## Modern contact investigation methods for enhancing tuberculosis control in Aboriginal communities

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The Aboriginal communities in Canada are challenged by a disproportionate burden of TB infection and disease. Contact investigation (CI) guidelines exist but these strategies do not take into account the unique social structure of different populations. Because of the limitations of traditional CI, new approaches are under investigation and include the use of social network analysis, geographic information systems and genomics, in addition to the widespread use of genotyping to better understand TB transmission. Guidelines for the routine use of network methods and other novel methodologies for TB CI and outbreak investigation do not exist despite the gathering evidence that these approaches can positively impact TB control efforts, even in Aboriginal communities. The feasibility and efficacy of these novel approaches to CI in Aboriginal communities requires further investigation. The successful integration of these novel methodologies will require community involvement, capacity building and ongoing support at every level. The outcome will not only be the systematic collection, analysis, and interpretation of CI data in high-burden communities to assess transmission but the prioritization of contacts who are candidates for treatment of LTBI which will break the cycle of transmission. Ultimately, the measure of success will be a clear and sustained decline in TB incidence in Aboriginal communities.

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lthough Canada is considered a low tuberculosis (TB) incidence country, TB affects Aboriginal persons living on and off reserve with reported rates far greater than that of the overall population (1). The burden of TB in Aboriginal communities is not uniform across the country, and it often involves multiple inter-related medical and social issues (2). These issues include community-level factors such as geographic isolation, inadequate housing, underemployment, and limited access to health care, in addition to individuallevel risk factors such as chronic diseases (e.g. diabetes), substance use and mental health issues (2,3). Elevated rates of TB in some communities reflect recent transmission and outbreak activity, as well as reactivated disease from a large background pool of historic latent TB infection (LTBI).

In Canada, the public health priority has shifted away from active case management alone towards focused contact investigation (CI) as the principal method to identify people who have been exposed to TB, to evaluate these people for active TB (acquired through either "upstream" or "downstream" transmission with respect to the index case), and LTBI, and to provide appropriate treatment (4,5). Persons recently infected with TB are at increased risk of developing active disease and treatment of LTBI can prevent this occurrence and subsequent transmission (4). Combining these activities with effectively targeting those at greatest risk for progression to active TB once infected (e.g. persons with HIV infection) should reduce TB incidence.

Despite targeted testing and enhanced surveillance efforts, national TB rates have generally reached a plateau in Aboriginal persons though in some areas, incidence is rising, particularly in more remote Northern communities (1). Successful CI, which includes the treatment of latent TB in infected contacts, is extremely important in

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Aboriginal communities because of the disproportionate burden of disease. Novel approaches to CI, as a means to better identify and treat those contacts with TB infection, as well as contacts who may actually have active disease, may lead to improvements in TB control efforts in communities.

#### **Tuberculosis contact investigations**

## Guidelines and evidence base for tuberculosis contact investigations

Present CI practices are based upon consensus expert opinion and originated from the advent of available and effective treatment for TB and LTBI (6–8). Strategies for the evaluation of contacts have historically given priority to close, household contacts or those at greatest risk for infection (e.g. young children) or progression to active disease (e.g. HIV infected persons). The closeness of contact has been defined by the amount of time spent in a shared airspace per week with minimal emphasis on specific environmental or social factors. Expanding the screening circle to non-household, casual and community contacts often depends on the results of initial tuberculin skin testing (TST) screening in close contacts.

It is well known that TB transmission also depends on the period and level of infectiousness (e.g. smear status, chest radiograph findings) of the source case as well as the environment (e.g. large open space with good ventilation vs. small enclosed space) in which exposure occurs. While contact vulnerability and other risk factors play a key role in TB infection and subsequent disease, the determination of a precise infectious period, which ultimately influences the prioritization of contacts, remains difficult in many cases. National and international guidelines on tuberculosis CI are available and vary widely on recommendations though none are specific to Aboriginal communities (6–8). However, the challenges of contact tracing within marginalized groups or in remote communities, are acknowledged in all.

## Challenges with present tuberculosis contact investigation strategies

Several limitations in CI have been documented including issues with contact identification, screening completion and LTBI treatment initiation and completion (9,10). These problems are amplified in certain vulnerable groups, such as homeless and other marginalized persons. Conventional CI relies on a person knowing all of their contacts and their willingness to share their contacts names, and does not easily account for contacts of highly mobile persons, especially when their daily activities do not follow a fixed permanent routine, or in transient circumstances. Standard practice has often focused on the person alone, ignoring the role that non-traditional environments (e.g. non-household places of social aggregation) and casual contacts play in the transmission of TB (11). Although locations are important factors in TB transmission, the routine use of location-based screening is not widespread. Also, approaches to eliciting contacts are generally unstructured and rely on histories gathered by health care workers with different levels of contact interview experience (12). Finally, the completion of LTBI treatment, one of the main reasons to do CI in the first place, remains a significant barrier both within and outside of communities.

## Tuberculosis contact investigation in Aboriginal communities

Published literature on routine CI in Aboriginal communities is limited. Detection of LTBI in Aboriginal communities is often done through local community screening and surveillance programs. Given the burden of TB in Aboriginal communities, one can argue that successful completion of CI is a very important public health measure. Anecdotally, there are inherent challenges to conducting effective CI in some settings including community isolation, language and cultural barriers, as well as the social stigma associated with TB. Human power and resource shortages also represent an important challenge in Aboriginal health as there is often no permanent or full-time nurse available in a given community to implement TB programming. Also, access to the internet and up to date information technology is not always available in community. Other responsibilities that extend beyond TB (e.g. H1N1 pandemic planning) can impact a nurse's ability to provide recommended TB programming. Further, CI often involves generating long lists of persons identified for evaluation and subsequent follow up, and tracking of contacts quickly becomes cumbersome. Incomplete and inadequate CI leads to missed opportunities to identify secondary active cases and ensure the identification and treatment of infected contacts, both of which can limit the cycle of transmission and lessen the burden of TB. Successful treatment of LTBI is the main purpose of contact tracing. The importance of treating infected contacts cannot be overemphasized though is not the focus of this discussion.

# Newer methodologies available for use in tuberculosis contact investigations in Aboriginal communities

Due to the limitations of routine CI and the negative consequences of inadequate CI, new approaches are under investigation, and in some cases in use, to ensure effective TB control in those persons and communities at greatest risk. A recent publication detailed some of these newer methodologies in the context of TB contact tracing in low prevalence (e.g. developed) countries including social network analysis (SNA), geographic information systems (GIS) and genomics (13). How these approaches could be implemented in Aboriginal communities facing a significant burden of TB is not yet clear and requires investigation. A thorough examination of each methodology is out of the scope of this manuscript but a brief description of how these novel methodologies have facilitated TB control in Aboriginal communities to date is outlined below. It should be emphasized that routine or traditional CI is always indicated for infectious TB cases and that the expectation is that additional resources should be sought to implement newer methods.

#### Social network analysis

The success of a network-informed approach to CI in sexually transmitted infections (STIs) led to its use in TB control, in particular for its potential to identify how TB cases are connected to one another and to identify and prioritize contacts for evaluation (14,15). Social network methods, alone and in combination with conventional and molecular epidemiology, have been used to examine TB clusters and outbreaks both retrospectively and prospectively in both Aboriginal and non-Aboriginal settings (16-23). Network methods have also clearly documented that locations are key to the evaluation of TB transmission. Focusing on locations and locationbased contacts has been shown to link cases and contacts which otherwise do not fit the traditional expectations of contact interactions (23). With respect to Aboriginal TB control, network analysis has helped to understand outbreak boundaries, locations of transmission and the risk of TB in contacts in remote communities in Manitoba. These methods were also used to investigate a developing TB outbreak involving Aboriginal persons living on and off reserve in British Columbia, as well as a northern shelter outbreak (V. Cook, UBC. Verbal communication, Shah L, PhD Student, McGill University. 2011 May 1).

#### Geographic information systems

Geographic information systems (GIS) and global positioning systems (GPS) are tools used to visualize data involving distance and location. These techniques have been used to examine the distribution of TB cases, risk factors for acquiring disease, and the relationship of TB to the surrounding environment and health care system (24-26). In lower incidence settings, TB rates are most often attributed to immigration patterns. However it is interesting to note that investigators have clearly demonstrated that it is the deprivation of certain ethnicities, not only high prevalence immigration backgrounds, which influences TB disease rates (24). There are no published studies looking at GIS/GPS specifically in Aboriginal communities. However, the results available to date, particularly where they relate to the determinants of health, may be highly relevant and applicable in some communities.

#### Genomics

Current molecular epidemiology methods for investigating TB include simple DNA fingerprinting techniques such as RFLP/PFGE and more advanced techniques based on sequencing, such as MIRU-VNTR. While these methods can readily identify clusters of related cases, they cannot provide further detail, such as the resolution of individual transmission events within a cluster. Rapid advancements in DNA sequencing technology have made whole genome sequencing of bacteria like Mycobacterium tuberculosis quite tractable - a genome can be sequenced in as little as 1 day for 50-250 – and the resulting data can now be used to understand transmission dynamics at a much higher resolution. In a recent TB outbreak investigation involving Aboriginal persons, genomic data from the outbreak organisms was able to identify transmission events, individuals acting as superspreaders, and confirm parallel related, yet distinct, outbreaks within the community (27). This investigation integrated clinical data, social network analysis and genomics to better characterize a TB outbreak that had significantly affected community members. It also confirmed that social factors played a larger role in the outbreak than organism virulence or ethnicity.

# Recommendations for the integrating novel approaches to tuberculosis CI in Aboriginal communities

The feasibility and efficacy of network methods and other novel approaches to CI in Aboriginal communities is unknown but it will be important to develop multidisciplinary initiatives to enhance the understanding of TB in Aboriginal populations using available technologies. A systematic and coordinated approach to CI, both in outbreak and non-outbreak settings and across jurisdictions (e.g. both on and off reserve), will be essential to integrate these novel approaches and strengthen TB control efforts. GIS/GPS, molecular and conventional epidemiology, social networks and genomics will likely all play an important role in facilitating TB CI and further understanding of TB transmission in Aboriginal populations.

It must be emphasized that novel methods are meant to supplement and not supplant routine activities. Success depends on a strong foundation of routine contact tracing in community which relies on community buy-in, the interview skills of local health care workers, as well as dedicated resources to undertake thorough contact evaluation and follow-up. Efforts should be made to develop contact tracing interview tools that are culturally sensitive or adapt those in use for Aboriginal communities whether network methods, or other novel approaches, are in use or not.

Key recommendations were detailed in a recent publication on novel approaches to TB CI and are relevant to their use in Aboriginal communities (13). These recommendations focused on questionnaire development and adaptation, electronic data management and software needs, capacity building and coordinated consultant expertise. In the absence of local expertise in every jurisdiction, governing bodies should identify and train epidemiologists and analysts to integrate these novel techniques into standard CI practice. It has been suggested that these "TB epidemiology specialists" act as expert consultants to support CI activities in the field. For example, this position could support the development of dedicated teams or units that facilitate network and other novel methods for TB CI across the country to complement the work of field epidemiologists.

#### **Future directions**

There are many important areas for further investigation in the use of novel methodologies to support TB control in Aboriginal communities. Given that SNA has been successfully implemented in some communities with a higher burden of TB disease, a research plan might choose to focus on ensuring the approach is systematic and applicable to most groups. Future research has been detailed previously in the literature (13). Key areas include: the development and validation of a network-informed CI interview tool; the type, extent and use of CI data collected, including places of social aggregation; infrastructure needs and available local expertise; and the utility, feasibility and evaluation of coordinated approaches that use one or more novel methodologies. To successfully integrate these newer methodologies to TB CI in Aboriginal communities, it will be imperative to:

- (a) Develop culturally sensitive and appropriate interview tools that can be adapted for and in consultation with Aboriginal populations
- (b) Determine the presently available infrastructure in Aboriginal communities and determine those communities that may benefit from integrating novel methodologies
- (c) Support capacity building by facilitating basic CI training for health care professionals working in TB, particularly for those working in high incidence communities
- (d) Determine if SNA and other methodologies (either alone or in combination) are feasible, useful and cost effective to supplement TB CI in Aboriginal communities both in routine (up front) use or during outbreak investigation
- (e) Evaluate potential deployment strategies in Aboriginal communities
- (f) Develop a network of experts both locally and nationally for communities to access for support in

implementing novel CI strategies, and to support the systematic collection and analysis of CI outcomes using these novel techniques

From the available data, it seems clear that novel approaches to CI may enhance TB control efforts in Aboriginal communities. Specific deployment strategies have been discussed in the literature and can be adapted for use in Aboriginal communities (13). A networkinformed approach to TB CI, which could begin with social network analysis, should be considered in, but not limited to, the following circumstances:

- (a) Outbreak scenarios or in communities with a continuing high incidence or burden of TB cases (endemic TB)
- (b) Sporadic (non-outbreak) TB cases if the source is highly infectious or marginalized, or is diagnosed in a community challenged by social determinants of health
- (c) Smear positive case and/or culture positive respiratory TB cases, if no clear single source is identified
- (d) Clustered cases (in the sense of time and place) before genotyping results become available, especially if no single source is identified or in small, geographically isolated communities where there has been historical documentation of consistent genotype(s)
- (e) Pediatric TB or pleural TB (e.g. primary TB reflecting recent transmission) if no clear single source is identified

#### Conclusions

The Aboriginal communities in Canada are challenged by a disproportionate burden of TB infection and disease. Contact investigation (CI) guidelines exist but these strategies do not take into account the unique social structure of different populations. The incidence of TB disease in Aboriginal people living on and off reserve will not decline in the absence of effective and organized CI. Guidelines for the routine use of network methods and other novel methodologies for TB CI and outbreak investigation do not exist despite the gathering evidence that these approaches can positively impact TB control efforts, even in Aboriginal communities. The feasibility and efficacy of these novel approaches to CI in Aboriginal communities requires further investigation. Work that has already taken place in communities requires analysis and dissemination. The successful integration of these novel methodologies will require community involvement, capacity building and ongoing support at every level. The outcome will not only be the systematic collection, analysis, and interpretation of CI data in high-burden communities to assess transmission but the

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