success than purple-flowered plants when yellow was rare and suffered lower reproductive success when yellow was common.

Gigord and colleagues calculated the relative reproductive success of yellow orchids as

$$RRS_y = \frac{2(RS_y)}{RS_y + RS_p}$$

where RS_y and RS_p are the absolute reproductive success of yellow and purple orchids. The relationship between relative reproductive success via male function and the frequency of yellow flowers is given by the best-fit line in Figure 6.21b. It is

$$RRS_y = -0.66F_y + 1.452$$

where F_y is the frequency of yellow flowers.

We can incorporate this relationship into a population genetics model. We might imagine, for example, that flower color is determined by two alleles at a single locus and that yellow is recessive to purple. We set the starting frequency of the yellow allele to an arbitrary value. We assign fitnesses to the three genotypes as we have before, except that the fitnesses change each generation with the frequency of yellow flowers. When we use a computer to track the evolution of our model population, we discover that the frequency of the yellow allele moves rapidly to equilibrium at an intermediate value. This value is precisely the allele frequency at which yellow flowers have a relative fitness of 1. We get the same result if we imagine that yellow flowers are dominant. Again the equilibrium value for the yellow allele is the frequency at which yellow and purple flowers have equal fitness.

The dashed vertical lines in Figure 6.24b and c indicate the predicted equilibrium frequencies Gigord and colleagues calculated for each of their fitness measures. The predictions are 61%, 69%, and 72% yellow flowers. The researchers surveyed 20 natural populations in the region where they had placed their experimental arrays. The actual frequency of yellow flowers, $69 \pm 3\%$, is in good agreement with the predicted frequency. Our model has passed its fourth test.

Gigord et al.'s study of Elderflower orchids demonstrates that frequency-dependent selection can have an effect similar to heterozygote superiority. Both patterns of selection can maintain genetic diversity in populations.

Compulsory Sterilization

We can use population genetics models to evaluate whether eugenic sterilization could have accomplished the aims of its proponents, had their assumptions about the heritability of traits been correct. The answer depends on the frequency of the alleles in question, and on the criteria for success.

The theory of population genetics, despite its simplifying assumptions, allows us to predict the course of evolution. Our four tests show that the model we have developed works remarkably well. So long as we know the starting allele frequencies and genotype fitnesses, the model can predict how allele frequencies will change, under a variety of selection schemes, many generations into the future. The requisite knowledge is easiest to get, of course, for experimental populations living under controlled conditions in the lab. But Gigord et al.'s study of Elderflower orchids shows that the model can even make fairly accurate predictions in natural populations. Given its success in the four tests, it is reasonable to use our model to consider the evolutionary consequences of a eugenic sterilization program. The proponents of eugenic sterilization sought to reduce the fitness of particular genotypes to zero and thereby to reduce the frequency of alleles responsible for undesirable phenotypes. Would their plan have worked?

The phenotype that caught the eugenicists' attention perhaps more than any other was feeblemindedness. The Royal College of Physicians in England defined a feebleminded individual as "One who is capable of earning his living under favorable circumstances, but is incapable from mental defect existing from birth or from an early age (a) of competing on equal terms with his normal fellows or (b) of managing himself and his affairs with ordinary prudence" (see Goddard 1914). Evidence presented in 1914 by Henry H. Goddard, who was the director of research at the Training School for Feebleminded Girls and Boys in Vineland, New Jersey, convinced many eugenicists that strength of mind behaved like a simple Mendelian trait (see Paul and Spencer 1995). Normal-mindedness was believed to be dominant and feeblemindedness recessive.

A recessive genetic disease is not a promising target for a program that would eliminate it by sterilizing affected individuals. As Figures 6.19a and 6.20a show, rare recessive alleles decline in frequency slowly, even under strong selection. On the other hand, eugenicists did not believe that feeblemindedness was especially rare (Paul and Spencer 1995). Indeed, they believed that feeblemindedness was alarmingly common and increasing in frequency. Edward M. East (1917) estimated the frequency of feeblemindedness at three per thousand. Henry H. Goddard reported a frequency of 2% among New York schoolchildren. Tests of American soldiers during World War I suggested a frequency of nearly 50% among white draftees.

We will assume a frequency for feeblemindedness of 1% and reproduce a calculation reported by R. C. Punnett (1917) and revisited by R. A. Fisher (1924). Let *f* be the purported allele for feeblemindedness, with frequency q. If 1% of the population has genotype *ff*, then, by the Hardy–Weinberg equilibrium principle, the initial frequency of *f* is

$$q = \sqrt{0.01} = 0.1$$

If all affected individuals are sterilized, then the fitness of genotype *ff* is zero (or, equivalently, the selection coefficient for genotype *ff* is 1). Using the equation developed in Computing Consequences 6.6, we can calculate the value of q in successive generations, and from q we can calculate the frequency of genotype *ff*.

The result appears in Figure 6.25. Over 10 generations, about 250 years, the frequency of affected individuals declines from 0.01 to 0.0025.

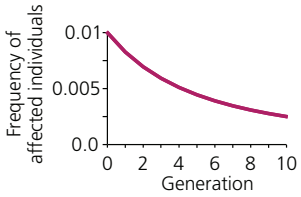

Figure 6.25 Predicted evolution due to sterilization The graph shows the change in the frequency of homozygotes for a putative allele for feeblemindedness under a eugenic sterilization program that prevents homozygous recessive individuals from reproducing.

Whether geneticists saw this calculation as encouraging or discouraging depended on whether they saw the glass as partially empty or partially full. Some looked at the numbers, saw that it would take a very long time to completely eliminate feeblemindedness, and argued that compulsory sterilization was such a hopelessly slow solution that it was not worth the effort. Others, such as Fisher, dismissed this argument as "anti-eugenic propaganda." Fisher noted that after just one generation, the frequency of affected individuals would drop from 100 per 10,000 to 82.6 per 10,000. "In a single generation," he wrote, "the load of public expenditure and personal misery caused by feeblemindedness . . . would be reduced by over 17 percent." Fisher also noted that most copies of the allele for feeblemindedness are present in heterozygous carriers rather than affected individuals. Along with East, Punnett, and others, Fisher called for research into methods for identifying carriers.

While their evolutionary logic was sound, the eugenicists' models were built on dubious genetic hypotheses. It is not entirely fair to use modern standards to criticize Goddard's research on the genetics of feeblemindedness. Mendelian

genetics was in its infancy. Still, looking back after nearly a century, we can see that Goddard's evidence was deeply flawed. We will consider three problems.

First, the individuals whose case studies he reports are a highly diverse group. Some have Down syndrome; some have other developmental challenges. At least one is deaf and appears to be the victim of a woefully inadequate education. Some appear to have been deposited at Goddard's training school by widowed fathers who felt that children from a prior marriage were a liability in finding a new wife. Some may just have behaved differently than the directors of the school thought they should. Concluding the first case report in his book, Goddard writes of a 16-year-old who has been at the school for seven years:

> Gertrude is a good example of that type of girl who, loose in the world, makes so much trouble. Her beauty and attractiveness and relatively high [intelligence] would enable her to pass almost anywhere as a normal child and yet she is entirely incapable of controlling herself and would be led astray most easily. It is fortunate for society that she is cared for as she is.

Second, Goddard's methods for collecting data were prone to distortion. He sent caseworkers to collect pedigrees from the families of the students at the training school. The caseworkers relied on hearsay and subjective judgments to assess the strength of mind of family members—many of whom were long since deceased.

Third, Goddard's method of analysis stacked the cards in favor of his conclusion. He first separated his 327 cases into various categories: definitely hereditary cases; probably hereditary cases; cases caused by accidents; and cases with no assignable cause. He apparently placed cases in his "definitely hereditary" group only when they had siblings, recent ancestors, or other close kin also classified as feebleminded. When he later analyzed the data to determine whether feeblemindedness was a Mendelian trait, Goddard analyzed only the data from his "definitely hereditary" group. Given how he had filtered the data ahead of time, it is not too surprising that he concluded that feeblemindedness is Mendelian.

Although feeblemindedness is not among them, many genetic diseases are now known to be inherited as simple Mendelian traits. Yet eugenic sterilization has few advocates. One reason is that most serious genetic diseases are recessive and very rare; sterilization of affected individuals would have little impact on the frequency at which new affected individuals are born. A second reason is that mainstream attitudes about reproductive rights have changed to favor individual autonomy over societal mandates (Paul and Spencer 1995). A third reason is that, as we discuss in the next section, a growing list of disease alleles are suspected or known to be maintained in populations by heterozygote superiority. It would be futile and possibly ill advised to try to reduce the frequency of such alleles by preventing affected individuals from reproducing.

6.4 Mutation

Cystic fibrosis is among the most common serious genetic diseases among people of European ancestry, affecting approximately 1 newborn in 2,500. Cystic fibrosis is inherited as an autosomal recessive trait. Affected individuals suffer chronic infections with the bacterium *Pseudomonas aeruginosa* and ultimately sustain severe lung damage (Pier et al. 1997). At present, most individuals with cystic fibrosis