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To link to this article: http://dx.doi.org/10.1080/0035919X.2017.1290709

Published online: 18 Apr 2017.
An epidemic uncurbed: tuberculosis in Cape Town, South Africa, 1910–2010

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Cape Town is unique among currently high-TB-burdened settings because detailed records are available, which span 100 years of public health attempts to bring the disease under control. Over the century, public health TB interventions were implemented which contemporarily mirrored those implemented in the industrialised cities of the Northern Hemisphere. Longitudinal observational data allow an exploration of associations between observed epidemiological changes and specific interventions. TB was never truly generalised but was consistently linked to socio-economic disadvantage. In the first half of the century TB treatment was focused on sanatorium treatment. While patients were observed to clinically improve immediately after admission, no long-term individual or public health impact was discernible. Following the introduction of chemotherapy in the 1950s, case fatality declined markedly but with less impact on non-European TB notifications. TB remains the commonest cause of natural death in the city. TB meningitis, a particularly pernicious form of the disease, frequently affecting children, peaked in the 1940s followed by a 100-fold decline and remains at low levels. In contrast, childhood TB also peaked in the 1940s but has returned to rates higher than those reported 100 years ago. High childhood TB rates are indicative of ongoing transmission and the recent HIV epidemic has further exposed failure to control TB transmission. While Cape Town TB has waxed and waned over the decades, TB rates remain among the highest in the world and are at levels recorded 100 years ago. A fundamental question is, why have public health measures failed to control TB?

Keywords: Cape Town; tuberculosis; tuberculous meningitis; notification rate; mortality rate; sanatorium; mass radiography

INTRODUCTION

The tuberculosis (TB) epidemic of the late nineteenth and early twentieth centuries has been strongly associated with the large industrialised cities of the Northern Hemisphere where long-term records are available (Dubos & Dubos, 1952). The introduction of compulsory death certification in the late nineteenth century enabled quantification of TB as a major cause of mortality. Compulsory TB case notification in the early twentieth century enabled assessment of TB population disease burden. In contrast, the historical trajectory of TB in currently high burdened settings such as China, Indonesia, sub-Saharan Africa and the Indian sub-continent has been limited due to the absence of both death and TB notification registries in these countries. The South African City of Cape Town, with a current population of 3.4 million, has an enormous annual TB burden, equivalent to the national caseloads of the USA, Canada, UK and France combined (Wood et al. 2011; World Health Organization, 2016). Cape Town is unique among currently high burdened settings because it was among the first cities globally to introduce compulsory TB notification. Therefore, for over 100 years, the city has reported TB specific data from an enumerated population while implementing contemporary TB treatments and control measures.

The first decade of the twentieth century saw the introduction of embryonic public-health efforts against TB in the City of Cape Town. Dr Anderson was employed as the first full-time Medical Officer of Health (MOH) in 1903 and he introduced compulsory notification of TB cases in 1904, almost a decade prior to the UK. Failure to notify TB cases resulted in a hefty £10 fine. An anti-spitting ordinance was instituted in 1905. The City Hospital for Infectious Disease, which had been in military control during the Anglo-Boer War, was transferred to civic control and became the hub for TB diagnosis and management in 1901. The scale of the urban TB burden was recognised to require increased resources and civil society engagement by the founding of the Society for Prevention of Consumption in 1911, whose membership enabled funding of the Nelspoort TB sanatorium (Pelteret, 2008).

The Cape Town historical records from 1910, therefore, provide a unique opportunity to observe long-term ecological data and concurrent control measures within an established TB public health programme. The period of observation incorporates sequential TB control measures, both before and after the availability of chemotherapy in the 1950s, and the impact of the more recent HIV epidemic. However, the reliability of TB reporting by healthcare staff may have varied over time and the more severe forms of TB, particularly hospitalised childhood TB, may have been under-reported (Du Preez et al., 2011).
METHODS

Population denominators

Estimated mid-year populations of Cape Town were extracted from the MOH annual reports and the National Department of Health Information System Programme (Statistics South Africa http://www.statssa.gov.za). Age and racial strata were calculated from population pyramids of national censuses performed in 1911, 1922, 1960, 1970, 1980, 1985, 1991, 1996 and 2001 (Statistics South Africa http://www.statssa.gov.za). Age and racial denominators were interpolated for the intervening years between censuses.

TB case identification

TB case and TB meningitis notifications, stratified by age and racial group, were abstracted from the MOH annual reports 1910–1994. After 1995 TB notifications were no longer stratified by racial group but case numbers were extracted from the City TB Progress Report 1997–2003 (Cape Town TB control 1997–2003) and subsequently TB notifications, stratified by age and HIV status, from the city electronic TB record for the years 2004 to 2009.

TB mortality, notifications and case fatality

TB death certifications including TB meningitis deaths were abstracted from MOH reports from the Cape Town Burden of Disease study (Groenewald et al., 2008) and annual Statistics SA reports. TB case fatality was calculated from annual TB deaths as a proportion of annual TB notifications.

RESULTS

Population growth

The growth of Cape Town populations stratified by racial group is shown in Figure 1. Two major defining periods for the city occurred: in 1913 with the amalgamation of the central with surrounding metropolitan areas, and in 1996 with the creation of the Cape Town Unicity.

Prior to 1913, Cape Town consisted of the harbour area and the surrounding natural amphitheater enclosed by a backdrop of Devil’s Peak, Table Mountain, Lion’s Head and Signal Hill. The pre-amalgamation population was 67 531, consisting of 50% European and 50% non-Europeans predominantly mixed race. Immediately following amalgamation the population increased to 144 731 and the city area increased 10-fold (MOH reports; Cape Town History and Heritage http://www.capetown.at/heritage/history/1910.htm). In the decades following the creation of the metropolitan area, the city grew in all directions, South along the Atlantic Coast, East around Devil’s Peak and North East along the shore of Table Bay.

In 1996 the Cape Town metropolitan area was expanded to include six municipalities; Cape Town Central, Tygerberg, South Peninsula, Blaauwberg, Oostenberg and Helderberg. These boundary changes, together with inward migration, increased the population to over 2 million. The 2009 population of the Cape Town Unicity was estimated to be 3.4 million consisting of 44% mixed race, 35% black African, 19% European and 2% Asian (MOH reports; Cape Town History and Heritage http://www.capetown.at/heritage/history/2006.htm).

Social changes

Cape Town exists within the complex socio-political environment of South Africa. In the early British era, after the release of slaves in the 1830s, large numbers of “free blacks” required housing in Cape Town. They had only limited incomes and former slave owners took advantage of the situation to develop slum areas. District 6 was one slum community made up of former slaves, artisans, merchants and immigrants and was home to almost a tenth of the city’s population. Most houses were small, without water or sewerage, jumbled together between narrow alleyways, many consisting of only one room housing as many as 16 people (Cape Town History and Heritage http://www.capetown.at/heritage/city/district%206.htm, South African History Online, 2011).

The Second World War brought convoys of ships through Cape Town which greatly boosted the demand for food and clothes, resulting in rising food prices and scarcity of meat and fish. Requests to the government for equitable food rationing were rejected. Frustrated by the lack of action, housewives marched upon Parliament to demand food rationing and a ministry of food. The result was price controls at Salt River Market and mobile markets in poorer districts. In 1941 severe flooding on the Cape Flats resulted in the formation of soup kitchens and a Flood Relief Board (Legassick, n.d.; South African History Online, 2011).

During the war and post-war boom, African migration increased due to improved work opportunities. However, in the 1940s the City was granted wide powers to reverse inward African migration by influx control (Legassick, n.d.; South African History Online, 2011). The election of the Nationalist Party in 1948 and the subsequent Group Areas Act of 1950 initiated 40 years of forced removals of large segments of the non-European populations. Between 1957 and 1961 over 100 000 people were removed from Lansdowne and in 1966 over 60 000 people were forcibly removed from District Six to townships on the Cape Flats (Legassick, n.d.). The City of Cape Town remains a very unequal society with a Gini coefficient (Gini, 1997) of 57 in 2010.

Following the democratisation of South Africa in 1994 the 61 municipalities of Greater Cape Town were amalgamated into seven local government authorities. In 2000, the Municipal Structures Act led to the establishment of the Cape Town Unicity, providing an integrated metropolitan tax base to address the inequitable provision of services of the apartheid era (Swilling & Annecke, 2012). Within a relatively short period the population of Cape Town mushroomed with an increase in the proportion of black citizens and the incorporation of crowded informal settlements.

TB control measures

A timeline of TB interventions sequentially implemented in Cape Town is shown in Figure 2. Cape Town was also one of the first cities to introduce the Edinburgh TB management scheme in 1910. The Edinburgh integrated TB management system, developed by Sir Robert W. Philip, remained the basic framework for TB diagnosis, treatment and care in the
city and throughout the British dominions and colonies until the advent of chemotherapy in the 1950s (Wallace, 1961). TB cases were diagnosed and triaged by clinical, laboratory and radiology at the TB dispensary located in the City Hospital. Early cases were identified for sanatorium therapy and advanced cases were sent for terminal care to the old smallpox isolation hospital at Rentzkies Farm Hospital, which later became the site of Brooklyn Chest Hospital. Before the opening of the dedicated Nelspoort Sanatorium in 1924, rest and open-air “sanatorium” therapies were provided in small wooden chalets located in the grounds of the City Hospital. Health inspectors were employed from 1913 to perform fortnightly visits of all TB cases to ensure adequate patient nutrition, compliance with rest and for disinfection of premises.

A watershed for TB treatment occurred in the 1950s with initially single streptomycin therapy, quickly followed by free anti-tuberculosis combination chemotherapy in 1953. The 1950s also saw a large programmatic drive for active TB case finding with mass radiography. An interesting observation included in the annual reports was the finding that many of the cases identified radiologically were surprisingly asymptomatic. Universal immunisation of neonates with intradermal Bacillus Calmette–Guérin (BCG) was introduced in 1959 (MOH reports). While most major medical advances in TB management were expeditiously implemented over the following decades, the implementation of antiretroviral therapy was delayed because of political intransigence.

Sanatorium

Edward Prince of Wales in 1924 formally opened a 460-bed sanatorium in Nelspoort, located 300 km from Cape Town in the Karoo. In common with most other heavily burdened cities, sanatorium capacity quickly fell below demand. In the 1924, 24% of the City notified cases were treated at Nelspoort sanatorium but a decade later less than 8% of new notifications could be accommodated. During the initial admission period a majority (60%) of patients were assessed as clinically improved however, less than 50% could be confirmed to be alive after 3 years.

Active TB case finding

A total of 3.3 million miniature radiograph examinations were performed between 1948 and 1994, 2.3 million (68%) at Chapel Street (1948–1996), 737 000 (22%) in mobile units (1965–1995) and 324 000 (9.8%) in Langa township (1966–1984). More than 10% of the population was screened per annum between 1952 and 1982, reaching a peak of 16% (123 000 radiographs) in 1975. The Langa facility opened in 1966 predominantly to screen new workers arriving in the City from rural areas and closed in 1984 when the unit was burnt down during civil unrest. Twenty thousand cases were identified by mass radiography with mean annual yields of 1616/100 000 at Langa. Diagnostic yields for the mobile and Chapel Street clinics decreased from 1123/100 000 in 1949–1958 to 86 per 100 000 between 1986 and 1995. The forced removal of 60 000 people from District 6 in 1966 removed a heavy TB burdened population away from the Chapel Street radiological screening facility. TB notifications steadily increased between 1970 and 2010, coincident with declining numbers and yield of active screening.

Tuberculosis notification and mortality

TB notification and mortality rates for 5-year periods between 1910 and 2009 are shown in Figure 3. The initial decline in TB notification rate was followed by an increase to a peak in the 1940s, a decline to a nadir in the 1960s and a sustained increase to peak again in 2010. The total population TB mortality rate paralleled the notification rate until a marked decline after the introduction of chemotherapy. The mean annual case fatality remained around 60%, which was unaffected by tuberculin treatment given between 1912 and 1923, the purchase of pneumotherapy apparatus and the Nelspoort

Figure 1. Mean 5-year population numbers in millions of the three main racial groupings of Cape Town between 1910 and 2010.
Figure 3. Total population tuberculosis (TB) notification (red bars) and TB mortality (blue bars) rates expressed as means for each 5-year period per 100 000 population between 1910 and 2010. Case fatality (TB deaths/TB notifications) is shown as a broken line corresponding to values on right-sided vertical axis.

Figure 2. A timeline showing the initiation of major tuberculosis (TB) control measures between 1910 and 2010.
sanatorium from 1924 to 1950. Following the introduction of chemotherapy the mean annual case fatality declined markedly to less than 5%.

TB notification and mortality rates for the European population and non-European populations of Cape Town for 5-year periods between 1910 and 1994 are shown in Figure 4 and Figure 5, respectively. From 1910 to 1950 both populations followed the temporal pattern observed in Figure 3, albeit with 3- to 4-fold higher rates in the non-European population. However, after the 1950s TB almost completely disappeared in the European population and showed an increasing decline until racial data was no longer recorded in 1994. In contrast, case fatality was similar in both populations both pre- and post-chemotherapy, indicating equitable access to chemotherapy for all notified cases regardless of race.

**Tuberculous meningitis**

Tuberculous meningitis (TBM) mortality rates are shown for 1910–1994 and TBM notifications from 1925 to 1994 in Figure 6. TBM is one of the most devastating manifestations of TB, and is almost always fatal in the absence of treatment. TBM predominantly affected the non-European population (80%) with children under 5 years bearing the highest (62%) burden. Reported case fatality remained around 95% until the availability of streptomycin in the late 1940s and combination therapy in the 1950s. The case notification rates mirrored those of non-meningeal TB; however TBM cases markedly peaked in the 1940s with a 76% decline in the 1950s (anteriorating the introduction of universal neonatal BCG) and a 77% decline in the 1960s. It is unclear what factors may have increased the TBM notifications in the 1940s. However, similar increases were observed in European, non-European and childhood notifications during this period.

**Childhood and adolescent TB**

The TB notification rates for children <5 years and 5–15 years are shown in Figure 7. Childhood tuberculosis notification data would have been impacted by the prevailing case definitions, the availability of chest radiology, with intensified contact tracing and in more recent years with chemoprophylaxis. The rates for <5 years were greater than 3-fold higher than 5–15 year-olds; however, troughs and peaks were closely mirrored in both age groups. In particular there was a marked decrease in case notification between 1945 and 1975.

**Human immunodeficiency virus epidemic**

TB notifications increased two-fold between 1990 and 2010, coinciding with an increasing HIV epidemic. TB epidemiologic data changed from MOH reports to the electronic TB record, which no longer included racial group nor included human immunodeficiency virus (HIV) status. However, by 1999 a majority of TB cases (87%) were tested for HIV, enabling the HIV-associated TB burden to be estimated at 50%. Retreatment TB constituted 30% of both HIV-associated and non-HIV-associated TB. The HIV-negative population contributed almost half of the overall disease burden and cumulative lifetime risks remained similar to those reported in the pre-chemotherapy era. Childhood TB rates, a measure of ongoing TB transmission, increased steadily between 1990 and 2010. The variable case survival estimated in the 1990s may have

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**Figure 4.** European population tuberculosis (TB) notification (red bars) and TB mortality (blue bars) rates expressed as means for each 5-year period per 100 000 population between 1910 and 2010. Case fatality (TB deaths/TB notifications) is shown as a broken line corresponding to values on right-sided vertical axis.
Figure 5. Non-European population tuberculosis (TB) notification (red bars) and TB mortality (blue bars) rates expressed as means for each 5-year period per 100,000 population between 1910 and 2010. Case fatality (TB deaths/TB notifications) is shown as a broken line corresponding to values on right-sided vertical axis.

Figure 6. Total population tuberculosis (TB) meningitis notification (red bars) and TB meningitis mortality (blue bars) rates expressed as means for each 5-year period per 100,000 population between 1910 and 2010. TB meningitis was not separately notified between 1910 and 1925. Case fatality (TB deaths/TB notifications) is shown as a broken line corresponding to values on right-sided vertical axis.
been sensitive to the completeness of TB case and TB death notifications. During the early HIV epidemic, euphemisms for HIV/AIDS were used to avoid consequential stigma. However, in the late 1990s, the method of collecting and collating statistics was reviewed and enhanced through training and standardisation (Bradshaw et al., 2006). HIV testing of TB cases within the TB control programme increased from 3% in 2003 to 92% in 2009. After 2002 public sector antiretroviral therapy (ART) increased rapidly and likely was associated with the downturn in case fatality.

**DISCUSSION**

We have presented unique data documenting a century of TB epidemiology from Cape Town covering two major civic re-organisations (1913 and 1996), 40-years of pre-chemotherapy, 40-years of combination chemotherapy followed by 20-years of an HIV co-epidemic. The time period also spans two world wars and post-1948 government sponsored forced removal of large proportions of the city population. The trajectory of the TB epidemic in the European population mimicked the time-course of TB in industrialised settings such as New York and London (Hermans et al., 2015). However, despite multiple sequential TB control efforts, the current TB caseload in the predominantly black and coloured populations remains at levels recorded in the early 1900s. The challenge is to develop some causal hypotheses from data that may contain spurious associations. Inference for causation is increased by the strength of association, temporality, plausibility, specificity and demonstration of biological gradient (Hill, 1965).

The halving of TB notification and TBM death rates following the municipal amalgamation of 1913, in the absence of any effective therapy, can be sufficiently explained by a doubling in population denominator with little increase in TB numerators, as more rural populations were incorporated into the city.

The relatively stable TB notification rate, TB mortality rate and case fatality rate between 1915 and 1950, was observed in both European and non-European populations supporting a hypothesis of minimal population impact of the current TB interventions over that period. The plausibility of this lack of effectiveness of the Edinburgh system of TB management is supported by evidence that recipients of sanatorium therapy, the major curative modality during this period, had no improvement in long-term survival.

The introduction of combination chemotherapy in 1953 was associated with a rapid decline in case fatality and mortality rate in European and non-European populations. A biological gradient is further demonstrated by the decline in TBM case fatality observed 5 years earlier than the general population fatality, which was consistent with the use of streptomycin, a partially effective monotherapy that became available in limited quantities during the late 1940s. However, the impact of chemotherapy on TB notifications is far less clear. European TB notifications consistently declined after 1954 and contribute minimally to the current population burden of disease. While non-European TB notifications declined 50% by 1970, rates gradually returned to pre-chemotherapy levels by 1995. The decline in TB notifications coincided temporally with a period of effective active case finding by widespread population-based mass radiography. Other potential explanations...
for adult disease include socio-environmental hazards for TB transmission, such as forced removals away from centrally placed TB facilities, crowding in transport and work environments (Richardson et al., 2016) and an increase in recurrent disease among a rapidly increasing population of TB survivors (Uys et al., 2009).

TB is a serious and more easily recognised form of TB, with an extremely high-untreated mortality that remained around 95% between 1910 and 1945. The highest TB rates coincided with periods of high childhood and adolescent notifications. Childhood TB rates represent recently acquired TB infection and are a measure of prevailing force of infection. However, the dramatic increase in TBM cases peaking in 1945–1950 indicates further probable unrecognised biological or socio-environmental factors. The initial decline of MTB caseload was associated with a decrease in other childhood TB but continued to decline to <5/100 000 following the introduction of the neonatal Bacillus Calmette–Guérin (BCG) vaccine programme in 1959. BCG given at birth is proposed to decrease the more serious forms of TB including TBM (Fourie, 1987). In contrast to decline to <5/100 000 in 1990 and >700/100 000 in 2005 (Kritzinger et al., 2003).

Inferences from observational data are subject to major caveats that the quality of observational data is subject to the vagaries of standardised diagnoses and variable data collection quality over long periods of time. The magnitude of HIV co-infection remained uncertain during the 1990s due to a failure to systematically collect HIV status data. Data collection also changed from a citywide perspective to a TB clinic-based data collection system in 1996. On a more conceptual level, a TB burden expressed as cases per 100 000 is predicated based data collection system in 1996. On a more conceptual level, a TB burden expressed as cases per 100 000 is predicated on an assumption that TB is homogeneous within that level, a TB burden expressed as cases per 100 000 is predicated on an assumption that TB is homogeneous within that observed racial grouping. Racial grouping is rather a surrogate indicator of socio-environmental factors that determine acquisition and progression of TB. Identification of heterogeneity of TB within populations will require more refined geographical analyses to identify such socio-environmental determinants.

In summary, the epidemiologic course of TB over the last century differed considerably from descriptions from industrialised settings (Hermans et al., 2015). TB rates in Cape Town have remained among the highest in the world. TB has never been a generalised epidemic but always linked to areas of socio-environmental deprivation. Chemotherapy, which has revolutionised individual prognosis, has been insufficient to control TB and a wider focus to address the socio-environmental conditions maintaining high rates of TB transmission is required.

ACKNOWLEDGEMENTS

We gratefully acknowledge the Health Department, City of Cape Town for the access to TB notification data and ongoing collaborative efforts to understand the TB epidemic in Cape Town, and the University of Cape Town Medical Library for access to the City of Cape Town Medical Officer of Health Historical Reports.

References


