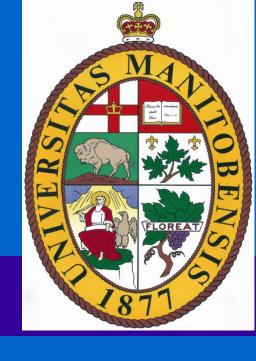
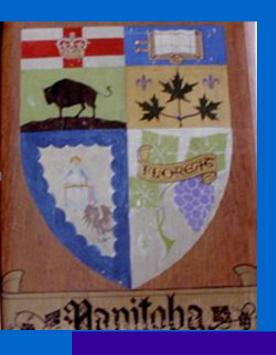
Prof. Kelly MacDonald & Dr. Kamran Kadhoka





Depts. of Medicine,
(Infectious Diseases) and
Medical Microbiology
University of Manitoba,
Cadham Provincial Laboratory

 37-year-old male mechanic, who lives in downtown Winnipeg, presents with rash of 5 days duration



What is the diagnosis?

- A. Eczema
- B. Erythema multiforme
- C. Psoriasis
- D. Seborrheic dermatitis
- E. Tinea corporis (ringworm)





What is the diagnosis?

- A. Eczema
- B. Erythema multiforme
- C. Psoriasis
- D. Seborrheic dermatitis
- E. Tinea corporis (ringworm)
- . None of the above





What other history?

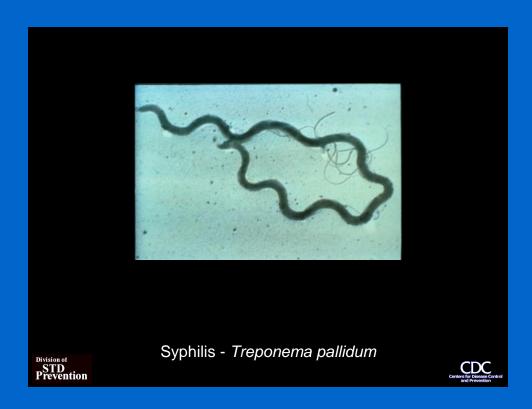
- no travel history
- no pets/animal contacts
- meets men on the internet and has occasional casual sexual encounters (only knows the internet IDs of 9 contacts in the last 3 months)
- also complaining of hair loss

What is his diagnosis UPO?

- A. Primary Syphilis
- Secondary Syphilis
- C. Tertiary Syphilis
- D. Latent Syphilis
- E. Neurosyphilis

Syphilis – the Basics

- Re-emerging disease (since 2000)
- Treponema pallidum, spp. pallidum



Syphilis – the Basics

Direct (sexual) contact; blood transfusion; congenital

Incubation Period: 10-90 days

 Stages – primary, secondary, early latent, late latent, and tertiary

Infectious Syphilis

- Primary Ulcers (chancres) on penis/vagina
- Secondary Rash (any kind except vesicular); may be on palms of hands or soles of feet; systemic illness
- Latent Asymptomatic (12 months)

Primary Syphilis



Primary Syphilis





Primary Syphilis (Extragenital)



Secondary Syphilis



Secondary Syphilis (Palms and Soles)





Secondary Syphilis (Condylomata)



Condylomata lata



acuminata (HPV)

Serology - Testing Algorithm

Treponemal Test (CMIA)

No current or previous treponemal infection

Non-reactive

Reactive

Non Treponemal Test (VDRL/RPR)

RPR + TPPA +

RPR - TPPA +

RPR +
TPPA -

RPR -

Most likely diagnosis

Active treponemal infection

Old treated treponemal infection

Biologic false positive

False positive

Other diagnoses

Treated after many years of infection "serofast"

Latent active treponemal infection

Early active treponemal infection

Early active treponemal infection

Can J Infect Dis Med Microbiol 2015;26 (Supp A)

Cadham Provincial Laboratory General Requisition



ONLY ONE SPECIMEN TYPE PER REQUISITION

All areas of the requisition must be completed (please print clearly) See back for requisition/specimen instructions

Cadham Provincial Laboratory P.O. Box 8450 750 William Avenue Winnipeg, MB R3C 3Y1 Tel: (204) 945-6123 Fax: (204) 786-4770 E-mail: cadham@gov.mb.ca Website: www.gov.mb.ca/health/publichealth/cpl

Ordering serology

SEROLOGY					
Serology Test Panels (see #1 over)					
STI Panel Prenatal Panel					
☐ Post Exposure: So			al HIV OP		
□ Post Exposure: Exposed Panel (1) □ Blood-borne Pathogen			hogen		
HIV (4) HIV1/2A	Ab	Syphili	s Screen		
Hepatitis					
☐ HAV IgG (Immunity) ☐ HBsAb (Immunity)			y)		
☐ HAV IgM (acute HA	AV)	☐ HBsAç			
☐ HBcAb (Total)		☐ HCV A	Λb		
Nucleic Acid (Plasma	Nucleic Acid (Plasma Only) ⁽⁵⁾				
☐ HBV PCR/Quant	☐ HC\	/ PCR/Quant	[☐ WNV PCR	
☐ HCV PCR/Qual	☐ HC\	/ Genotyping			
Miscellaneous Serology					
Acute	Immune Status		Acute	Immune Status	
CMV ☐ IgM	☐ IgG	Parvo B19	☐ IgM	☐ IgG	
EBV 🗌 IgM	☐ IgG	Rubella	☐ IgM	☐ IgG	
HSV ☐ IgM	☐ IgG	Toxoplasma	□ IgM	□ IgG	
Measles IgM	☐ IgG	Varicella WNV	□ IgM	☐ IgG	
Mumps 🗌 lgM	□ IgG	VVIVV	☐ IgM		
☐ Lyme Ab	☐ H. pylori Ab	□ Мус	oplasma p	neumoniae IgM	

Syphilis: How to treat?

	First	Second	Allergy
SYPHILIS (Primary, Secondary, Early latent)	Benz Pen G 2.4 M units IM X1 (?Azithro 2g)	Ceftriaxone 1g IM daily x10 d	Doxycycline 100mg PO BID x14 d
SYPHILIS (Late latent)	Benz Pen G 2.4 M units IM wkly X3	Ceftriaxone 1g IM daily x10 d	Doxycycline 100mg PO BID x28 d
Neurosyphilis	Cryst Pen G 3-4 M units IV q4h X10- 14 d	Proc Pen G 2.4 M units IM daily X10-14 d (+ probenecid) or Ceftriaxone 2g IM/IV daily x10- 14 days	

How to obtain Bicillin®?

- Benzathine penicillin G (Bicillin®) 2.4 million units
 IM in a single session (separated into 2 injections)
- Bicillin[®] in preloaded syringes provided free of charge by Manitoba Health
- Can only be obtained by faxing a completed Manitoba Health STD Medication Administration Form (call Materials Distribution Agency at 945-0570 or download form:

http://www.gov.mb.ca/health/publichealth/cdc/protocol/form11.pdf

Manitoba Health STI Medication Order Form (PLEASE PRINT)



Fax order to: Taché Pharmacy - Fax: (204) 231-1739 • Phone: (204) 233-3469 • For Inquiries only e-mail tache@mts.net Contact Person: (yyyy/mm/dd) Facility Name: Physician: Address: Telephone #: Refer to Sexually Transmitted and Slood-Sorne Infections webpage http://www.gov.mb.ca/health/publichealth/ede/sti/index.html All treatments provided to patients must be recorded and reported to Manitoba Health using the STI Administration Form (http://www.gov.mb.ca/health/publichealth/cdc/protocol/stiadminform.pdf) Units Ordered Drug Dosage Forms & Unit Quantity Indication CHANCROID Ceftriaxone 250 mg x 1 vial First line treatment for adults and adolescents Alternative treatment for cephalosporin or penicillin allergy. 250 mg x 56 tablets Erythromycin base Azithromycin 250mg x 4 tablets CHLAMYDIA^{*} Azithromycin 250 mg x 4 tablets First line treatment in children > 9 years of age and adults Daxycycline 100 mg x 14 capsules Alternative treatment in children > 9 years of age and adults Erythromycin base 250 mg x 56 tablets Prognant and lectating women Amoxicitiin 500 mg x 21 capsules Prognant and lactating women allergic to crythromycin or azithromycin GONORRHEA² Cefixime 400 mg x 2 tablet First line treatment in combination with 1 g azithromycin Ceftriaxone 250 mg x 1 vial First line treatment in combination with 1 g azithromycin Azithromycin 250 mg x 4 tablets First line treatment treatment in combination with refixime OR reftriesone 250 mg x 8 tablets Azithromycin Alternative treatment when there is severe cophalosporin allergy LGV 100 mg x 42 capsules Daxycycline First line treatment Erythromycin base 250 mg x 168 tablets Alternative treatment Azithromycin 250 mg x 12 tablets Alternative treatment PID Recommended treatment for scute PID (in combination with doxycycline and Ceftriaxone 250 mg x 1 vial mctronidasolc) Recommended treatment for soute PID (in combination with coftriaxone and Daxycycline 100 mg x 28 capsules metronidasole) Secommended treatment for soute PID (in combination with dovereding and ceftriaxone). 250 mg x 56 tablets McCronidazole is included to provide optimal anacrobic coverage. 250 mg x 7 tablets (1 tablet daily for Azithromycin Alternative treatment for scute PID (in combination with oral metronidacole) for patients 7 days) OR 250 mg x 8 tablets (4 tablets once with cophalosporin contraindication. Azithromycin weekly for 2 weeks) SYPHILIS Benzathine Pirst line for primary, secondary, and early latent stages of infection and epidemiologic 1.2 MU x 2 syringes Penicitlin G+ (Bicitlin) treatment of sexual contacts Benzathine First line for late latent infection, infection of unknown duration and tertiary syphilis NOT 1.2 MU x 6 syringes Penicillin G+ (Bicillin) Alternative treatment for penicillin allergic adults and adolescents staged with primary, 100 mg x 28 capsules Daxycycline accondary or early latent infection Alternative treatment for penicillin allergic adults and adolescents staged with late latent Daxycycline 100 mg x 56 capsules infection, infection of unknown duration or tertiary syphilis NOT involving the CNS Azithromycin alone should not be routinely used as a treatment option for early or Azithromycin 250 mg x 8 tablets incubating syphilis as asithromycin resistance has been reported and is increasing? * Pediatric dosing available upon request. *In exceptional circumstances, azithromycin should be reserved for suspect syphilis cases (at the time that serology is performed) only if Bicillin (Benzathine Penicillin G) is not readily available, with the understanding that the patient will require Bicillin if their serology confirms that they have syphilis. +Must be stored in a refrigerator that is temperature monitored and kept between 2-8°C.

	 	-
with a distance		at a state of the state of

http://www.gov.mb.ca/health/publichealth/cdc/protocol/form11.pdf

SYPHILIS			
	Benzathine Penicillin G† (Bicillin)	1.2 MU x 2 syringes	First line for primary, secondary, and early latent stages of infection and epidemiologic treatment of sexual contacts
	Benzathine Penicillin G† (Bicillin)	1.2 MU x 6 syringes	First line for late latent infection, infection of unknown duration and tertiary syphilis NOT involving the CNS
	Doxycycline	100 mg x 28 capsules	Alternative treatment for penicillin allergic adults and adolescents staged with primary, secondary or early latent infection
	Doxycycline	100 mg x 56 capsules	Alternative treatment for penicillin allergic adults and adolescents staged with late latent infection, infection of unknown duration or tertiary syphilis NOT involving the CNS
	Azithromycin	250 mg x 8 tablets	Azithromycin alone should not be routinely used as a treatment option for early or incubating syphilis as azithromycin resistance has been reported and is increasing*

 $[\]mbox{\ensuremath{\,^{\mu}}}\xspace Pediatric dosing available upon request.$

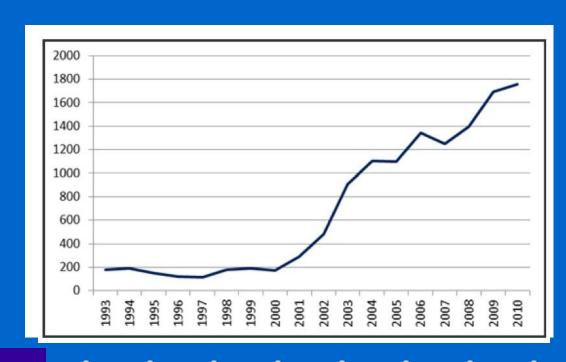
 $^{^\}dagger\text{Must}$ be stored in a refrigerator that is temperature monitored and kept between 2-8°C.

|--|

^{*}In exceptional circumstances, azithromycin should be reserved for suspect syphilis cases (at the time that serology is performed) only if Bicillin (Benzathine Penicillin G) is not readily available, with the understanding that the patient will require Bicillin if their serology confirms that they have syphilis.

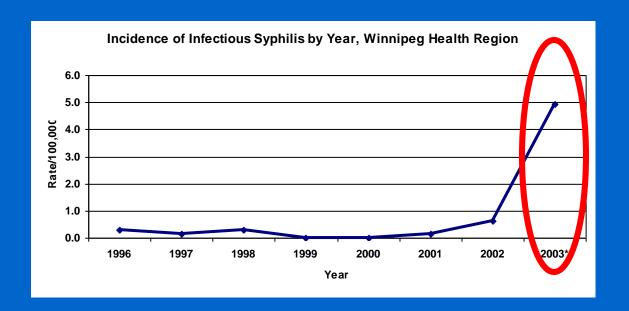
Background - Canada

- Since 2000, there have been outbreaks of infectious syphilis reported in Vancouver, Calgary, Edmonton, Toronto, Ottawa, Montreal, Halifax ...
- Vancouver MSM
- Calgary MSM/Hetero
- Edmonton MSM/Hetero
- Toronto MSM
- Ottawa MSM
- Montreal MSM
- Halifax MSM



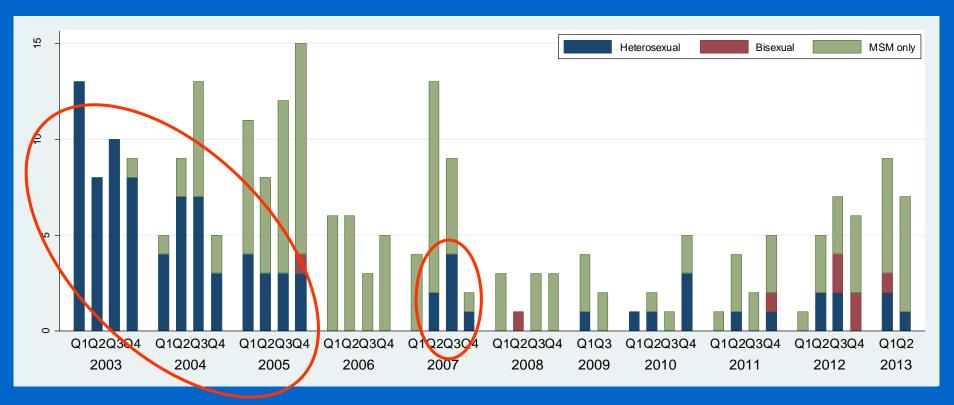
Background - Winnipeg

- Until January 2003, the incidence of syphilis infection (imported cases) had remained stable at less than 1 case per 100,000 population
- No locally acquired infectious syphilis since 1995



Infectious Syphilis Cases - WHR

N=238



Source: Syphilis Surveillance Database, Population and Public Health Program, Winnipeg Regional Health Authority, June 2013

Outbreak Demographics

Predominant risk factors

- 2007 cluster
 - place of meeting at inner city bars
 - significant alcohol use
 - casual unprotected sex (male-female)
 - no link to sex trade work
 - numerous sexual networks ranging in size from 2 to more than 15 individuals

Outbreak Demographics

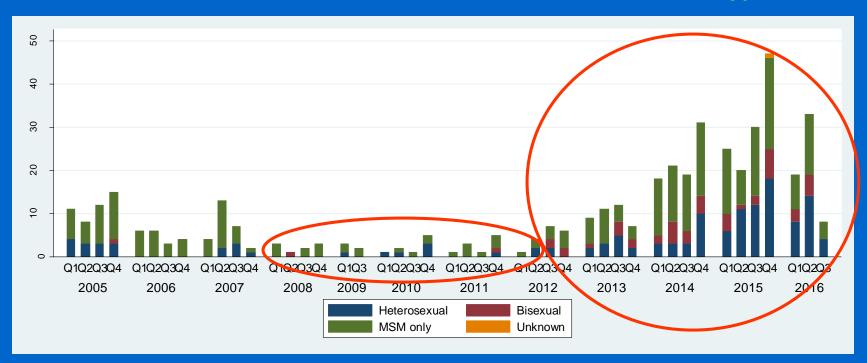
Predominant risk factors

- December 2003 to January 2009
 - exclusively MSM
 - frequenting MSM-specific meeting places
 - anonymous unprotected sex (male-male)

40-50% HIV +

Infectious Syphilis Cases – WHR*

N = 456



Source: Syphilis Surveillance Database, Population and Public Health Program, Winnipeg Regional Health Authority, October 2016

*Has postal code in WHR or is identified as resident in WHR; excludes cases not resident in Winnipeg

•

Demographics (WHR* cases 2012-16)

>320 Infectious Cases (since 2012 Q3)

83% male (63% MSM + 16% bisexual)

 Downtown (30%), Point Douglas (13%), and River Heights (9%)

• 83% "locally acquired" (10% "imported")

Demographics (WHR* cases 2012-16)

42% "meeting" on social media

 19% HIV (?resistant) – although much lower recently – 7% in 2016

71% primary/secondary

76% 20-49 yo

Infectious Syphilis – Rural Mb

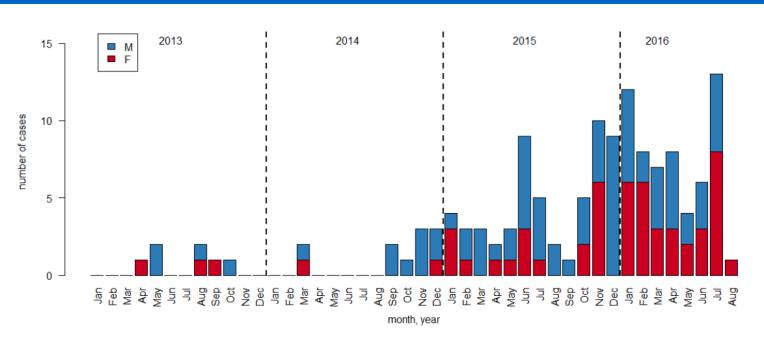


Figure 5: Distribution of infectious syphilis per month and by sex at the Northern RHA 01 Jan 2013 to 29 Aug 2016.

Outbreak summary

Predominant risk factors

- September 2012 to October 2016
 - mostly MSM/MSMW
 - meeting online or via mobile phone apps
 - anonymous unprotected sex (male-male)
 - increasing heterosexual transmission (?bisexual bridges, sex trade)

Less than 10% are HIV + (all male)

INFECTIOUS SYPHILIS

MANAGEMENT TOOL

WHO SHOULD I TEST?

ALL PERSONS WHO PRESENT WITH SYMPTOMS OF SYPHILIS

such as painless genital, anal or oral ulcers, generalized maculopapular rash (typically including palms and soles) and/or lymphadenopathy.

See Manitoba Health, Healthy Living and Seniors (MHHLS) protocol (below) for details on clinical presentations

IN ADDITION TO TESTING SYMPTOMATIC PERSONS, ALSO SCREEN THE FOLLOWING PERSONS:

- ALL pregnant persons congenital syphilis is often severe, disabling, and life-threatening
- ALL persons reporting unprotected sex with casual or anonymous partners should be routinely tested for sexually transmitted infections (STI) every 3-6 months
- · ALL persons requesting STI testing
- ALL persons with any confirmed or suspected STI such as gonorrhea, chlamydia or HIV
- · consider offering serology for all patients as part of routine care

WHO IS INFECTIOUS?

PRIMARY SYPHILIS: painless genital, anal or oral ulcerative lesions, +/- inguinal lymphadenopathy. The initial ulcer typically heals spontaneously.

SECONDARY SYPHILIS: usually a generalized maculopapular nonpruritic rash (typically including palms and soles) */- other rash types. */- fever. */- generalized lymphadenopathy */-alopecia */- condy loma lata.

EARLY LATENT SYPHILIS: cases are asymptomatic, only detected with serologic screening.

NOTE: neurosyphilis can occur during any stage of infection. Consult ID if neurologic symptoms.

HOW DO I TEST?

- 5-10 ml blood in a red-stoppered tube or a serum separator tube (red top with vellow cap)
- Cadham Provincial Laboratory (CPL) requisition form should request syphilis serology testing and HIV antibody testing; and should provide information on reason for testing, including symptoms or suspected stage of syphilis. (Consider choosing CPL's STI panel which includes serology testing for syphilis, HIV and hepatitis B and test for hepatitis C as well.)
- Swab ulcers, sores, or moist skin lesions with a dacron swab (ex: swab from GenProbe package) of the lesion and place into viral transport medium. The sample must remain refrigerated until sent to CPL and the CPL requisition should clearly indicate the site and test requested: T. pallidum PCR testing.

WHAT IS THE TREATMENT?

- Benzathine penicillin G (Bicillin®) 2 injections of 1.2 million units IM in a single session (2.4 MU total). See MHHLS protocol for information on allergy, pregnancy and HIV positive persons.
- The Bicillin® in preloaded syringes is provided free of charge by MHHLS (see order form below).
- Sex contacts of known syphilis cases MUST ALSO immediately be offered treatment for syphilis, without awaiting testing results.
- When staging is questionable in asymptomatic person, consider staging as Early Latent for reporting purposes, but treating as Late Latent (3 weekly treatments of Bicillin).
- Follow serologic response as per provincial protocol and current outbreak response. If titres do not decrease as per protocol, repeat HIV testing and consult ID.

IS IT REPORTABLE? Cases of syphilis are reportable under The Public Health Act, as are identified contacts of cases. If you are contacted by a public health nurse for follow up of your patient who has an STI, your collaboration and assistance would be greatly appreciated.

WHERE CAN I GET MORE INFO?

- Any complicated cases, all cases of neurosyphilis, or for assistance, consult Infectious Diseases.
- Consult Pediatric Infectious Diseases for any pregnant patient diagnosed with syphilis, any newborn if maternal syphilis was diagnosed at any time during pregnancy, or if congenital syphilis is suspected.
- MHHLS Syphilis Protocol http://www.gov.mb.ca/health/ publichealth/cdc/protocol/syphilis.pdf
- CPL -Cadham Provincial Laboratory Serology section: 204-945-6123
- MHHLS STI Medication Order Form http://www.gov.mb.ca/health/ publichealth/cdc/protocol/form11.pdf





POSITIVE SYPHILIS SEROLOGY

CLIENT HISTORY OR CADHAM LAB DOCUMENTATION OF REMOTE POSITIVE SYPHILIS SEROLOGY?

NO

LATENT

SYMPTOMS/

EXPOSURE

IN LAST 12

MONTHS?

OR 4 FOLD RISE IN

VDRL/RPR TITRE?

YES:

FARIY IATENT

NO:

LATE LATENT

NO NEW INFECTION:

REPEAT SYPHILIS SEROLOGY SAME DAY AS TREATMENT
TEST FOR GONORRHEA, CHLAMYDIA, HIV & HEPATITIS B AND C

DO A SEXUAL HEALTH HISTORY & PHYSICAL TO STAGE INFECTION

STAGING: SYMPTOMS?1

CHANCRE

ORAL, ANAL, VAGINAL, PENILE SWAB FOR SYPHILIS PCR

PRIMARY

RASH ALOPECIA, IYMPHADENOPATHY

SECONDARY

TREAT (2.4 MU BICILLIN) x1
FOLLOW SEROLOGY
AS PER PROTOCOL

ABOUT CONTACTS

COMPLETE FORM FOR CONTACT TRACING

TREAT (2.4 MU BICILLIN)
WEEKLY x3
FOLLOW SEROLOGY

NEWBORNS: IF MATERNAL SYPHILIS WAS DIAGNOSED AT ANY TIME DURING PREGNANCY, OR IF CONGENITAL SYPHILIS IS SUSPECTED, CONSULT PEDIATRIC INFECTIOUS DISEASES.

NEUROSYPHILIS CAN OCCUR DURING ANY STAGE OF INFECTION.
CONSULT ID IF NEUROLOGIC SYMPTOMS.

POSSIBLE REMOTE CASE:

ABOUT PREVIOUS INFECTION

DO SEXUAL HEALTH & IMMIGRATION
HISTORY AND PHYSICAL

TEST FOR GONORRHEA, CHLAMYDI.
HIV & HEPATITIS B AND C

SYMPTOMS?

YES: EFER TO NEW INFECTION

NO.

EXPOSURE TO INFECTIOUS CASE, CURRENT JNPROTECTED SEX, RISE IN VDRL/RPR, OR OTHER REASON TO SUSPECT NEW INFECTIONS

NO: KELY AN OLD

YES: RETEST IN 7-21 DAY

4 FOLD RISE

IN VDRL/RPR:

HISTORY OF TREATMENT:

NO FOLLOW U

NO HISTORY OF TREATMENT:

TAGE AND TREAT

NO CHANGE IN VDRL/RPR:

> RETEST IN 2-3 MONTHS

STAGE AND TRE







Outbreak Interventions

- Assertive Testing Strategy (SasP)
- Bathhouse Outreach
- Case Management (TasP)
- Social media advertising
- Health Care Provider Information
- Mapping ("frequent transmitters")
- Contact Notification (anonymity)

Assertive Testing Strategy

- Offer q3mo syph testing to all previous syphilis cases (phone/text/email reminders)
- Only 22% completed 3/6/9/12 mo testing
- 20 repeat syphilis infections detected (10% of all cases/12 mo; 2 new HIV)
- Very positive PHN/client interaction
- Future focus on "core transmitting networks" =
 MSM/MSMW, <35 yo, past Hx STBBI (HIV), low income



Case One:

28 y. pregnant female with a history of spontaneous first trimester abortion x 2, and is seen at 10 weeks of pregnancy for a first screening visit. She has no complaints and is in a monogamous relationship. She has no chronic illnesses and no history of STI.

Physical Exam: normal

Lab Tests:

HBSAg - HBSAb + , HIV-

Rubella - Chlamydia, GC both negative,

Syphilis: CMIA +, TPPA+, RPR -

Case One cont'd

① What does this test result mean?

Two different Treponema specific screening tests are positive but RPR neg.

- could be very early syphilis, late-latent or treated syphilis
- ② What should you do next?

Repeat test in 7-10 days

③ Is treatment advised? If so what?

If persistently positive, treat as late-latent syphilis, since patient is pregnant, worst case scenario is passing syphilis to fetus, Treat with 3 doses of IM penicillin 2.4 mil. U x 3 doses

④ Is anything advised after treatment?

Document Treatment! Since RPR negative no need to follow titers.

Case Two



A 63 year old female Filipino bookkeeper returns from an ophthalmologist referral with confirmed uveitis. PMH: hypertension, elevated lipids.

Review of systems is negative, Social History: married with adult sons. No history of TB or STI.

Physical Exam: normal, eye exam not done

Lab Tests: HBSAg – , HBSAb + , Toxo -, CMV-, HIV-

Syphilis: CMIA +, TPPA-, RPR -

Case two cont'd

① What does this test result mean?

The CMIA indicates a positive screening Treponemal test for syphilis but the TPPA, a second Treponemal test for syphilis aimed at a different antigen is negative, as is the RPR, a non-Treponemal test.

② What should you do next?

Since both a second Teponema test and non-Treponemal test are negative, we conclude the first test (CMIA) is a False Postive and *no further testing is necessary*

- ③ Is syphilis treatment advised? If so what? **NO!**
- ④ Is contact tracing advised? No
- What about the uveitis? It still needs workup! TB, lymphoma, spondyloarthritis etc...

Summary

- Syphilis outbreak in 2005-2006 was in large part heterosexual, traditional risk factors operated, traditional control measures were successful to manage it
- Recent outbreak in 2013-16 is more -social media driven, fewer imported cases, highly infectious, multifocal –all over province: rural as well as northern,
- Large infectious MSM component with bisexual men bridging the epidemic into the female population
- Traditional control methods less successful, resorting to novel methods such as assertive or intensive testing strategies in key populations have other risk factors.

Acknowledgements

Kamran Kadkhoda my colleague and expert on syphilis diagnostics in Manitoba Allan Ronald who taught me about Syphilis first hand in the public health clinics of Nairobi as a 4th year medical student) Pierre Plourde Medical Officer of Health in charge of STD's in Winnipeg

Information:

Cadham Provincial Lab:

cadham@gov.mb.ca

Tel. 204-945-6123

www.gov.mb.ca/health (use search word "syphilis")

Public health Canada (search on PHAC-Syphilis)

http://www.phac-aspc.gc.ca/sti-its-surv-epi/rep-rap-2012/rep-rap-3-eng.php

