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Medical Genetics: Recent Advances with Legal Implications

By Charles J. Epstein, M.D.*

Except for their role in paternity assignment, scientists working in the field of human genetics and its more medically applied sub-science, medical genetics, have had little involvement with legal processes. Recent advances in the area of medical genetics, however, both technical and conceptual in nature, have raised issues that have, or in the near future will have important legal implications. The purpose of this paper is to discuss the scientific and medical aspects of three of these areas: chromosomal abnormalities and behavior, a subject of active legal and medical discussion at present; prenatal diagnosis and management of genetic diseases, an area which raises important questions about existing abortion laws; and the genetic effects of environmental agents, an area that will undoubtedly generate legal problems in the future.

Chromosomal Abnormalities and Behavior

A most important recent technical development in medical genetics was the visualization and analysis of human chromosomes. Chromosomes are structures present within the nucleus of each cell of the body that carry the genetic information necessary for human development and function. Although they had been studied earlier, the correct enumeration and description of the human chromosome complement did not occur until 1956. It was then discovered that each human cell contains 46 chromosomes. Forty-four of the chromosomes occur in 22 pairs differing in size and general appearance. These chromosomes are referred to as the autosomes. The remaining two chromosomes in the complement are the sex chromosomes; they are, as their name implies, responsible for sex determination. In both males and females one of the two sex chromosomes is an X-chromosome. In females the other sex chromosome is also an X-chromosome; but in males it is a very small chromosome designated as the Y-chromosome.

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The female chromosome complement is designated 46,XX,¹ the male complement, 46,XY.

Although chromosomes can be visualized in many types of cells, the cells generally employed for human chromosome analysis are the lymphocytes present in blood. The lymphocytes are placed in a culture medium² and stimulated to divide by the addition of a specific chemical.³ After three days in culture, another chemical is added to stop cell division;⁴ the chromosomes, now trapped in their most readily visualized state, are spread on microscope slides and stained. Complete sets of chromosomes are examined microscopically and enlarged photographic prints are analyzed carefully.

The discovery of chromosomal abnormalities followed shortly after the determination of the normal human chromosome complement. There are many types of abnormalities, but most often they involve the addition or deletion of chromosomes from the normal set of 46. The effects of these abnormalities depend on the specific chromosomes affected. In general, abnormal numbers of autosomes are associated with severe mental retardation and multiple physical anomalies.⁵ That such patients may have aberrations of behaviour is obvious; no real legal problems result, however, because they are rarely competent. The effects of abnormalities of the sex chromosomes are more subtle in nature, at least as far as behavior is concerned.

A common sex chromosome abnormality is the Klinefelter syndrome.⁶ Patients with this condition have a chromosome complement of 47,XXY, and therefore can be considered males with an extra X-chromosome. Detection of such individuals has been facilitated by the discovery that a characteristic body, the sex chromatin body, is present on the edge of the nuclei of cells from all individuals with two X-chromosomes.⁷ Because they have two X-chromosomes, both the cells

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1. A total of 46 chromosomes including two X-chromosomes.
2. A culture medium is a rich broth containing nutrients in which the lymphocytes will develop.
3. Pytohemagglutinin.
6. A syndrome is a number of symptoms and signs which occur together as a group and usually indicate a particular disease or diseased condition. Patients with the Klinefelter syndrome are male in general appearance and development, are tall, have enlarged breasts but small genitalia, and are sterile.
7. This sex chromatin body actually represents one of the two X-chromosomes in the cell. Cells scraped from the inside of the cheek are usually employed for this test, and, as opposed to several days for a full chromosome study, the results can be
of normal females and those of patients with Klinefelter's syndrome will have sex chromatin bodies present. Individuals in both groups are classified as sex chromatin positive.

The incidence of Klinefelter's syndrome in the total population of newborn males is about 1 in 500 or 0.2 percent. Surveys of institutions for the mentally subnormal (retarded) found the incidence of sex-chromatin positive males to be about 1 in 125 or 0.8 percent—four times higher than in the "normal" newborn population. Tests of males in mental hospitals produced similar results. The combined results of these tests show a clear increase in the proportion of sex-chromatin positive men in groups with mental aberrations involving retardation, behavioral disturbances, or a combination of the two. The reason for this increase is not known; however, it has been suggested that a combination of factors, including organic brain deficits and sexual abnormalities leading to psychological problems, might be responsible. Although the increased frequency of XXY men in institutions has been recognized for a long time, the chromosomal abnormality has not been regarded as a cause of aberrant behavior.

In the course of the investigations of institutionalized patients, studies were made of inmates in two English maximum security hospitals that dealt principally with mentally retarded, dangerous, and aggressive criminals. Of 943 men studied, 21 (2.2 percent) were sex-chromatin positive. Fourteen of these patients had a 47,XXY chromosome complement (two having a XXY/XY mosaic); while seven were 48,XXYY (two having a XXYY/XYY mosaic). Since the only XXYY's previously recognized had been patients with various congenital abnormalities, the latter finding was unexpected. Because of the supposition that two Y-chromosomes might have an adverse ef-

obtained within a hour. Unfortunately, the same type of test cannot be used to study other human chromosomes.

9. The chromosome complement of those tested is presumed to be 47,XXY. The combination of general male characteristics and a sex chromatin positive determination of the test employed form the basis of the presumption.
10. Polani, supra note 8, at 379.
11. Id. at 382.
12. The sexual abnormalities include infertility, lack of libido, and enlarged breasts.
13. Polani, supra note 8, at 365.
15. Id. at 54. Because of the two X-chromosomes the patients were chromatin positive and, thus, detectable by the screening test, despite the second Y chromosome.
fect on behavior, a search was made for individuals with a 47,XYY chromosome complement. Such a survey required full chromosomal analysis, rather than sex chromatin determinations, since XYY individuals have only one X-chromosome and, thus, are sex chromatin negative.

In a Scottish maximum security hospital for persons with dangerous, violent, or criminal propensities, 315 patients were investigated, and nine (2.9 percent) were 47,XYY. These nine XYY males were subjected to intensive scrutiny. Except for a tendency to be taller than the other inmates, the XYY men did not have any distinctive physical characteristics. Their first criminal convictions, however, had occurred an average of 5 years earlier than those of the other inmates (13 versus 18 years) and 90 percent of their offenses were against property. Most of them had behavioral problems early in childhood. Moreover, of 31 of their brothers and sisters, only one had been convicted of a criminal offense, a figure much lower than that which applied to the siblings of a control group randomly chosen from the same hospital. As summarized by W. Court Brown, XYY individuals were characterized as psychopathic individuals lacking in any ordinary capacity for feeling, apparently without much depth of emotion, who seemed incapable of making any rational plans for the future, and who on the whole posed behavioural problems from childhood. These individuals, drawn from all social classes, stood out as the black sheep of their families and as the apparently inexplicably erring sons in otherwise reasonably well adjusted families.

It was further concluded that

This picture strongly favors the idea that the additional Y-chromosome genetically predisposes the 47,XYY male to the development of a psychopathic personality and to consequent aberrant behaviour and antisocial conduct.

Following the initial identification of XYY individuals in maxi-

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16. The search was made even though the few individuals with a 47,XYY chromosome complement that had been identified were children with physical abnormalities.
18. The reader should keep in mind the small number of cases studied.
19. Court Brown, Males with an XYY Sex Chromosome Complement, 5 J. MED. GENET. 341 (1968) [hereinafter cited as Court Brown].
20. Id. at 348.
21. Id.
22. Id.
23. Id.
24. Id. at 348-49.
mum security hospitals, there has been considerable scientific activity in four directions: Attempting to detect biochemical and psychological differences between XYY and XY men, validating the psychological profile of the XYY patents, determining whether the same high frequency of the XYY chromosome complement is true of other criminal populations, and assessing the incidence of XYY individuals in normal populations. So far, medical studies have not been very informative—to date, only two reasonably controlled observations have been published. One observation reveals that XYY men have an electrocardiographic abnormality. This observation is of little importance to this discussion. The other, possibly more significant for an understanding of the syndrome, is that XYY men have a higher level of one of the pituitary hormones. Considerably more work, however, is necessary to confirm this finding.

Psychological investigations have been relatively few. One recently published report contradicts some aspects of the opinion of Court Brown noted above, and claims that family instability may be a significant factor leading to criminal and sociopathic behavior.

Because of the observed increase in the height of XYY's and the desire to maximize the chance of detecting affected individuals, most of the population studies have been conducted on prisoners and inmates selected for height. Pooling of several such studies reveals that 6.6 percent of the men tested had an XYY chromosome complement. If the initial English and Scottish studies are eliminated, the frequency is still 4.1 percent. What the figures would be for the whole population of men in the same institution is not known; none of a control population of 401 normal men, 6 feet or taller in height, however, was found to be XYY. Similarly, only 1 out of 1185 newborn males studied by Court Brown was XYY, although a frequency as high as 1 in 250 has been indicated by other reports. Because of the small number of

28. See Court Brown, supra note 19, at 350-52. The individuals selected are usually a minimum of six feet in height.
29. See id. at 355.
30. Id.
31. Id at 354.
individuals tested, it is difficult to ascribe any particular significance to these different estimates. Nevertheless, even though its exact value is in question, the frequency of the XYY complement in the newborn population appears to be significantly lower than that in the tall criminal population. As a rough estimate based on available studies, the frequency of the XYY complement in the entire criminal population is about 1 in 500 (0.2 percent).\textsuperscript{33} Even this estimate must be qualified by the fact that most of the criminal groups surveyed were in hospitals for the criminally insane or similar institutions.

Numerous articles have appeared in the popular press commenting on the relationship of the XYY chromosome complement to criminal behavior and describing the efforts of attorneys to have their XYY clients acquitted.\textsuperscript{34} The usual plea has been innocence by reason of insanity; and in one Australian case the plea was accepted.\textsuperscript{35} So far, this plea has not been accepted in the United States.\textsuperscript{36}

The use of the XYY chromosome complement as a justification of criminal actions has raised questions that have not, as yet, been successfully answered. These questions can be posed as follows. Does the XYY complement always lead to criminal behavior? If not, can it be considered a significant factor in the predisposition of an XYY person to such behavior? And, if either of the above is established, how should the XYY individual be dealt with both before and after commission of a criminal act? The answer to the first and second questions depends upon accurate knowledge of the frequency of XYY individuals in the newborn population, of their fate, and of the frequency of XYY men in the normal noninstitutionalized adult-male population. If it could be shown that all or most newborn XYY's ultimately commit criminal acts and are eventually placed in penal institutions, it would be established that the XYY complement leads directly to criminal behavior. Similarly, if it were shown that the proportion of all adult XYY's who were in prisons and hospitals is significantly higher than the total male proportion in the same institutions, we would have reasonably acceptable evidence that a relationship exists between the genetic make up of the individual and his criminal behavior. Although the data summarized above suggests that a significant proportion of the XYY's do get into difficulty, the information presently available is not

\begin{itemize}
\item 33. Marinello, note 27 supra, at 324.
\item 34. \textit{E.g.}, Stock, \textit{The XYY and the Criminal}, N.Y. Times, Oct. 20, 1968, § 6 (Magazine), at 30.
\item 35. \textit{Id.} at 96.
\end{itemize}
sufficient to establish a valid, workable rule. Court Brown estimated that if the frequency of the XYY abnormality in the newborn male group is taken as at least 1 in 1000,\(^\text{37}\) then there is a large gap between the numbers that are present in the male population and the numbers that are being recognized in prisons, maximum security hospitals, mental subnormality hospitals, and the like.\(^\text{38}\)

For example, Court Brown calculated that only 2 percent of the XYY's in Scotland have so far been identified.\(^\text{39}\) Therefore, on the basis of present information, it is not possible to claim a direct cause and effect relationship between the chromosomal make up and behavior. If most XYY's do not get into difficulty, it cannot be claimed that those who do have done so because they are XYY's. As a corollary, it cannot be inferred that an XYY child will ultimately and necessarily become a criminal. If the presently available figures are taken at face value, the chances are quite high that he will not. For this reason, most geneticists have been inclined to recommend that neither a child found to be XYY nor his parents be informed of this finding and that no attempt be made to treat the child prophylactically to forestall the emergence of criminal tendencies.\(^\text{40}\) On the other hand, the probability that most XYY's will turn out to be normal does not negate the possibility that the XYY complement could still be a factor in the development of a psychopathic or sociopathic personality and resulting criminal behavior.\(^\text{41}\) How this predisposition might operate is not known, but once operative, it is reasonable that it should be taken into account. Furthermore, as McWhirter has suggested, the proper time for considering this factor is in the ultimate disposition of XYY criminals, at the time of their sentencing in court and their rehabilitation in prison.\(^\text{42}\)

If the original psychological evaluations are valid (they still must be confirmed) then the XYY criminal can be expected to be a habitual offender whose criminal acts cannot always be attributed to environmental factors and who may not be amenable to the usual corrective measures. This does not mean that he is legally insane in that he is unable to distinguish right from wrong or to appreciate the nature of his

\(^\text{37}\) Court Brown, supra note 19, at 357.

\(^\text{38}\) Id.

\(^\text{39}\) Id.

\(^\text{40}\) This recommendation is aided by the fact that there is no effective preventative.

\(^\text{41}\) The terms psychopathic and sociopathic are used in the commonly accepted medical sense and have no specific legal connotations.

acts, although it does imply that he may have great difficulty in controlling his acts. This will have to be taken into account when determining and applying corrective measures.

It should be apparent to the reader that many questions remain to be answered about the relationship of chromosomal disorders to behavior. Until such time as these questions are unequivocally answered, the making of critical policy decisions concerning these chromosomal disorders should be avoided.

The Prenatal Diagnosis and Management of Genetic Diseases

An important aspect of the practice of medical genetics is genetic counseling—the advising of patients or parents with regard to genetic risks. Counseling usually occurs after an abnormal child is born, or the family becomes aware of a hereditary or chromosomal disorder present in themselves or their relatives. The advice given usually forms the foundation of a couple's decision whether or not to have additional children.

The degree of risk to which a couple is exposed varies with the condition present in the family; it can range from a low of 0.1 percent to a high of 50 percent. The risk of recurrence for diseases due to abnormal genes is usually on the order of 25-50 percent, while the risk for most chromosomal disorders involving visible defects in the chromosomes is generally less than 2 percent. But if a group of chromosomal anomalies is transmissible within families, and if a couple has had one abnormal child or if a parent is a "carrier" of the abnormality, the risk of having an affected child can reach 20 percent for each pregnancy.

Depending on the severity of the disease and the risk the family is willing to take in order to have a normal child, a couple that has received genetic counseling may or may not elect to have children. The decision is made on the basis of probabilities rather than on the basis of specific knowledge. As a result, this type of counseling has not

43. For a good discussion of genetic prognosis and counseling see Motylsky & Hecht, Genetic Prognosis and Counseling, 90 AM. J. OBSTET. & GYN. 1227 (1964).
44. Genes are small regions of chromosomes concerned with the transmission of specific hereditary characteristics. An individual gene can be defined as a unit of heredity; one of the constituents of chromosomes which carry hereditary characteristics and traits.
45. Motylsky, supra note 43, at 1229.
46. Id. at 1231.
47. Carr, Chromosomal Abnormalities in Clinical Medicine, 6 PROG. MED. GENET. 1 (1969).
been considered wholly satisfactory by either counselors or their patients. Therefore, a search was begun for better methods of dealing with these situations. The result of this search is prenatal diagnosis, a diagnosis made before birth. In practice this diagnosis is most often made during the fourth and fifth months of pregnancy, utilizing fetal cells obtained from the amniotic fluid. The tests used in diagnosis are time consuming and require expert performance, but if they are properly performed, the answer is a specific one—the child will or will not be affected.

If treatment of the fetus could prevent the appearance of disease, then prenatal diagnosis would, as in any other medical situation, merely be the prelude to therapy. However, except for Rh negative women who are reacting immunologically against their Rh positive fetuses, this has not proven to be the case. The therapy of hereditary and chromosomal disorders is limited, and those conditions that can presently be treated are as well treated after birth as before. Consequently, the principal present usefulness of prenatal diagnosis is in deciding whether a pregnancy should be terminated.

Today, most physicians require both that the couple be willing or, more precisely, desirous of terminating the pregnancy by aborting the abnormal fetus and that the obstetrician be willing and able to do so. Otherwise, the entire procedure becomes one which potentially may be psychologically very traumatic to the pregnant woman.

Therapeutic abortion per se is not a new practice in the management of genetic disorders. Situations have frequently arisen in the past in which an already pregnant woman with a risk of 25-50 percent of...
having an affected infant has sought and been granted an abortion. Often the abortions are coupled with a sterilization procedure. The usual legal justification for these therapeutic abortions, provided by the abortion law concerned, is the potential grave injury to the mental health of the mother.50 While such abortions have been and still ought to be carried out on an emergency basis, the fact remains that many normal fetuses will be aborted. On the other hand, the use of therapeutic abortion coupled with prenatal diagnosis provides a much more selective method. The function of preventing the birth of a defective individual becomes secondary to the function of insuring the birth of a normal one. In most instances in which prenatal diagnosis is carried out on a prospective, rather than emergency basis, it is expected that the goal of the parents is to have normal children, even if several pregnancies are required. Understood in this light, the genetic counselor who uses prenatal diagnosis and, when necessary, therapeutic abortion for the management of "genetically high risk" pregnancies is as concerned, perhaps more concerned, with the physical health of the fetus as with the mental health of the mother. The entire process is intended to be a positive medical act rather than merely a negative act of fetal destruction. Furthermore, in contrast to the earlier use of therapeutic abortion, the decision is made not on probabilities but on specific knowledge of the status of the fetus.

Unfortunately, the law in most states has not kept pace with these developments.51 While it may be possible to justify therapeutic abortion on the grounds that a mother's belief that her fetus is abnormal would be injurious to her mental health, this seems to be an unduly cumbersome and undesirable approach. It puts the burden on what might be or become wrong with the mother rather than on what is wrong with the fetus. Again, it must be emphasized that the status of the fetus can only be determined after careful investigation in a well controlled laboratory under the supervision of a qualified physician; otherwise, the possibility of errors is significant. It would be much simpler and more logical to make serious fetal abnormality a specific justification for termination of pregnancy. This approach has been recommended in a statement by the Executive Board of the American College of Obstetricians and Gynecologists:

Therapeutic abortion may be performed . . . when continuation of the pregnancy would result in the birth of a child with grave

physical deformities or mental retardation.\textsuperscript{52}

Similar wording is present in the section on abortion in the Model Penal Code proposed by the American Law Institute:

A licensed physician is justified in terminating a pregnancy if he believes there is a substantial risk\textsuperscript{53} . . . that the child would be born with grave physical or mental defect.\textsuperscript{54}

Wording of this type has been written into the laws of a few states,\textsuperscript{55} but, unfortunately, was specifically deleted\textsuperscript{56} from the California abortion law passed in June, 1967.\textsuperscript{57}

In a recently published poll, a majority of 1011 adult Californians, both Catholic (58 percent) and non-Catholic (81 percent), favored restoration of the provision specifically deleted from the California law.\textsuperscript{58} Despite a degree of agreement on this matter, the subject of therapeutic abortion continues to be highly charged with emotional and moral considerations. Some liken abortion of an abnormal child to euthanasia.\textsuperscript{59} Others argue that the unborn child would almost certainly choose life with defects as against no life at all.\textsuperscript{60} With regard to these objections, however, it must be realized that the diseases under consideration do not merely involve minor or even major abnormalities compatible with a relatively normal life. They involve, for the most part, conditions that usually lead to severe mental retardation or to grave illness and early death. Stated in another way, no one would knowingly and willingly subject a normal infant to a 20-50 percent risk of developing some very serious disease, either physical or mental. Why then should an unborn fetus be subjected to such a risk? To argue that, in such situations, adoption is preferable to abortion is to ignore that many parents would prefer to retain their own children, that society has recognized therapeutic abortion as a legitimate practice, and that, ex-

\textsuperscript{52} Medical World News, May 24, 1968, at 22-23 (quoting the Board).
\textsuperscript{53} It should be pointed out that in the limited context of the prenatal diagnosis of genetic disorders, substantial risk is tantamount to certainty. Even for most of the diseases not detectable in the prenatal stage, the risks usually run 25-50 percent. Risks of this degree are considered substantial by medical geneticists.
\textsuperscript{54} Model Penal Code § 230.3(2) (Proposed Official Draft, 1962).
\textsuperscript{56} Monroe, How California's Abortion Law Isn't Working, N.Y. Times, Dec. 29, 1968 § 6 (Magazine), at 10.
\textsuperscript{57} Cal. Health & Safety Code § 25950-54.
\textsuperscript{60} Id. See also America, March 1, 1969, at 239.
cept in the emergency situations, abortion would only be carried out for proven fetal abnormality. In the light of the above discussion, it is submitted that language such as that proposed in the Model Penal Code\textsuperscript{61} should be inserted into California abortion laws.

The Genetic Effects of Environmental Agents

Physical agents, such as radiation, have long been known to have adverse genetic effects. Organisms exposed to X-rays, \( \gamma \)-rays, or even ultraviolet light develop mutations or genetic alterations which are usually deleterious. In higher organisms, the genetic damage can often be visualized as structural alterations of the chromosomes.\textsuperscript{62}

Despite the widespread public interest in radiation and its effects stimulated by the atom bombings and the known relationship between radiation and cancer, relatively little interest in the possible genetic effects of chemicals was manifested until the occurrence of two events: the thalidomide "disaster" and the widespread use of lysergic acid diethylamide (LSD).

The congenital abnormalities caused by thalidomide are not genetic in origin but, rather, represent a relatively specific sensitivity of certain tissues during a critical period of fetal development. Nevertheless, thalidomide focused public interest, as perhaps nothing had previously, on the potentially harmful effects of widely distributed chemicals and drugs. It has also led to an increasing scrutiny of and sensitivity, in some cases hypersensitivity, to such drugs by governmental agencies charged with protecting the health of the public. Given this sensitivity, reports of the induction of chromosomal aberrations by LSD generated interest out of proportion to the public's concern for the health of the users. For the first time, an agent being consumed by many individuals was reported to damage chromosomes. Since use of LSD was illegal, no additional legislative action was required; however, governmental authorities increased investigations of other chemical agents that might possibly cause harmful genetic effects.

Three types of genetic effects have been attributed to LSD: damage to the chromosomes of cells of the user or, in the case of a pregnant woman, of her fetus; damage to the male germ cells, the cells which

\textsuperscript{61} See text accompanying note 54 \textit{supra}.

\textsuperscript{62} These alterations are of many types including breaks in the chromosomes, joining of part or all of one chromosome to another (translocations), loss of part of a chromosome (deletions), and even fragmentation or loss of entire chromosomes. Similar effects can also be produced in cultured cells by the use of various chemicals which have been termed "radiomimetic" (like radiation in their effects).
produce the sperm; and the production of mutations which might not become manifest until later generations. Controversy among scientists attends each of these areas. Authorities are equally divided on the question whether LSD taken orally damages the chromosomes. In all cases, it is the chromosome complement of the blood lymphocytes grown in culture for two or three days that is being discussed. The difficulty in obtaining consistent results derives from many factors, including variations in dosage, frequency, purity of the drug, the possible ingestion of other drugs, and various technical problems. Even if it is conceded that ingestion of LSD does damage lymphocyte chromosomes, the relevance of this effect to the future health of the individual and his offspring is questionable. At present it is impossible to answer this question, although by way of analogy to radiation the possibility of malignancy appearing at some later date cannot be ruled out.

More important from the genetic point of view are the effects, both visible and invisible, of LSD on the chromosomes of the germ cells. Chromosome damage is transmissible only when it occurs in the chromosomes of the germ cells, because these are the chromosomes that are contributed by the parents to the newly-conceived embryo and serve as the templates for all of the chromosomes in the developing fetus body. Information on this point is even more deficient; but again the claim is that LSD given in sufficient amounts to animals will damage the chromosomes of the male germ cells and might, by inference, cause fetal abnormalities. It has yet to be shown, however, that malformations found in human infants were the result of a chromosomal aberration induced by LSD before the time of conception, despite unproven claims that ingestion of LSD by a pregnant woman can result in fetal abnormalities.

63. Mutations are microscopic alterations of genes.
64. Among those authors claiming chromosome damage see Cohen, Hirshhorn & Frosch, *In Vivo and In Vitro Chromosome Damage Induced by LSD-25*, 277 NEW ENG. J. MED. 1043 (1967); Irwin & Egozque, *Chromosomal Abnormalities in Leukocytes from LSD-25 Users*, 157 SCIENCE 313 (1967).

Among those authors claiming no chromosome damage by LSD see Bender & Sankar, *Chromosome Damage Not Found in Leukocytes of Children Treated with LSD-25*, 159 SCIENCE 749 (1968); Longhman, Sargent & Israelstam, *Leukocytes of Humans Exposed to Lysergic Acid Diethylamide: Lack of Chromosome Damage*, 158 SCIENCE 508 (1967).

65. As of this date, no cases of cancer resulting from LSD ingestion have been reported.
With all of the uncertainty about the relatively short-term genetic and developmental effects of LSD, it is not difficult to understand why nothing of value can be said about its long-term effects. While it is possible that such effects might exist, it will be very difficult to demonstrate them in man; even in the case of humans exposed to large doses of radiation at Hiroshima and Nagasaki, more than twenty years of observation has not demonstrated any specific genetic damage to succeeding generations of children. Perhaps the length of time that has elapsed is still too short.

This abbreviated account of LSD and its effects is given, not because of the special legal importance of this drug, but because it illustrates the difficulties which attend the establishment of a specific relationship between drug or chemical use and genetic damage. It will not be easy, except in the most unusual circumstances, to prove such a relationship; yet, situations have already arisen in which attempts were made to do so; and it is likely that similar undertakings will arise in the future. From the point of view of the legal profession, each time a widely used drug or chemical is suspected, the possibility of extensive and difficult litigation arises and important legal questions are raised. To what extent is a producer or distributor responsible for such potential genetic effects? What proof should be required to establish that a drug or chemical is genetically deleterious? How should such agents be regulated?

Consider in this light the artificial sweetening agents, the cyclamates, which are very widely used in diet foods and beverages. A decomposition product of these drugs is known to be injurious to the chromosomes of cultured cells and purportedly to those of the germ cells of male mice. The cyclamates themselves, in sufficiently high concentration, will also damage the chromosomes of cultured cells. By analogy to LSD and radiation, but with even less support in fact, the possibility of deleterious genetic effects arises. Although no reports have as yet appeared of damage to human chromosomes after ingestion of cyclamate, the Food and Drug Administration has suggested that consumption of these agents should be voluntarily limited by the user. It is still too early to know whether any attempt will be made to officially restrict the use of this chemical.

68. Some attempts were made to prove that malformed babies are the result of LSD ingestion.
It is impossible to predict what other materials will be called into question on genetic grounds; it could be the caffeine in coffee, or the sodium nitrite in luncheon meats, both of which can cause chromosomal or genetic damage in the proper experimental circumstances. It is almost certain that occasions will arise in which drugs or chemicals will be deemed genetically injurious and in which legal remedies will be sought by those who were exposed.

Summary

The three areas described in this review represent problems that are of current legal interest or that are likely to be of interest in the near future. Everyone involved with criminal practice should be aware of the significance of the XYY chromosome complement and of the current uncertainties about its true relevance to the determination of behavior. Likewise, the uncertainties of establishing a causal relationship between the ingestion of drugs or chemicals and genetic damage, both immediate and future, must be taken into account when questions are raised about their safety and regulation. Finally, a need for changes in the present therapeutic abortion laws has been created by our new capabilities for diagnosing serious genetic disorders early in pregnancy and thereby ensuring the birth of healthy children to parents who have a high risk of having genetically defective offspring. As the science of genetics progresses, it is likely that other problems of legal importance will develop.

71. Sanders, Chemical Mutagens—the Road to Genetic Disaster, CHEM. & ENG’R NEWS, May 19, 1969, at 90; Sanders, Chemical Mutagens—An Expanding Roster of Suspects, CHEM. & ENG’R NEWS, June 2, 1969, at 54.