

Abraham Lincoln's DNA  

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*and Other Adventures in Genetics*

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Philip R. Reilly



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# Genes and Violence

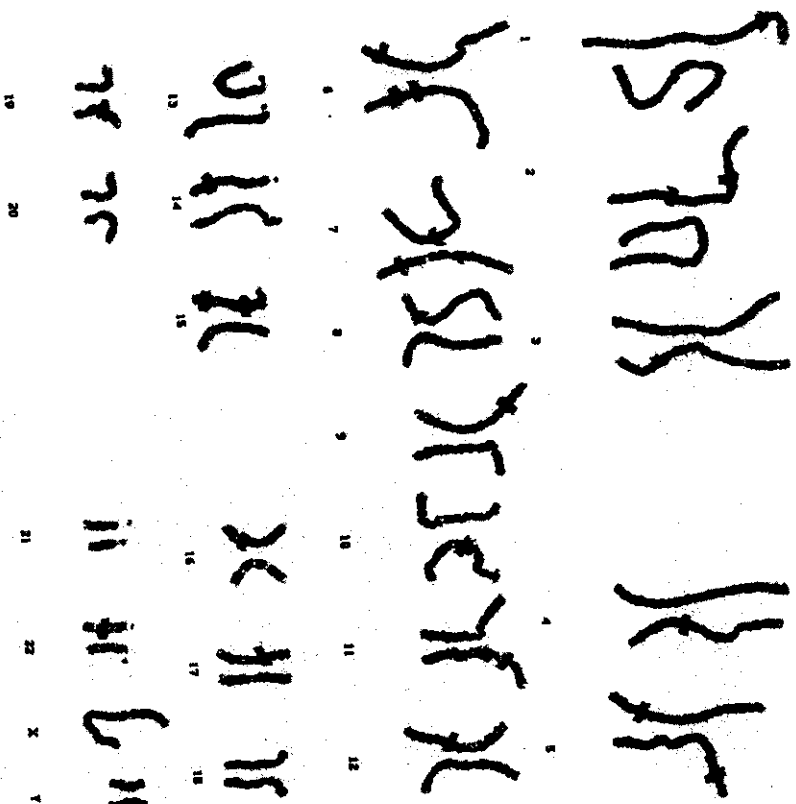
## Do Mutations Cause Crime?

### THE XYY SYNDROME

On Christmas day, 1965, Patricia Jacobs, a promising young cytogeneticist, and her colleagues published an astounding report of their studies of the chromosomes of 197 men who had been committed to the Carstairs Hospital for the criminally insane in Scotland.

The 1960s was the golden age of cytogenetics, a period when, after a dark age, our knowledge of human chromosomes grew immensely. Since 1902, the year that Sutton and Boveri proposed that chromosomes carried the hereditary material (the word gene was not yet in use), cell biologists had labored to understand them. In the case of human tissue, however, their tools were of such limited value that for more than 30 years scientists had accepted an erroneous report by Theodosius Painter that each human cell had 48 chromosomes (23 pairs of autosomes and 1 pair of sex chromosomes). In the early 1920s when Painter did his work, it was not possible to count chromosomes (which under the microscope looked like a plate of spaghetti) in most types of tissue. Knowing that the cell replication cycle of germ cells made them a better object of study, Painter sought permission to dissect the testicles of two inmates of the Texas State Insane Asylum whom authorities had castrated in an effort to control their behavior. In his first paper, he suggested the correct number was either 46 or 48; in his second, he asserted that 48 was the correct count. It was not until 1956 when Tio and Levan, two scientists working in New York, developed a new method to spread out chromosomes so fewer overlap each other that the correct count was discovered to be 46.

In 1958, the French geneticist, Jerome Lejeune, discovered that persons with Down syndrome had 47 chromosomes (the normal complement plus an extra number 21), thus confirming a hypothesis about the



Eight-year-old boy evaluated for behavioral problems and learning disabilities. The prominent glabella and long face are compatible with the presence of an extra Y chromosome (47, XYY syndrome). (Photo reprinted, with permission, from Jones 1988.) (Karyotype courtesy of Genzyme Genetics.)

cause of Down syndrome that had been proposed nearly 30 years earlier. This extremely important discovery triggered huge interest among other scientists. Over the next few years, other researchers made rapid progress in finding abnormal numbers of chromosomes and associating them with physical or mental abnormalities. But no one was prepared for Dr. Jacobs' report.

Jacobs was acting on a hunch. She knew that another cytogeneticist had recently counted the chromosomes in white blood cells taken from 942 men housed in English institutions for criminal and/or mentally retarded men. He had found that 21 of them had an extra X chromosome, and that of these, 7 also had an extra Y chromosome. These findings contrasted sharply with a large study of 2607 mentally subnormal men without significant behavioral problems of whom only 2 had been shown to have the extra Y. Jacobs and her associates wondered "whether an extra Y chromosome predisposes its carriers to unusually aggressive behaviour." If this were true, one would expect to find an unusually large number of men with an extra Y among groups of men with a history of unusually violent behavior.

The Carstairs Hospital housed 203 men, of whom 197 agreed to undergo study. Among them, Jacobs and her colleagues found 12 men with an abnormal karyotype (chromosome count), of whom 7 had an extra Y chromosome. At the time, almost nothing was known about the physical or clinical consequences of being born with an extra Y, but the finding that 3.5% of the Carstairs Hospital population had XYY syndrome was without question much higher than would be expected in a random sample of the normal male population. For example, Jacobs had studied 1500 apparently normal men and found only one with an extra Y. If one assumed that about 1 in 1000 newborn boys had an extra Y, the Carstairs group had more than 30 times the expected number. The other interesting finding that emerged from the Carstairs study was that men with an extra Y chromosome were very likely to be much taller than their counterparts. Those men had an average height that was a full 6 inches greater than the other 190.

Jacobs entitled her brief paper: "Aggressive Behaviour, Mental Subnormality and the XYY male." She closed the report on a provocative note, writing: "At present it is not clear whether the increased frequency of XYY males found in this institution is related to their aggressive behaviour or to

their mental deficiency or to a combination of these factors." The implication was clear; in her opinion, the XYY syndrome might include an in-born tendency to aggressive behavior. Thus was born the notion of the "criminal chromosome," an idea that she did not propagate, but which fascinated the world's journalists.

The report generated intense interest and spirited (sometimes bitter) debate in the scientific and forensic community. As clinical geneticists found and studied more men with XYY syndrome, they learned that in addition to being tall, some of them had coarse facial features, scars from severe acne, and low intelligence. In a word, many of them looked much like Hollywood's portrayal of a hulking criminal. On the other hand, most men with XYY syndrome looked normal, were clearly of normal intelligence, and were leading ordinary lives. A number of researchers argued that the reason that persons with an extra Y chromosome were more likely to turn up in prison populations was because if they committed petty crimes they were more likely to get caught, and if they were tried before a jury they were, because of their "criminal look," more likely to be convicted.

In 1968, thinking that it might settle the controversy over whether a second Y chromosome predisposed to violent behavior, several physicians at Harvard initiated a project to examine the chromosomes of thousands of newborns and then follow those with the XYY and other abnormal chromosomal constitutions through childhood and adolescence. As word got out, the project drew a storm of protest, especially from a Boston-based group called Science for the People, whose members argued that the study was scientifically worthless and likely to harm the children. In their view, parents of children who were found to have the extra Y were likely, despite the advice of the researchers, to view their child as having a behavioral abnormality. This would create a self-fulfilling prophecy. If the parents treated the children as though they were abnormal it was likely that they would develop behavioral problems. The scientific debate became rancorous and was soon immersed in confrontational politics. Faced with mounting adverse publicity, the physicians abandoned the study. To this day, there have been far fewer studies of the developmental course of children with XYY syndrome than of similar cytogenetic conditions such as Klinefelter syndrome (in which boys are born with an extra X chromosome) or Turner syndrome (in which girls are born with only one X).

The controversy largely subsided after the publication of a major study of XYY men in the prestigious journal, *Science*, in 1976. A team of scientists concluded that, as had been posited, many of the XYY men in prisons had wound up there because borderline intelligence and low socioeconomic status had put them at higher than usual risk of being caught and convicted. They were, for example, less likely than others to have a personal attorney and less likely to obtain a successful plea bargain.

Despite the resolution of the scientific debate, defense attorneys became intrigued with the possibility that they might be able to defend clients on trial for violent crimes by invoking a "criminal chromosome" defense. This started in 1968 when a court in Australia acquitted a man who had murdered a 77-year-old woman on the grounds that he was insane because of XYY syndrome. A few weeks later, a French court convicted Daniel Hugon of murder, but reduced his sentence to 7 years because he had an extra Y chromosome. In the United States there were at least seven murder trials in which the defense tried to win an acquittal or obtain a lighter sentence because the defendant had an extra Y chromosome. Only two judges even permitted the evidence to go before the jury. In each case, the prosecution won a guilty verdict. In the only American murder trial in which the defense was permitted to fully develop an argument that the XYY syndrome should be grounds for acquittal based on the presumption that the individual could not control his behavior, a New York jury convicted a 6-foot, 8-inch defendant named Sean Farley.

The insanity defense, a relatively new addition to Anglo-American law, emerged during the late 19th century. Trying cases in which the defendant had engaged in strikingly abnormal behavior that seemed devoid of motive, courts on both sides of the Atlantic concluded that some persons might be incapable of judging right from wrong. For them the concept of guilt had no meaning. In a closely related line of cases, the courts also recognized that there could be rare instances in which persons could be placed in situations in which it was conceivable that they could suddenly lose all measure of self-control and succumb to an unpremeditated, "irresistible impulse." Throughout its history, the insanity defense has been used sparingly, and although it is widely known through movies and plays, it is rarely successfully invoked in real life.

The idea that the XYY syndrome might actually predispose to behavioral abnormalities that might lead to an application of the insanity de-

fense has been dormant during the last two decades. However, there has been no shortage of creative tactics by defense counsel, especially those involved in murder trials. In the last 20 years, low blood sugar levels, high blood sugar levels, premenstrual syndrome, and posttraumatic stress syndrome have all been offered—almost always unsuccessfully—as a basis for an insanity plea.

We now know that the vast majority of people with XYY syndrome do not commit violent crimes. However, we also know that a significant fraction of people in prison and an even higher percentage on death row are of borderline intelligence or have mild mental retardation, and that many of them have a history dating to early childhood of severe behavioral problems. It is probable that many of these (mostly) men have gene variants that contribute to their low intelligence and to their behavioral problems. It is possible, although by no means proven, that in a few individuals a gene defect may have constituted a major etiologic factor in criminal acts. One recent murder trial shows how tenacious defense attorneys will be in trying to make that case.

#### MONOAMINE OXIDASE A DEFICIENCY

In February, 1991, Stephen Mobley, a young man with a long history of brushes with the law, shot and killed the manager of a Domino's Pizza store in Oakwood, Georgia. Because he had already cleaned out the cash register and had met no resistance during the robbery, the motive was unclear. In the ensuing month before Mobley was apprehended, he committed six more armed robberies. When he was finally caught, he confessed to the murder and, while waiting for trial, often bragged to fellow inmates about it. He kept a Domino's Pizza box in his cell and, reportedly, threatened guards by telling them that they looked like Domino's delivery boys.

At trial, Mobley's attorneys tried an innovative strategy. Instead of portraying him in the best possible light, they emphasized his troubled childhood, his violent past, and his prior convictions. They filed a motion asking the court to order the State to provide funds so that they could obtain testing that might reveal that Mobley suffered from a genetic defect that caused abnormal levels of a key chemical in his brain. If so, they argued, he might well be driven by violent impulses that were beyond his

control. The attorneys based their motion on two arguments. First, they provided biographical information about a dozen of Mobley's relatives over four generations. They portrayed a family, many of whose members could not control their behaviors, drank heavily, and often committed crimes.

Their brief is eerily reminiscent of the stories of the Jukes, the Kallikaks, and other families studied by eugenicists a century ago. These now quaint case reports once struck fear into the American public with their lurid depictions of huge families in which a strong propensity to criminality and prostitution were as surely inherited as eye color and the family chin. With only a few exceptions, the attorneys asserted, the Mobley family tree bore similarly poisoned fruit. Specifically, they argued that Stephen Mobley and some of his relatives might well be burdened with the same genetic disorder as was a family in The Netherlands in which a new genetic disease had been diagnosed.

The discovery in The Netherlands began early in 1978 when a young woman walked into a genetics clinic at a hospital in Nijmegen and told a physician that she was worried by the history of mental retardation in her family. She wanted to know if there was a test to show whether she would be at risk for bearing a son with similar problems. As Dr. Hans Brunner, a clinical geneticist, talked with her, he soon realized that the family history of mental retardation was only the tip of the iceberg. Virtually all the men with mental retardation also sometimes behaved with extreme violence. As the months passed, Dr. Brunner was able to review family records that made it impossible to dismiss his concern. He discovered that 30 years earlier, an unaffected granduncle of the woman who had come to him, convinced that there was a family curse, had compiled detailed accounts of all living relatives that he could locate. The granduncle had identified 9 male relatives with mental retardation, all of whom had periodically had bursts of extraordinarily violent behavior, many involving sexual assaults against their sisters. Since then, the family had grown to include five more men who were both mildly mentally retarded and violent.

Brunner realized that the family might well be burdened with a heretofore undescribed genetic disorder. He and his colleagues, with the grateful cooperation of the family, decided to try to find the abnormal gene. Over the years, they were able to find, examine, and draw blood for DNA analysis from 24 family members, 8 of whom were men with mild to

borderline mental retardation. All 8 men, who came from four different nuclear families, had behavioral problems. They seemed to undergo periodic bursts of severe aggression lasting for several days during which they slept little and, when sleeping, experienced severe night terrors. One young man had raped his sister. Several years later, while in prison on a work detail, he had stabbed a guard who had reprimanded him for a minor infraction in the chest with a pitchfork. Another man had attempted to run down the supervisor of his sheltered workshop with an automobile after that man had mildly chastised him for laziness. Other men had exposed themselves in public. A third man had on several occasions attempted to rape his sisters at knife point. Two others had committed arson. In all four families, the young women relatives refused to be alone with the men because of their frequent, inappropriate sexual advances.

The family history overwhelmingly suggested that, if the mental retardation and violence were due to a faulty gene, it almost certainly was on the X chromosome. Brunner and his team used DNA markers known to reside on that chromosome to map the location of the gene in which a defect might lie. The goal was to find a marker (a short stretch of repetitive DNA that because of wide variation in length among individuals can be used as a molecular address in an individual) that would distinguish men with the disorder from those who did not have the disorder. Using 26 different markers, the researchers were soon able to identify a region on the long arm of X that was highly likely to contain a faulty gene. That is, they found a DNA marker that was always present in affected men and absent in unaffected men, a fact that strongly suggested that the short stretch of DNA was tightly linked to and co-inherited with the abnormal allele. They next asked which of the genes in that region might, if defective, predispose to such bizarre behavior.

Among the candidate genes known to reside in the suspect region was a gene that codes for a protein called monoamine oxidase A. This protein is found in neurons in the brain and is responsible for regulating the level of important neurotransmitters called catecholamines. Although no one had ever described a patient with a solitary defect in monoamine oxidase A (MAOA), there had been case reports of persons missing chunks of this region of the X chromosome who were severely retarded. Brunner's group tested the urine of the affected men to look for evidence of abnormal levels of MAOA. The results suggested that these men made either very little

of this important brain chemical or none at all. The evidence strongly suggested, but did not prove, that these men had a mutation in the gene coding for MAOA.

Just a few months later, Dr. Xandra Breakfield, a molecular biologist at the Massachusetts General Hospital who had agreed to collaborate with Dr. Brunner, found that the men in this family did have a mutation in the MAOA gene, a tiny defect that prevented production of a functional protein. Their paper stands as the first definitive proof that a mutation in a single gene can drive behaviors that are universally considered to be aberrant.

In their petition to the court to permit genetic testing, Mobley's attorneys relied heavily on the work done by Dr. Breakfield and presented an affidavit showing that she had agreed to perform the relevant tests should the court authorize them. The prosecution countered that despite the violent family history, there was little reason to suspect that Mobley was afflicted with a genetic disorder involving MAOA. In Mobley's family, both women and men exhibited violent behavior; furthermore, none was mentally retarded. Stephen Mobley himself had a normal IQ. Also important was the lack of evidence to connect any genetic condition with a propensity to commit any violent crime. After comparing the Mobley family history with the papers written by Brunner, the trial judge rejected the defense motion, asserting that the "theory of genetic connection . . . is not at a level of scientific acceptance that would justify its admission." On February 20, 1994, a jury found Mobley guilty of murder and sentenced him to death. As part of his appeal to the Supreme Court of Georgia, Mobley again asked to undergo genetic testing for evidence of MAOA deficiency. The court rejected the appeal. Mobley is now living on death row.

As our understanding of the role that genes can play in shaping behavior grows, it is only a matter of time before courts will be sufficiently impressed with evidence that a genetic defect drove a behavior that they will do exactly what Mobley's attorneys sought—permit such evidence to form the basis of an insanity defense or factor it into guidelines on sentencing. We can already see the first glimmers of such thinking. In 1990 a California judge decided not to disbar an attorney, in part because he presented evidence that the alcoholism that had made him fail his duties to his clients had a genetic basis that was beyond his control. Even more dramatic was the decision in 1994 by an Atlanta judge to release a woman

from prison who was serving a life sentence for murdering her son on the grounds that she had done so under the influence of Huntington disease, a dominantly inherited, adult-onset disorder in which certain brain cells die.

On the night of July 7, 1985, Glenda Sue Caldwell walked into her 19-year-old son's bedroom and fired three shots, killing him instantly. She then went to her daughter, Susan's, room and fired at her. The bullet came so close that it burned the young woman's face. For some reason Glenda Sue did not fire again, and Susan was able to disarm her without a struggle. At the trial, Glenda Sue's lawyer argued that his client, who had lost a father and a brother to Huntington disease, almost certainly was also afflicted, and that the condition had rendered her mentally ill. At the time there was no definitive test for the disorder. As is permitted in Georgia, the jury found her guilty, but mentally ill. Judge Kenneth Kilpatrick imposed a life sentence. In prison Glenda Sue deteriorated rapidly. In 1988 she underwent brain surgery for a tumor in the frontal lobe, and in 1992 she was officially diagnosed with Huntington disease, a disorder in which cells in part of the brain called the substantia nigra die off. Although the best-known feature of the disorder, formerly called Huntington chorea, is the inability to control the movements of the limbs, some affected persons do have psychiatric problems as well.

In prison Glenda Sue suffered alone. Her marriage had ended shortly before she killed her son, and her daughter was so distraught that for two years she could not bring herself to have any contact with her mother. By the time that the diagnosis of Huntington disease was unequivocal, however, Susan had come to accept that her mother was insane the night she killed Susan's brother.

In 1992 Susan and Glenda's lawyer set out to obtain a new trial based on the fact that the doctors who made the diagnosis were willing to testify that they were certain that she was already affected with Huntington disease on the night of the killing. On August 25, 1994, after a retrial without a jury, Judge Kilpatrick reversed himself and found that Glenda was not guilty by reason of insanity. Although she was no longer in the state prison, Glenda was now incarcerated in a far more terrible way. She had deteriorated so much that she was unable to leave the Georgia Regional Hospital where she had been staying before the trial. Ironically, the day after her mother was found not guilty, Susan learned from DNA testing that

she too would someday develop Huntington disease. In an interview with the *Atlanta Constitution*, she was eager to talk about her predictive diagnosis. She intended, she said, to live fully and openly, capturing as many good years as she can before Huntington disease destroys her.

#### WHAT IF THERE ARE GENE VARIANTS THAT PREDISPOSE TO CRIME?

Glenda's is a tragic story, and most people would probably agree that the judge acted properly in freeing her. But what if there are persons who are genetically driven to commit heinous crimes, yet who seem by the usual methods of evaluation to be sane? Child molesters are especially likely to commit their crimes again and again. Many such individuals even express relief when they are arrested. It is possible that some of them will turn out to have a genetic abnormality that alters the manner in which certain cells in their brains respond to testosterone (the actual levels are normal). There certainly is a basis for speculating along these lines. We know that many serial sex offenders respond well to regular injections of Depo-Provera, a drug that mimics the female hormone, progesterone, and which suppresses testosterone production.

It is an extremely uncomfortable fact that criminal behavior clusters in families. According to the National Bureau of Justice, 37% of the 771,000 inmates in state prisons in 1991 have a close relative who has also been in prison. More than half of all juvenile delinquents who are imprisoned have immediate family members who have also been in prison. The more serious the crime for which a juvenile is imprisoned, the more likely he (the vast majority are teenage boys) is to have a close relative who has been in prison. Criminologists interpret these data to argue that criminality is learned, not in the streets, but at home. But it is not difficult to see how a lay person could suspect that a genetic force was at work.

Although such research is politically incorrect today, during the 1930s in Europe and the United States there were many studies of crime in families that sought evidence of a genetic influence by comparing concordance rates among groups of monozygotic (identical) twins with those among groups of dizygotic (fraternal) twins. Those studies were flawed because there were no tests to prove that twins assumed to be so were in fact

identical. More problematic is that the research, especially in Germany, was done at a time when eugenic thinking was at its zenith. Allowing for these facts, the studies repeatedly found that if one monozygotic twin had been convicted of a serious crime, it was highly likely that the co-twin would have a similar history. The concordance among dizygotic twins (who share only one-quarter of their genes) was generally much lower.

In 1977 a criminologist named K. O. Christiansen reviewed the nine published studies of criminality among twins. Among them were investigations conducted in Germany (3), Holland, Finland, Japan, Norway, and the United States (2). In total, the researchers studied 216 pairs of monozygotic twins and 214 pairs of dizygotic twins. In every study the concordance rate for criminality was higher among MZ twins than among DZ twins. When he pooled the data, Christiansen found the MZ rate to be .69 and the DZ rate to be .33, strongly suggesting, but by no means proving, the influence of genetic factors. More recently (1984), sociologist David Rowe conducted a survey on delinquent behavior by sending questionnaires to virtually all twins who were in the eighth to twelfth grades in Ohio public schools. Rowe received completed questionnaires from 168 MZ and 97 same-sex DZ twin pairs (a response rate of about 50%). There was a significantly higher percentage of MZ twin pairs than DZ pairs in which both admitted delinquent behavior. Rowe concluded that the results supported a strong role for genetic factors influencing asocial behavior.

During the middle of the 20th century, a number of criminologists used adoption studies as a tool to investigate the role of genetic factors in crime. The largest effort studied all nonfamily adoptions in Denmark from 1924 to 1947. The researchers identified 14,427 adoptees and sought to study them and their biological and adoptive parents. After rigorously excluding individuals about whom there were not enough data, they still had more than 4000 male adoptees about whom they could attempt to assess parental influence on criminality. Among boys who had neither adoptive nor biological criminal parents, 13.5% had at least one criminal conviction. Where one adoptive parent had a criminal conviction, the conviction rate among the adopted boys was 14.7%. Where one biological parent had a conviction, the rate for the boys was 20%. In cases where both an adoptive and a biological parent had a conviction, the rate among the boys rose to 24.5%.

The data are more dramatic when one studies the children of recidivists. Parents with three or more convictions were three times more likely than noncriminal parents to have sons who, despite adoption into non-criminal families, went on to be convicted of crimes. Only 4% of the male adoptees became chronic criminals, but they were responsible for 69% of all convictions among adoptees. A similar large study in Sweden conducted in the early 1980s, and an American study in the 1970s, also found a strong correlation of the criminal history of biological parents with the risk of criminal conviction in children adopted away from them at birth.

Assuming there are individuals who cannot control their violent acts and who are shown to suffer from a genetic abnormality that drives them to such behavior, should they when found culpable be judged not guilty by reason of insanity and incarcerated indefinitely in a state hospital? How will new knowledge about the biologically driven behavior reshape our society's view of guilt and innocence? For the moment, these questions are purely speculative, and we have ample time to debate them. I think it likely that we will discover individuals with rare gene variants who are so driven to abnormal behavior that we will have to redefine the insanity defense to manage their disposition. Will such discoveries ultimately lead us to medicalize the definition of crime? Someday will those who are determined to have committed certain acts be diagnosed as having a neurodevelopmental disorder and then subjected to compulsory treatment rather than an incarceration? Given the fact that we have barely opened the book of the human genome and that our understanding of behavioral genetics is primitive, there is virtually no evidence to make such a prediction. Nor, of course, is there evidence upon which to reject such a future.

Discoveries like the one linking a mutation in the gene for MAOA and violent behavior pose other troubling scenarios. It would be possible to test all the young boys in each generation of the Dutch family and identify those who inherited the mutation. Should the family, working with physicians, psychologists, and others, try from infancy to influence the development of those boys in the hope of countering their violent predispositions? What if such an effort required the use of mind-altering drugs with serious potential side effects? When, if at all, should such drugs be given? How would we ever determine when to start? How would teachers and neighbors react to such children? How should doctors respond to the women in the family who seek prenatal diagnosis, not to avoid bearing a

child with mild mental retardation, but to avoid bearing a boy who in manhood may be highly likely to attack women?

Questions like these bring us perilously close to the edges of what we wish to know about ourselves. Indeed, in regard to a possible link between genetics and violence, there are some who would prefer that the matter not be pursued at all. In 1992, after it came under attack for funding a conference of genetics and criminal behavior, the National Institutes of Health revoked a \$78,000 award it had made to support a conference on that topic. This led David Wasserman, a researcher at the University of Maryland to whom the grant had been given, and his university to threaten a suit, alleging a violation of the First Amendment. After lengthy negotiations and a three-year delay, the conference was eventually held, only to be disrupted by a 1960s style sit-in. Despite the turbulence at the meeting, the scholars in attendance seemed to agree that it would be stupid to attempt genetic studies of criminal behavior, as crime is an ever-changing social construct.

As we learn more about the genetics of behavior, especially of major mental illnesses (see Chapter 9), it is very likely that we will over time develop drugs and other therapies to alter inborn predispositions. At the least, such advances will shake our faith in the 19th-century notion of "free will" that provides a cornerstone to the foundation of the criminal justice system.