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Alaska's Ongoing Journey with Tuberculosis

A Brief History of Tuberculosis in Alaska and Considerations for Future Control

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Introduction

Tuberculosis (TB) is an ancient disease that has had a devastating impact on Alaska in the past. Despite massive and ongoing public health effort and advances in diagnostic tools, chemotherapy, and medical care, TB continues to cause serious illness and occasionally death among Alaskans. The purpose of this report is to provide a short review of Alaska's TB history and the challenges we face going forward. While great strides have been made controlling TB in Alaska, the dream of TB elimination is not at hand, and until that time, the threat of TB transmission and disease will remain.

Early History of Tuberculosis in Alaska

One of the oldest human diseases, people have been living and dying with TB for millennia. DNA fragments of *Mycobacterium tuberculosis*, the causative agent for TB, have been found in Egyptian mummies dating back to 3400 BC.¹ Tuberculosis was common in both ancient Greece and Imperial Rome and widespread in Europe and many U.S. cities in the 1800s.² Archeologic investigations have documented the presence of TB in the western hemisphere long before the arrival of the first European explorers.³ Studies of frozen human remains on St. Lawrence Island and Barrow suggest there may have been some TB transmission occurring in Alaska for at least 1,500 years.⁴

Alaska's current TB epidemic started in the late-1700s to the mid-1800s with the arrival of white explorers, fur traders, whalers, gold miners, and other immigrants, many of whom came from areas with high TB rates.⁵ During that period, TB was a leading cause of death in the U.S. and in many European countries.⁴ Tuberculosis rapidly spread among Alaska Native people, a susceptible population living under conditions ideal for TB transmission and dissemination, especially those with close contact to the incoming colonists (Box).⁴

During the first half of the 20th century, Alaska had some of the highest rates of TB ever seen anywhere in the world. Alaska Native people experienced extraordinary rates of disease and death from TB.

A 1934 review of death certificates by Dr. FS Fellows, Director of the Alaska Medical Service, U.S. Office of Indian Affairs, found the following: "*Among the native Indians and Eskimos tuberculosis stands out far above any other cause of death, with a death rate of 655 per 100,000 for the whole native population of Alaska. Tuberculosis constitutes 35 percent of all deaths among the [Alaska] natives, a figure which does not vary greatly in the different divisions.*"⁶ Mortality rates were highest among Native children under age 5 (900 cases per 100,000 children).⁶

In 1945, 20% of all deaths in Alaska were from TB and, until 1950, TB was the leading cause of death in Alaska.⁴

Surveys conducted from 1948–1951 found that TB was most serious along the lower Yukon and Kuskokwim Rivers where 75% of Alaska Native children aged <8 years (and 92% of those aged 7–8 years) had positive tuberculin skin tests. The average annual infection rate was 25% among children aged 0–3 years. In radiographic surveys, 30% of adults had radiographic findings of past or present pulmonary TB. In other regions, 32% of Alaska Native children in Southeast Alaska and the Aleutian Islands and 56% of children in the Interior region were found to be infected with TB.⁷

Before effective antibiotic treatment for TB, isolation and supportive care of persons with TB disease in hospitals and sanitariums was the mainstay of care. Sanitarium care offered fresh air, sleep, wholesome food, and exercise. Alaska's first sanitariums opened in

Box. An excerpt from *Must We All Die? Alaska's Enduring Struggle with Tuberculosis*, by Dr. Robert Fortune⁴

"With the first shore settlements of the Russian American Company at the beginning of the 19th century came a period of harsh living conditions, near starvation, and warfare, all of which were conducive to the development of tuberculosis among rank and file Russian workers, many of whom may have arrived in Alaska with the disease.

Within a few decades, living conditions had improved considerably in the colony and basic medical services were available. By mid-century, consumption was recorded as the main cause of death at Sitka and Kodiak, particularly among the Creoles and Aleut women, both groups living in close and sometimes intimate contact with the Russians. Other types of tuberculous disease were also recorded, including scrofula, bone and joint involvement, meningitis, and hectic fevers.

Based on available evidence, there was little tuberculosis among the Tlingit living in their own village in Sitka, with whom the Russians had limited contact."

former Army hospitals in Skagway in 1945, Seward in 1946, and in Sitka in 1947.⁴

The efficacy of sanitarium care was unproven. Some studies found a modest reduction in mortality rates among persons treated in sanitariums, others did not. Isolation of persons with TB in sanitariums likely reduced the burden of disease and the risk of disease transmission in their home communities, but at great psychological and emotional distress for patients, families, and communities.

The 1954 Parran Report, *Alaska's Health: A Survey Report to the United States Department of the Interior*, clearly described to Federal and Territorial officials Alaska's dire TB situation and critical need for personnel, programs, and equipment to control the epidemic:

*"Tuberculosis is the Alaskan scourge. Only by a "crash" attack carried on with increasing intensity during the next five years will it be possible to break the back of this Number 1 killer of young men and women andcrippler of children. Such a program involves not only the full-scale employment of all proven methods such as systematic case finding, the hospitalization of every person needing it, but the immunization of infants and the extensive use of anti-tuberculosis drugs which are widely used in the states to break the chain of infection."*⁸

Period of Dramatic Decline in TB Incidence

Alaska's TB epidemic started to decline considerably by the late-1950s (Figure 1). Many factors contributed to turning the tide, but most important were the advent of effective chemotherapy in the early 1950s and a coordinated, collaborative effort by an array of Territorial (later State) and Federal agencies, including the Alaska Department of Health and Welfare, the U.S. Public Health Service, and the Indian Health Service.^{4,6}

Streptomycin was first used in Alaska in 1947, followed by P-aminosalicylic acid (PAS) in 1951 and isoniazid in 1952. Combination treatment with these three drugs for 18–24 months was required for cure.⁴ Studies in Alaska in the 1950s also demonstrated the effectiveness of isoniazid prophylaxis in preventing active (infectious) TB disease among persons with latent TB infection (LTBI).^{5,7,9}

In the Alaska Native population, the incidence of TB dropped from 1,854 cases per 100,000 population (649 cases) in 1952 to 436 cases per 100,000 population (188 cases) in 1960.¹⁰ Similarly, the Alaska Native TB death

rate dropped from 650 deaths per 100,000 population (227 deaths) in 1950 to 26 deaths per 100,000 population (11 deaths) in 1960.^{4,10} In the Yukon Kuskokwim Delta, the average annual TB infection rate among children aged 0–3 years dropped from 25% per year in 1950 to 1% per year in 1960.⁷

Alaska's TB epidemic was the driving force for the creation of the 200-bed Mt. Edgecumbe Hospital in Sitka that opened in 1950, the 400-bed Alaska Native Hospital in Anchorage that opened in 1953, and regional hospital facilities and clinics throughout the state. By 1954, there were over 800 TB beds available in Alaska.⁴

At the same time, the Territory of Alaska had established a formal public health program with epidemiologic and laboratory services and public health nurses. Public health nurses and village "chemotherapy aides" (now Community Health Aides) played a vital role in case-finding and TB treatment.

Since the 1960s, Alaska TB control has focused on case finding, isolating and treating persons with active TB, and finding and treating persons with LTBI. Because of these intensive efforts and the availability of effective chemotherapy, Alaska's TB incidence and mortality declined sharply over the next 30 years: the incidence dropped from 99 cases per 100,000 in 1960 to 12 cases per 100,000 in 1990, and the mortality rate dropped from 6 deaths per 100,000 to <1 death per 100,000 over the same period.⁴ Moreover, short course (6- to 9-month) treatment for active TB became possible in the early 1970s when rifampin and ethambutol became available.⁴

Recent History of Tuberculosis in Alaska

While the incidence of TB in Alaska has continued to decline since the precipitous drop in the 1950s and 1960s, Alaska continues to have the highest or second highest TB incidence in the nation.¹¹ In 2016, Alaska's TB rate was nearly three times higher than the national rate (Figure 2).¹²

During 2011–2015, 334 Alaskans were identified with active TB; 73% were Alaska Native people and 17% were Asian/Pacific Islanders. Many of the Asian/Pacific Islander cases acquired TB infection in their home country prior to arriving in Alaska. Alaska Native people from the Northern and Southwest regions of Alaska, the areas devastated by TB half a century ago, continue to be disproportionately burdened with TB.¹³

Flare-ups of TB in rural villages are an ongoing problem, triggered by activation of disease in persons with untreated infection and persons previously treated for active disease. Controlling these outbreaks requires an intensive, extended, and collaborative response. The cost of controlling a large TB outbreak in one Yukon-Kuskokwim Delta village in 2013 was estimated to be >\$1,000,000.¹⁴

Anchorage has had ongoing problems with TB in its homeless population. Transmission in homeless camps and possibly shelters, an influx of persons with active disease from rural villages, and limited housing and healthcare services are likely contributing factors.

Drug resistant TB is a growing problem globally and in the United States. During 2010–2015, 30 cases of isoniazid resistant TB were reported to the Section of Epidemiology.¹³ Many of the recent isoniazid resistant cases are attributable to one village outbreak that has not yet been completely controlled.¹³ During 2010–2015, seven cases of multi-drug resistant (MDR) TB were reported to the Section of Epidemiology,¹³ one each in 2010, 2012, 2014, and four in 2011. Two of the MDR cases in 2011 were from the same household; one of these cases was in a foreign-born person. The other two cases of MDR TB in 2011 were in unconnected foreign-born individuals. The one case of MDR TB in 2012 was from an individual whose only other risk factor for TB was volunteering at various sites in a post-Soviet state just prior to illness. The MDR case from 2014 was in a foreign born individual from Southeast Asia.¹³

Alaskans continue to die with TB. During 2011–2015, 17 deaths were determined to be related to TB.¹³ Some were only diagnosed post-mortem, never having received medical evaluation.

Both in Anchorage and elsewhere in Alaska, excessive alcohol use is a complicating problem for many persons

with active TB. During 2011–2015, 38% of active cases had excessive alcohol use documented.¹¹ Heavy alcohol use is associated with higher risk for TB acquisition. Moreover, persons with TB and excessive alcohol use are more difficult to treat, often experience treatment interruption and delayed culture conversion, and are at increased risk of death from TB, other medical conditions, environmental exposures, and trauma.¹³

For >20 years, directly observed therapy (DOT) has been the standard of care for persons with active TB in Alaska.¹⁵ This has helped ensure that persons complete therapy quickly and safely. However, Alaska continues to encounter persons who are non-compliant or become lost to follow-up. Often these persons have challenging personal situations, including homelessness, alcoholism, and mental health issues.

The past 5 years have seen the arrival of new TB diagnostic tools in Alaska. The Quantiferon test, an interferon gamma release assay (IGRA), is being used in Anchorage and several other locations for testing persons for TB infection. This test is especially useful for testing foreign-born persons with prior BCG vaccination. The Alaska State Public Health Laboratory (ASPHL) now has the GeneXpert MTB/Rif PCR system to rapidly test for *M. tuberculosis* and rifampin-resistance mutations. Molecular testing for drug resistance mutations is available at the Centers for Disease Control and Prevention (CDC) and the National Jewish laboratories, with results returning in a few days compared to the several weeks required for standard drug resistance testing.

Also new in the past 5 years are short course regimens for LTBI: a) isoniazid and rifapentine once weekly by DOT for 12 weeks, and b) rifampin daily for 4 months. These regimens are increasingly being used whenever possible to enhance the likelihood of LTBI treatment completion.

Figure 1. Alaska and the United States TB Incidence Rates, 1952–2016

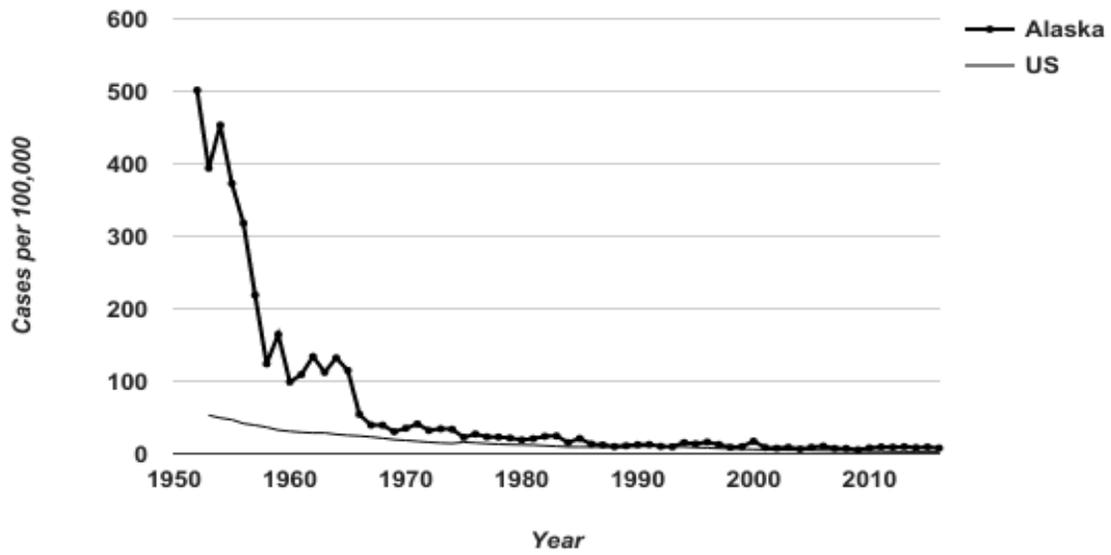
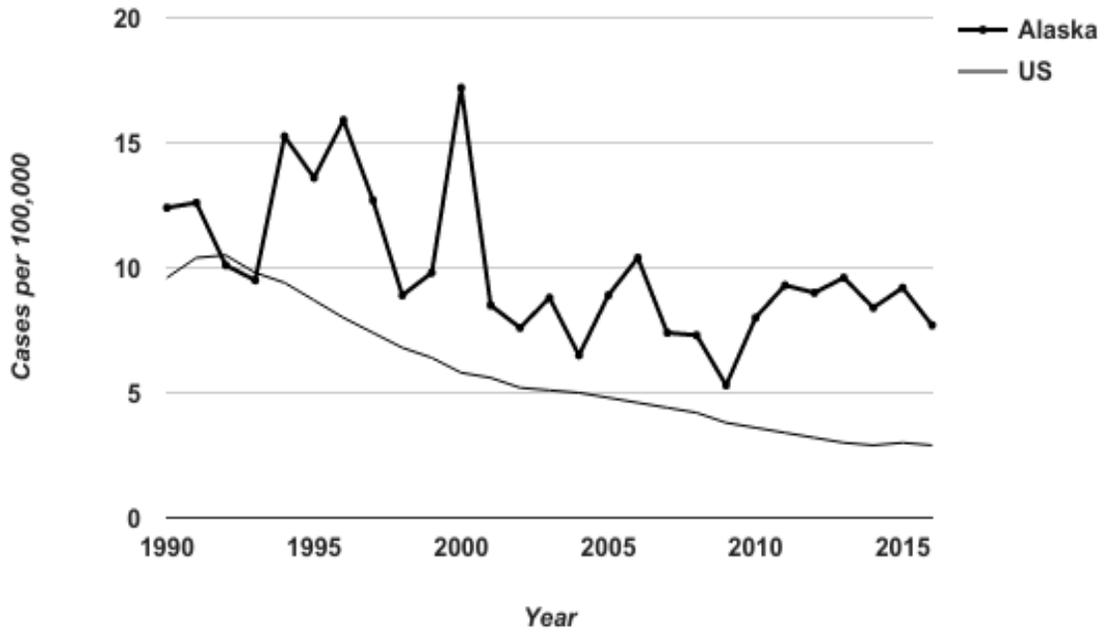


Figure 2. Alaska and the United States TB Incidence Rates, 1990–2016



Ongoing Challenges

1. Tuberculosis treatment is not easy, cheap, or quick. Despite extensive and ongoing research for a shorter treatment regimen, a person with fully susceptible TB still requires combination treatment with multiple drugs by DOT for a minimum of 6 months. New TB treatment guidelines in 2016 favor daily DOT at least 5 days per week. The minimum recommended DOT frequency is 3 days per week; twice weekly treatment is no longer recommended due to the higher risk of relapse.¹⁶ Persons with MDR TB require a minimum of 18 months of daily DOT, with a combination of medications often costing well over \$100,000, in addition to intensive monitoring, medical care, and case management.
2. Alaska's vast land area, cold climate, and dependence on airplanes for travel to many rural regions pose challenges not found elsewhere in the Nation.
3. Tuberculosis control in Alaska and elsewhere is ever-threatened by limited and often diminishing public health funding, personnel, and resources.
4. In 1952, René and Jean Dubos wisely noted in *The White Plague: Tuberculosis, Man, and Society*: "Tuberculosis is a social disease, and presents problems that transcend the traditional medical approach. Its understanding demands that the impact of social and economic factors on the individual be considered as much as the mechanisms by which the tubercle bacilli cause damage to the human body." Sixty years later, many Alaskans with TB struggle with additional complicating problems, such as homelessness, drug and alcohol abuse, mental health impairments, poverty, and difficulties accessing needed health care and social services. Successful TB treatment often depends on simultaneous attention to every patient's unique personal and medical needs, which is often more challenging than treating the disease itself.
5. Further curbing TB transmission in Alaska will require extra effort to find and treat persons with latent TB infection to prevent future disease. Since the arrival of effective TB chemotherapy in the 1950s, the first priority of TB control has been on finding, isolating, and treating persons with active disease. But even in the 1950s, public health experts recognized the need to find contacts and to treat persons with LTBI to prevent them from developing TB disease in the future.

Sixty years later, we continue to have new eruptions of TB in different communities and villages, triggered by a person who develops TB disease often years or decades after becoming infected.

6. More work is needed to destigmatize TB. Persons who are newly diagnosed with TB sometimes experience profound fear that others will learn of their illness and they will suffer negative social consequences. As such, they may be reluctant to name their close contacts to clinicians and public health practitioners or to allow a DOT aide to come to their home. Public education is the cornerstone of destigmatizing TB, and can include targeted, culturally-appropriate campaigns (e.g., for foreign-born persons, Alaska native or American Indian people living in villages, and the homeless population) to relay the importance of TB as a personal and public health threat, the symptoms to look for, how to access testing services, and the concept of LTBI.¹⁷
7. We must think TB to find TB. Many persons view Alaska's TB problem as a historical footnote, not an ongoing problem. Thanks to a half-century of hard and dedicated work, many Alaskans in urban areas are unaware of Alaska's ongoing TB problem. Many health care professionals in Alaska now have limited TB education, training, and experience. We continue to see patients with a delayed diagnosis because they were thought to have cancer or other conditions; sometimes their real diagnosis only becomes clear after death. The need for further education never ends.

Conclusion

More than 100 years after the discovery of *M. tuberculosis* and more than 50 years after the advent of effective chemotherapy, the struggle to control TB in Alaska (and globally) continues, and eradication is not in sight. The World Health Organization estimates that in 2015, 10.4 million people contracted TB and 1.8 million died from it. Moreover, the challenges of controlling TB are mounting with the increasing incidence of drug resistant TB worldwide. In 2015, 480,000 of the new TB cases globally had MDR TB and only 1 in 5 people who needed treatment for MDR TB received it.¹⁸

Fortunately, research is ongoing on developing a) vaccines to prevent TB infection and disease, b) new drugs and new drug combinations that will allow shorter treatment regimens for both drug susceptible and drug resistant TB, and c) better diagnostic tools.

But for now, the focus remains on controlling TB with the resources we have. Now more than ever, successful TB control depends on a coordinated and collaborative alliance of Alaska's medical and social services providers and institutions; public health epidemiologists, laboratorians, pharmacists, and public health nurses; and DOT and community health aides who do the hard day-to-day work of finding cases, testing contacts, and administering DOT.

Recommended TB Resources

1. Alaska Section of Epidemiology Tuberculosis Program Manual. Available at:
http://dhss.alaska.gov/dph/Epi/id/SiteAssets/Pages/TB/TB_Manual.pdf
2. Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis. Available at:
https://www.cdc.gov/tb/publications/guidelines/pdf/clin-infect-dis.-2016-nahid-cid_ciw376.pdf
3. The Alaska Directly Observed Therapy (DOT) Manual. Available at:
<http://dhss.alaska.gov/dph/Epi/id/SiteAssets/Pages/TB/Tuberculosis%20DOT%20Manual.pdf>
4. Alaska Section of Epidemiology, Tuberculosis website. Available at:
<http://dhss.alaska.gov/dph/Epi/id/Pages/tb.aspx>
5. The Curry International Tuberculosis Center's "Drug-Resistant Tuberculosis: A Survival Guide for Clinicians, 3rd edition." Available at:
<http://www.currytbcenter.ucsf.edu/products/cover-pages/drug-resistant-tuberculosis-survival-guide-clinicians-3rd-edition>

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