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A are metabolized distinctly in cardiac muscle. Glucose is converted in the cytoplasm into pyruvate, which passes into mitochondria for conversion into acetyl-CoA that then undergoes oxidation. FFAs are converted to acyl-CoA in the cytoplasm and acetyl-CoA in the mitochondria. Acetyl-CoA enters the citric acid (Krebs) cycle to produce ATP by oxidative phosphorylation; ATP then enters the cyto plasm from the mitochondrial compartment. Intracellular adenosine diphosphate (ADP), resulting from ATP breakdown, enhances ATP production.

PART 6 Disorders of the Cardiovascular System In the fasted, resting state, circulating FFAs furnish most of the heart’s acetyl-CoA (~70%). In the fed state, with elevations of blood glucose and insulin, glucose oxidation increases and FFA oxidation subsides. Increased cardiac work, inotropic agents, hypoxia, and mild ischemia all enhance myocardial glucose uptake, production (glyco genolysis), and metabolism to pyruvate (glycolysis). Exercise raises circulating lactate levels and myocardial utilization of acetyl-CoA. By contrast, β-adrenergic stimulation raises the circulating levels and metabolism of FFAs in favor of glucose. Severe myocardial ischemia inhibits cytoplasmic pyruvate dehydrogenase, producing incomplete glucose metabolism to lactic acid (anaerobic glycolysis). Anaerobic glycolysis produces much less ATP per mole of glucose than does aerobic glucose metabolism. High concentrations of circulating FFAs, which can occur when adrenergic stimulation is superimposed on severe ischemia, reduce oxidative phosphorylation, and the myocar dial content of ATP declines, impairing contraction. In addition, FFA breakdown products may exert toxic or arrhythmogenic effects on cardiac cell membranes. Myocardial energy is stored as creatine phosphate (CP), which is in equilibrium with ATP, the immediate energy source. In states of reduced energy availability, the CP stores decline first. Cardiac hypertrophy, fibrosis, tachycardia, increased wall tension due to ven tricular dilation, and increased intracytoplasmic [Ca2+] all contribute to increased myocardial energy needs. When coupled with reduced coronary flow reserve, as occurs with obstruction of coronary arteries or abnormalities of the coronary microcirculation, an imbalance in myocardial ATP production relative to demand may occur, and the resulting ischemia can worsen or cause heart failure. ■ ■CARDIAC CELLULAR INTERVENTIONS: REGENERATION AND REPAIR Adult mammalian myocardial cells are fully differentiated and have little or no regenerative potential; however, there is evidence that the immature mammalian heart has some limited regenerative potential that rapidly becomes constrained with increasing maturity

and work load. Considerable current effort is being devoted to evaluating the utility of various approaches to facilitate the transient release of these constraints on regeneration to enhance cardiac repair after injury. Recent work has also shown that by engineering chimeric antigen receptors on T lymphocytes (CAR-T), it may be possible to reverse fibrosis in the heart. The success of such approaches would offer the exciting possibility of reconstructing an infarcted or failing ventricle. ■ ■FURTHER READING Bautch VL, Caron KM: Blood and lymphatic vessel formation. Cold Spring Harb Perspect Biol 7:a008268, 2015. Dejana E et al: The molecular basis of endothelial cell plasticity. Nat Commun 8:14361, 2017. Green DJ et al: Vascular adaptation to exercise in humans: Role of hemodynamic stimuli. Physiol Rev 97:495, 2017. Libby P et al (eds): Braunwald's Heart Disease: A Textbook of Cardio vascular Medicine, 11th ed. Philadelphia, Elsevier, 2022. MacLeod KT: Recent advances in understanding cardiac contractility in health and disease. F1000Res 5(F1000 Faculty Rev):1770, 2016. Page E et al (eds): Handbook of Physiology: A Critical Comprehensive Presentation of Physiological Knowledge and Concepts. Section 2: The Cardiovascular System, Volume I: The Heart. New York, Oxford University Press, 2002. Rurik JG et al: CAR T cells produced in vivo to treat cardiac injury. Science 375:91, 2022.

Spinale FG: Assessment of cardiac function—Basic principles and approaches. Compr Physiol 5:1911, 2015. Srivastava D: Making or breaking the heart: From lineage determination to morphogenesis. Cell 126:1037, 2006. Taegtmeyer H et al: Cardiac metabolism in perspective. Comp Physiol 6:1675, 2016. J. Michael Gaziano, Thomas A. Gaziano

Epidemiology of

Cardiovascular Disease Cardiovascular disease (CVD) is now the most common cause of death worldwide. Before 1900, infectious diseases and malnutrition were the most common causes, and CVD was responsible for <10% of all deaths. In 2022, CVD accounted for over 19 million deaths worldwide (33%), with the same rate now occurring in both high-income countries and low- and middle-income countries. THE EPIDEMIOLOGIC TRANSITION The global rise in CVD is the result of an unprecedented transforma tion in the causes of morbidity and mortality during the twentieth century. Known as the epidemiologic transition, this shift is driven by industrialization, urbanization, and associated lifestyle and demo graphic changes and is taking place in every part of the world among all races, ethnic groups, and cultures. The transition is divided into four basic stages: pestilence and famine, receding pandemics, degen erative and man-made diseases, and delayed degenerative diseases. A fifth stage, characterized by an epidemic of inactivity and obesity, is emerging in many countries that have moderate economic develop ment (Table 245-1). The age of pestilence and famine is marked by malnutrition, infec tious diseases, and high infant and child mortality that are offset by high fertility. Tuberculosis, dysentery, cholera, and influenza are often fatal, resulting in a mean life expectancy of about 30 years. CVD, which accounts for <10% of deaths, takes the form of rheumatic heart disease and cardiomyopathies due to infection and malnutrition. Despite advances in treatment of those with rheumatic heart disease, incidence and prevalence rates increased between 1990 and 2019. Per capita income and life expectancy increase during the age of receding pandemics as the emergence of public health systems, cleaner water supplies, and improved nutrition combine to drive down deaths from infectious disease and malnutrition. Infant and childhood mor tality also decline, but deaths due to CVD increase to between 10 and 35% of all deaths. Rheumatic valvular disease, hypertension, coronary heart disease (CHD), and stroke are the predominant forms of CVD. Almost 40% of the world's population

is currently in this stage. The age of degenerative and man-made diseases is distinguished by mortality from noncommunicable diseases—primarily CVD—surpassing mortality from malnutrition and infectious diseases. Caloric intake, particularly from animal fat, increases. CHD and stroke are prevalent, and between 35 and 65% of all deaths can be traced to CVD. Typically, the rate of CHD deaths exceeds that of stroke by a ratio of 2:1 to 3:1. During this period, average life expectancy surpasses the age of 50. Roughly 35% of the world's population falls into this category. In the age of delayed degenerative diseases, CVD and cancer remain the major causes of morbidity and mortality, with CVD accounting for 40% of all deaths. However, age-adjusted CVD mortality declines, aided by preventive strategies (for example, smoking cessation pro grams and effective blood pressure control), acute hospital manage ment, and technologic advances, such as the availability of bypass

TABLE 245-1 Five Stages of the Epidemiologic Transition STAGE DESCRIPTION Pestilence and famine Predominance of malnutrition and infectious diseases as causes of death; high rates of infant and child mortality; low mean life expectancy Receding pandemics Improvements in nutrition and public health lead to decrease in rates of deaths related to malnutrition and infection; precipitous decline in infant and child mortality rates Degenerative and man-made diseases Increased fat and caloric intake and decrease in physical activity lead to emergence of hypertension and atherosclerosis; with increase in life expectancy, mortality from chronic, noncommunicable diseases exceeds mortality from malnutrition and infectious disease Delayed degenerative diseases CVD and cancer are the major causes of morbidity and mortality; better treatment and prevention efforts help avoid deaths among those with disease and delay primary events; age-adjusted CVD morality declines; CVD affecting older and older individuals Inactivity and obesity Overweight and obesity increase at alarming rate; diabetes and hypertension increase; decline in smoking rates levels off; a minority of the population meets physical activity recommendations Abbreviations: CHD, coronary heart disease; CVD, cardiovascular disease. Source: Data from AR Omran: The epidemiologic transition: A theory of the epidemiology of population change. Milbank Mem Fund Q 49:509, 1971; and SJ Olshansky, AB Ault: The fourth stage of the epidemiologic transition: The age of delayed degenerative diseases. Milbank Q 64:355, 1986. surgery. CHD, stroke, and congestive heart failure are the primary forms of CVD. About 15% of the world's population is now in the age of delayed degenerative diseases or is exiting this age and moving into the fifth stage of the epidemiologic transition. In the industrialized world, physical activity continues to decline while total caloric intake increases. The resulting epidemic of over weight and obesity may signal the start of the age of inactivity and obesity. Rates of type 2 diabetes mellitus, hypertension, and lipid abnor malities are on the rise, trends that are particularly evident in children. As these risk factor trends continue, age-adjusted CVD mortality rates that have fallen for decades during the fourth phase have started to increase in recent years during this fifth phase. ■ ■PATTERNS IN THE EPIDEMIOLOGIC TRANSITION Unique regional features have modified aspects of the transition in var ious parts of the world. High-income countries experienced declines in CVD death rates by as much as 50–60% over the past 60 years, whereas CVD deaths increased by 15% over the past 20 years in the low- and middle-income range and the rate of change has been faster. However, given the large amount of available data, the United States serves as a useful reference point for comparisons. The age of pestilence and famine occurred before 1900, with a largely agrarian economy and population. Infectious diseases accounted for more deaths than any other cause. By the 1930s, the country proceeded through the age of receding pandemics. The establishment of public health infrastruc tures resulted in dramatic

declines in infectious disease mortality rates. Lifestyle changes due to rapid urbanization resulted in a simul taneous increase in CVD mortality rates, reaching ~390 per 100,000. Between 1930 and 1965, the country entered the age of degenerative and man-made diseases. Infectious disease mortality rates fell to fewer than 50 per 100,000 per year, whereas CVD mortality rates reached peak levels with increasing urbanization and lifestyle changes in diet, physical activity, and tobacco consumption. The age of delayed degen erative diseases took place between 1965 and 2000. New therapeutic approaches, preventive measures, and exposure to public health cam paigns promoting lifestyle modifications led to substantial declines in age-adjusted mortality rates and a steadily rising age at which a first CVD event occurs. Currently, the United States is entering what appears to be a fifth phase. The decline in the age-adjusted CVD death rate of 3% per year through the 1970s and 1980s has tapered off in the 1990s to 2% through 2010. There was then limited reduction in the 2010–2019 period, and in 2020 and 2021, there was an increase in CVD mortality rates that had not been seen since the early 1960s. Competing trends appear to be at play. On the one hand, an increase in the prevalence of diabetes and obesity, a slowing in the rate of decline in smoking, and a leveling off

DEATHS RELATED TO CVD, % PREDOMINANT CVD TYPE <10 Rheumatic heart disease, cardiomyopathies caused by infection and malnutrition CHAPTER 245 10–35 Rheumatic valvular disease, hypertension, CHD, and stroke (predominantly hemorrhagic) 35–65 CHD and stroke (ischemic and hemorrhagic) Epidemiology of Cardiovascular Disease 40–50 CHD, stroke, and congestive heart failure <40 CHD, stroke, and congestive heart failure, peripheral vascular disease in the rate of detection and worsening treatment for hypertension are in the negative column. On the other hand, cholesterol levels continue to decline in the face of increased statin use. Many high-income countries (HICs)—which together account for 15% of the population—have proceeded through four stages of the epi demiologic transition in roughly the same pattern as the United States. CHD is the dominant form of CVD in these countries, with rates that tend to be two- to fivefold higher than stroke rates. However, variations exist. Whereas North America, Australia, and central northwestern European HICs experienced significant increases then rapid declines in CVD rates, southern and central European countries experienced a more gradual rise and fall in rates. More specifically, central European countries (i.e., Austria, Belgium, and Germany) declined at slower rates compared to their northern counterparts (i.e., Finland, Sweden, Denmark, and Norway). Countries such as Portugal, Spain, and Japan never reached the high mortality rates that the United States and other countries did, with CHD mortality rates at 200 per 100,000, or less. The countries of Western Europe also exhibit a clear north/south gradient in absolute rates of CVD, with rates highest in northern countries (i.e., Finland, Ireland, and Scotland) and lowest in Mediterranean countries (i.e., France, Spain, and Italy). Japan is unique among the HICs, most likely due to the unique dietary patterns of its population. Although stroke rates increased dramatically, CHD rates did not rise as sharply in Japan. However, Japanese dietary habits are undergoing substantial changes, reflected in an increase in cholesterol levels. Patterns in low- and middle-income countries (LMICs; gross national income per capita $11,666) depend, in part, on cultural dif ferences, secular trends, and responses at the country level, with regard to both public health and treatment infrastructure. Although com municable diseases continue to be a major cause of death, CVD has emerged as a significant health concern in LMICs. With 85% of the world’s population, LMICs are driving the rates of change in the global burden of CVD (Fig. 245-1). In most LMICs, an urban/rural gradient has emerged for CHD, stroke, and hypertension, with higher rates in urban centers. However, although CVD rates are rapidly rising globally, vast dif ferences exist among the

regions and countries, and even within the countries themselves (Fig. 245-2). The East Asia and Pacific regions appear to be fully in the third phases of the epidemiologic transition. CVD is a major cause of death in China, but like Japan, stroke causes more deaths than CHD in a ratio of about three to one. Vietnam and Cambodia, on the other hand, are just emerging from the pestilence and famine transition. The Middle East and North Africa regions also appear to be well into the third phase of the epidemiologic transition, with increasing life expectancy and CVD death rates just below those of HICs. In general, Latin America appears to be in the third phase of

Highincome countries… INJ 7.61% Low- and middleincome countries, 80.99% PART 6 Disorders of the Cardiovascular System CMNN 18.03% CVD 32.84% ONC 41.52% CVD ONC CMNN INJ FIGURE 245-1 Global deaths by cause, 2019. CMNN, communicable, maternal, neonatal, and nutritional disorders; CVD, cardiovascular diseases; INJ, injuries; ONC, other noncommunicable diseases. (Based on data from Global Burden of Disease Study 2017. Global Burden of Disease Study 2017 [GBD 2017] Results. Seattle, United States: Institute for Health Metrics and Evaluation [IHME], 2020.) the transition, although there is vast regional heterogeneity with some areas in the second phase of the transition and more in the fourth. The Eastern Europe and Central Asia regions, however, are firmly in the peak of the third phase, with the highest death rates due to CVD (~55%) in the world. Importantly, deaths due to CHD are not limited to the elderly in this region and have a significant effect on working-age populations. South Asia—and more specifically, India, which accounts for the greatest proportion of the region’s population—is experiencing an alarming increase in heart disease. The transition appears to be in the Western style, with CHD as the dominant form of CVD. However, rheumatic heart disease continues to be a major cause of morbidity and Latin America and the Caribbean Middle East and North Africa 26.9% (619 million) 41.8% (437 million) High-income 31.5% (1139 million) Sub-Saharan Africa 13.1% (1087 million) FIGURE 245-2 Cardiovascular disease deaths as a percentage of total deaths and total population in seven economic regions of the world defined by the World Bank. (Based on data from Global Burden of Disease Study 2017. Global Burden of Disease Study 2019 [GBD 2019] Results. Seattle, United States: Institute for Health Metrics and Evaluation [IHME], 2023.)

mortality. As in South Asia, rheumatic heart disease is also an impor tant cause of CVD morbidity and mortality in sub-Saharan Africa, which largely remains in the first phase of the epidemiologic transition. Many factors contribute to this heterogeneity among LMICs. First, the regions are in various stages of the epidemiologic transition. Second, vast differences in lifestyle and behavioral risk factors exist. Third, racial and ethnic differences may lead to altered susceptibili ties to various forms of CVD. In addition, it should be noted that for most countries in these regions, accurate country-wide data on causespecific mortality are not complete. ■ ■GLOBAL TRENDS IN CARDIOVASCULAR DISEASE Over the past 5 years, there have been changes in the trends of CVD that are reflective of both trends in demographics and management of disease, but also of the way deaths and diseases have been measured and estimated. In 2017, the Global Burden of Disease (GBD) Study updated its estimates with several important changes based on newly available data, refinement in the causes of death, and the introduction of new modeling techniques. The major changes include the addition of an independent estimation of population and fertility, the addition of over 127 country-years of vital registration and verbal autopsy data, revisions of some deaths from “misclassified” to dementia, Parkinson’s disease and atrial fibrillation, and the addition of new diseases such as nonrheumatic calcific aortic and degenerative mitral valve disease. CVD accounts for 32% of deaths worldwide, a number expected to increase. In 2019, CHD accounted for 16.2% of

all deaths globally and the largest portion (10%) of global years of life lost (YLLs) and disabilityadjusted life-years (DALYs) (7.2%). Stroke moved from the third to the second largest cause of death (11.6% of all deaths) and remained the third largest contributor to global YLLs (7.5%) and DALYs (5.7%). Together, CHD and stroke accounted for more than a quarter of all deaths worldwide. The burden of stroke is of growing concern among LMICs. The impact of stroke on DALYs and mortality rates is more than three times greater in LMICs as compared to HICs. Europe and Central Asia 55.1% (875 million) South Asia 27.5% (1813 million) Southeast and East Asia and Pacific 40.2% (2257 million)

CVD Deaths per 100,000

Year World Bank lower middle income World Bank high income World Bank upper middle income World Bank low income Global FIGURE 245-3 Age-standardized cardiovascular diseases (CVD) death rate per 100,000 from 1990 to 2019, by World Bank income. (Based on data from Global Burden of Disease Study 2019. Global Burden of Disease Study 2019 [GBD 2019] Results. Seattle, United States: Institute for Health Metrics and Evaluation [IHME], 2023.) With 85% of the world's population, LMICs largely drive global CVD rates and trends. More than 15 million CVD deaths occurred in LMICs in 2019, compared to 3.5 million in HICs. Globally, there is evidence of significant delays in age of occurrence and/or improve ments in case fatality rates; between 1990 and 2019, the number of CVD deaths increased by 54%, but age-adjusted death rates decreased by 32.4% in the same period. Age-standardized death rates, however, have declined faster in HICs than in middle-income and lower-income regions (Fig. 245-3). Population growth has been greater in LMICs compared to HICs. As a result of slower rates of population growth in HICs, overall CVD deaths remained steady. However, in the LMICs, the population aging and growth outstripped gains in age-adjusted mortality reductions such that overall CVD deaths continued to climb over the past 25 years (Fig. 245-4).

Number of CVD Deaths in Millions

Year World Bank high income World Bank lower middle income World Bank upper middle income World Bank low income Global FIGURE 245-4 Number of cardiovascular diseases (CVD) deaths from 1990 to 2019, by World Bank income. (Based on data from Global Burden of Disease Study 2019. Global Burden of Disease Study 2017 [GBD 2019] Results. Seattle, United States: Institute for Health Metrics and Evaluation [IHME], 2023.)

Although HIC population growth will be fueled by immigration from LMICs, the populations of HICs will shrink as a proportion of the world's population. The modest decline in CVD death rates that began in the HICs in the latter third of the twentieth century will continue, but the rate of decline appears to be slowing. However, these countries are expected to see an increase in the prevalence of CVD, as well as the absolute number of deaths as the population ages.

CHAPTER 245 Significant portions of the population living in LMICs have entered the third phase of the epidemiologic transition, and some are enter ing the fourth stage. Changing demographics play a significant role in future predictions for CVD throughout the world. For example, the population in Eastern Europe declined by 3% between 2010 and 2023, whereas it grew by 30% in South Asia. CVD rates will also have an eco nomic impact. Even assuming no increase in CVD risk factors, most

countries, but especially India and South Africa, will see a large num ber of people between 35 and 64 die of CVD over the next 30 years, as well as an increasing level of morbidity among middle-aged people related to heart disease and stroke. Epidemiology of Cardiovascular Disease ■ ■RISK FACTORS Global variation in CVD rates is related to temporal and regional variations in known risk factors and behaviors. Ecologic analyses of major CVD risk factors and mortality demonstrate high correlations between expected and observed mortality rates for the three main risk factors—smoking, serum cholesterol, and hypertension—and suggest that many regional variations are based on differences in conventional risk factors. Behavioral Risk Factors • TOBACCO Over 1.3 billion people use tobacco worldwide. Tobacco use currently causes about 8.7 mil lion deaths annually (15.4% of all deaths), 3.2 million of which are CVD related. The population of the HIC group smokes (21.6%) at almost double the rate of the low-income countries (11.2%), whereas the middle-income country group's smoking rate (19.5%) approxi mates the global average (22.3%). From 2007 to 2017, smoking rates decreased across low-, middle-, and high-income country groups, with relative reductions of 19%, 12%, and 20%, respectively. By 2030, the global average smoking rate is expected to decline from 19% to 16% (women, 4%; men, 28%); however, the number of tobacco users is expected to rise owing to population growth. Secondhand smoke is another well-established cause of CVD, responsible for 598,000 CVD deaths of nonsmokers in 2019. Although smoking bans have both immediate and long-term benefits, implementation varies greatly between countries. DIET Total caloric intake per capita increases as countries develop. With regard to CVD, a key element of dietary change is an increase in intake of saturated animal fats and hydrogenated vegetable fats, which contain atherogenic trans fatty acids, along with a decrease in intake of plant-based foods and an increase in simple carbohydrates. Fat contrib utes <20% of calories in rural China and India, <30% in Japan, and over 35% in the United States. Caloric contributions from fat appear to be increasing in the United States but falling in the other HICs. PHYSICAL INACTIVITY The increased mechanization that accompa nies the economic transition leads to a shift from physically demand ing, agriculture-based work to largely sedentary industry- and office-based work. Physical inactivity is responsible for 1.3 million global deaths in 2019. The global prevalence of physical inactivity has remained steady between 2001 and 2016 (28.5% to 27.5%). Mor tality rates attributable to inactivity are highest in North Africa and the Middle East and in Central and Eastern Europe and lowest in sub-Saharan Africa. ■ ■METABOLIC RISK FACTORS Examination of trends in metabolic risk factors provides insight into changes in the CVD burden globally. Here we describe four metabolic risk factors—lipid levels, hypertension, obesity, and diabetes mellitus— using data from the Global Burden of Disease, Injuries, and Risk Factors Study (GBD 2019). The GBD project identified and compiled mortality and morbidity data from 195 countries from 1980 to 2017.

Lipid Levels Worldwide, high low-density lipoprotein cholesterol levels are estimated to play a role in 41% of ischemic heart disease deaths and 9% of stroke deaths, amounting to 4 million deaths in 2019. Although mean population plasma cholesterol levels tend to rise as countries move through the epidemiologic transition, mean serum total cholesterol levels have decreased globally between 1980 and 2008 by 0.08 mmol/L per decade in men and 0.07 mmol/L per decade in women. Large declines occurred in Australasia, North America, and Western Europe (0.19–0.21 mmol/L). Countries in the East Asia and Pacific region experienced increases of >0.08 mmol/L in both men and women. More recent research including Mendelian studies sug gests that lipoprotein(a) may act as an individual predictor of CVD risk beyond traditional total or low-density lipoprotein cholesterol through increased cellular lipid accumulation, endothelial dysfunction, and impacts on

coagulation. It appears to be elevated in ~20% of the global population, although fewer data are available from LMICs. Non randomized data suggest higher rates among those of African descent with twice the levels of Caucasians, with East Asians and South Asians having intermediate levels. There are limited clinical trial data on clini cal agents that target lipoprotein(a), although PCSK9 inhibitors lower it or other specific targets, so this remains an area of intense research. Hypertension Elevated blood pressure is an early indicator of the epidemiologic transition. Observational studies show increased risk of CVD beginning with systolic blood pressures (SBPs) >110–115 mmHg. Between 1990 and 2015, the global prevalence of SBP ≥110–115 mmHg increased from 73,119 to 81,373 per 100,000, whereas the prevalence of SBP ≥140 mmHg rose from 17,307 to 20,526 per 100,000. In 2015, of the estimated 3.47 billion adults with SBP ≥110–115 mmHg, 874 million (25%) had SBP ≥140 mmHg. While SBP ≥140 mmHg accounts for only 25% of those with elevated blood pressure, it accounted for 73% (7.8 million) of deaths due to SBP of ≥110–115 mmHg in 2015. Worldwide, 53% of stroke deaths (3.44 million) and 53% of CHD deaths (4.86 million) are attributable to high blood pressure, account ing for 10.8 million deaths in 2019. From 1990 to 2015, the number of deaths related to SBP ≥140 mmHg increased in all LMIC groups but fell in HICs. Between 1980 and 2008, the age-standardized prevalence of uncontrolled hypertension decreased even as the number of people with uncontrolled hypertension increased due to population growth and aging. However, concerning trends of declining hypertension control rates were seen in the United States since 2016 with many middle-income countries now outperforming high-income nations. Rising mean population blood pressure also occurs as populations industrialize and move from rural to urban settings. For example, the prevalence of hypertension in urban India is 33.8%, but varies between 14.5 and 31.7% in rural regions. One major concern in LMICs is the high rate of undetected, and therefore untreated, hypertension. This may explain, at least in part, the higher stroke rates in these countries in relation to CHD rates during the early stages of the transition. The high rates of hypertension throughout Asia, especially undiagnosed hypertension, likely contribute to the high prevalence of hemorrhagic stroke in the region.

PART 6 Disorders of the Cardiovascular System Obesity In 2025, an estimated 892 million adults will be obese. Global obesity prevalence is projected to be 16.1% among adults and is increasing throughout the world, particularly in developing coun tries where the trajectories are steeper than those experienced by the developed countries. High body mass index (BMI) contributed to 5.0 million deaths worldwide (7.1% deaths from any cause); CVD was the leading cause of these deaths (1.95 million) and also of associated DALYs (160 million) followed by diabetes (0.6 million deaths, 30.4 million DALYs). Women are more affected by obesity than men; from 1975 to 2014, global mean age-standardized BMI increased from 22.1 to 24.4 kg/m2 in females and from 21.7 to 24.2 kg/m2 in males, whereas the prevalence of obesity increased from 6.4% to 14.9% in females and 3.2% to 10.8% in males. The proportion of the world’s adult women who are either overweight or obese rose from 29.8% to 38.0% between 1980 and 2013, while an increase from 28.8% to 36.9% was observed for men. Country and regional differences are observed. The highest prevalence of male obesity is in the United States, Southern and Central

Latin America, Australasia, and Central and Western Europe. For females, the highest prevalence of obesity is in Southern and North Africa, the Middle East, Central and Southern Latin America, and the United States. The lowest prevalence for both males and females was observed in South and Southeast Asia and in East, Central, and West Africa. Diabetes Mellitus As a consequence of, or in addition to, increas ing BMI and decreasing levels of physical activity, worldwide rates of

diabetes—predominantly type 2 diabetes—are on the rise. According to the most recent data from the GBD project, the prevalence of diabe tes increased 129.7% for males and 120.9% for females between 1990 and 2017. An estimated 476 million people worldwide have diabetes, and the International Diabetes Foundation predicts this number will reach 693 million by 2045. Nearly 50% of people with diabetes are undiagnosed, and 80% live in LMICs. The Middle East and North Africa have the highest regional age-standardized prevalence (8.7% of the population) and incidence rates (400 per 100,000) of diabetes, whereas East Asia and the Pacific have the lowest (5.8%; 249 per 100,000). Future growth will also largely occur in the Middle East and Africa, along with other LMICs in South Asia and sub-Saharan Africa. COVID-19 The impact of COVID-19 on CVD was significant. First, patients with acute conditions were hesitant to present to hos pitals for fear of infection, resulting in delayed presentation for those with acute coronary syndrome (ACS) or stroke and missing critical early care. Additionally, even those who presented with ACS had worse outcomes sometimes related to testing delays. Furthermore, the pres ence of obesity and/or diabetes mellitus worsened outcomes. Finally, control rates of hypertension and dyslipidemia may have been exacer bated due to difficulty of access to providers. ■ ■GENETIC RISK FACTORS A great deal of effort has recently been invested in understanding how genes affect cardiovascular health in populations. These efforts have focused on germline genetic variants that are related to specific CVDs as well as those that are associated with cardiovascular risk factors. In both cases, every year, the number of associated variants has increased meaningfully to the point that it appears that hundreds or even thou sands of variants are associated with these conditions, each explaining a small amount of the population variability in disease and risk fac tors. Collections of variants have been combined in polygenomic risk scores, but these too explain only a small amount of the variability of the disease in the population. Much more data will emerge in the com ing years about these associations, the mechanisms that explain these associations, the relationships of variants that are specific to certain tis sues such as the heart or the brain, and the interactions between genetic and lifestyle factors in causing disease. Currently, most of the data are among those with European ancestry; however, large-scale efforts are underway to understand the relationships between genes and diseases and their risk factors around the world. The early data suggest non trivial differences among various world populations. Beyond germline risk, there appears to be increased cardiovascular risk associated with age-related expansion of hematopoietic clones with somatic mutations, including loss-of-function alleles of certain genes. Individuals with these mutations without other hematologic abnormalities are defined as having clonal hematopoiesis of indeterminate potential (CHIP). Recent studies suggest those with CHIP have up to a twofold increased risk of developing CHD. SUMMARY Although CVD rates are declining in the HICs, they are increasing in many other regions of the world. The consequences of this preventable epidemic will be substantial on many levels, including individual mor tality and morbidity, family suffering, and staggering economic costs. Three complementary strategies can be used to lessen the impact. First, the overall burden of CVD risk factors can be lowered through population-wide public health measures, such as national campaigns against cigarette smoking, unhealthy diets, and physical inactivity. Sec ond, it is important to identify higher risk subgroups of the population

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