Public Health Updates for Halton Physicians: Screening and Treating Tuberculosis March 31, 2022





The webinar will begin at 7 p.m. If you run into technical difficulties, please email Javier.Rincon@halton.ca

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Indigenous Land acknowledgement

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Placeholder for video

Boozhoo, She:kon, Tanshi, Greetings!

Halton Region acknowledges the Treaty Lands of the Mississaugas of the Credit First Nation as well as the Traditional Territory of the Haudenosaunee, Huron-Wendat and Anishinabek on which we gather.

In stewardship with Mother Earth and the enduring Indigenous presence connected to these lands we acknowledge the Indigenous Nations of the past, present and future.

In the spirit of ally-ship and mutual respect, we will take the path of Truth and Reconciliation to create change, awareness and equity as we strive to elevate the collective consciousness of society.

Miigwetch, Nia:wen, Marsi, Thank you



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Agenda

- TB in Halton local context
- Epidemiology, reporting, supports
 Dr. Deepika Lobo

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- Screening and treating TB Dr. Ananda Ghosh
- Question & Answer Session



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Housekeeping

REGION



Use the Q&A function to ask, vote or comment on a question

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Learning Objectives

Overall series learning objective:

• By attending the Public Health **Updates for Halton Physicians** series, participants will be able to identify and discuss relevant and recent information about approaches to the prevention, diagnosis and management of key public health issues impacting their family medicine practice in both rural and urban settings.

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By the end of this session,

participants will be able to:

- Identify risk factors for TB and re-activation of TB
- Screen for TB using TST or IGRA
- Differentiate between LTBI and active TB
- Describe treatment options for LTBI, the treatment referral process for active TB and reporting requirements for TB and LTBI



Mitigating Potential Bias

All data, resources and recommendations presented are based on current scientific literature and data.

While some treatments may be referred to by their pharmaceutical name, there is no relationship between us and the pharmaceutical companies referenced in this presentation.

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Disclosure of Financial Support

- This program is hosted and organized by Halton Region Public Health.
- I am a paid employee with Halton Region Public Health.

Potential for conflict(s) of interest:

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 Halton Region Public Health receives funding from the Province of Ontario who also provides funding for public health research, programs and resources that may be discussed today.



We are here TB in Halton

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Global comparison (crude rate/ 100,000 2020)

Global Rank	Country	Rate per 100,00
1	Monaco	0
2	San Marino	0
3	United Arab Emirates	0.8
4	Israel	2.1
5	Saint Lucia	2.2
6	Antigua and Barbuda	2.3
7	Jamaica	2.4
8	United States of America	2.4
9	Barbados	2.4
10	Grenada	2.8
31	Canada	5.9
185	Papua New Guinea	441
186	Namibia	460
187	Marshall Islands	483
188	Timor-Leste	508
189	Democratic People's Republic of Korea	523
190	Gabon	527
191	Philippines	539
192	Central African Republic	540
193	South Africa	554
194	Lesotho	650

Ontario 4.5 Halton 2.7



Active TB Cases by Origin of Birth: Ontario, 2017-2021



Unknown origin (n=285; 8.3%)

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Of those born outside of Canada, five countries accounted for 62.9% (1,838/2,920) of all cases:

- India (n=856; 29.3%)
- Philippines (n=479; 16.4%)
- China (n=264; 9.0%)
- Vietnam (n=122; 4.2%)
- Pakistan (n=117; 4.0%

Origin of birth varies by geography:

- GTA (Toronto, Peel, York):
 - 88.8% of cases born outside Canada
- Northwestern Ontario (Northwestern, Thunder Bay, Porcupine):
 - 70.3% of cases Canadian-born Indigenous

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Data sources: Ontario's integrated Public Health Information System (iPHIS) [extracted March 23, 2022]; Statistics Canada population estimates



Slide credit: PHO Rounds World Tuberculosis Day 2022 (March 29, 2022)

Active cases in Halton over time (# of cases)



confirmed suspect

TB trends in Halton (# of cases)



Primary care and IMS

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- Public Health is notified by Immigration Refugees and Citizenship Canada (IRCC) that the individual is placed on IMS.
- Public Health provides a package to IMS clients and advises them to follow-up with a primary care provider.
 - Package includes a letter to physician, Tuberculosis Medical Surveillance Assessment Form and resources
 - Client is encouraged to bring their overseas medical report
 - The goal is to assess and rule out active TB disease (pulmonary and extra-pulmonary) and consideration for LTBI treatment

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What is TB – Active vs Latent

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ACTIVE

- Symptomatic
- Capable of infecting others if pulmonary/ laryngeal
- TB germs are active, multiplying and destroying tissue
- Needs medications to treat the disease

– LATENT (LTBI)

- Asymptomatic
- Cannot spread to others
- May develop active TB in the future
- Needs treatment to prevent conversion to active disease

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Publicly vs privately funded TST

Publicly funded

- Active TB contacts
- Deemed to be "medically necessary" by physician
- <65 age who are entering a Long-term care facility
- Students when required for school admission/continuing education
- Free TB testing solution can be ordered through the <u>online vaccine ordering</u> <u>system on halton.ca/physicians</u>

Privately funded

- For employment, volunteer placement, entry into retirement homes.
- Physician can purchase test solution and charge the patient or give a prescription to the individual





Access to TB medications

- Medications for treatment of active TB and LTBI are provided at no cost to patients, regardless of OHIP coverage, through Public Health
- In Halton, the ordering physician should:

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- fax prescription directly to Pharmex at 905-847-8271 or
- call 905-847-8224.
- Halton Region Public Health works in collaboration with Pharmex to provide the medications to the patient
- Public Health also conducts directly observed therapy (DOT) for treatment of active pulmonary TB cases.

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Reporting TB to Public Health

- Physician who reads the TST or orders the IGRA must <u>report positive results to</u> <u>Public Health</u>
- <u>TB Physician Reporting Form</u> (Halton)
- Fax results to 905-825-8797
- Telephone support
 - 905-825-6000 ext. 7341 live answer during business hours (Monday to Friday, 8:30 a.m.-4:30 p.m.)

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Dr. Ananda Ghosh, MD FRCP

Infectious Diseases Consultant, Physician Lead, Quality and Patient Safety Medical Lead, COVID-19 Assessment Centres and Vaccination Clinic Halton Healthcare

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Tb screening and treatment

Ananda Ghosh MD FRCPC Mar 31, 2022

Disclosures

- No grants/research support
- Funded by Halton Healthcare Services (Quality & Patient Safety, Infection Prevention & Control)
- Participant in Gilead Sciences and ViiV Healthcare HIV therapies advisory boards (not related to TB treatment)

Outline

- Tuberculosis (Tb) what is it?
 Natural history and pathogenesis of Tb
- Latent Tb (Infection)
 - Diagnosis
 - Treatment
- Active Tb (Disease)
 - Diagnosis
 - Treatment

What is tuberculosis?

- Bacterial infection caused by Mycobacterium tuberculosis
 - Enveloped (acid-fast)
 - Aerobic
 - Gram-positive
 - Bacillus
 - Slow growing





Natural History

Inhalation of aerosol droplets containing M. tb:

- Immediate clearance (no infection)
- Immune response to establish granuloma(ta) and contain (latent tuberculosis infection)
 - May later have immune escape leading to active disease (reactivation disease)
- Limited or inadequate immune response allowing immediate progression to active disease(primary disease)

Diagnosing Latent Tb

Diagnosing tuberculosis infection

Diagnosing latent Tb infection

- Looking for immune response, not Tb bacilli
- T-cell mediated response (Gell and Coombs type IV)
- Mantoux tuberculin skin test (TST)
- Interferon-Gamma release assay (IGRA)

Mantoux tuberculin skin test (TST)

Placing TST

- Inject 0.1 mL Tb purified protein derivative (PPD)
- Intradermal administration
 - Needle at 10-15° from skin
 - Bevel of needle up
 - Create small wheal



cdc.gov/tb/topic/testing/tbtesttypes.htm

Reading TST

- 48 to 72 hours later
- Measure millimeters of induration (not erythema)



Mantoux tuberculin skin test (TST)

TST Result	Situation in which reaction is considered positive						
<5 mm	In general, this is considered negative						
≥5mm	People living with HIV Known recent (<2 years) contact with a patient with infectious TB disease Fibronodular disease on chest x-ray (evidence of healed, untreated TB) Prior to organ transplantation and receipt of immunosuppressive therapy Prior to receipt of biologic drugs, such as tumor necrosis factor alpha inhibitors, or disease-modifying antirheumatic drugs Prior to receipt of other immunosuppressive drugs, such as corticosteroids (equivalent of ≥15 mg per day of prednisone for at least one month) Stage 4 or 5 chronic kidney disease (with or without dialysic)						
≥10 mm	Recent (<2 years) conversion of TST from negative to positive Diabetes (controlled or uncontrolled) Malnutrition (<90% of ideal body weight) Current tobacco smoker (any amount) Daily consumption of >3 alcoholic drinks Silicosis Hematologic malignancies (lymphomas and leukemia) and certain carcinomas (such as cancers of head, neck, lung and/or gastrointestinal tract) Any population considered at low risk of disease.						

Report measurement of induration in addition to interpretation

Canadian Tb Standards, 8th Ed.

IGRA

- Laboratory-based method to assess T-cell mediated immune response to Tb antigens
- Blood exposed to (more specific than PPD) M. tb antigens
- Release of IFN-γ in response is detected/measured
- Low probability of cross reacting from BCG vaccine or NTM infection
- Not covered by OHIP (cost ~\$100)

BCG vaccine

- Live attenuated vaccine (strain of M. bovis)
 - Developed by Calmette and Guérin
- Limited efficacy at preventing latent Tb (infection)
- Modest (unclear) efficacy at preventing active Tb (disease)
- Likelihood of causing false positive TST depends on:
 - Age of administration (<12 months vs >12 months)
 - Time since administration

Choosing TST vs IGRA

- Patient preference and access
- IGRA preferred if:
 - Child <10 years old with history of BCG vaccine
 - Any age with BCG vaccine dose after 12 months old
 - Unlikely/unable to present for reading of TST
- TST preferred for:
 - Planned serial testing (i.e. on-going exposure risk)

Treating Latent Tb

Tuberculosis preventative treatment

Decision to treat

- Weigh risk of reactivation/progression to active disease
 against
- Risk of toxicity or intolerance of therapy and
- Patient values and preference
- Practical considerations may influence decision (e.g. employment, barrier to potential future therapeutics)

Risk of progression to active disease

Pick factor	Annual risk of TB disease for the first 2-3	Poferonco
	years after testing positive (%)	Reference
VERY HIGH RISK		
People living with HIV	1.7 to 2.7	2,56
Child or adolescent (<18y) tuberculosis contact	2.9 to 14.6	56,57
Adult (≥18y) tuberculosis contact	0.8 to 3.7	2,56
Silicosis	3.7	2
HIGH RISK		
Stage 4 or 5 chronic kidney disease with or without dialysis	0.3 to 1.2	2
Transplant recipients (solid organ or hematopoietic)	0.1 to 0.7	2
Fibronodular disease	0.2 to 0.6	Extrapolated from: 75–77
Receiving immunosuppressing drugs (eg, tumor necrosis factor a inhibitors or steroids) ^b	0.5	2
Cancer (lung, sarcoma, leukemia, lymphoma or gastrointestinal)	0.1 to 0.4	Extrapolated from: 70
MODERATE RISK		
Granuloma on chest x-ray	0.1	Extrapolated from: 77,78
Diabetes	0.1 to 0.2	Extrapolated from: 83
Heavy alcohol use (at least 3 drinks/day)	0.1 to 0.2	Extrapolated from: 79
Heavy tobacco cigarette smoker (at least 1 pack/day)	0.1	Extrapolated from: 80–82
LOW RISK		
General (adult) population with no known risk factor	0.03	2
Persons with a positive two-step TST booster and no known risk factor	0.02	Extrapolated from: 84,85

Canadian Tb Standards, 8th Ed.

Before starting latent Tb treatment

Essential to rule out active disease

Minimum:

- Thorough history for symptoms
- Chest X-ray within previous six months and after last exposure
- Physical exam and further investigations based on above

Tb preventative therapy regimens

Rifampin daily for 4 months

- Dosed 10mg/kg up to 600mg once daily
- Counsel regarding:
 - Nausea/vomiting/diarrhea (typically mild, improves)
 - Change in colour of urine, sweat, tears
 - Mild rash can usually be treated through
 - Any severe rash (involving palms, soles, mucous membranes) STOP THERAPY IMMEDIATELY (SJS is rare but known risk)
- Review regular medications for interactions
 - Rifampin is a potent CYP450 inducer

Tb preventative therapy regimens

Isoniazid daily for 9 months

- Dosed 5mg/kg up to 300mg once daily
- Only used when rifampin not an option due to longer duration and higher risks of adverse events
- Counsel regarding:
 - Hepatotoxicity (monitoring bloodwork if age >40)
 - Peripheral neuropathy (co-administer 25mg pyridoxine daily)
 - Avoid Et-OH consumption while on therapy

Follow up

- Typically 2-4 weeks after initiating therapy to ensure
 - Receipt of therapy
 - Adherence
 - Tolerance
- At completion of therapy to ensure
 - Completion of recommended course
 - Counsel:
 - No need for further TST
 - No 'test of cure'
 - Provide documentation of successful completion

Diagnosing Active Tb

Diagnosing tuberculosis disease

Diagnosing active Tb

- Looking for the Tb bacilli, not the immune response
- Limited (?no) role for TST/IGRA in diagnosis of active Tb
 - Positive test does not confirm latent vs active
 - Negative test does not rule out active Tb

Go fishing where the fish are

Sample site of suspicion

Pulmonary

- Pleural
- Lymphadenitis
- Urogenital
- Bone and joint
- Bone marrow
- Skin
- Meningitis



Establishing a microbiological Dx

- Order "AFB stain and mycobacterial culture"
- For pulmonary Tb, sputum samples to start (3 samples, at least an hour apart)
 - High suspicion may required induced sputum or BAL
- For other sites, tissue biopsy for culture higher yield than body fluids (sample not in formalin, for micro studies)
- Important not only to confirm diagnosis of Tb disease
- Drug susceptibility results guide therapy

Treating Active Tb

Therapy for tuberculosis disease

Principles of treating active Tb

- ALWAYS have at least two confirmed active agents
- Intensive or induction phase
 - 3 active agents (pyrazinamide is preferred 3rd agent)
 - 2 months
- Continuation phase
 - 2 active agents (ideally one is rifampin)
 - 4 months minimum
 - Longer continuation phase if not using rifampin or high burden of disease and cultures not cleared by end of intensive phase

Nuances of treating active Tb

- Counselling and monitoring for adverse drug events
- Managing adverse drug events
 - Which can be treated through
 - Which necessitate interruption of therapy
 - Re-introduction of therapy after adverse drug events
- Expected (or unexpected) clinical course paradoxical reactions
- Collaboration with PH for DOT to support adherence

Regimens for susceptible active Tb

Table 2.	Recommended	treatment	regimens fo	r known	or :	suspected	drug	-susceptible	pulmonary	ТВ.	
										/	

	Initial phase (first two months)	Continuation phase
Suspected drug susceptible Preferred regimen	INH ^b RMP PZA EMB ^c daily ^d	INH RMP EMB daily for 4months
Alternative regimen ^e Alternative regimen ^e Alternative regimen ^e	INH RMP EMB daily INH RMP PZA EMB daily INH RMP EMB daily	INH RMP EMB daily for 7 months INH RMP EMB 3x per week ⁹ for 4 months INH RMP EMB 3x per weeks for 7 months
Known drug susceptible Preferred regimen	INH RMP PZA dailyd	INH RMP daily for 4 months
Alternative regimen ^e Alternative regimen ^e Alternative regimen ^{e,t}	INH RMP EMB daily INH RMP PZA daily INH RMP EMB daily	INH RMP daily for 7 months INH RMP 3x per week9 for 4 months INH RMP 3x per week9 for 7 months

Abbreviations: TB, tuberculosis; INH, Isoniazid; RMP, rifampin; PZA, pyrazinamide; EMB, ethambutol; DOT, directly observed therapy. "INH: Isoniazid, RMP: rifampin, PZA: pyrazinamide, EMB: ethambutol.

Canadian Tb Standards, 8th Ed.

Key messages

- Spectrum of clinical disease with interplay between pathogen factors and host immune response
- Classical paradigm of Latent Tb and Active Tb still a useful and practical approach
- Diagnosis of Latent Tb = detection of host immune response (TST or IGRA)
- Diagnosis of Active Tb = detection of mycobacteria (microbiologic diagnosis)

(more) Key messages

- Must rule out Active Tb before treating Latent Tb
- 4 months rifampin is preferred Latent Tb regimen
- Management of Active Tb should be referred for specialist care

Thank you

back to Heather...

TB resources for primary care

- TB resources for primary health care sheet will be emailed to attendees
- <u>halton.ca/physicians</u> > Communicable diseases > Tuberculosis
- TST skin test video, Ottawa Public Health

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- Call 311
- TB Public Health Nurse
 - 905-825-6000, ext. 7341



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Questions?

Email <u>doctors@halton.ca</u> Call 311 or 905-825-6000, ext. 7341





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Thank you!

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