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TABLE 1.1 **Ten Leading Causes of Death and Their Percentages of All Deaths, United States, 2020**

Rank	Cause of Death	Number of Deaths	Percent of Total Deaths	Age-Adjusted Death Rate Per 100,000
	All Causes	33,83,729	100	
1	Heart disease	6,96,962	20.6%	168.2
2	Cancer	6,02,350	17.8%	144.1
3	COVID-19	3,50,831	10.4%	85
4	Accidents (unintentional injuries)	2,00,955	5.9%	57.6
5	Stroke (cerebrovascular diseases)	1,60,264	4.7%	38.8
6	Chronic lower respiratory diseases	1,52,657	4.5%	36.4
7	Alzheimer's disease	1,34,242	4.0%	32.4
8	Diabetes	1,02,188	3.0%	24.8
9	Influenza and pneuomnia	53,544	1.6%	13
10	Kidney disease	52,547	1.6%	12.7

Murphy SL, Kochanek KD, Xu JQ, Arias E. *Mortality in the United States, 2020.* NCHS Data Brief, no 427. Hyattsville, MD: National Center for Health Statistics; 2021. Available at: https://dx.doi.org/10.15620/cdc:112079. Accessed May 08, 2023.

the COVID-19 pandemic have emerged and the incidence of tuberculosis has increased, infectious diseases are once again becoming major public health problems. Table 1.1 shows the 10 leading causes of death in the United States in 2014. The three leading causes—heart disease, cancer, and COVID-19—account for almost 55% of all deaths, an observation that suggests specific targets for prevention if a significant reduction in mortality is to be achieved.

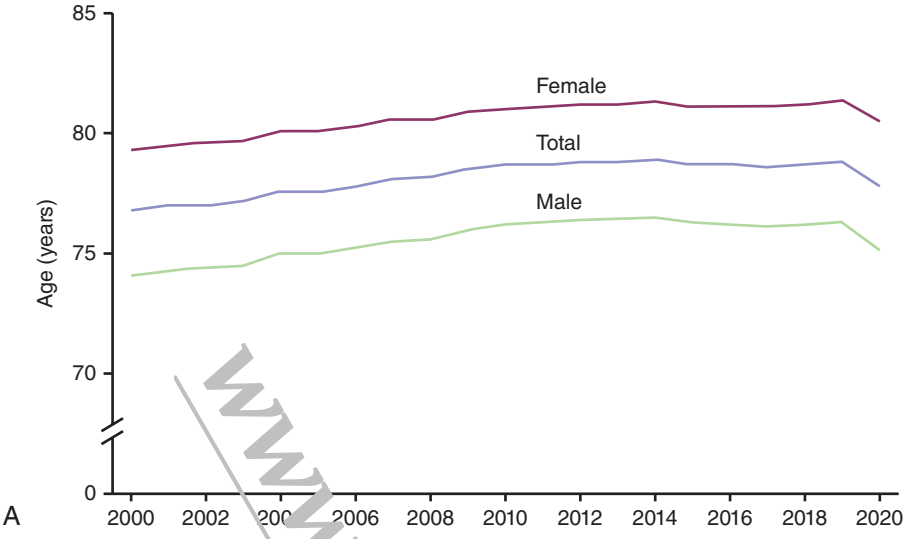
Another demonstration of changes that have taken place over time is seen in Fig. 1.3, which shows the life expectancy at birth by sex between 2002 and 2020 (panel A) and by Hispanic origin and race in 2019 and 2020 (panel B) in the United States.

While the life expectancy has dramatically increased in both sexes over 20 years, most of these public health gains have been swept by the COVID-19 pandemic deaths as we can see from the sharp decline in life expectancy in both sexes and all races.

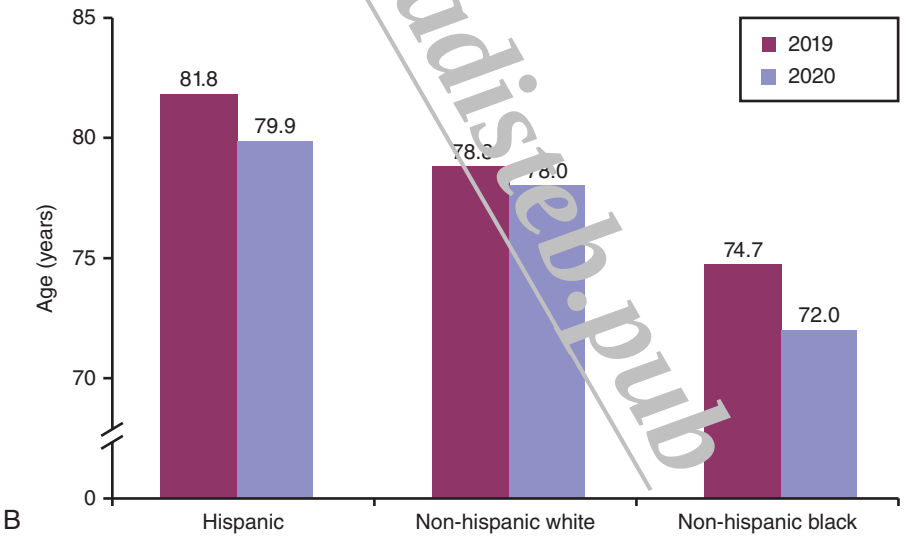
EPIDEMIOLOGY AND PREVENTION

A major use of epidemiologic evidence is to identify subgroups in the population who are at high risk for disease. Why should we identify such high-risk groups? First, if we can identify these high-risk groups, we can direct preventive efforts, such as screening programs for early disease detection, to populations who may not have been screened before and are most likely to benefit from any interventions that are developed for the disease. In sub-Saharan Africa, targeted HIV counseling and testing to men and women who are not aware of their status can effectively reduce epidemics if they are linked to care, started on antiretroviral therapy, and continued in care such that their viral load is undetectable.

Second, if we can identify such groups, we may be able to identify the specific factors or characteristics that put them at high risk and then try to modify those factors. It is important to keep in mind that such risk factors may be of two types. Characteristics such as age, sex, and race, for example, are not modifiable, although they may permit us to identify high-risk groups. On the other hand, characteristics such as obesity, smoking, diet, sexual practices, and other lifestyle factors may be potentially modifiable and may thus provide an opportunity to develop and introduce new prevention programs aimed at reducing or changing specific exposures or risk factors.



Notes: Life expectancies for 2019 by hispanic origin and race are not final estimates; see technical notes. Estimates are based on provisional data from January 2020 through June 2020.
Source: National center for health statistics, National vital statistics system, Mortality data.



Notes: Life expectancies for 2019 by hispanic origin and race are not final estimates; see technical notes. Estimates are based on provisional data from January 2020 through June 2020.
Source: National center for health statistics, National vital statistics system, Mortality data.

Fig. 1.3 **(A)** Life expectancy at birth by sex: United States, 2000–2020. **(B)** Life expectancy at birth by Hispanic origin and race: United States, 2019 and 2020. (From Arias E, Ejada-Vera B, Ahmad F. Provisional life expectancy estimates for January through June, 2020. Vital Statistics Rapid Release; no 10. Hyattsville, MD: National Center for Health Statistics. February 2021.)

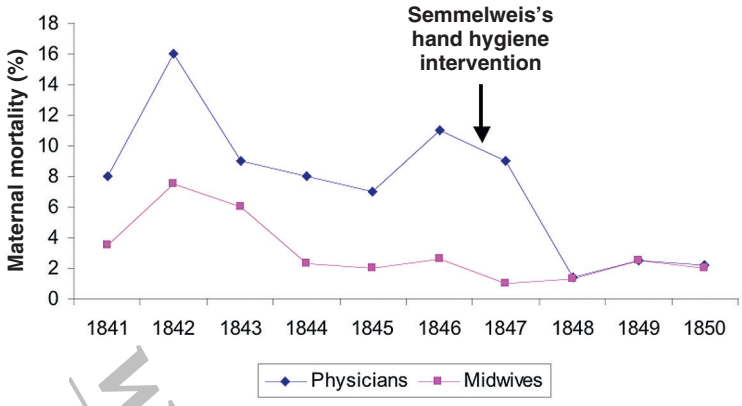


Fig. 1.12 Maternal mortality due to childbed fever, by type of care provider, General Hospital, Vienna, Austria, 1841–1850. (Modified from Marshall GC. *Hospital Epidemiology and Infection Control*. 2nd ed. Philadelphia: Lippincott Williams & Wilkins; 1999.)

Unfortunately, for many years Semmelweis refused to present his findings at major meetings or to submit written reports of his studies to medical journals. His failure to provide supporting scientific evidence was at least partially responsible for the failure of the medical community to accept his hypothesis of causation of childbed fever and his further proposed intervention of handwashing before examining each patient. Among other factors that fostered resistance to his proposal was the reluctance of physicians to accept the conclusion that by transmitting the agent responsible for childbed fever, they had been inadvertently responsible for the deaths of large numbers of women. In addition, physicians claimed that washing their hands before seeing each patient would be too time consuming. Another major factor is that Semmelweis was, to say the least, undiplomatic and had alienated many senior figures in medicine. Because of all of these factors, many years passed before a policy of handwashing was broadly adopted. An excellent biography of Semmelweis by Sherwin Nuland was published in 2003.[7]

The lessons of this story for successful policy making are still relevant today to the challenge of enhancing both public and professional acceptance of evidence-based prevention policies. These lessons include the need for clearly presenting supporting scientific evidence for a proposed intervention, the need for implementation of the proposed intervention to be perceived as feasible and cost-effective, and the need to lay the necessary groundwork for the policy, including garnering professional as well as community and political support.

Years later, the major cause of childbed fever was recognized to be a streptococcal infection. Semmelweis's major findings and recommendations ultimately had worldwide effects on the practice of medicine. Amazingly, his observations and suggested interventions preceded any knowledge of germ theory and thus proved that it is possible to implement a prevention strategy even when the exact cause of the disease is not known. However, it is also of interest that, although the need for handwashing has now been universally accepted, recent studies have reported that many physicians in hospitals in the United States and in other developed countries still fail to wash their hands as prescribed (Table 1.3).

TABLE 1.3 Compliance With Hand Hygiene Among Physicians, by Specialty, at University of Geneva Hospitals

Physician Specialty	No. of Physicians	Compliance With Hand Hygiene (% of Observations)
Internal medicine	32	87.3
Surgery	25	36.4
Intensive care unit	22	62.6
Pediatrics	21	82.6
Geriatrics	10	71.2
Anesthesiology	15	23.3
Emergency medicine	16	50.0
Other	22	57.2

Data from Pittet D. Hand hygiene among physicians: performance, beliefs, and perceptions. *Ann Intern Med*. 2004;141:1–8.

Fig. 1.13 Portrait of Edward Jenner. (From the Wellcome Historical Medical Museum and Library, London.)

Fig. 1.14 *Une des premières vaccinations d'Edward Jenner* ("One of the first vaccinations by Edward Jenner"), by Gaston Melingue. (Reproduced by permission of the Bibliothèque de l'Académie Nationale de Médecine, Paris, 2007.)

Edward Jenner and Smallpox

Edward Jenner (Fig. 1.13) was born in 1749 and became very interested in the problem of smallpox, which was a worldwide scourge. In the late 18th century, 400,000 people died from smallpox each year and one-third of survivors were blinded as a result of corneal infections. It was known that those who survived smallpox were subsequently immune to the disease, and consequently it became a common preventive practice to infect healthy individuals with smallpox by administering to them material taken from smallpox patients, a procedure called *variolation*. However, this was not the optimal method: some variolated individuals died from the resulting smallpox, infected others with smallpox, or developed other infections.

Jenner was interested in finding a better, safer approach to preventing smallpox. He observed, as had other people before him, that dairy maids, the young women whose occupation was milking cows, developed a mild disease called cowpox. Later, during smallpox outbreaks, smallpox appeared not to develop in these young women. In 1768 Jenner heard a claim from a dairy maid, "I can't take the smallpox for I have already had the cowpox." These data were observations and were not based on any rigorous study, but Jenner became convinced that cowpox could protect against smallpox and decided to test his hypothesis.

Fig. 1.14 shows a painting by Gaston Melingue of Edward Jenner performing the first vaccination in 1796. (The term "vaccination" is derived from *vacca*, the Latin word for "cow.") In this painting, a dairy maid, Sarah Nelmes, is bandaging her hand after just having had some cowpox material removed. The cowpox material is being administered by Jenner to an 8-year-old "volunteer," James Phipps. Jenner was so convinced that cowpox would be protective that 6 weeks later, to test his conviction he inoculated the child with material that had just been taken from a smallpox pustule. The child did not contract the disease. We shall not deal in this chapter with the ethical issues and implications of this experiment. (Clearly, Jenner did not have to justify his study before an institutional review board!) In any event, the results of the first vaccination and of what followed eventually saved literally millions of human beings throughout the world from disability and death caused by the scourge of smallpox. The important point is that Jenner knew nothing about viruses and nothing about the biology of the disease. He operated purely on observational data that provided him with the basis for a preventive intervention.

In 1967 the World Health Organization (WHO) began international efforts to eradicate smallpox using

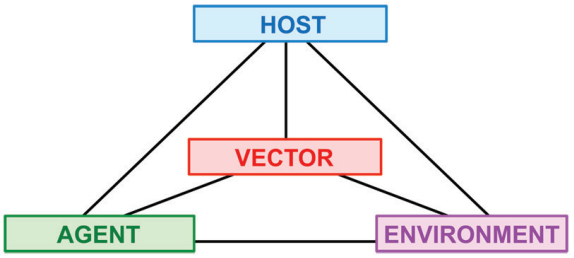


Fig. 2.1 The epidemiologic triad of a disease.

TABLE 2.1 Factors That May Be Associated With Increased Risk of Human Disease

Host Characteristics	Types of Agents and Examples	Environmental Factors
Age	Biologic	Temperature
Sex	Bacteria, viruses	Humidity, Altitude
Race	Chemical	Crowding
Religion	Heavy metals, alcohol, smoke	Housing
Customs	Physical	Neighborhood
Occupation	Trauma, radiation, fire	Water
Genetic profile	Nutritional	Milk
Marital status	Lack, excess	Food
Family background		Radiation
Previous diseases		Air pollution
Immune status		Noise

BOX 2.1 Modes of Disease Transmission

1. Direct
   a. Person-to-person contact
2. Indirect
   a. Common vehicle
      1) Single exposure
      2) Multiple exposures
      3) Continuous exposure
   b. Vector

Indirect transmission can occur through a common vehicle such as a contaminated air or water supply or by a vector such as the mosquito. Some of the modes of transmission are shown in Box 2.1.

Fig. 2.2 is a classic photograph showing droplet dispersal after a sneeze. It vividly demonstrates the potential for an individual to infect many people in a brief period of time. As Mims has pointed out:

> *An infected individual can transmit influenza or the common cold to a score of others in the course of an innocent hour in a crowded room. A venereal infection also must spread progressively from person to person if it is to maintain itself in nature, but it would be a formidable task to transmit venereal infection on such a scale.*[2]

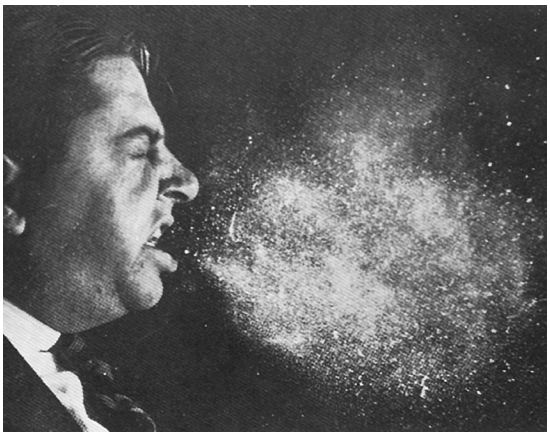


Fig. 2.2 Droplet dispersal following a violent sneeze. (Reprinted with permission from Jennison MW. *Aerobiology*. 17:102, 1947. Copyright 1947 American Association for the Advancement of Science.)

Thus, different organisms spread in different ways, and the potential of a given organism for spreading and producing outbreaks depends on the characteristics of the organism, such as its rate of growth, the route by which it is transmitted from one person to another, and the number of susceptible persons in the community.

Fig. 2.3 is a schematic diagram of human body surfaces as sites of microbial infection and shedding. The alimentary tract can be considered as an open tube that crosses the body, and the respiratory and urogenital systems are shown as blind pockets. Each offers an opportunity for infection. The skin is another important portal of entry for infectious agents, primarily through scratches, bites, or injury. Agents that often enter through the skin include streptococci or staphylococci and fungi such as tinea (ringworm). Two points should be made in this regard: first, the skin is not the

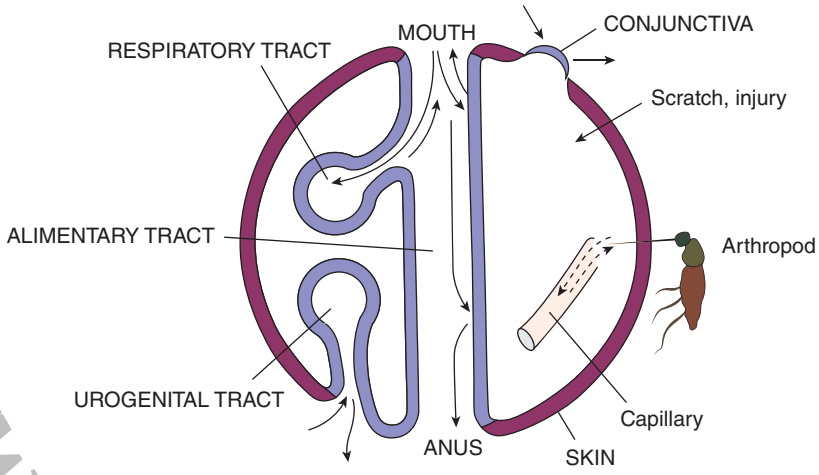


Fig. 2.3 Body surfaces as sites of microbial infection and shedding. (From Mims CA, Nash A, Stephen J. *Mims' Pathogenesis of Infectious Disease*. 5th ed. London: Academic Press; 2001.)

exclusive portal of entry for many of these agents, and second, infections can be acquired through more than one route. The same routes also serve as points of entry for noninfectious disease-causing agents. For example, environmental toxins can be ingested, inspired during respiration, or absorbed directly through the skin. The clinical and epidemiologic characteristics of many infectious and noninfectious conditions often relate to the site of the exposure to an organism or to an environmental substance and to its portal of entry into the body.

Another example of more than one mode of transmission is the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative virus of coronavirus disease 19 (COVID-19). While the primary mode of transmission of SARS-CoV-2 is through exposure to respiratory fluids carrying infectious virus by inhalation of air carrying infectious virus, deposition of virus carried in droplets onto exposed mucous membranes or touching infected mucous membranes with hands that were contaminated with droplet-containing infectious virus may occur.[3]

CLINICAL AND SUBCLINICAL DISEASE

It is important to recognize the broad spectrum of disease severity. Fig. 2.4 shows the iceberg concept of disease. Just as most of an iceberg is under water and hidden from view with only its tip visible, so it is with disease: only clinical illness is readily apparent (as seen

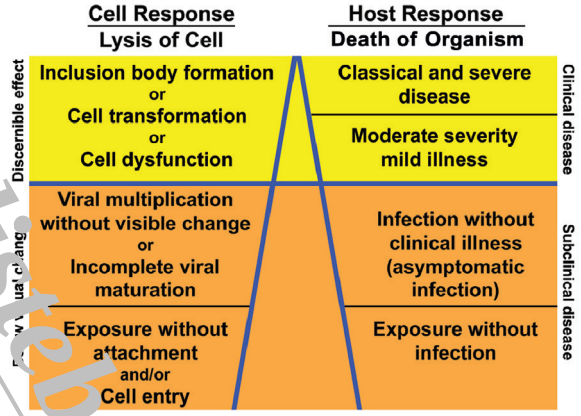


Fig. 2.4 The "iceberg" concept of infectious diseases at the level of the cell and of the host. (Modified from Evans AS, Kaslow RA, eds. *Viral Infections of Humans: Epidemiology and Control*. 4th ed. New York: Plenum; 1997.)

under *Host Response* on the *right* side of Fig. 2.4). However, infections without clinical illness are important, particularly in the web of disease transmission, although they are not clinically apparent. In Fig. 2.4, the corresponding biologic stages of pathogenesis (biologic mechanisms) and disease at the cellular level are seen on the *left*. The iceberg concept is important because it is not sufficient to count only the clinically apparent cases we see; for example, most cases of polio in prevaccine days were subclinical—that is, many people who contracted polio infection were not clinically ill.