STBBI in Saskatchewan

Presentation at the SASKPIC Education Conference

September 2023

Healthy People, Healthy Saskatchewan
The Saskatchewan Health Authority works in the spirit of truth and reconciliation, acknowledging Saskatchewan as the traditional territory of First Nations and Métis People.
Slides adapted from the “Syphilis in Saskatchewan: Epidemiology and Analyses to Inform Public Health Action” presentation

Healthy People, Healthy Saskatchewan
The Saskatchewan Health Authority works in the spirit of truth and reconciliation, acknowledging Saskatchewan as the traditional territory of First Nations and Métis People.
Vision, Mission, Values and Philosophy of Care

Vision

Healthy People, Healthy Saskatchewan

Mission

We work together to improve health and well-being. Every day. For everyone.

Values

Safety: Be aware. Commit to physical, psychological, social, cultural and environmental safety. Every day. For everyone.

Accountability: Be responsible. Own each action and decision. Be transparent and have courage to speak up.

Respect: Be kind. Honour diversity with dignity and empathy. Value each person as an individual.

Collaboration: Be better together. Include and acknowledge the contributions of employees, physicians, patients, families and partners.

Compassion: Be caring. Practice empathy. Listen actively to understand each other’s experiences.

Philosophy of Care: Our commitment to a philosophy of Patient and Family Centred Care is at the heart of everything we do and provides the foundation of our values.
We acknowledge that we are gathering on Treaty 4 territory and the Homeland of the Dakota, Lakota and Métis.

Recognizing this history is important to our future and our efforts to close the gap in health outcomes between Indigenous and non-Indigenous peoples.

www.saskhealthauthority.ca/trc

Treaty Territories and Saskatchewan Health Authority Areas

Depictions of Treaty boundaries are subject to variation. These boundaries are usually not surveyed and are estimated based on written descriptions.

This map displays the Pre-1975 Treaties (Historic Treaties) in colour, as provided by Crown-Indigenous Relations and Northern Affairs Canada. The grey lines indicate alternate boundaries compiled from various sources.
Learning objectives

- Describe the epidemiology of syphilis in Saskatchewan
- Describe the epidemiology of syphilis in Regina
- Highlight the challenges and successes experienced by public health staff in syphilis clinical management
- Explore the impact of the current syphilis outbreak
- Explore the operational impacts of the current syphilis outbreak
Syphilis Update: A limerick

There was a young man from back bay
Who thought syphilis just went away
He believed that a chancre
Was only a canker
That healed in a week and a day

But now he has acne vulgaris
Or whatever they call it in Paris
On his skin it has spread
From his feet to his head
And his friends want to know where his hair is

There is more to his terrible plight:
His pupils won’t close in the light
His heart is cavorting
His wife is aborting
And he squints through his gun barrel sight

Arthralgia cuts into his slumber
His aorta is in need of a plumber
But now he has Tabes
And sabershinned babies
While of gumma he has quite a number

He has been treated in every known way
But his spirochetes grow day by day
He’s developed paresis
Has long talks with Jesus
And thinks he is the queen of the May

Key messages

- From 2017 to 2022, Saskatchewan’s syphilis rates have increased over 400%.
- In 2019, syphilis cases were largely in the North West area of the province.
- Syphilis transmission spread diagonally north-south.
  - This trend is the same for syphilis, infectious syphilis, child-bearing years, congenital.
- Over the same period, the epidemiology shifted from predominately middle aged men, with higher testing rates among males, to predominately women of child-bearing years, with higher testing rates among women.
- SK reported zero congenital syphilis cases between 2013 and 2018, to n = 68 since 2019.
- Syphilis now exists throughout the province.
- Saskatchewan ranks 2nd highest infectious syphilis rates in Canada (behind MB) and has the highest rates of congenital syphilis in Canada.
Key messages

All cases have complex mix of risk factors associated with infection:

- Substance misuse
- Unstable housing
- Transiency/Frequent movement
- Anonymous or multiple sex partners
- No condom use
- History of multiple sexually transmitted infections, including re-infection
Syphilis by the numbers
Epidemic curve: All Syphilis, 2017 – 2022

All syphilis cases, Saskatchewan, January 2017 to December 2022 (n = 7042)

*PHAC Date (month and year) used, confirmed cases only
**2022 is subjected to change - data as of February 1st, 2023
Epidemic curve: All Syphilis by Stage, 2017 – 2022

All syphilis cases by stage, Saskatchewan, January 2017 to December 2022 (n = 7042)

*PHAC Date (month and year) used, confirmed cases only
**2022 is subjected to change - data as of February 1st, 2023
### All syphilis distribution by sex, 2017-2022

<table>
<thead>
<tr>
<th>Year</th>
<th>Females (%)</th>
<th>Males (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2017</td>
<td>7.5</td>
<td>92.5</td>
</tr>
<tr>
<td>2018</td>
<td>28.3</td>
<td>71.7</td>
</tr>
<tr>
<td>2019</td>
<td>46.2</td>
<td>53.8</td>
</tr>
<tr>
<td>2020</td>
<td>52.0</td>
<td>48.0</td>
</tr>
<tr>
<td>2021</td>
<td>52.1</td>
<td>47.9</td>
</tr>
<tr>
<td>2022</td>
<td>53.9</td>
<td>46.0</td>
</tr>
<tr>
<td>2017 – 2022</td>
<td>51.2</td>
<td>48.8</td>
</tr>
</tbody>
</table>

- **Sex trend reversal from 2017 to 2022**
- **Median age, in 2022:**
  - Males = 32 years
  - Females = 28 years

*PHAC Date (year) used, confirmed cases only
**2022 is subjected to change - data as of February 1st, 2023*
Syphilis and age trends

*All syphilis cases including congenital and stillbirths; PHAC Date (year) used, confirmed cases only

**2022 is subjected to change - data as of February 1st, 2023
**Preliminary estimates for 2022 data**

**All syphilis includes staged and unstaged cases**
Epidemic Curve: Infectious, Late Latent, and Unstaged Syphilis by Stage, 2017 - 2022

Infectious, Late Latent, and Unstaged Syphilis Cases, January 2017 to December 2022 (n = 6967)

*PHAC Date (month and year) used, confirmed cases only
**2022 is subjected to change - data as of February 1st, 2023
~ Unknown/blank refers to syphilis cases with unknown or blank information captured under staging information
Syphilis in females of child-bearing years
Epidemic Curve: Infectious, Late Latent, and Unstaged Females of Child-bearing Years (15-45), 2017-2022

Infectious syphilis, late latent and unstaged cases in females of child-bearing ages (15-45 years), Saskatchewan, January 2017 - December 2022 (n = 3430)

*PHAC Date (month and year) used, confirmed cases only
**2022 is subjected to change - data as of February 1st, 2023
~ Unknown/blank refers to syphilis cases with unknown or blank information captured under staging information
Congenital syphilis
Epidemic Curve: Congenital Syphilis + Infectious, late latent and unstaged female of child-bearing years (15-45), 2019-2022

*PHAC Date (month and year) used, confirmed cases only

**46 cases of infectious, late latent and unstaged cases in females of child-bearing years reported from January 2017 to December 2018 are not included in the above epi curve. Caution should be utilized while interpreting the graph as cases in women of child-bearing years and pregnancy gestation are not aligned.

~ Blank refers to syphilis cases with unknown or blank information captured under staging information
Only four moms (6%) received prenatal care; 63% had no prenatal care.
28% received sporadic prenatal care; 3% had no information reported.
Nearly all mothers did not receive effective treatment (n = 67; 99%).
Where treatment occurred, 50% treated post delivery.
At least half became infected or were re-infected during pregnancy (primary, secondary).
All mothers (n = 68; 100%) had at least one of the following risk factors:
- Substance misuse, unstable housing, transiency, anonymous or multiple sex partners, no protection used, previous STIs.
The minority of moms were entirely under First Nations jurisdiction (ISC and/or NITHA) (n = 26; 38%) but frequent movement between public health jurisdictions, particularly in the northern areas.
The view from Regina
Overall disease counts and disease-specific rates of confirmed STI cases, 2019 - 2022, Regina, Saskatchewan

<table>
<thead>
<tr>
<th>Disease</th>
<th>2019</th>
<th>2020</th>
<th>2021</th>
<th>2022</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlamydia Trachomatis Infection</td>
<td>1417</td>
<td>1062</td>
<td>978</td>
<td>1126</td>
</tr>
<tr>
<td>Gonococcal Infection</td>
<td>551</td>
<td>445</td>
<td>386</td>
<td>465</td>
</tr>
<tr>
<td>HIV</td>
<td>47</td>
<td>52</td>
<td>61</td>
<td>70</td>
</tr>
<tr>
<td>Syphilis</td>
<td>61</td>
<td>155</td>
<td>511</td>
<td>528</td>
</tr>
</tbody>
</table>

| Rate per 100,000              | 518.5| 382.0| 357.7| 404.1|
| Chl. Trach rate               | 201.6| 160.1| 141.2| 166.9|
| Gono. Infection rate          | 17.2 | 18.7 | 22.3 | 25.1 |
| HIV rate                      | 22.3 | 55.8 | 186.9| 189.5|

*PHAC Date (month and year) used, confirmed cases only
**2022 is subjected to change - data as of February 1st, 2023
~ Unknown/blank refers to syphilis cases with unknown or blank information captured under staging information
Crude rate per 100,000, infectious syphilis, fRQHR 2015-2022, by sex

<table>
<thead>
<tr>
<th>Year</th>
<th>Female cases</th>
<th>Male cases</th>
<th>Female rate</th>
<th>Male rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>2015</td>
<td>2</td>
<td>5</td>
<td>1.4</td>
<td>3.5</td>
</tr>
<tr>
<td>2016</td>
<td>1</td>
<td>31</td>
<td>0.7</td>
<td>20.7</td>
</tr>
<tr>
<td>2017</td>
<td>2</td>
<td>27</td>
<td>1.3</td>
<td>17.5</td>
</tr>
<tr>
<td>2018</td>
<td>6</td>
<td>23</td>
<td>4</td>
<td>15.0</td>
</tr>
<tr>
<td>2019</td>
<td>23</td>
<td>38</td>
<td>16.9</td>
<td>27.6</td>
</tr>
<tr>
<td>2020</td>
<td>75</td>
<td>80</td>
<td>54.4</td>
<td>57.1</td>
</tr>
<tr>
<td>2021</td>
<td>244</td>
<td>265</td>
<td>179.4</td>
<td>192.9</td>
</tr>
<tr>
<td>2022</td>
<td>258</td>
<td>260</td>
<td>186.3</td>
<td>185.5</td>
</tr>
</tbody>
</table>
Characteristics of a cohort of STI patients in Regina area, 2019 - 2022

<table>
<thead>
<tr>
<th></th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of cases (%)</td>
<td>4900 (57.1)</td>
<td>3681 (42.9)</td>
</tr>
<tr>
<td><strong>STBBI cases by disease type</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chlamydia Trachomatis Infection</td>
<td>2907 (63.4)</td>
<td>1675 (36.6)</td>
</tr>
<tr>
<td>Gonococcal Infection</td>
<td>1002 (54.3)</td>
<td>845 (45.7)</td>
</tr>
<tr>
<td>HIV</td>
<td>118 (51.3)</td>
<td>112 (48.7)</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>68 (40)</td>
<td>102 (60)</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>194 (40.1)</td>
<td>282 (59.9)</td>
</tr>
<tr>
<td>Syphilis</td>
<td>605 (48.2)</td>
<td>650 (51.2)</td>
</tr>
</tbody>
</table>

STI cases and rates per 100,000 by Regina area residence

<table>
<thead>
<tr>
<th></th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regina 1 (North)</td>
<td>1057 (771.4)</td>
<td>676 (487.0)</td>
</tr>
<tr>
<td>Regina 2 (East)</td>
<td>661 (482.4)</td>
<td>455 (327.8)</td>
</tr>
<tr>
<td>Regina 3 (South)</td>
<td>827 (603.5)</td>
<td>616 (443.8)</td>
</tr>
<tr>
<td>Regina 4 (Central)</td>
<td>1965 (1434.0)</td>
<td>1149 (827.7)</td>
</tr>
<tr>
<td>Regina NA</td>
<td>390 (284.6)</td>
<td>785 (565.5)</td>
</tr>
</tbody>
</table>

*PHAC Date (month and year) used, confirmed cases only
**2022 is subjected to change - data as of February 1st, 2023
~ Unknown/blank refers to syphilis cases with unknown or blank information captured under staging information
Syphilis by disease stage, 2022

- **Primary**: 131, 25%
- **Secondary**: 94, 18%
- **Early latent**: 86, 17%
- **Late latent**: 71, 14%
- **Early congenital**: 2, 0%
- **Tertiary other than neurosyphilis**: 2, 0%
- **Unknown**: 131, 25%
- **Early neurosyphilis (<1 year after infection)**: 3, 1%
- **Tertiary other than neurosyphilis**: 2, 0%

Legend:
- Blue: Primary
- Orange: Secondary
- Yellow: Late latent
- Blue: Early neurosyphilis (<1 year after infection)
- Gray: Unknown
- Gray: Early congenital
Syphilis by risk factor

Female (n=259)

- No condom
- Previous STI
- Non-injection drug use
- Street involved
- More than 2 partners last 3 months
- IDU
- No RF
- Alcohol use
- Sex with a known case
- Unknown/anonymous partnering
- Homeless
- Pregnant
- Victim of sexual assault
- Goods received in exchange for sex
- e-partnering
- Goods provided in exchange for sex
- Travel outside Canada

Male (n=261)

- No condom
- Previous STI
- Non-injection drug use
- Alcohol use
- More than 2 partners last 3 months
- Unknown/anonymous partnering
- Street involved
- Sex with a known case
- No RF
- IDU
- e-partnering
- Homeless
- MSM
- Travel outside Canada
- Goods provided in exchange for sex
- Victim of sexual assault
- Goods received in exchange for sex
- Correctional facility resident
## Risk factor profile of sexually transmitted cases in Regina 2019 - 2022

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex without protective barriers</td>
<td>1973 (22.99)</td>
</tr>
<tr>
<td>Sex with two or more partners in the last three months</td>
<td>1556 (18.13)</td>
</tr>
<tr>
<td>Sex with an anonymous partner</td>
<td>976 (11.37)</td>
</tr>
<tr>
<td>Cases with a history of injectable substance use</td>
<td>607 (7.07)</td>
</tr>
<tr>
<td>Cases with a history of non-injectable substance use</td>
<td>584 (6.8)</td>
</tr>
<tr>
<td>Sex with a known case</td>
<td>479 (5.58)</td>
</tr>
<tr>
<td>Cases meeting partners online</td>
<td>471 (5.49)</td>
</tr>
<tr>
<td>Cases who are street-involved</td>
<td>424 (4.94)</td>
</tr>
</tbody>
</table>
Impacts of Syphilis Epidemic in Public Health

- Increased workload
- Hard to reach population with coexisting social and health issues
- Increased lost to follow up rates
- Difficulty with retention in care
- Limited healthcare worker capacity
- Coinfections
Thank you for listening.

Questions?
With thanks to...

- Cara Benz
- Helen Bourget
- Kathy Lloyd
- Lara Murphy
- Laurel Stang
- Maureen Anderson
- Maurice Hennink
- Molly Trecker
- Muhammad Siddiqui
- Priyanka Mahajan
- Taegen Fitch
- Tania Diener
- CD team
- Sexual health clinic team
- Our patients
- Provincial epidemiologists
- SHA epidemiologists
Extras
Syphilis Diagnosis
Syphilis Update: Clinical History and Examination

Assessment
- History of syphilis
- Known contact to an infectious case of syphilis
- Signs or symptoms of syphilis in the past 12 months
- Most recent serologic test for syphilis

Examination
- Oral cavity
- Lymph nodes
- Skin of torso
- Palms and soles
- Genitalia and perianal area
- Neurologic examination
- Abdomen
Laboratory tests

Syphilis screening tests:

- **Venereal disease research laboratory (VDRL) test.** The VDRL test checks blood or spinal fluid for an antibody that can be produced in people who have syphilis. This antibody is not produced as a reaction to syphilis specifically, so the test result could be "abnormal" for reasons other than syphilis.

- **Rapid plasma reagin (RPR) test.** The RPR test also finds syphilis antibodies.

Syphilis confirmation tests:

- **Enzyme immunoassay (EIA) test.** This blood test checks for syphilis antibodies. A positive EIA test should be confirmed with either the VDRL or RPR tests.

- **Fluorescent treponemal antibody absorption (FTA-ABS) test.** This test also checks for antibodies. It can be used to find syphilis except during the first 3 to 4 weeks after exposure. The test can be done on a sample of blood or spinal fluid.

- **Treponema pallidum particle agglutination assay (TPPA).** This test also checks for antibodies. It is used after another method tests positive for syphilis. This test is not done on spinal fluid.

Adapted from Syphilis Tests. Available at [https://www.healthlinkbc.ca/medical-tests/hw5839](https://www.healthlinkbc.ca/medical-tests/hw5839)
### Laboratory testing

<table>
<thead>
<tr>
<th>Syphilis screen</th>
<th>RPR</th>
<th>TPPA</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>n/a</td>
<td>n/a</td>
<td>No serologic evidence of past or current syphilis infection. In the setting of recent exposure, or signs/symptoms of primary syphilis, repeat testing in 2 to 4 weeks.</td>
</tr>
<tr>
<td>Reactive</td>
<td>Reactive</td>
<td>n/a</td>
<td>Consistent with syphilis infection. Clinical manifestations and treatment history is required to refine interpretation: i) Infectious syphilis (primary, secondary or early latent) ii) Late latent syphilis iii) Tertiary syphilis iv) Treated syphilis with persistent reactive RPR</td>
</tr>
<tr>
<td>Reactive</td>
<td>Non-Reactive</td>
<td>Non-Reactive</td>
<td>No serologic evidence of past or current syphilis infection. Screening test is most likely falsely reactive. In the setting of recent exposure, or signs/symptoms of primary syphilis, repeat testing in 2 to 4 weeks.</td>
</tr>
<tr>
<td>Reactive</td>
<td>Non-Reactive</td>
<td>Indeterminate</td>
<td>Syphilis serology inconclusive. Recommend repeat testing in 2 to 4 weeks. If results remain inconclusive upon repeat testing, this may represent falsely reactive serology or distant prior infection (treated or untreated).</td>
</tr>
<tr>
<td>Reactive</td>
<td>Non-Reactive</td>
<td>Reactive (or Repeat Reactive)</td>
<td>Consistent with syphilis infection. Clinical manifestations and treatment history is required to refine interpretation: i) Primary syphilis before RPR seroconversion ii) Secondary syphilis with RPR prozone effect (notify lab if suspected) iii) Late latent syphilis after RPR seroreversion iv) Treated syphilis Note: These results are also consistent with non-syphilitic treponematosis (bejel, yaws or pinta)</td>
</tr>
</tbody>
</table>
Syphilis Diagnosis
Laboratory tests

- Screening test - IgG & IgM (By itself is not reportable to MHO)
- RPR - Rapid Plasma Reagin (non-treponemal): Quantitative
  - Guides treatment and re-infection for previous cases
  - NR, 1:1, 1:2, 1:4, 1:8, 1:16, 1:32, 1:64, 1:128, 1:256, 1:512,....
- TPPA - T. pallidum Particle agglutination assay
  - Treponemal test (specific for T. pallidum antibody)
  - Reportable (Reactive or Indeterminate)
  - Remains “Reactive” for life
- Direct Detection Test - Sent to NML, Winnipeg
- PCR - Polymerase chain reaction - UTM swab taken from “chancre”
  - Tests for genes: polA, bmp, tpp47
### Laboratory testing algorithm

<table>
<thead>
<tr>
<th>T. pallidum Total Antibody Screen</th>
<th>RPR</th>
<th>TPPA</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Negative</strong></td>
<td>n/a</td>
<td>n/a</td>
<td>No serologic evidence of past or current syphilis infection. In the setting of recent exposure, or signs/symptoms of primary syphilis, repeat testing in 2 to 4 weeks.</td>
</tr>
</tbody>
</table>
| **Reactive**                      | Reactive | n/a  | Consistent with syphilis infection. Clinical manifestations and treatment history is required to refine interpretation:  
|                                   |       |      | i) Infectious syphilis (primary, secondary or early latent)  
|                                   |       |      | ii) Late latent syphilis  
|                                   |       |      | iii) Tertiary syphilis  
|                                   |       |      | iv) Treated syphilis with persistent reactive RPR |
| **Reactive**                      | Non-Reactive | Non-Reactive | No serologic evidence of past or current syphilis infection. Screening test is most likely falsely reactive. |
| **Reactive**                      | Non-Reactive | Indeterminate | Syphilis serology is inconclusive. Recommend repeat testing in 2 to 4 weeks. |
| **Reactive**                      | Non-Reactive | Reactive (or Repeat Reactive) | Consistent with syphilis infection. Clinical manifestations and treatment history is required to refine interpretation |

Source: Syphilis testing algorithm: [https://rrpl-testviewer.ehealthsask.ca/SCI/What%20is%20new%20at%20SDCL/Syphilis%20Algorithm%20Interpretation%20v3.1.pdf](https://rrpl-testviewer.ehealthsask.ca/SCI/What%20is%20new%20at%20SDCL/Syphilis%20Algorithm%20Interpretation%20v3.1.pdf)
Syphilis serology

Timing of serologic responses in syphilis infection

- Higher numbers correspond to higher level of antibodies in patient’s serum
- Number determined by progressive dilution of serum until it becomes non-reactive
- A two-fold change such as 1:32 to 1:16 is generally considered within margin of test error
- Sustained four-fold change such as 1:64 to 1:16 is considered significant

https://doi.org/10.1212/01.CPJ.0000435752.17621.48
Case Management
Syphilis Update: Management

- Penicillin G, administered parenterally, is the preferred drug for treating patients in all stages of syphilis

- Preparation used (i.e., benzathine, aqueous procaine, or aqueous crystalline) including dosage, and treatment duration depend on:
  i. the stage; and
  ii. clinical manifestations

- Treatment for Primary, Secondary, & Early Latent is Benzathine penicillin G 2.4 million units provided as a deep IM single dose (Bicillin L-A®) - two syringes

- In cases of penicillin allergy, Doxycycline 100 mg orally twice daily for 14 days

- Alternative agents (exceptional circumstances)

- Ceftriaxone 1 g IV or IM daily for 10 days

Syphilis Treatment

Primary, Secondary or Early Latent Syphilis

- Benzathine penicillin G 2.4 million units intramuscularly in a single dose (Bicillin L-A®)

Late latent syphilis or syphilis of unknown duration

- Benzathine penicillin G 2.4 million units IM once weekly for 3 weeks

Tertiary syphilis with normal CSF examination

- Benzathine penicillin G 2.4 million units IM once weekly for 3 weeks

If penicillin allergic

- Doxycycline 100 mg orally twice daily for 14 days, or
- Tetracycline 500 mg orally 4 times daily for 14 days
Syphilis in pregnancy

- Treat with Bicillin L-A® according to stage:
- **Doxycycline is contraindicated**, clients who are skin-test-reactive to penicillin should be desensitized in the hospital and treated with Bicillin L-A®.
- Missed doses >9 days between doses are not acceptable for pregnant women receiving therapy for late latent syphilis
- Pregnant women who miss a dose of therapy should repeat the full course of therapy

<table>
<thead>
<tr>
<th><strong>Recommended Regimen for Syphilis During Pregnancy</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnant women should be treated with the recommended penicillin regimen for their stage of infection</td>
</tr>
</tbody>
</table>
Post treatment serology

Primary, Secondary, Early Latent:
- One, three, six & twelve months
- Add twenty-four months for HIV infected clients

Late latent:
- Twelve & twenty-four months

Neurosyphilis:
- Six, twelve and twenty-four months after treatment.
- Patients with CSF abnormalities require follow up CSF at 6 monthly intervals until normalization of CSF parameters.
- Other clinical follow up may be indicated on a case-by-case basis.