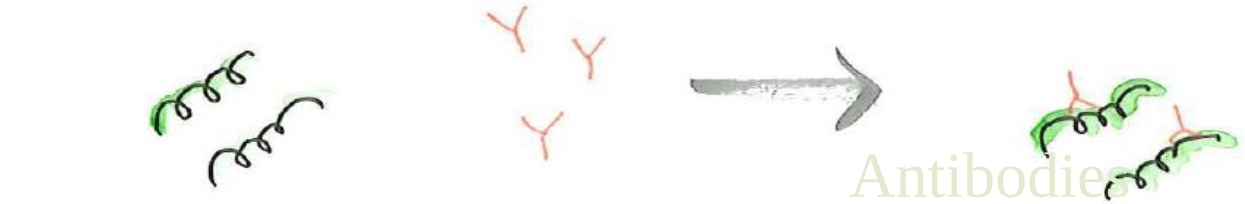
- Tuskagee
  - In 1932 US Public Health Service followed African American with untreated syphilis
  - Heavily criticized on ethical grounds
    - Rockwell .Arch Intern Med 1964 114:792 -798
- Rosahn
  - Reviewed all autopsies form 1917 to 1941 at Yale
    - Rosahn J Vener.Dis.Infect. 1947 :21(suppl)

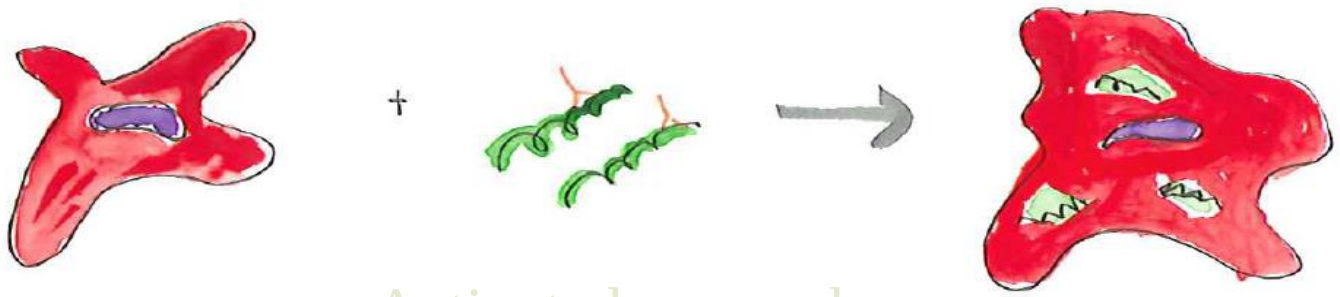
- Summary :
  - 15 to 40% of patients with untreated syphilis develop recognizable late complications
  - Higher mortality rate noted
  - Men twice as likely to develop late complications
  - Suggested that African American more likely to develop cardiovascular syphilis ,white more likely to develop neurosyphilis
    - Singh Clin Microbiol Rev 1999,12(2) :187



"Borrowed "from


macrophage
activated macrophage
T
T
+
T Lymphocytes
Interferon γ
T pallidum
B Lymphocyte activating signals
+
B
B
B lymphocytes
B
B
plasma cells
antibodies
Local immune response



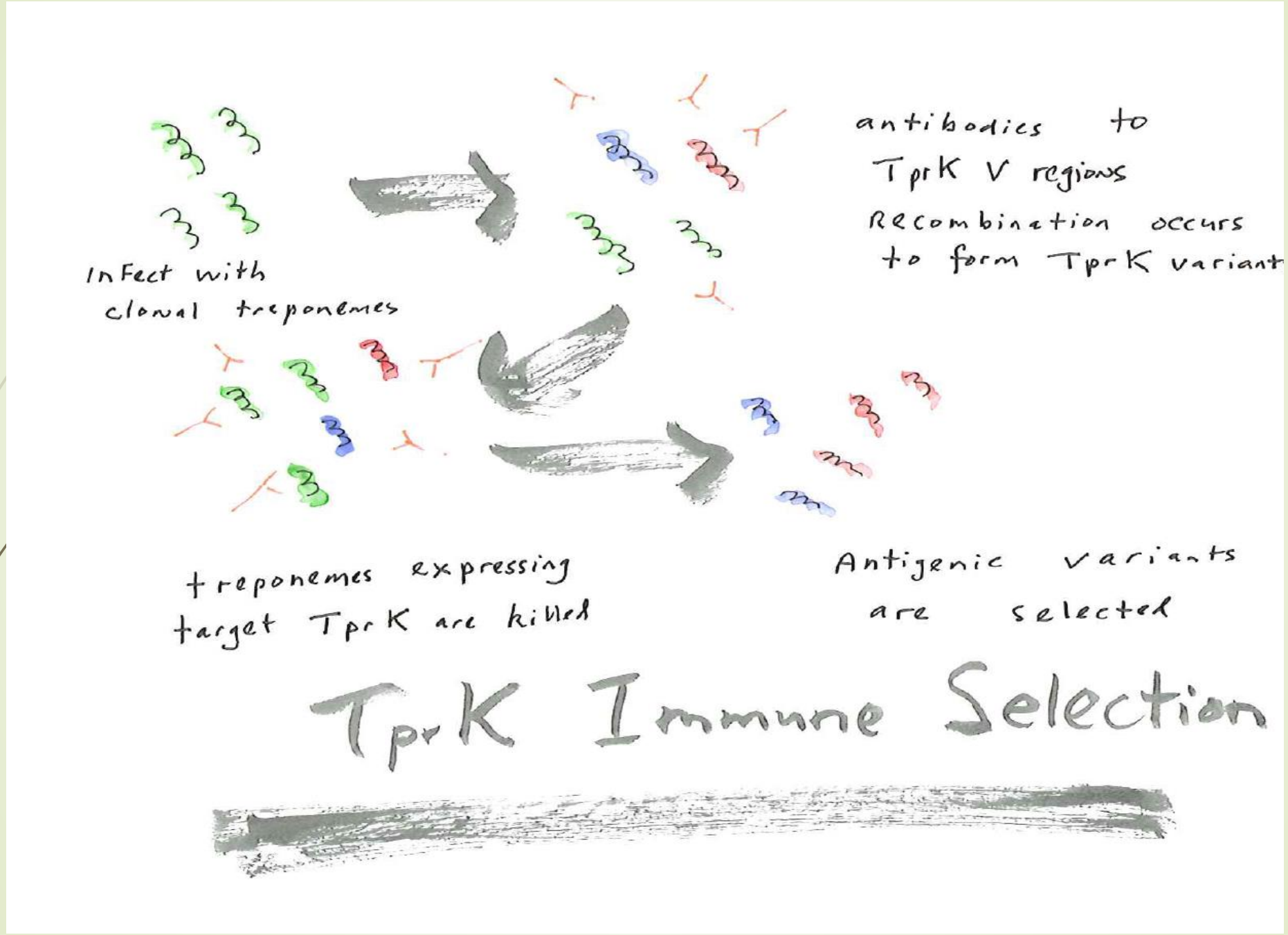


Clearance of T pallidum from Early Lesions

- “Stealth “ pathogen – low concentrations of integral membrane proteins
- Antigenic variation changing the antigens exposed to immune response
  - Phase variation : ON - OFF
  - On but changed in variation

TprK

- Translocated Promoter Region
- This gene is highly expressed and located in outer membrane
- Induces robust early immune response
- Sequences variable in 7 discrete regions
- => Immune evasion & re-infection


Infect with clonal treponemes
antibodies to TprK V regions
Recombination occurs to form TprK variant
treponemes expressing target TprK are killed
Antigenic variants are selected
TprK Immune Selection

Tests

- Dark Ground
  - Experience is disappearing
- Direct Fluorescent-antibody Test for Treponemes
  - Invalid for mouth lesions because of commensal treponemes
- PCR
  - For use with ulcers .Uses orange top tube CHL ask for syphilis PCR

Serological

- Non-Treponemal
  - Rapid Plasma Reagin (RPR), Venereal Disease Research Laboratory (VDRL)
  - can get false positives
  - 25% will turn negative without treatment
  - Most will turn negative with treatment but if syphilis is long standing may become serofast
  - with secondary syphilis get rising titres
  - 13 -41 % negative with chancre
    - Hutchinson CM Med Clin North AM 1990 74:1389

Serology

- Treponemal Tests
- eg T pallidum haemagglutination assay (TPHA),T pallidum particle agglutination (TPPA) ,Syphilis enzyme immunoassay(EIA) (IgG and IgM) ,Treponema pallidum Immunoblot
- Once positive tend to remain positive even with treatment,Tend to become positve before non treponemal tests around 2 weeks after infection

Treatment

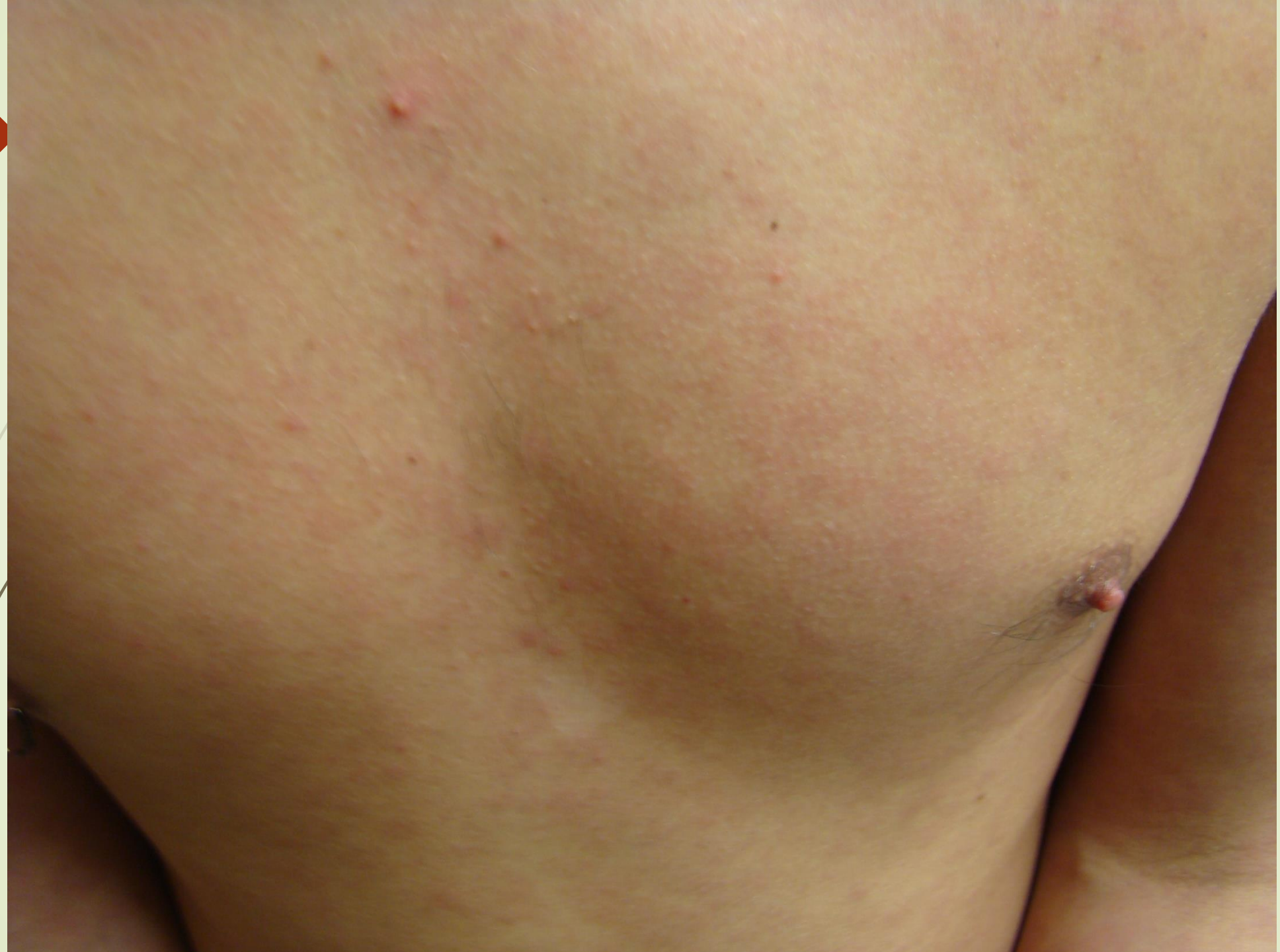
- Penicillin remains treatment of choice.
- This is long acting ie benzanthine penicllin
- In NZ this is Penicillin G benzathine(BICILLIN LA 2.4)
- For early syphilis 2.4 megaunits stat by intramuscular injection
- For late latent 2.4 megaunits ,stat ,1 week and 2 weeks
- NOT **Benzylpenicillin**
- **LA long acting ,LA long acting ,LA long acting**

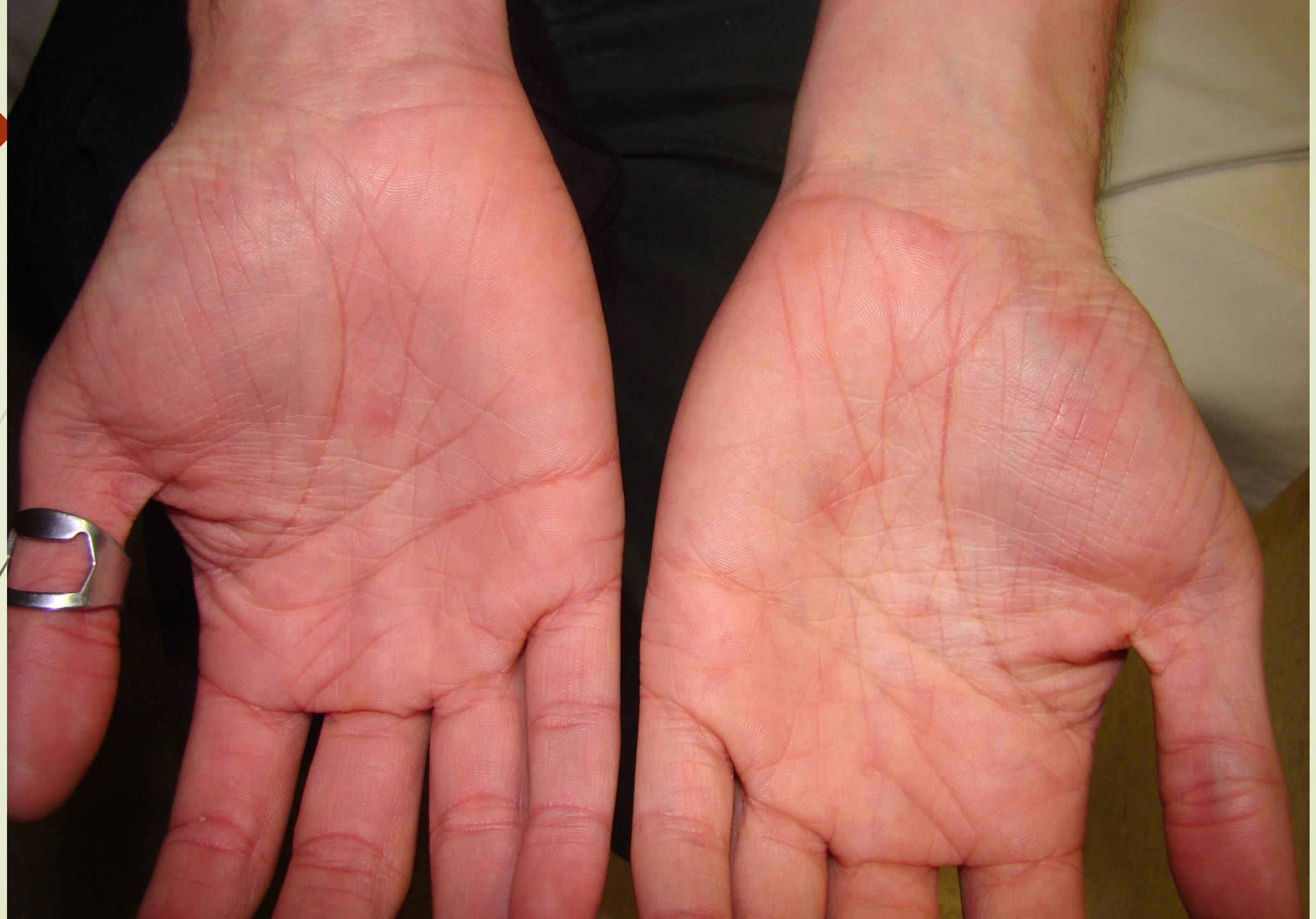
Elimination

In adults with normal kidney function plasma half-life is approximately 30 minutes. Most of the administered dose (50 to 80%) is eliminated along renal pathways in an unchanged form (85 to 95%). Tubular excretion is inhibited by probenecid which is sometimes given to increase plasma-penicillin concentrations. Biliary elimination of the active medicine accounts for only a minor fraction (about 5% of the dose).

Rx: 3 days - Benzylpenicillin Sodium 1 x 10[6]IU inj (equiv. 600 mg) • 2.4 mu IM . o
S/OS : 2.4 mu IM . one injection per week for 3 wks

- A is 22 year old young man
- Referred by GP for mangement of syphilis.
- He had presented with a rash on his torso which had not resolved (quite subtle)
- => syphilis serology had been done
- => RPR 1:32
- TPHA :reactive
- Syphilis EIA :reactive





- He reported these sexual contacts over the last 6 m or so;
  - D
  - M
  - S

D

- Had been referred here by his GP afew months previously
- Had penile ulcer with negative serology
- Negative dark ground ,Negative HSV
- Positive DFA for treponemes (but took a week or so to come back)
- Then
- RPR 1:2 ,TPHA pos EIA pos

D

- He only gave history of contact with 3 females

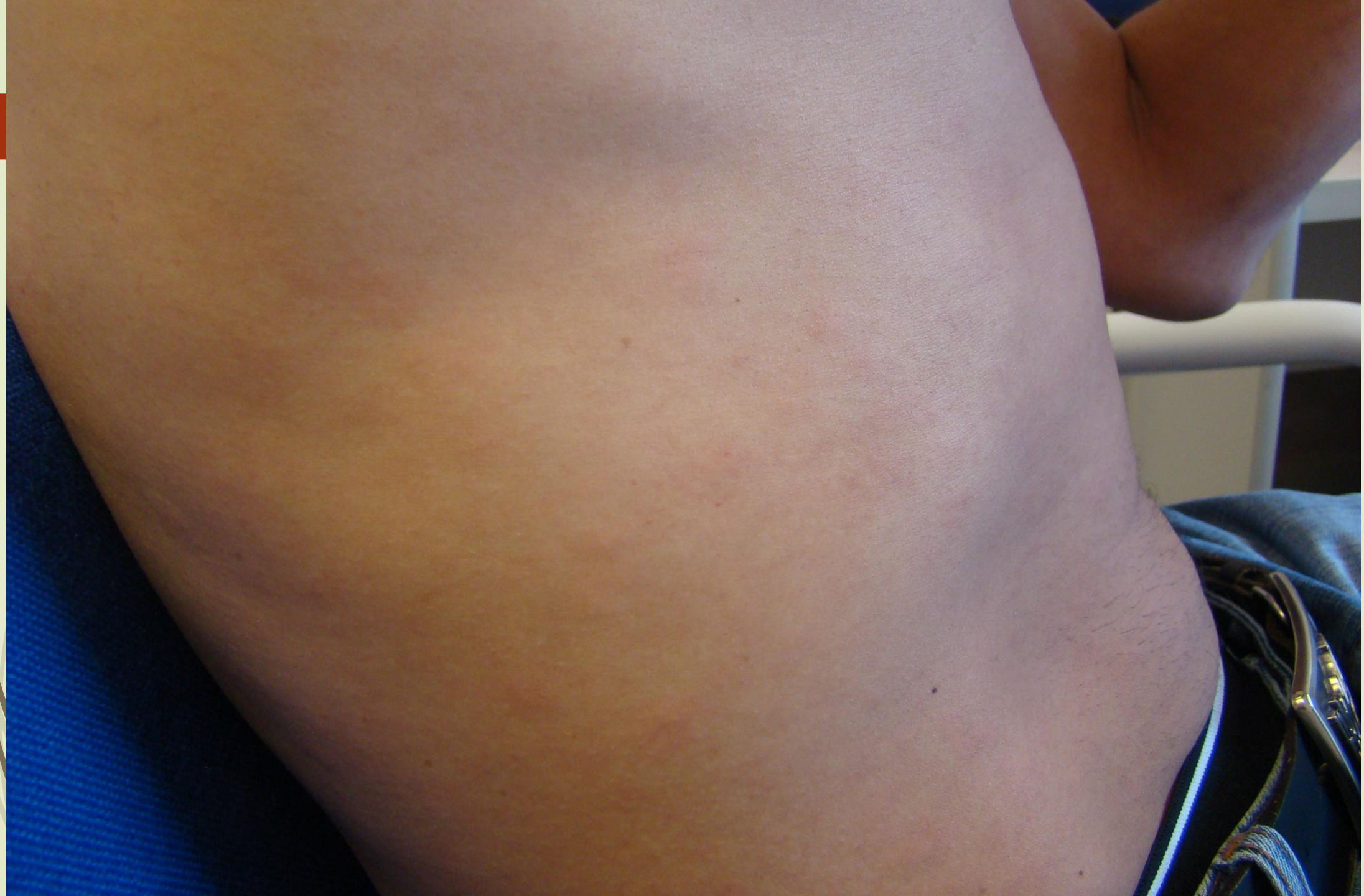
M

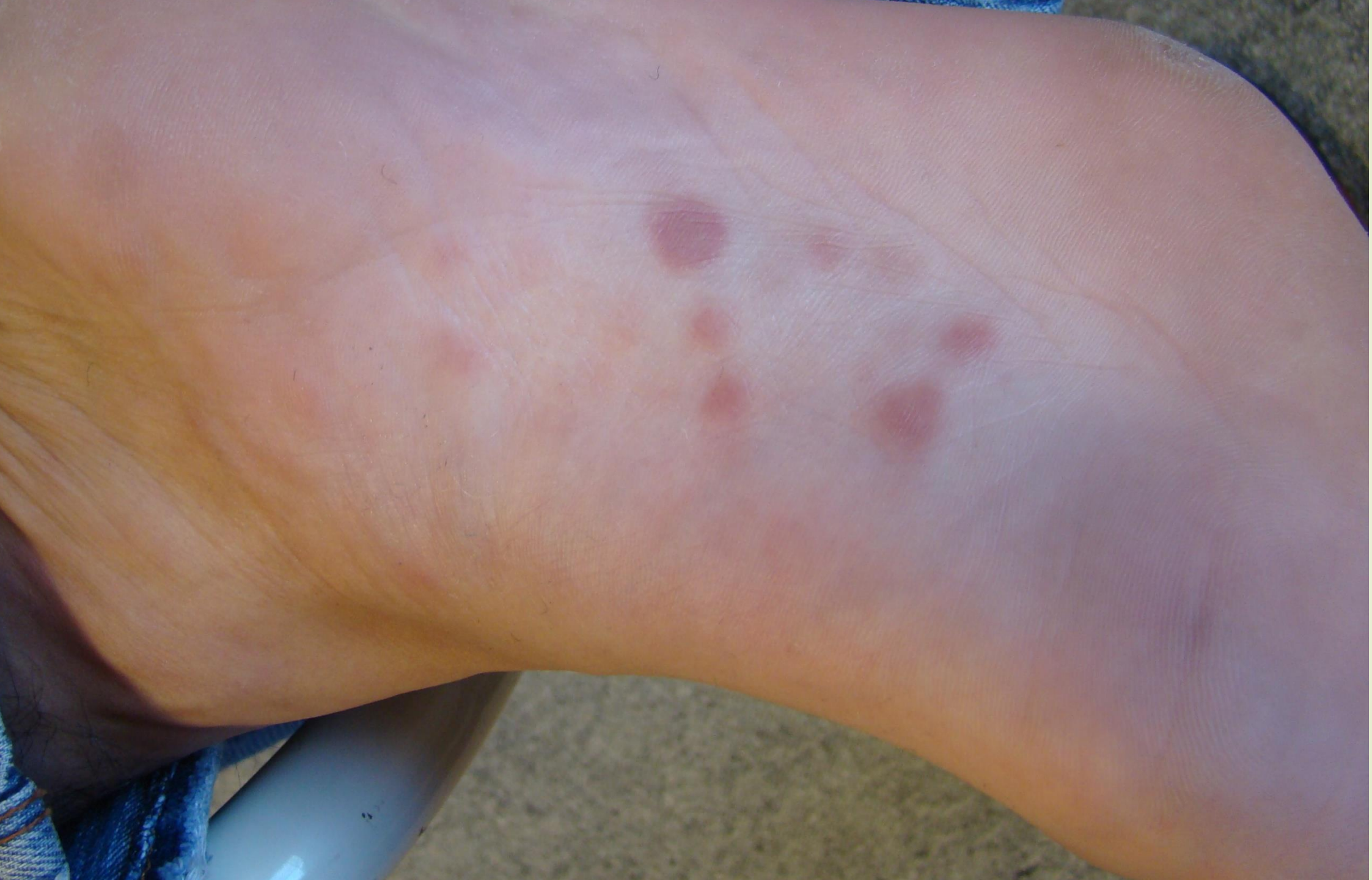
- Some what older at 39
- Had negative serology
- Treated as a contact

- And S
- negative serology as well and treated as a contact

- He was treated with Benzathine Penicillin (BICILLIN LA) 2.4 megaunits by intra muscular injection
- JHR discussed ie **Jarisch-Herxheimer reaction**

- J was a young MSM referred by his GP who on routine screening found to have positive serology ie RPR 1:64.He reported no symptoms

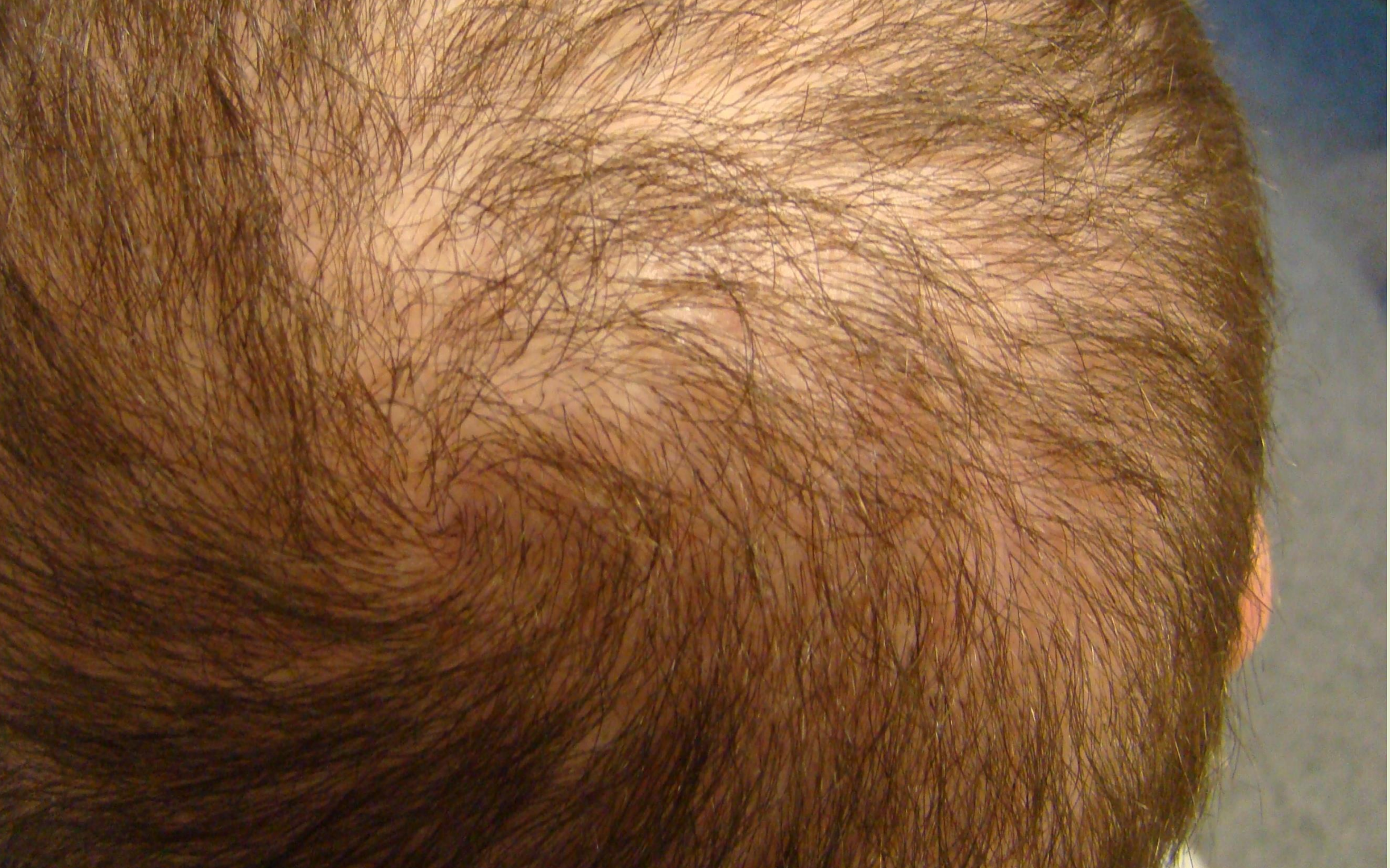


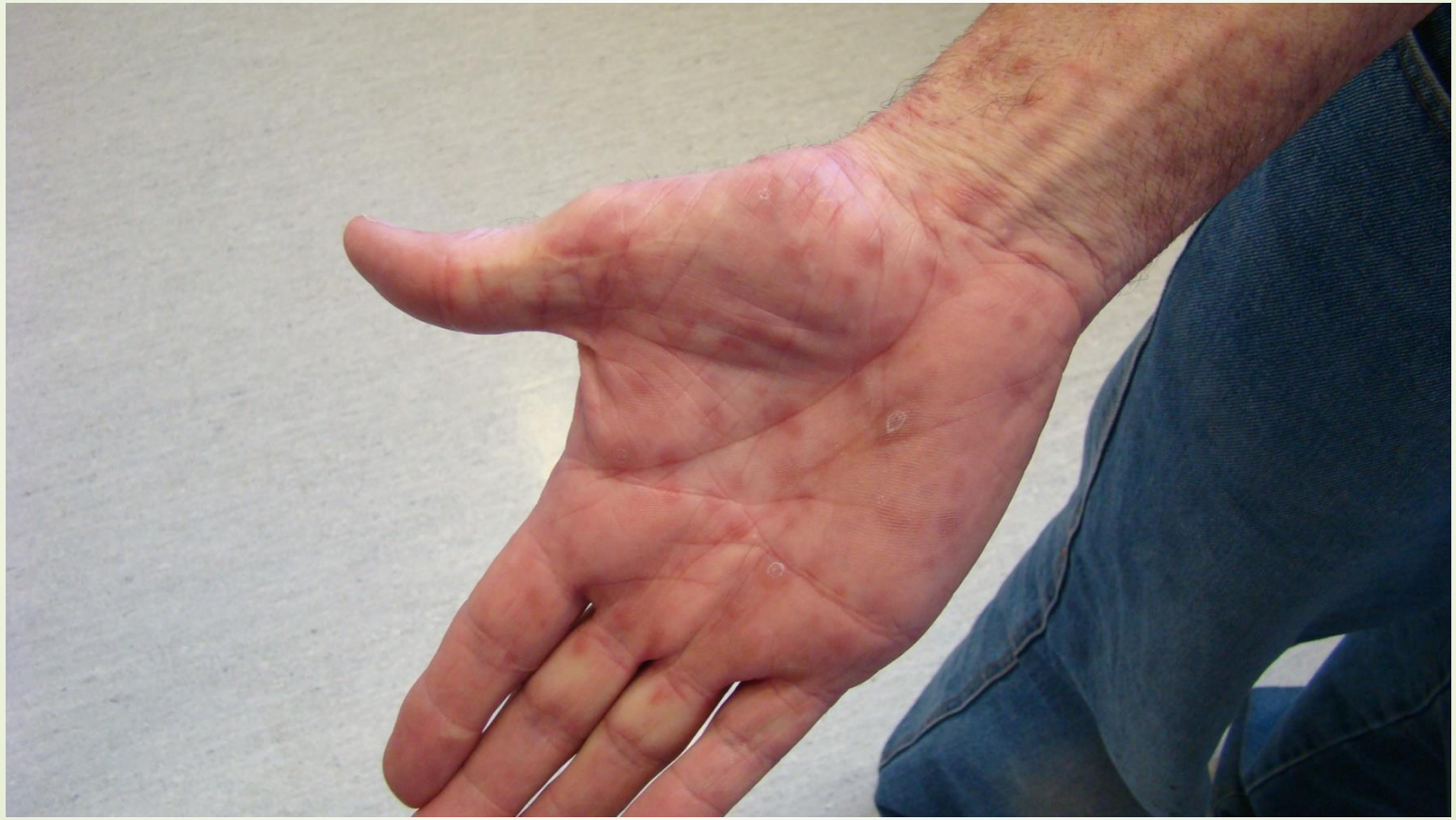


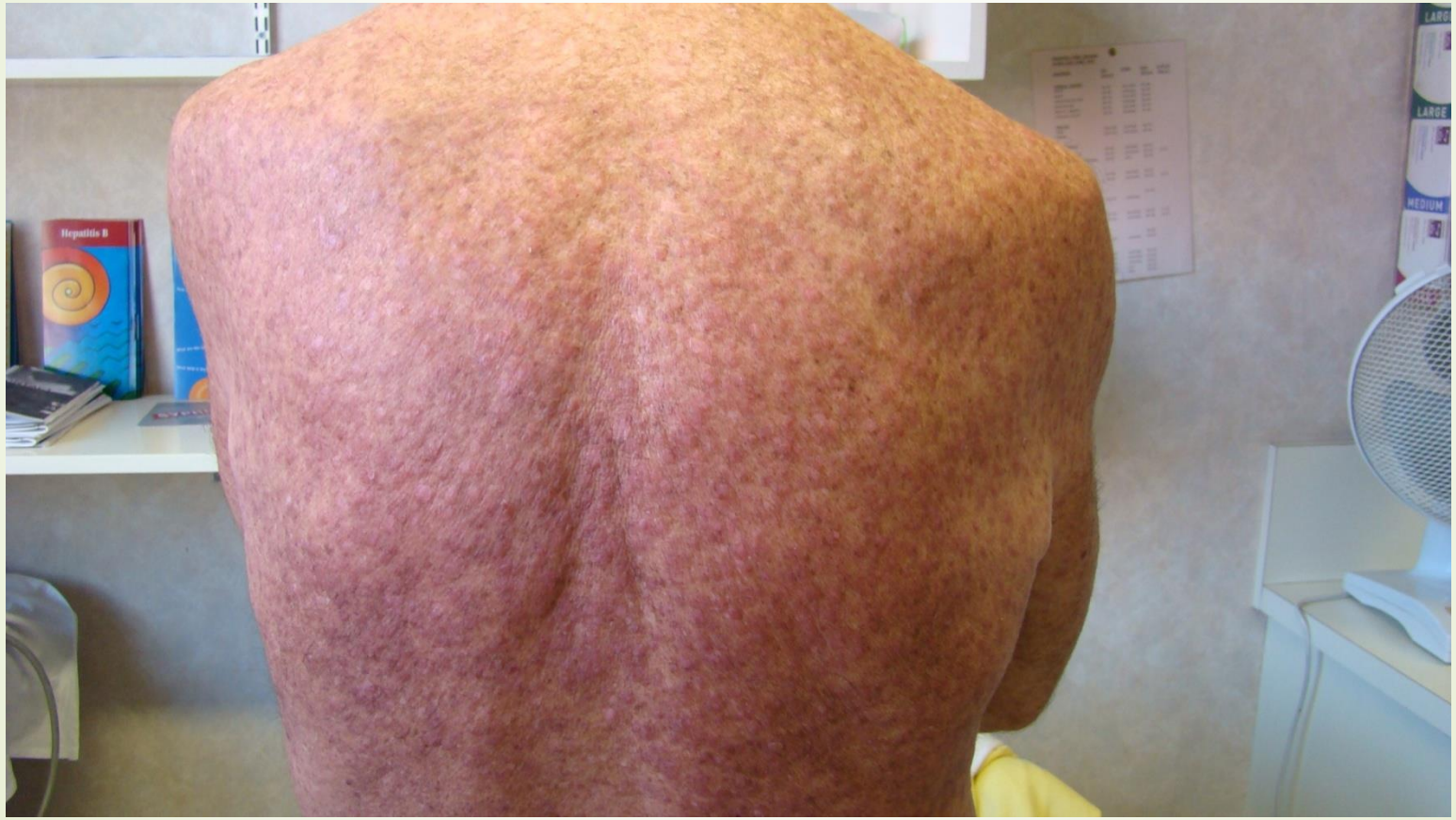
Other presentations

- Right upper quadrant pain,abnormal liver function tests and hep A.,B,C negative .
- Great response to i.m. penicillin

- Persistent “snuffles” and alopecia






Hepatitis B
LARGE
LARGE
MEDIUM

Pregnancy

- Untreated syphilis during pregnancy can profoundly affect pregnancy outcome, resulting:
  - in spontaneous abortion,
  - stillbirth, non-immune hydrops fetalis
  - , intrauterine growth restriction,
  - premature delivery, and perinatal death,
  - congenital syphilis
    - ***Sex Transm Infect*** *2000;**76:**73-79 doi:10.1136/sti.76.2.73*

- Harman published a report in England on the outcome 1001 pregnancies in 150 women with untreated syphilis and 826 pregnancies in a control group of 150 women with similar social status. Among the syphilitic group, 17.2% of the pregnancies resulted in a spontaneous abortion, 22.9% in newborn death, and 21% in congenital syphilis. Healthy infants were delivered in 38.9% of the cases, almost half of that in the control group.
- Harman N. *Staying the Plague*. London: Methuen, 1917.
  - ***Sex Transm Infect*** *2000;**76:**73-79 doi:10.1136/sti.76.2.73*

- In a study of 59 cases of untreated maternal syphilis, half of the mothers with primary or secondary syphilis delivered a premature or stillborn child, and the other half had syphilitic infants. The rate of congenital syphilis and perinatal accidents decreased slightly in early latent syphilis. With the late latent syphilis, approximately 10% of the infants were stillborn, and another 10% had congenital syphilis.
- *Fiumara N, Fleming W, Dowing, et al. The incidence of prenatal syphilis at the Boston City Hospital. N Engl J Med 1952;247:48–52.*
  - ***Sex Transm Infect** 2000;**76:**73-79 doi:10.1136/sti.76.2.73*

- . A commonly held but erroneous obstetric principle stated that infection of the fetus does not occur before 18 weeks.[1] Silver and immunofluorescence staining of the fetal tissue,[2] or polymerase chain reaction and rabbit infectivity testing of amniotic fluid[3] showed that *T pallidum* gains access to the fetal compartment as early as 9–10 weeks
  - *1)Dippel A. The relationship of congenital syphilis to abortion and miscarriage, and the mechanism of uterine protection. Am J Obstet Gynecol 1944:369–79.*
  - *2) C, Benirschke K. Fetal syphilis in the first trimester. Am J Obstet Gynecol 1976;124:705–11.*
  - 3)*Nathan L, Bohman V, Sanchez P, et al. In utero infection with Treponema pallidum in early pregnancy. Prenat Diagn 1997;17:119–23.*
    - ***Sex Transm Infect** 2000;**76:**73-79 doi:10.1136/sti.76.2.73*

Congenital Syphilis

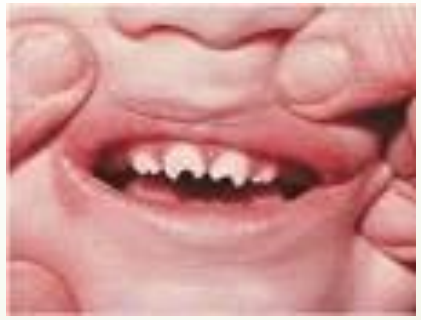
- Can involve almost all fetal organs
- Early(<2 years) and late congenital syphilis
- Nasal discharge – 15 to 60% if have clinical evidence of congenital,
- Myriad cutaneous lesions
- Hepatosplenomegaly and haematological changes
- Characteristic skeletal involvement
- CNS

Congenital Syphilis

- Marked differences according to stage of maternal infection
  - If infection early in pregancy
    - then incidence of still birth was 25%
    - Infected infant 41%
  - If infection late in pregnancy
    - Still birth 12%
    - Infected infant 2%
      - Ingraham 1951 Acta Dermato-Venerol 31(supp24):60-88

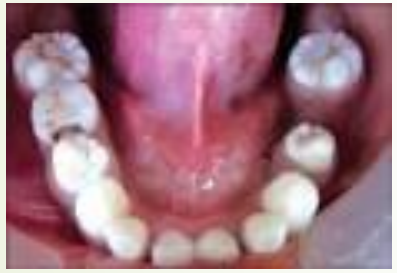
Late Congenital Syphilis

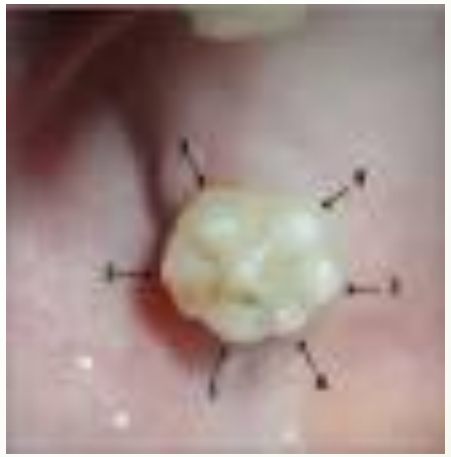
- Delayed consequences of localised inflammatory processes established at sites of treponemal infection
- Frontal bossing
- Saddle nose deformitys,saber shins
- Teeth = Hutchinsons teeth – molars –conical ,tapered to apex , notched



- Primary lesion heals with local host response
- BUT secondary syphilis follows with chronic infection
- Evasion of the immune response

Mulberry Molar





- Interstitial keratitis
- Deafness
- Cluttons joints
- neurosyphilis

Summary

- If painless genital ulcer(s) with or without inguinal lymphadenopathy, consider primary syphilis.
  - Do a viral swab for herpes simplex virus (HSV), organise syphilis serology, and arrange sexual health assessment for syphilis polymerase chain reaction (PCR) swab

Summary

- If any of the following, conduct syphilis serology:
  - any genital ulceration.
  - all men who have sex with men (MSM) at least annually, especially if HIV positive
  - for unusual clinical presentations e.g., lymphadenopathy, unexplained abnormal liver function tests, alopecia, pyrexia of unknown origin.
  - Rash on palms of hands /soles of feet
  - Torso rash if not explained especially prior to biopsy
  - Rash in MSM
  - if patient has had sexual contact with a person diagnosed with syphilis (serology usually carried out by sexual health clinic