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Editorial

The Rise and Fall of Tuberculosis and Atherosclerosis: First There Is a Mountain…

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See article by Tu et al., pages 378–384 of this issue.

First there is a mountain, then there is no mountain, then there is.

—Zen proverb and song by Donavan, British singer (1968)

By the beginning of the 19th century, tuberculosis had killed 1 in 7 of all individuals who had ever lived. In Europe, rates of tuberculosis began to rise in the early 17th century to a peak level in the 19th century, when it caused nearly 25% of all deaths. Among writers, Jane Austen, the Brontë sisters, John Keats, Elizabeth Browning, Anton Chekhov, Albert Camus, Franz Kafka, Henry David Thoreau, and George Orwell all succumbed. Urban poverty and overcrowding were strong risk factors for tuberculosis, but its reach extended to all levels of society.

In what is generally considered to be the first randomized controlled clinical trial in medicine, streptomycin was shown to reduce mortality in a series of young patients with active pulmonary tuberculosis.[1] However, by the time this study was published in 1948, the threat from tuberculosis had largely receded in Europe and North America. A better understanding of the pathophysiology of the disease, improved living conditions, better diagnosis, isolation of active cases, and better treatment all are assumed to have contributed to the decline in tuberculosis incidence and mortality.

Myocardial infarction was first clearly described in 1912.[2] The incidence of coronary heart disease (CHD) increased rapidly over the ensuing decades, peaking in the mid-1960s in North America and about a decade later in Western Europe. In 1977, it was belatedly recognized that CHD mortality had been falling in the United States for more than a decade, with an age-adjusted decline of approximately 25% across all age groups.[3] Since then, both the incidence and the case fatality rate of CHD have steadily decreased in the United States, with reductions in age-adjusted CHD mortality between 1980 and 2009 of 66% in men and 67% in women.[4] The incidence of stroke peaked earlier and has shown similar declines.

In this issue of the *Canadian Journal of Cardiology*, Tu et al.[5] describe the changes between 1994 and 2014 in hospitalization rates in Ontario for 6 major atherosclerotic cardiovascular disease (ASCVD) conditions and trends in mortality rates for ischemic heart disease, cerebrovascular disease, and noncirculatory disease. This information is derived mainly from the Canadian Institute for Health Information Hospital Discharge Abstract Database and serial Canadian Community Health Surveys.

The changes over these 2 decades are breathtaking. Age-standardized hospitalizations for the 6 ASCVD conditions decreased by 54% in both men and women. Ischemic heart disease and cerebrovascular disease mortality decreased by 53% in both sexes, whereas noncardiovascular mortality declined by "only" 22%. During this period, age-standardized rates of percutaneous coronary intervention (PCI) increased from approximately 100 to > 300 per 100,000 population in men and from approximately 40 to 110 per 100,000 population in women, whereas the rates or coronary bypass surgery fell to a lesser extent.

How Do We Explain These Improvements?

Tu et al.[5] attribute the fall in ASCVD hospitalizations and mortality to better control of risk factors—specifically, smoking, hypertension, and greater use of cholesterol-lowering therapy—along with increasing rates of PCI. As they point out, similar improvements have been described over this period in the United States and Western Europe, although not simultaneously for all 6 of the ASCVD conditions tracked in this study.

Several investigators have provided precise estimates of the contributions of different factors to the fall in CHD mortality. For example, 1 group stated that 25% of the decline in CHD mortality from 1980-1990 could be attributed to primary prevention, whereas 29% was explained by a secondary reduction in risk factors in patients with CHD and 43% by other improvements in the treatment of patients with CHD.[6] In serial population surveys from Norway, the incidence of CHD decreased by 3% per year between 1994 and 2008.[7]

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Changes in coronary risk factors accounted for 66% of the decline, with improvements in cholesterol levels contributing 32%, whereas reduced blood pressure, giving up smoking, and physical activity contributed 14%, 13%, and 9%, respectively.

Although studies such as these appear highly credible, in part because they provide a high degree of precision, they in fact describe associations and do not prove causality. Nevertheless, plans to reduce ACSVD usually revolve around risk factor reduction strategies. In the United States, eg, Healthy People 2020 aims to reduce fatal ASCVD by 20% by 2020, with a strategy based mainly on risk factor reduction.[8]

The New Mountain

Although tuberculosis was conquered in the first half of the 20th century, it did not vanish but only retreated to niches where it could thrive, such as disadvantaged inner cities, Canadian aboriginal communities, and developing countries. The spread of HIV has led to a resurgence of tuberculosis. In 1997 worldwide, new cases of tuberculosis totaled almost 8 million, with 1.87 million deaths and a global case fatality rate of 23%.[9] Latent tuberculosis is present in approximately 2 billion individuals across the globe.

There are ominous signs to suggest that ASCVD is not about to fade from view either. Tu et al.[5] note that the rates of decline in ASCVD "were least evident among those aged 20-49 for both sexes." Reports from the United States, the United Kingdom, and Australia also indicate that ASCVD rates are not decreasing and indeed in some instances appear to be increasing slightly in younger age strata, particularly in women.[10-13] A change in the case fatality rate does not appear to account for the flattening or increased CHD mortality curve in younger groups; rather, this more likely results from an increase in risk factors,[13] specifically surging rates of obesity and diabetes.

More than 80% of deaths from ASCVD now occur in low- and middle-income countries, where the incidence continues to rise.[14,15] Rates of ASCVD and ASCVD mortality are higher in low- and middle-income countries compared with high-income countries, despite a lower risk factor burden.[15] The obvious reason for this disparity is the very low rates of treatment of risk factors in low- and middle-income countries and lower rates of coronary revascularization compared with high-income countries.[15] Furthermore, risk factors are becoming more prevalent in low- and middle-income countries, presaging a worsening of their ASCVD epidemics.[16]

Social Deprivation

The relationship between childhood deprivation and life expectancy is most colorfully depicted in a map of the London Underground created by the geographer James Cheshire in 2012, with life expectancy shown at each Underground stop.[17] Going east on the Central Line for 8 stops, between Oxford Circus and Mile End, life expectancy decreases by 18 years, and crossing the Thames between the Pimlico and Vauxhall stations sees life expectancy drop by 6 years.

Social deprivation, both on a country level and for disadvantaged groups within a country, has long been linked to an increased risk of ACSVD. However, higher risk is not limited to just the lowest stratum of deprivation. In the influential Whitehall study of 17,530 British civil servants, all of whom were employed and none of whom were considered to be socially deprived, 10-year CHD mortality was 2.2%, 3.6%, 4.9%, and 6.7% across job grade from the highest to the lowest, a difference that remained statistically significant even after controlling for risk factors.[18]

Lack of access to affordable effective health care contributes to social deprivation. Living in a disadvantaged neighborhood compared with an advantaged one increases the risk of a coronary event, even after adjustment for personal socioeconomic status.[19] Social support and social networks are often deficient for individuals experiencing social deprivation. In a study of 32,624 male health care professionals, those in the lowest stratum of social support had a relative risk of 1.9 for cardiovascular mortality and 2.2 for incident stroke compared with those in the highest stratum.[20]

Social deprivation may increase cardiovascular risk by increasing depression and anxiety.[21] Depression and depressive symptoms have been linked to increased cardiovascular morbidity and mortality in many studies, and the effect persists after adjustment for other risk factors.[21] In patients with cardiovascular disease (CVD), depression is associated with higher levels of inflammatory markers and other biomarkers of risk, greater platelet reactivity, reduced heart rate variability, and impaired vascular function.[21]

Future Directions

Further reductions in ASCVD incidence and mortality should not be taken for granted. We must apply secondary prevention more comprehensively. Among patients with established ASCVD in the United States, statin drug use was at 49.8% in 2002-2003 and despite a decrease in cost, increased to only 58.1% in 2012-2013, with less than one-third of patients prescribed a high-intensity statin drug.[22]

We must pay attention not just to primary prevention but to primordial prevention—the prevention of the appearance of risk factors. This leads us to focus on young adults and children. Although we treat individuals, we must also engage in population-based initiatives to improve community health and reduce socioeconomic disparities.

The prevalence of both tuberculosis and atherosclerosis are strongly influenced by social determinants of health. The World Health Organization broadly defines the social determinants of health as the circumstances in which people are born, grow, live, work, and age and the systems put in place to deal with illness.[23] We need to see ASCVD in this larger context, just as we have with tuberculosis. We must shrink the mountain and not just have it move somewhere else.

Disclosures

The author has no conflicts of interest to disclose.

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