Prologue

All truth passes through three stages: First, it is ridiculed; Second, it is violently opposed; and Third, it is accepted as being self-evident. This quote by Arthur Schopenhauer, a 19th-century German philosopher, resonates deeply with my own 50-year journey. As one of the first to alert the United States (US) physicians and cardiologists about the heightened risk of heart disease in Indians, I encountered significant resistance and skepticism within the American cardiology community.

India and Indians face a significant burden of coronary artery disease, characterized by disproportionately high rates of heart attacks, particularly in younger individuals (under 50 years, and even under 40 years of age). Despite seemingly similar cardiovascular risk profiles across populations, Indians experience a nearly two-fold increased risk of heart attacks compared to whites, even after adjusting for traditional risk factors. The London Life Sciences Population (LOLIPOP) study, which followed 25,000 individuals (South Asians and Whites) for 20 years, further emphasizes this disparity. This landmark study revealed a persistently elevated risk of heart disease in younger South Asians, with the incidence of heart attacks among South Asian women approaching that of white European men. Notably, the risk of heart attack was highest in South Asians younger than 45 years, underscoring the urgency of this critical public health challenge.

This book delves into the heart of India's alarming heart disease epidemic—a significant public health challenge within the South Asian population. South Asians refer to people of ancestral origin from the Indian subcontinent nations, including India, Pakistan, Bangladesh, Nepal, Bhutan, and Sri Lanka, with Indians accounting for 70–75% of South Asians. Most studies among the Indian immigrants have been aggregated and commingled with other South Asians. While Pakistanis, Bangladeshis and other South Asian ethnicities exhibit even higher heart disease, this book focuses on the unique challenges and complexities of heart disease within the Indian population.

It is important to note that while vegetarianism is prevalent in India, a significant portion of the population, including vegetarians, consumes a diet high in saturated and trans fats, often found in fried foods. This can occur while simultaneously having a low intake of essential nutrients like whole grains, fruits, vegetables, nuts, seeds, and non-tropical vegetable oils.

Heart disease disproportionately accounts for two-thirds of the burden of atherosclerotic cardiovascular disease (ASCVD) in India, and ASCVD itself constitutes two-thirds of all cardiovascular diseases (CVDs) within this population. This significant burden of heart disease among Indians, compared to other CVDs like stroke, underscores the critical need to address this major health challenge. My research, spanning over five decades, has exclusively focused on understanding the specific factors contributing to the high burden of heart disease in Indians.

The catalysts for my research. As a young Resident Physician in Chicago in the early 1970s, I was deeply disturbed by the case of a fellow first-year resident physician from India who suffered a heart attack at the tender age of 29 years. He presented to the emergency department with chest pain over several days but was unfortunately and repeatedly sent home with reassurance due to his young age. This tragic event, which unfortunately still occurs today, served as a stark reminder of the vulnerability of even the healthiest individuals to this silent killer. After surviving the initial heart attack, his disease progressed relentlessly, and he tragically succumbed to heart disease before reaching 50 years of age while awaiting a heart transplant.

Another poignant case involved a 37-year-old colleague who, despite seemingly minimal initial disease, experienced a rapid and aggressive progression of coronary atherosclerosis. Within a decade, he was debilitated by severe chest pain and heart failure, ultimately requiring multiple complex surgeries (more in the Epilogue). This case underscores the potential for rapid disease progression, even in seemingly low-risk individuals.

Another 39-year-old patient was diagnosed with inoperable heart disease following his first heart attack. Tragically, he died of a stroke just over 5 years later, highlighting the close connection and shared risk factors between heart attacks and strokes.

These tragedies were further compounded by the cases of three more young Indian physicians in their forties. One experienced a devastating cascade of events, suffering a heart attack followed by an aortic dissection a year later, necessitating emergency surgery. Another, despite undergoing bypass surgery, suffered a massive heart attack within a year, resulting in permanent disability and a significant decline in his quality of life. The third suffered cardiac arrest while enroute to the hospital, narrowly surviving but sustaining significant disabilities.

Witnessing the devastating impact of heart disease on these vibrant young colleagues, most of whom were dedicated to serving others, left an indelible mark on my soul. These experiences ignited a deep sense of urgency and a burning desire to understand the underlying causes of this alarming trend and to develop effective strategies for prevention and intervention. These and other similar case studies served as the driving force behind my initiation of the landmark coronary artery disease in Indians (CADI) study.

The CADI study confirms high rates of heart disease in Indian Americans. The CADI study, a ground-breaking investigation involving nearly 2,000 Indian-American physicians and their families, conducted by the author and commissioned by the American Association of Physicians of Indian Origin (AAPI), confirmed high rates of heart disease in Indian Americans. This landmark study found that Indian American men were four times more likely to develop heart disease compared to the general US population. Furthermore, it revealed the "Indian Paradox," where traditional cardiovascular risk factors, while contributing to heart disease, do not fully explain the disproportionately high rates observed in this population, suggesting the need to explore additional, potentially genetic factors.

Elevated lipoprotein(a) [Lp(a)] found in one in four Indians. The study found that one in four Indians has elevated Lp(a) levels, a potent genetic risk factor for heart attacks. This finding, initially met with skepticism, has gained widespread recognition within the scientific and Indian communities. The evidence strongly suggests that Lp(a) is a major

independent risk factor for heart attacks, particularly in young individuals (less than 50 years) and very young individuals (less than 40 years). The risk is doubled in individuals with elevated Lp(a) and further amplified to fourfold among those with other risk factors, such as diabetes or elevated LDL cholesterol.

In the INTERHEART Lp(a) study, the contribution of Lp(a) to heart attack was double in Indians than in whites (10% vs. 5%). The landmark Prospective Urban Rural Epidemiology (PURE) study has demonstrated that risk factors like high cholesterol, high blood pressure, smoking, diabetes, obesity, metabolic syndrome, physical inactivity, air pollution, and poor diet remain crucial, as these risk factors account for approximately 70% of cardiovascular disease globally.

The Global Burden of Elevated Lp(a). The 2018 special report by the National Heart, Lung, and Blood Institute (NHLBI) highlighted the global burden of elevated Lp(a), affecting approximately 1.43 billion individuals worldwide. The report revealed that 25% of Indians have high Lp(a) levels, compared to 20% of whites and 10% of Chinese. The "I" special report established the following Lp(a) classifications:

- *Normal:* <30 mg/dL
- *Moderately high:* 30–50 mg/dL
- *High:* >50 mg/dL

American guidelines embrace and incorporate seminal CADI research findings. Our research achieved a significant milestone in 2018 when the American College of Cardiology and American Heart Association (ACC/AHA) incorporated key findings from the CADI study into their Clinical Practice Guidelines. This landmark decision, recognizing both Lp(a) and South Asian ethnicity as significant risk-enhancing factors for heart disease, has profound implications. It empowers physicians to personalize treatment plans, including the use of statin therapy, based on individual risk profiles, thereby improving the prevention and management of heart disease in the Indian population.

Notably, Lp(a) levels can be measured as early as age 5–10 years, providing a crucial window of opportunity for early detection and preventive interventions, potentially averting a cardiac catastrophe decade in advance. While new medications specifically targeting Lp(a) are anticipated, the good news is that we already have the knowledge, diagnostic tools, and treatments to substantially reduce heart disease risk.

Empowering Indians with Knowledge

By combining these efforts with personalized strategies based on individual risk factor profiles, significant progress has been made in reducing heart disease rates among South Asians in Canada (personal communication with Salim Yusuf and Sonia Anand) and the US, achieving near-parity with the dominant white population. This progress is attributed to the efforts of organizations like the CADI Research Foundation, which have championed awareness and educational initiatives.

This book aims to empower individuals with the knowledge to understand heart disease and its contributing factors, enabling them to actively participate in their healthcare journey. It delves deeply into the complexities of heart disease in Indians, exploring its impact on heart attacks, strokes, and other cardiovascular events.

Across 17 chapters, this book comprehensively examines key risk factors, including tobacco use, hypertension, diabetes, cholesterol, and the critical role of Lp(a). It also explores the latest treatment strategies, including statin therapy and emerging non-statin therapies. Furthermore, the book provides extensive guidance on preventing heart attacks, managing stable angina, cardiovascular kidney metabolic syndrome, atrial fibrillation stroke, and heart failure.

Three chapters are dedicated to prevention, including one chapter focused on diet and another dedicated to "Life's Essential 8," recognizing the need for a tailored approach to heart health within this high-risk population.

While a comprehensive resource for cardiologists, this book is also written in an accessible style, making it understandable for individuals with no medical background. My sincere gratitude goes to my Co-author and Editor, Basil Varkey, whose legendary expertise and meticulous attention to detail ensured the brevity, clarity, and readability of each chapter. His invaluable contributions resulted in the book being trimmed by at least 100 pages without omitting any valuable data.

The book concludes with an epilogue, offering a personal touch as it traces the author's 50+-year journey and contributions. This blend of scientific expertise and personal reflection makes it a compelling resource for understanding and addressing heart disease in the Indian context.

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