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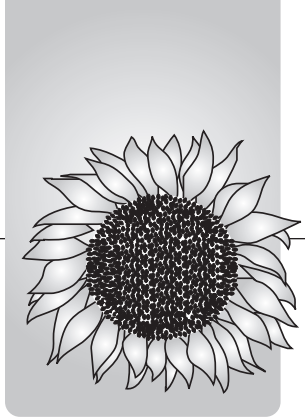

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Contraception, Population, and the Environment

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As we write this chapter, the earth's population of humans exceeds 7.7 billion. Hopefully our collective work in family planning will slow the rate of population growth over the next 80 years. If we are lucky, population will peak at just over 11 billion around 2100 before gradually stabilizing in the next millennium.[1] Achieving this goal will require us to rapidly reach a global total fertility rate (TFR) of about 2.1, a feat yet to be accomplished. We remain optimistic in pursuit of this objective as the consequences of failure are unacceptable.

Our global predicament provides evidence that Earth struggles to adequately support the current population of humans. Our ecologic footprint is not just a "catchphrase." Around 1970, the resources used daily surpassed what the Earth can maintain, meaning that Earth cannot generate resources fast enough to support our growing population.[2] Already, nations compete vigorously for the finite resources of Earth, with rising nationalism, war, famine, and migration of displaced people symptoms of massive inequality of wealth and resource distribution.[3] How will we respond to the addition of 4 billion more inhabitants by the end of the current century?

Fifty years ago, Professor Paul Ehrlich of Stanford University alerted the world to the hazards of unchecked population growth through publication of *The Population Bomb*.[4] Widely criticized as Malthusian sensationalism, his predications of exponential population growth leading to food insecurity and environmental degradation generally reflect the dilemma of our modern world.[3] In a 2014 commentary, Ehrlich urged greater activism: "All scientists should be allocating a significant amount of effort to promoting understanding and action to deal with the major drivers of environmental destruction: population growth, overconsumption by the rich, and socioeconomic inequity."[5]

Our calling of voluntary family planning represents the most humane and respectful approach to a better collective future. As health care providers, we have the privilege of delivering family planning services, and the obligation to advocate for universal access to these tools. This chapter provides a framework to view the history of contraception as a story of human innovation, dignity, and empowerment of women.

Human Population Growth

About 2 million years ago, hominoids began their ascent on the African continent and spread throughout the world.[6] By 40,000 years ago, the era of speciation of humans had ended, with only *Homo sapiens* remaining.[7] World population remained stable, and in balance with resource consumption throughout most of human history. The total human population did not reach 1 billion until about 1827.[8] Due to emerging technologies allowing exploitation of new energy resources, advances in disease prevention, and improved agricultural techniques, we reached the second billion in less than 100 years. Population growth advanced quickly to 7 billion within the next 100 years **(Table 1.1)**.[8]

It is useful to consider that the technologic achievements associated with this explosive population growth have been appreciated only recently. A 1966 report commissioned by NASA placed these gains into perspective.[9] If we consider that eight hundred human lifespans of only 60 years span roughly 50,000 years, then among the generations of those 800 people:

- 650 spent their lives in caves.
- Only the last 70 had a truly effective means of communication.
- Only the last 6 saw the printed word.
- Only the last 4 could measure time with precision.
- Only the last 2 used an electric motor.
- The majority of items that make up our current world were developed within the lifespan of the 800th person.

Correcting for one or two additional generations from 1966 does not make the comparison less remarkable today!

Peak Population

We live in the era of peak population. While we cannot change history, our collective actions today influence the future, and history should inform our

Table 1.1 Human Population Growth

Year	Population (Billions)	Years to Reach the Next Billion
1827	1	93
1920	2	37
1957	3	17
1974	4	13
1987	5	12
1999	6	12
2011	7	?

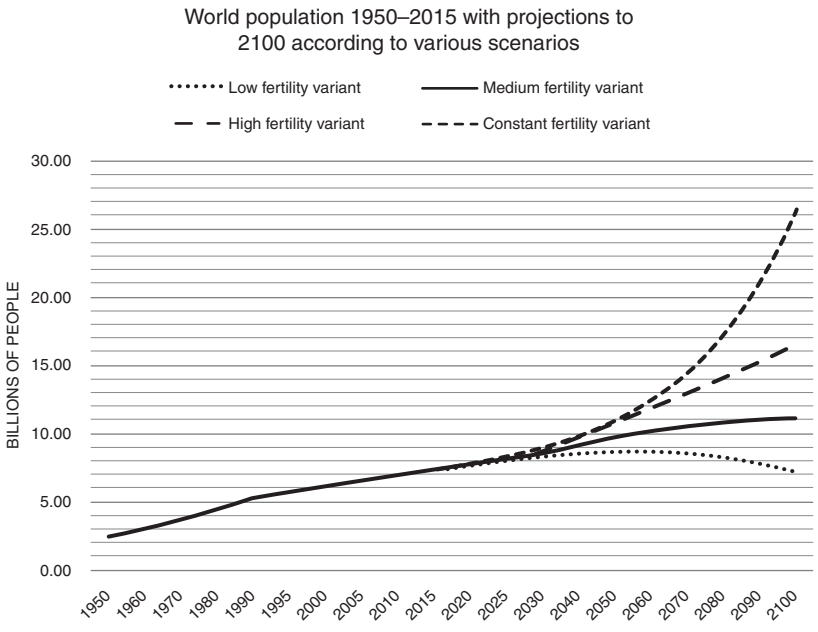

Figure 1.1 World population 1950–2015 with projections to 2100 according to various total fertility rate (TFR) scenarios. Medium fertility variant: assumes total fertility in all countries averages 1.85 children/woman; high fertility variant, 0.5 children above the medium variant; low fertility variant, 0.5 children below medium variant; constant fertility variant, assumes fertility remains at 2000–2005 estimate for each country. (Source: United Nations, Department of Economic and Social Affairs, Population Division (2017). World Population Prospects: The 2017 Revision, Volume I: Comprehensive Tables (ST/ESA/SER.A/399).)

actions and decisions. **Figure 1.1** illustrates four potential scenarios based on the United Nations Population Division's 2017 revised estimates of fertility patterns projected to 2050. The TFR provides an estimate of the number of children born per woman in a population calculated using current age-specific fertility rates. The TFR provides a better estimate of fertility and population growth than do crude birth rates, as it accounts for birth per woman over the reproductive lifespan. A TFR of 2.1 is considered replacement fertility.[1]

The United Nations Population Division's "medium" fertility estimate assumes that the TFR converges gradually to 1.85 in all nations over the next 50 years, but we can consider this more simply as reflecting replacement fertility (i.e., TFR 2.1). "High" and "low" fertility estimates assume an average of one-half a child more (or less); since women don't have half children, think of this as more women having a third child or more having only one or none. The global impact of the "third child" scenario cannot be understated. While population is expected to peak at around 11.4 billion in 2100 before stabilizing under the medium estimate, under the high fertility scenario (TFR 2.6), we

reach 11 billion by 2050 and surge to over 16 billion by 2100 with no end in sight.[10] In fact, even with a rapid decline to low fertility (TFR 1.6), population would continue to grow through midcentury with a peak of around 9 billion achieved in 2050 followed by a gradual decline by the end of the century to a population similar to today. Some economists believe economic growth and wealth require an ever-expanding population and place faith that scientific and technologic advances will provide for all. We feel science is better equipped to deal with the potential challenges of transition to a smaller population where people share scarce resources more equitably.

Worldwide, fertility has declined in most developed nations, with a TFR below replacement in China, Eastern and Western Europe, Canada, Japan, Australia, and New Zealand.[1] The TFR in the United States has hovered around 2.1 for the last few years largely due to higher fertility rates among recent migrants.[11] However, since 2016, the TFR in the United States has been below 2.0, most recently 1.78.[12] Today, almost all population growth occurs in developing countries. Ten countries will account for more than half of the world's projected population over the next 30 years (ordered by their expected contribution to global growth): India, Nigeria, the Democratic Republic of Congo, Pakistan, Ethiopia, the United Republic of Tanzania, the United States, Uganda, Indonesia, and Egypt. The United Nations Population Division estimates that by 2050, 90% of the total population of earth will live in less developed nations.[1]

The consequences of this demographic transition will affect all aspects of our modern lives. A growing literature links population growth and environmental decline to war, famine, terrorism, and human migration.[13] Over the last 20 years, between 3 and 4 million people each year migrated for economic reasons from low- and middle-income nations to high-income countries.[1] Those who remained behind in the poorest nations face environmental and political challenges that threaten their daily existence.

A bulging youth population drives future population growth in less developed nations. In Africa, for example, 60% of the population is less than 25 years old.[1] Poverty and limited opportunity for a better future in poor nations provide fertile ground for civil unrest and recruitment of terrorists. The fact that the population surge occurring in the poorest nations coincides with declining fertility and overconsumption in rich nations compounds the difficulty. A lack of opportunity in poor nations fuels resentment and contributes to war, terrorism, and displaced people. The surge in migrants to rich nations and clash of cultures has given rise to xenophobic nationalist regimes in many countries, including the election of Donald Trump in the United States.

The history of our era will be the story of how the minority of earth's inhabitants living in rich nations will either share or deny earth's finite resources to the majority of inhabitants living in poor nations. The unrelenting pressure of future population growth only intensifies our challenge. Unfortunately, the politics of population growth and income inequality interfere with discussion of population policies. For this reason, many environmental and social justice advocates hesitate to prioritize family planning

as a policy objective. This thinking fails to consider our fragile and interconnected earth. Both rich and poor nations have a responsibility to limit family size and future population growth. The world can sustain neither unchecked consumption in rich nations nor high fertility in poor nations.

Population and the Environment

In a 1971 paper published in *Science*,[14] Paul Ehrlich and John Holdren provided a useful formula linking environmental impact to population:

$$I = P \times A \times T$$

where:

I = environmental impact
P = population size
A = affluence (a measure of consumption)
T = technology (a measure of energy use to support the affluence)

This formula allows us to compare the relative environmental impact of different states. Rich nations like the United States, with high affluence and wasteful energy policies and a relatively large population size, have the greatest overall global environmental impact. In rich nations with stable populations, a dual strategy of embracing policies that reduce both the **T** (such as substituting renewable energy for coal) and **A** (changing the ethos to "enough" rather than "more") diminishes overall impact. While poor nations such as India with low per capita affluence and energy use have a comparatively lower global impact, we cannot neglect the contribution of a large and growing population. Understandably, citizens of poor nations aspire to gain the wealth common in rich nations, and as income rises, so does energy use and consumption. Even small gains in **A** and **T** contribute greatly to **I** with large and growing populations. Moreover, migrants to the United States and Europe from poor regions understandably seek to consume at North American and European levels, increasing global **I** even faster.

As biologists, we see a world of finite resources under significant stress at our current population under siege by a global economic policy that assumes human ingenuity will continue to provide for any number of humans. This ingenuity hypothesis faces an enormous test in the coming decades. Without population growth, at current rates of economic growth, China is projected to outpace the United States in use of all resources by 2035, consuming roughly two thirds of the world's production of grain and meat.[15] China is not the only nation seeking a bigger piece of the global resource pie. Will we see global cooperation or conflict as nations vigorously compete for earth's limited resources?

The wild-card effects of global warming and degradation of ecosystem services contribute further to our concerns about overpopulation. A recent assessment of the impact of rising temperatures on global yields of major crops predicted that each degree Celsius increase in global mean temperature

would, on average, reduce global yields of wheat by 6.0%, rice by 3.2%, maize by 7.4%, and soybean by 3.1%.[16] The overuse of aquifers and competition for freshwater sources also threaten agricultural productivity.[17]

The only variable that will reduce **I** under all scenarios is reduction in **P**. We cannot overemphasize the importance of voluntary contraception and global family planning policies as the most humane and practical approach to a just and peaceful future for our grandchildren. The Centers for Disease Control and Prevention (CDC) recognized the importance of these issues, citing family planning as one of the 10 great public health achievements of the 20th century.[18]

History of Contraception

Reproduction represents the most essential biologic activity. All species compete and expand populations to the limits of available resources. Natural constraints limit population growth, and the expression of fertility cycles continually throughout life for most species. Sex is a strong instinctive activity related to a natural need to repopulate the species. Since contraception violates this core hardwired behavior, it is not surprising that strong opinions follow. Unfortunately, many fundamentalist and orthodox religious scholars dismiss contraception as unnatural without painting most of the other medical conveniences that define our modern lives, such as vaccinations, antibiotics, and surgery, with the same brush.

Like all species, early humans struggled to survive. Groups prospered and populations increased during good times. Disease and famine had the opposite effect. Primitive humans lived in balance with the natural world. Births roughly matched deaths during the initial years of human evolution with well-defined gender roles and no need for contraception. The cycle of fertility controlled women's lives and limited opportunities. Pregnancy followed menarche, and prolonged lactational amenorrhea followed birth, until a woman became pregnant again. For these reasons, women in traditional societies experienced relatively few menstrual cycles.[19] Lifespan rarely surpassed the reproductive years due to death in childbirth and natural disease. Although women today may think that having a monthly menses is "natural," human women naturally experience lack of menses due to pregnancy and lactation as well as death prior to menopause.

In contrast, a modern woman will experience hundreds of menstrual cycles over her lifetime. Contemporary women also undergo earlier menarche and start having sexual intercourse at a younger age than past generations. Even though breastfeeding has increased in recent years, the duration of exclusive breastfeeding and related contraceptive lactational amenorrhea contributes minimally to fertility control in the developed world. Therefore, women today require highly effective modern contraceptive methods to limit family size.

The history of contraception is an amazing story of innovation and scientific discovery. Many excellent references, including earlier editions of this textbook, provide details beyond the scope of this chapter. To keep

the length of this edition manageable, we have compiled the comprehensive details of the history of various methods from previous editions into a supplemental chapter available in the eBook. Here, we present highlights of this amazing journey.

Contraception Prior to the Modern Era

It is impossible to unlink the history of contraception from the broader history of the women's movement. One cannot overstate the importance of highly effective reversible and permanent methods of contraception as essential tools for female empowerment. We believe that when women control their own fertility, they not only improve their own lives but also improve the lives of their children and their communities. Not surprisingly, those nations that deny women access to family planning and education suffer from poverty and social instability and rank among the most desperate places on earth.[20]

The introduction of the birth control pill in 1960 ushered in the modern era of contraception. Prior to that time, the limited available approaches for fertility regulation included the male condom, the female vaginal diaphragm, and withdrawal. Although intrauterine devices (IUDs) may have an ancient origin, devices designed specifically for contraceptive purposes did not appear until the beginning of the 20th century and did not enjoy extensive use until much later.[21]

Widespread income inequality has existed in the United States for centuries. The rich enjoy access to opportunities, including contraceptive methods, unavailable to poor persons. This great disparity has motivated many activists over the last century, including Margaret Sanger. Sanger worked tirelessly and at great peril to provide information about basic sexuality and contraception options to working-class women and men. Her activities included public speaking and the publications of pamphlets promoting the concept that every woman had a right to be "absolute mistress of her own body." This included the right to practice birth control, a term coined in *The Woman Rebel*, a series published between 1914 and 1915.[22] A 1916 pamphlet *Family Limitation* provided details on techniques for menstrual regulation and the use of vaginal pessaries (diaphragm).[23] These activities put her at risk for prosecution and imprisonment under the Comstock Act of 1873.

The Comstock Act prohibited the circulation of "obscene literature and items deemed for immoral use." Over the years, courts ruled that the Act also prohibited the distribution of contraceptive information and devices. Many states also passed laws that prohibited the use of contraceptives, even among married couples. With reproductive rights still under assault today, it is important to recognize that recognition of a constitutionally protected right to privacy that allowed married couples to use contraception did not occur until the landmark Supreme Court decision of Griswold versus the State of Connecticut in 1965. Eisenstadt versus Baird extended this right to unmarried couples in 1972.[24]

Sanger survived her legal battles and founded the American Birth Control League in 1920, which in turn became the Birth Control Federation

of America and eventually Planned Parenthood Federation of America in 1942. But arguably, her most important contributions involved her support for research to improve contraceptive methods through the development of oral contraception and the founding of the Population Council in 1952.

The Birth Control Pill Story and the Development of Hormonal Contraception

Few innovations in human history rival the social impact of the approval of oral contraception in 1960. Our limited space does not allow a complete presentation of this amazing story. We highly recommend *A Good Man*, the biography of Gregory Pincus written by Leon Speroff for a detailed history.[25] We borrow heavily from Speroff's book (with permission) for this summary. More detail on hormonal contraception is also presented in Chapter 2.

In 1951, Sanger introduced Gregory Pincus, a reproductive biologist at the Worcester Institute to Katharine McCormick, the first female graduate of the Massachusetts Institute of Technology and one of the richest women in the world. McCormick first met Sanger in 1917 and had long supported her efforts. Pincus, in collaboration with M.C. Chang, had demonstrated that progesterone could inhibit ovulation. McCormick provided Pincus with funding to develop a birth control pill, spending over $2 million between 1953 and 1958.

A birth control pill required the development of orally active and potent progesterone receptor agonists. The chemist Russell Marker solved the problem of supply by developing the synthetic steps to synthesize progesterone using the Mexican yam as a plant-based substrate. The importance of Marker's work to medicine cannot be overstated. The availability of large quantities of progesterone also provided the substrate for cortisol, in high demand for therapeutic use.

With a reliable source of substrate, G.D. Searle and Syntex, companies that we would call "start-ups" today, became involved in the synthesis of progesterone and cortisol. In collaboration with other chemists, notably Carl Djerassi, the scientists' and companies' cumulative efforts led to the development of novel synthetic highly potent orally active progestins. Pincus and Chang tested these compounds for effects on ovulation in animals and moved ahead with the Searle product norethynodrel.

Pincus recognized the need for a clinical collaborator and recruited Dr. John Rock, chief of gynecology and obstetrics at Harvard, for clinical trials of a birth control pill. Rock was a leading academic gynecologist with a research interest in fertility and menstrual disorders. For more than a decade, gynecologists had recommended porcine luteal extracts for the management of menstrual disorders, and Rock had also performed clinical experiments to understand the effects of newly available pure progesterone and the recently synthesized progestins.

The initial studies Rock performed on his patients demonstrated that progesterone 300 mg/d orally could inhibit ovulation in most women. A 20-day regimen beginning on cycle day 5 was picked to cover the expected time range for ovulation and to allow for normal monthly bleeding. When

the progestin norethynodrel became available in 1954, the investigative team switched to this novel agent and found complete ovulation inhibition in 50 women using 10 to 40 mg/d. Interestingly, the initial progestin products were contaminated with about 1% mestranol, a synthetic estrogen known today as the prodrug for ethinyl estradiol (EE). When women subsequently received a purified progestin without mestranol, they experienced irregular bleeding. As a result, estrogen was added back in the final design of the pill to improve cycle control, establishing the principle of cyclic combined hormonal contraception.

For those of us involved in clinical trials today, the pace of progress in the oral contraception development story seems breathtaking. Collaborating with Rock and Pincus, Celso-Ramon Garcia and Edris Rice-Wray, working in Puerto Rico, performed the first contraceptive human trial in 1956. In 1957, Enovid® (mestranol 150 μg/norethynodrel 9.85 mg) was approved by the U.S. Food and Drug Administration (FDA) for the treatment of miscarriages and menstrual disorders and, on June 23, 1960, for contraception. Lower-dose estrogen formulations followed quickly with Ortho-Novum (mestranol 60 μg/norethindrone 10 mg) approved in 1962 and Ovral (EE 50 μg/norgestrel 500 μg) in 1968.

By the late 1960s, concerns regarding an association between use of oral contraceptives and venous thromboembolism (VTE) led to government commissions investigating safety. In 1968, Vessey and Doll[26] reported a ninefold increase in the risk of VTE in users of oral contraceptives compared to nonusers. A follow-up publication by Inman in 1970 documented a clear relationship between estrogen dose and VTE.[27]

In 1969, concerns came to a head with the publication of *The Doctor's Case Against the Pill*. In this controversial book, medical journalist Barbara Seaman combined the testimony of physicians, medical researchers, and women who had used oral contraceptives to build a case against the safety of the Pill and to indict the medical-pharmaceutical establishment that had marketed it. Shortly after publication, U.S. Senator Gaylord Nelson read Seaman's book while he was conducting hearings on the pharmaceutical industry regarding alleged abuses in the use of antibiotics, barbiturates, and tranquilizers. After finishing Seaman's book, he decided to take on the birth control pill as well. The high profile and highly publicized Senate hearings in 1970 attacked the safety of the pill. More than 85% of reproductive age women followed the dramatic hearings.

One needs to put this timing in perspective. The sexual revolution that commenced during the tumultuous 60s was in full swing with new positive and permissive attitudes toward female sexuality and premarital sex, leading to a greater interest in contraception. Over the next few decades, the pharmaceutical industry introduced a number of different formulations of combined pills with novel progestins and lower doses of estrogen with the goal of improving safety and tolerability while maintaining efficacy. More recently, we have seen the introduction of nonoral combined contraceptives (vaginal rings, transdermal patches, and injectables) that provide alternatives

to daily administration. We discuss the key details of the pharmacology of combined hormonal contraception in Chapter 2 and management of combined hormonal contraceptive patients in Chapter 7.

Although the 1970 Senate hearings did not ultimately affect oral contraception availability, almost 20% of current users quit taking the pill in response to the reporting. These concerns led many women to turn to the vaginal diaphragm, the method of their mother's generation. For others, the solution was an IUD.

A Brief History of the Intrauterine Device

The modern history of IUD development begins with ring devices developed by Gräfenberg in Germany and Ota in Japan prior to World War II.[21] A resurgence in interest in intrauterine contraception followed the introduction of the pill, with multiple devices introduced in the 1960s and 1970s. In 1962, the Population Council sponsored the first international conference on IUDs in New York City. The most widely used devices in the sixties included the Lippes Loop, invented in 1962, and the Saf-T-Coil introduced in 1968. Both of these plastic frame devices came in multiple sizes and can be classified as inert or nonmedicated IUDs.

A.H. Robbins introduced the Dalkon Shield in 1970, the same year as the Senate hearings on the safety of oral contraceptives. The manufacturer aggressively marketed the device to clinicians using claims that the unique smaller "anatomic" design was particularly suitable for nulliparous women as a first-line contraception choice. In 1970, clinicians screened for gonorrhea by inoculating a chocolate agar bacteriologic plate and incubating this in a high carbon dioxide chamber. Chlamydia was unknown, and no reliable test existed to diagnose "nongonococcal urethritis." Not surprisingly, changes in sexual behavior and a decreased reliance on condoms for pregnancy prevention during this time led to a surge in rates of sexually transmitted infections (STIs).

Within 3 years of market introduction, clinicians recognized a high incidence of pelvic infection (including septic abortion and pelvic abscess) in Dalkon Shield users.[28] Tatum quickly pointed out that a unique design feature of the shield, a removal string that consisted of a multifilament thread enclosed in a plastic sheath, contributed to infection risk as it provided a pathway for bacteria to ascend into the upper genital tract protected from the barrier of cervical mucus.[29] Even though by the midseventies more effective copper-releasing IUDs had been introduced, the fear of infections due to the Dalkon Shield experience tainted all IUDs, and enthusiasm for their use plummeted along with sales. Although subsequent well-designed epidemiologic studies confirmed that the elevated risk of pelvic infections seen with IUDs was confined to users of the Dalkon Shield,[30] other manufactures withdrew their products. By 1984, only the 1-year progesterone-releasing Progestasert® IUD remained on the U.S. market.

The pharmaceutical industry abandoned the copper IUD in the 1980s for corporate business decisions related to concerns for profit and liability,