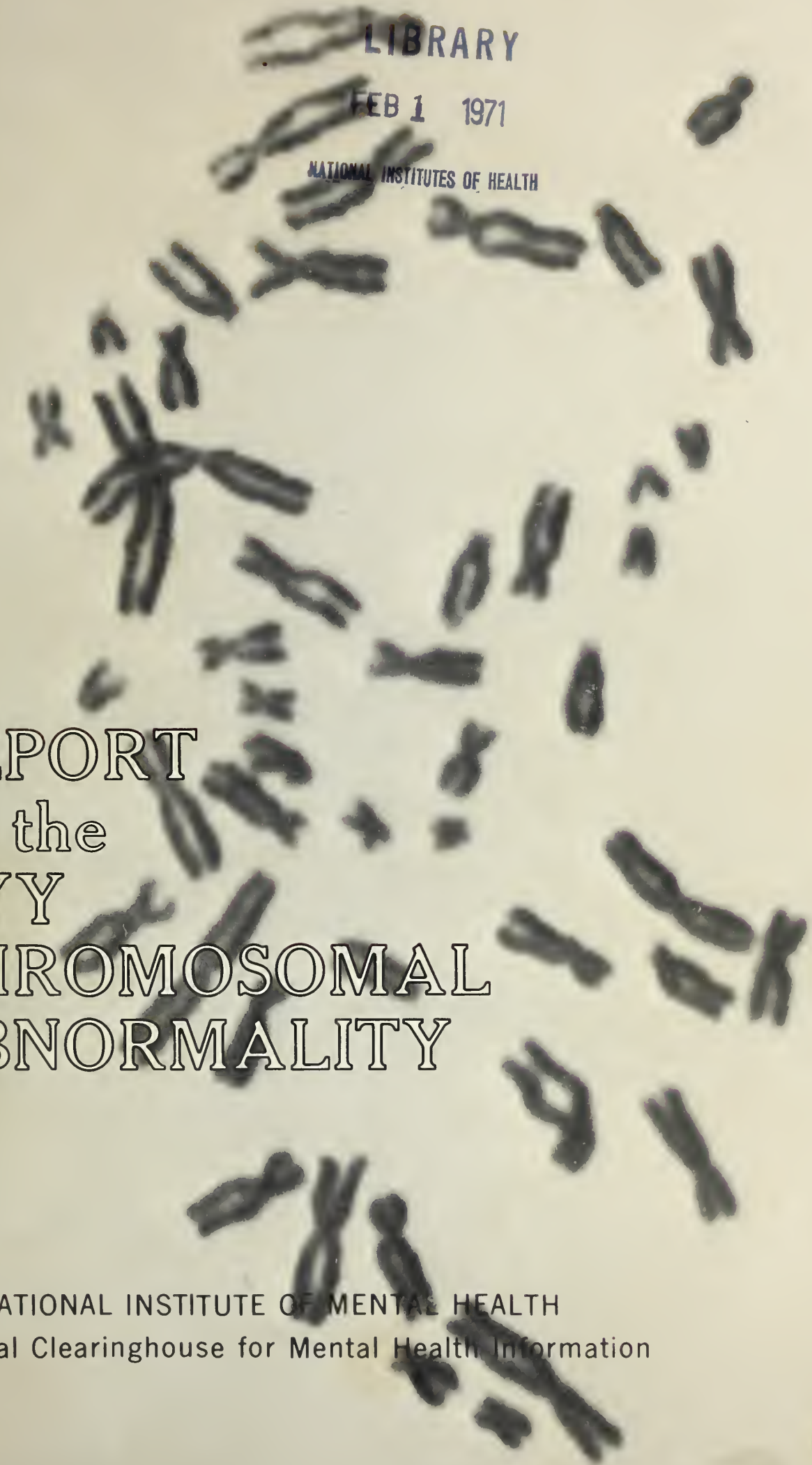

REPORT on the XYY CHROMOSOMAL ABNORMALITY

THE NATIONAL INSTITUTE OF MENTAL HEALTH
National Clearinghouse for Mental Health Information

REPORT

on the

XYY CHROMOSOMAL ABNORMALITY

U.S. National Institute of Mental Health
Center for Studies of Crime and Delinquency
5454 Wisconsin Avenue
Chevy Chase, Maryland 20015

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ON THE COVER: Photograph of chromosomes in a blood cell of an individual with the XYY abnormality.

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FOREWORD

This report is based in large measure on discussions held during a two day conference on the XYY chromosome anomaly, sponsored by the Center for Studies of Crime and Delinquency, National Institute of Mental Health, in June 1969. For purposes of this report, relevant citations from the scientific and professional literature have been provided for the various issues addressed at the conference. Moreover, in view of the considerable time which has elapsed since the two day meeting, an effort has been made to survey more recent reports in the scientific literature in order to update information concerning the XYY chromosome complement.

In a sense, therefore, this is not strictly a conference report. However, the major views, concerns, evaluative comments and recommendations made by the conferees have closely been followed. Also, the participants were given the opportunity to review drafts of this report and their comments have been incorporated. Nevertheless, the undersigned writer assumes final responsibility for this report and the shortcomings it may contain.

This report is presented for the general reader as well as for interested researchers and professionals in the field. However, the report is especially addressed to persons who are most likely to be confronted with important questions and decisions pertaining to the topic discussed, e.g., lawyers, judges, administrators of correctional, mental health and related programs, research administrators, legislators, and policy makers.

Readers not familiar with the basic terminology and principles of biology and genetics may wish first to read Appendix B, entitled "Background Information on Genetics," pages 37 to 40.[1] A glossary of key technical terms, many of which have been underlined in the report, is provided at the end of Appendix B, pages 41-42.

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[1] Readers interested in more information about the fundamentals of genetics may wish to consult some of the following items:

1. Asimov, I. Introduction to genetics. Seminars in Psychiatry, 1970, 2, 3-10.
2. Carter, C.O. An ABC of medical genetics. Boston: Little, Brown and Co., 1969.
3. Ford, C.E. & Harris, H. (Eds.) New aspects of human genetics. British Medical Bulletin, 1969, Vol. 25, No. 1. (117 pages)
4. McKusick, V.A. Human genetics. (Second edition). Englewood Cliffs, N.J.: Prentice Hall, 1969. (Available in paperback)
5. Stern, C. Principles of human genetics. San Francisco: W.H. Freeman, 1960.

The very generous cooperation and assistance of the participants (listed in Appendix A, page 35 is gratefully acknowledged, for both their contributions at the conference and subsequent suggestions during the preparation of this report. A note of thanks is also due to Dr. D. S. Borgaonkar, Division of Medical Genetics, The Johns Hopkins University School of Medicine, who generously made available pre-publication materials and provided other useful suggestions during the preparation of this report.

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INTRODUCTION

During 1968 a special branch of the science of genetics was drawn from the quietude of laboratories and professional journals and exposed to the glare of courtrooms and newspaper headlines. Since 1960 a number of geneticists and physicians had been studying the occurrence and effects of extra sex-determining chromosomes in humans. The first published report of a man with an extra Y, or male-determining chromosome (47,XYY), appeared in August 1961 (70). This individual was of average intelligence, without any physical defects, and had no criminal record. The reason his chromosomes were studied was to learn more about the presence of mongolism and other anomalies among his children.

In most of the reports published in the intervening years the individuals chosen for study had some mental or physical abnormality. Some investigators noted that several males with an XYY chromosomal constitution (47,XYY) had histories suggesting violent and aggressive behavior patterns. In addition, it was noted that such men were rather tall (16 & 46).

These observations led to numerous studies on chromosomal patterns among tall males institutionalized for mental illness, mental subnormality, or various forms of criminal behavior. The number of persons found to have the extra Y chromosome markedly exceeded the prevalence of the XYY pattern roughly estimated, but not yet rigorously confirmed, to exist in the general population.

The above findings led some investigators - and many news writers - to conclude that the extra Y chromosome predisposed such males to violent and aggressive behavior. Other scientists disagreed, arguing that the biased nature of the populations studied and the lack of accurate prevalence data for the general population put any causal links in doubt. The controversy remained largely within the scientific community.

The emergence in 1968 of the XYY research into the general public domain of controversy was precipitated by the murder trial in Paris of one Daniel Hugon. The defense attorney claimed his client had an extra Y chromosome and thus was not criminally responsible for his behavior. The Court appointed an expert panel to review the mental condition of the defendant. After trial and conviction, a reduced sentence was imposed, presumably because of the chromosomal defect (61).

At about the same time the press reported on the murder trial of Lawrence E. Hannell in Melbourne, Australia. Hannell was acquitted by reason of insanity; this verdict was allegedly influenced by testimony concerning his XYY constitution. However, more recent reports indicate that the defendant's chromosomal anomaly may actually have had little bearing on the acquittal since it was mentioned only perfunctorily in

the trial transcript, and there was considerable evidence about his mental deficiency, abnormal electroencephalogram, and temporal lobe epilepsy (6).

Again in 1968, Richard Speck, convicted of murdering eight Chicago nurses, was reported in the public press to have XYY chromosomes. It was also suggested that the purported finding of this anomaly might be raised in his projected appeal. Speck's attorney later announced that tests had shown his client's chromosomes to be normal.[1] Nevertheless, news items and professional articles still appear referring to Speck as an XYY type.

During and since these events many press and broadcast stories have appeared about the allegedly antisocial propensities of persons with the XYY chromosome abnormality. In addition, over 160 articles have appeared thus far in various scientific and professional journals (cf. 10 & 11).

Some segments of the general public and also of the scientific and legal communities seem to have accepted the belief that males with XYY chromosomes are more or less inexorably predisposed toward violent and antisocial behavior. On the other hand, many geneticists and behavioral scientists consider the above conclusions quite premature and seriously doubt that the available evidence can establish a cause and effect relationship between the presence of an XYY constitution and criminal or other socially deviant behavior.

The research findings thus far, the publicity, the scientific controversy, and various legal issues have generated some important medical-legal-ethical questions among researchers and those concerned with social policy. Thus, on the one hand there is a scientific as well as societal need to conduct further research to gain more knowledge. On the other hand, there are equally important social values which require that the rights, welfare, confidentiality and privacy of research subjects be safeguarded in such research endeavors (74). However, since a number of legal and social policy questions have been raised in regard to persons with the XYY chromosome complement, it is most essential that the answers to such questions be based upon sound and well-established scientific facts derived from rigorous and carefully designed studies.

Against this background of need for more precise and definite knowledge concerning the biological, behavioral, and social science contributions toward better understanding of deviant and antisocial behavior, the Center for Studies of Crime and Delinquency of the National Institute of Mental Health decided to give particular emphasis to an assessment of

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[1] See Chicago Herald Tribune, Nov. 26, 1968, 1A at 16, Col. 1.
See also, footnote 3, page 892 (61)

present knowledge in this field and to further research addressed to the subject of individual violent behavior.

On June 19-20, 1969, the NIMH Center for Studies of Crime and Delinquency at Chevy Chase, Md., convened a small group of scientists and researchers from the fields of genetics, medicine, psychiatry, psychology, sociology, and law to discuss this subject.*

The primary topics of the meeting were the current state of knowledge concerning the XYY chromosome anomaly, outstanding gaps in such knowledge, and the research methodologies which would permit more meaningful comparison of data from needed further studies. The conference also addressed some of the medico-legal issues involved in research on chromosome anomalies.

The participants indicated much need for careful research pertaining to other sex chromosome anomalies which have been found in relatively high rates among various institutionalized populations, e.g., the XXY chromosome constitution ("Klinefelter's syndrome"), which has a much longer research history.

Despite the considerable and often sensational publicity regarding the XYY chromosome anomaly -- indeed because of such publicity -- it seems most important that rather critical legal, social policy and related decisions should not become firm or rigid prior to the development of more adequate and definitive research findings.

Currently, one of the more important issues is the legal judgment concerning the criminal responsibility of defendants with an XYY chromosome constitution. The question is often asked whether persons with XYY chromosomes who are charged with criminal offenses can generally be regarded as suffering from mental disease or defect, and thereby exempt from criminal responsibility under an insanity defense or related legal doctrine.

The conference participants addressed themselves to this subject and their views and comments are discussed in Section III of the report, entitled "The XYY Karyotype and Criminal Responsibility." It seems important, however, to quote here the particular statement on which the conferees developed a formal consensus. Specifically responding to the above mentioned questions, the participants unanimously agreed that:

> "The demonstration of the XYY karyotype in an individual does not, in our present state of knowledge, permit any definite conclusions to be drawn about the presence of mental disease or defect in that individual. A great deal of further scientific evidence is needed."

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*The invited participants to the conference are listed in Appendix A, Page 35. Also present and listed as "observers" are members of the NIMH staff and persons from other Federal agencies.

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I

INCIDENCE AND PREVALENCE OF THE XYY CONDITION

A considerable part of the conference was devoted to discussing the fundamentally important question of the incidence and prevalence of the XYY chromosomal abnormality. Even among this expert group the two terms often were used as if they are interchangeable and thus have the same meaning, but they do not. Since the incidence and prevalence rates for a condition may be quite different, it is important to bear the different meanings of these terms in mind and to use them accurately. For purposes of this report, the following definitions have been applied throughout:

> Incidence: The rate at which new cases of a condition are added to a given population during a certain period of time or in relation to a particular event; more specifically, as related to the XYY condition or other genetic abnormalities, incidence is the rate of occurrence observed or estimated to exist in a given population at birth.
>
> Prevalence: The total number of cases of a condition that can be counted or estimated in all age groups in a given population at a particular point in time.

The first major deficit in our understanding of the XYY phenomenon pertains to the absence of precise and adequate data on its incidence as well as prevalence in the general population. This deficit prevents clear understanding of the effects upon the individual and society of the XYY condition and also interferes with efforts to mount economically the more precise and detailed investigations that are needed.

Data presently available on the aforementioned topic may be grouped and summarized into two major categories: 1) Surveys of institutionalized populations, and 2) surveys of newborn infants.[1]

1) Surveys of institutionalized populations. Most of the surveys conducted thus far have been among inmates of various institutions. In many instances the subjects for chromosomal screenings were selected for height, e.g., six feet (183 cm.) or taller. Since some of the earlier studies had suggested a possible association between an extra Y chromosome and aggressive behavior and had also noted that such males were tall (16 & 46), many investigators began to select tall inmates in mental and penal institutions in efforts to verify the above alleged association. Thus, in most of these surveys males six feet and over in height were screened. In a few instances, tall inmates were further selected on the basis of their "aggressive" and "dangerous" behavior (e.g., 81).

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[1] Here, as in other sections of this report, the information available at the time of the conference has been updated and revised in light of more recent material.

Table I provides a summary of a number of institutional surveys which have been conducted in the past few years; however, this list is not meant to be exhaustive. It is evident from the studies cited in this table that the majority of these investigations selected only tall males for chromosomal screening. Furthermore, there are numerous variations even in the more obvious features of these studies: a number of different populations has been studied (mentally ill, criminals, sexual offenders, defective delinquents, mentally subnormal, mentally disordered offenders, etc.); juveniles as well as adults have been screened; the sizes of the reference groups surveyed range from 11 to 607; the height selection criteria vary; and, the rough percentage figures for the XYY karyotypes discovered range from zero to 18.2.

Table I indicates that 103 subjects with a 47,XYY chromosome constitution (excluding the two 46,XY/47,XYY mosaics) were found among the total of 5342 persons screened. This would provide an overall prevalence rate of 1:52 among the specially selected institutional groups.

It should be emphasized that the selection factors inherent in the aforementioned surveys do not permit valid estimates of the XYY prevalence rate for the general institutional populations in the relevant studies.

In an attempt to obtain a rough prevalence rate for institutional populations generally, the findings from eight surveys (listed in Table I) which did not use any height selection criteria were considered. Keeping in mind the varying nature of these populations and the size of their reference groups, a prevalence rate of 1:140 is obtained.

Again, it needs to be reiterated that in view of the relatively small numbers in the samples surveyed and the very low base rates for occurrence of the XYY chromosome anomaly, rather wide variations in obtained frequencies could and indeed do result. Hence, the need to use and interpret the above figures with much caution pending availability of more meaningful and accurate prevalence rates for various institutional populations.

2) Surveys of newborn infants. A number of surveys of neonates have been undertaken in an effort to systematically determine the incidence rates for the XYY chromosomal constitution. During the conference data from five such neonatal surveys were available for review. Eliminating one study which had done selective screening, i.e., only normal appearing infants, a total of approximately 6,700 infants had been tested and 12 were found to have 47,XYY chromosomes.

These surveys were discussed extensively during the conference and determined to be so variable in techniques, methodology, and other relevant aspects, that firm incidence rates could not be derived from them. Taking account of these difficulties, the group accepted a tentative rate of about one XYY in 550 males at birth (1:550) as a rough working estimate.

TABLE I

Summary of Institutional Surveys Pertaining to the 47,XYY Karyotype[1]

Investigators	Reference Group Size	Classification	Height Selection (cm.)	No. XYY	Approx. XYY %
Casey et al 1966 (16)	100	Maximum Security Hospitals, England	183	16	16.0
Jacobs et al 1968 (47)	315	Mentally Disordered Offenders, Scotland	None	9	2.8
Akesson et al 1968 (2)	86	Two Mental Hospitals, Sweden	183	4**	2.3
Baker et al 1970[2] (4)	86	Juvenile Detention Center (14-16 yrs), Pa.	183	1	1.2
" "	42	Juvenile Detention Center (15-17 yrs), Pa.	183	0	0
" "	74	State Prisons, Pa.	183	2	2.7
" "	72	City Prisons, Pa.	183	1	1.3
" "	58	City Prison (penal & mentally ill), Pa.	183	1	1.7
" "	82	State Prison (penal & mentally retarded), Pa.	183	0	0
" "	102	State Hosp. for Criminally Insane, Pa.	183	3	3.0
" "	230	State & V.A. Hospitals, Pa.	183	0	0
" "	130	School for Mentally Retarded, Pa.	183	1	0.8
Welch et al 1967 (81)	20	"Defective Delinq." aggress. offenders, Md.	188*	0	0
" "	35	"Defective Delinquent" Offenders (various criteria, e.g., particular aggressivity.)	183*	1	3.0
Goodman et al 1967 (40)	52	Caucasian Prison Inmates, Ohio	185.4*	2	4.0
" "	100	Caucasian & Negro Prison Inmates, Ohio	185.4*	2	2.0
Griffiths & Zaremba 1967(41)	34	Wandsworth Prison, England	183	2	6.0
Weiner et al 1968 (83)	34	Adult Prisoners, Australia	175.3*	4	12.0
Hunter et al 1968 (45)	29	Boys in Approved Schools, England	"tall"	3	10.0
Court Brown 1968 (23)	71	Epileptic Colony, England	None	1	1.4
" "	605	Hospital for Mentally Subnormal, England	None	0	0
Cited by: Price & Jacobs 1970 (63)	607	New Entrants (1 yr), Scottish Borstals	None	1	0.2
" "	302	Allocation Center, Soughton Prison, Edinburgh	None	0	0
" "	204	Recidivist Criminals, Grendon Prison, England	None	2	1.0
" "	419	Inmates, all Scottish Prisons	178	1	0.3
" "	74	Young Offenders' Institution, Scotland	178	1	1.4
" "	17	Scottish Detention Center	178	0	0
" "	34	Wandsworth Prison, England	183	2	6.0
" "	24	Nottingham Prison, England	183	2	8.0
" "	40	Pentridge Prison, Australia	175	5	12.5
" "	19	Hospital for Mentally Subnormal, England	183	2	10.0
" "	11	Hospital for Mentally Subnormal, England	183	2	18.2
" "	30	Scottish Mental Subnormality Hospital	183	2	6.6
" "	183	Scottish Mental Disease Hospitals	183	2***	1.6
" "	40	English Mental Disease Hospitals	183	0	0
Melnyck 1969 (54)	200	Mentally Disordered Sex Offenders & Criminally Insane, Calif.	183	9	4.5
Nielsen 1968 (59)	41	State Hospital, Denmark	180	0	0
Nielsen et al 1968 (60)	37	Institution for Criminal Psychopaths, Denmark	180.3	2	5.4
Sergovich 1969 (72)	230	Hospital for Criminally Insane, Canada	None	4**	1.7
Daly 1969 (27)	210	Maximum Security Hospitals, U.S.A.	183	10	5.0
Marinello et al 1969 (52)	86	Attica State Prison, N.Y.	183	2	2.3
" "	76	State Mental Hospital, N.Y.	183	1	1.3
" "	57	Juvenile Offenders (Detention Home & Court Psychiatric Referrals), N.Y.	None	1	1.8
Abdullah et al 1969 (1)	18	Criminal Psychiatric Patients (known for violent behavior), N.Y.	183	1	5.5
" "	26	Psychiatric Patients (known for "violent, destructive behavior"), N.Y.	183	0	0

* Height converted to centimeters from inches
** Includes one mosaic - 46,XY/47,XYY
*** One 48,XXYY is not included in this figure

[1] This list is not meant to be complete or exhaustive of all institutional surveys conducted to date.

[2] Most recent information regarding studies previously cited by Telfer et al (75).

In light of the availability of additional and more recent information since the conference, the data used at the time have been updated. Table II provides currently available information on neonatal surveys. If data on only unselected infants are used, an incidence rate of 1:518 is obtained. This rate is extremely close to the rough working estimate of 1:550 determined by the conferees, and within the general range of 1-2 per 1000 discussed in the scientific literature.

In a recent publication Price and Jacobs (63) present some material pertaining to the frequency of 47,XYY males in the adult community at large. These data, summarized in Table III, encompass rather heterogeneous and somewhat unusual groups which, in many instances, could not be considered as very representative of a general adult male population. Once again, bearing in mind the aforementioned caveats concerning the limitations of such studies, the obtained prevalence rate (1:1036) is within the range generally estimated on the basis of neonatal incidence surveys, viz., 1-2 per 1000.

In summary, it may be noted that the data presented above provide no more than rough approximations of accurate incidence and prevalence rates for the XYY chromosome anomaly. Among the requirements for meaningful and precise frequency rates for chromosomal anomalies are: the careful delineation of well-defined and pertinent populations for study, assuring representative and random sampling, avoidance of biasing factors in the samples or populations studied and, preferably, use of large enough samples to minimize vagaries of sampling.[1]

The conferees were generally critical of the lack of information in many of the institutional and neonatal survey reports about the characteristics of the populations studied, criteria used for selection of the subjects, and details concerning various study procedures. In view of such variations and the lack of details concerning the study procedures, the value of pooling such data for estimating prevalence rates for various populations was viewed as being of dubious value. Further, the dangers of using such meager and inadequate data on the occurrence of the XYY karyotype for crucial decisions involving the welfare of individuals and groups or for social policy decisions was a recurrent theme during the conference. It was emphasized that the information needed for such decisions can be obtained only through properly designed and conducted prevalence studies of non-institutional as well as institutionalized populations in sufficient numbers to have statistical validity.

Further details concerning these and related problems are discussed later in section V - Some Methodological Problems.

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[1] For further discussion of these issues see: Borgaonkar, D.S. & Murphy, E.A. "On determining the frequency of chromosomally abnormal persons with particular reference to 47,XYY individuals." Manuscript submitted for publication, 1970.

TABLE II[1]

Surveys of 47,XYY Newborn Males in the General Population

Investigators	Location	No. Screened	No. XYY	Remarks
Sergovich et al, 1969 (73)	London, Ontario	1066	4	All liveborn infants.
Walzer et al, 1969 (80)	Boston, Mass.	1931	0	Phenotypical normal newborn infants*.
Lubs et al, 1968 (51)	New Haven, Conn.	2184**	3	Consecutive newborns in one hospital, over period of one year.
Turner, 1969	Pittsburgh, Pa.	1023	3	Quoted from Marinello et al, 1969 (52). No details available.
Ratcliffe et al, 1970	Edinburgh, Scotland	3496	5	Consecutive liveborn infants - April 1967 to October 1969.
	Totals	9700	15	

Incidence Rate 1:646

Incidence Rate excluding Boston data* 1:518

* Since only phenotypically normal infants were screened a bias was introduced in the study.

** Latest figures provided by Lubs. In this study a total of 4482 newborns were included; however, successful cultures were obtained in 4366 (2184 males and 2182 females). The difference between total number of cases included and the total number successfully cultured often confuses such calculations. (Personal communication from Lubs, April 8, 1970.)

See also: Lubs, H.A. & Ruddle, F.H. Chromosomal abnormalities in the human population: estimation of rates based on New Haven newborn study. Science, 1970, 169, 495-497.

[1] Adapted from: Borgaonkar, D.S. & Murphy, E.A. On determining the frequency of chromosomally abnormal persons with particular reference to 47,XYY individuals. (Manuscript submitted for publication, 1970.)

TABLE III[1]

Survey of "Normal" Adult Male Populations
Pertaining to the 47,XYY Karyotype

Population Studied	No. of Males Examined	No. of XYY Males
General Population Survey	207	0
Industrial Workers	189	0
Non-blood relatives of persons with a familial chromosome abnormality	87	0
Survey of tall (183 cm. or taller) workers in atomic energy establishments	629	0
Blood donors, randomly selected males, relatives of individuals with a chromosome abnormality, and males with neoplastic disease	1875	3
Males in community at large	6340	6
	9327	9

Prevalence Rate 1:1036

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[1] Based on Table IV and relevant information from Price & Jacobs (63), page 33.

II

THE XYY KARYOTYPE AND SOCIAL BEHAVIOR

Some Relevant Research

It was noted earlier that much of the recent publicity concerning the XYY chromosome complement relates to speculations regarding the increased likelihood for males with this karyotype to engage in aggressive, antisocial and other socially maladaptive behaviors. In efforts to verify some of the early findings of increased prevalence of this chromosomal anomaly among persons in mental and penal facilities, several studies have focused upon inmates of such institutions. It appears to have been assumed that the information obtained would shed some light, even if rather indirectly, on the relationship of this chromosomal constitution and social behavior.

For example, Welch et al (81) studied selected samples of inmates in a special institution for "defective delinquents." Men confined in this facility had demonstrated "persistent aggravated antisocial or criminal behavior." In the course of screening 35 males who were 72 inches or taller (some of whom had also been selected for aggressiveness and IQs below 75), a single XYY individual was found. However, when the investigators had asked the administration of the facility to list the 12 "most aggressive, dangerous or violent inmates" (who were also 72 inches or taller), they did not find a single XYY case in this group. These investigators concluded that their findings did not provide any support for a hypothesis suggesting a strong association between the XYY constitution and mental retardation or aggressive behavior.

Price and Whatmore (66) compared nine males with the 47,XYY karyotype with 18 controls (46,XY complement) located in a maximum security hospital at Carstairs, Scotland. Most of the patients in this hospital had convictions for criminal acts. It might be added, however, that the control patients were randomly selected from the hospital population and were not matched for length of institutionalization.

The following were the main conclusions drawn from this study:

1. The penal records of the XYY patients showed significantly fewer crimes against persons compared to the controls (four out of eight XYY males so convicted with mean number of convictions per man of 0.9 versus 17 out of 18 controls with such convictions, the mean number of convictions per man being 2.6). Moreover, within the hospital environment, the control patients were more openly hostile and violently aggressive outbursts were more common, as compared to the behavior of the XYY persons.
2. As a group, the XYY patients showed distinctly earlier manifestations of disturbed behavior than the controls. Mean age of first conviction was 13.1 years compared to 18.0 for the controls; the median age for first conviction was 14 years versus 17 years.

3. Considering criminal conduct among the families of the two groups, the frequency of crime among the siblings of the XYY patients was significantly lower. The 31 siblings of the XYY group had only one conviction, whereas there had been a total of 139 convictions among the 63 siblings for the controls. However, it should be noted that only seven of the 18 control families accounted for the above convictions.

4. The XYY patients were found to suffer from severe personality disorders and their criminal behavior was noted to have been resistant to conventional forms of treatment and corrective training. (In reference to this point it might be pointed out that the great majority, 74 percent, of the patients at Carstairs were considered to be suffering from "severe personality disorders" and thus, quite likely, were equally resistive to treatment and corrective training.)

In another study of the Carstairs patients done by Hope et al (44), seven XYY males were compared with 11 matched controls in regard to their performance on a number of psychological tests designed to assess hostility, direction of hostility, dependence, over-reactivity, and some other personality traits. Overall, there were very few significant differences between mean test scores obtained by the two groups. The XYY males did not differ markedly in either intelligence or in hostility; neither was there any difference in the direction of expression of hostility, i.e., whether hostile feelings were expressed inwards against the self or outwards against other persons. The XYY males were viewed as being somewhat lower in self-esteem, more obsessive or introverted, and described themselves as slower and more cautious in making decisions.

Social Definitions and Determinants of Deviancy

Stress was given during the conference to the importance of recognizing that antisocial behavior is a result of complex interactions between hereditary and environmental influences on the one hand, and behavioral norms established by society on the other. Behavioral patterns deviating from these norms are not absolute, but involve rather complex social interactions which depend upon the person committing the infraction, the social context in which it occurred, and the societal group evaluating the behavior.

It is also important to remember that "delinquency" and "crime" are not exact terms. The breaches of law encompassed by these terms are diverse and include greatly varied patterns of behavior. Furthermore, most successful criminals do not come to official attention, especially those from the upper social classes and better endowed in terms of intellectual, economic and social advantages. Of those who do come to official attention and are charged with crimes, a majority are not convicted. Offenders who are convicted and sentenced represent a rather small and non-representative sample of all those who come to official attention and are accused of violating criminal laws. Thus, the sample of incarcerated offenders

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may well tend to be over-represented by those who have relatively greater biological, psychological, social and economic handicaps, as compared to persons not detected or not convicted of their violations of the law.

A variety of social class factors is similarly involved in reference to persons suffering from mental disorders and institutionalized in public facilities.

To reiterate, the complex interactions between hereditary and environmental influences must be considered in understanding behavior. For example, a conference participant having experience with juvenile courts provided an illustration of the interactions between heredity, environment and societal norms for behavior in relation to the secondary sex characteristic of body size. When confronted with a disorderly group of juveniles, the police often tend to focus their attention on the taller boys, presuming these to be the older and stronger and therefore the ringleaders. Thus, the genetically determined trait of body height may lead to the environmental and social influences implicit in a police record, court rooms, detention homes and jails, as well as notoriety in neighborhood and school.

An Evaluation of Available Information

While a greater prevalence rate for XYY males among several groups of institutionalized criminals and mentally disordered offenders is not to be disputed, the widely publicized beliefs concerning aggressivity and antisocial behavior as typical characteristics of such individuals are premature and subject to error on at least two counts.

First, institutionalized offenders tend to represent a selected, recidivist, and somewhat more handicapped sub-group. Because of this fact, findings on institutionalized criminals cannot be generalized to all persons officially labelled as criminals. For example, XYY males, compared to other criminals, may simply be less adept at evading arrest and conviction.

The second problem pertains to establishing a direct causal relationship between the chromosomal disorder and socially deviant behavior. An association between two traits cannot be established simply by demonstrating their coincidence. The fact that criminal behavior is a complex and multi-determined phenomenon makes it extremely unlikely that the extra Y chromosome is the only, or even the major, causative factor.

It would appear that at least some of the interest in the XYY karyotype and criminality may relate to the view that if a single Y chromosome makes a contribution to maleness (the normal complement being 46,XY), then an extra Y will add to behavior traits believed to be associated with maleness, viz., aggressiveness. Indeed, persons with the 47,XYY karyotype have sometimes been referred to as "super-males."

In addition to the other reasons why the above line of reasoning is both overly simplified and faulty, there is a considerable amount of information that various other types of chromosomal abnormalities (e.g., 47,XXY or "Klinefelter's Syndrome"[1]) also have a higher prevalence rate among institutionalized populations than would be expected on the basis of their frequency in the general population. Indeed, in several institutional surveys the numbers of XXY cases have been found to equal or even exceed those with the XYY complements (see, e.g., 7, 17, 21, 22, 26 & 77). For example, in their survey of sex chromosome abnormalities in an English hospital for mentally subnormal and psychiatric patients, Close et al (18) had occasion to study 19 individuals over six feet tall. While two of these tall men were found to have XYY complements, a total of three had extra X chromosomes (XXY, XXXY, and XXYY).

In a recently reported study Clark et al (17) compared XXY and XYY males located in various institutions in Pennsylvania. They found comparatively little difference in the records of criminal convictions in the two groups. The number of convictions, including crimes against persons and those against property, were quite similar. One striking difference, which is consistent with the earlier finding of Price and Whatmore (66), was that the XYY males came into conflict with their families and society at an earlier age. Overall, these investigators concluded that XYY men had been falsely stigmatized and that their involvement in crimes and antisocial behavior might not be significantly different from normal (46,XY) individuals.

In what amounted to a summing up of the conference participants' assessment of the role played by the XYY chromosome constitution as a determinant of behavior, one conferee said: "It is through complex interactions of all kinds of contingencies and priorities mediated by language, culture and environment, that the inherited organic characteristics affect behavior. It is extremely speculative to assume there is a high predictability from genotype to complex behavior such as committing a crime. Moreover, until large numbers of non-institutionalized XYY males can be studied, generalizations about the behavioral correlates of the extra Y chromosome, e.g., increased aggressivity and antisocial behavior, should be held in abeyance."

A slightly different viewpoint was held by some others at the conference and was voiced along the following lines: It certainly could not be said that all infants with the XYY chromosome complement at birth will be confined in some institution. However, on the basis of our present knowledge they would appear to have an increased risk of developing socially maladaptive and deviant patterns of behavior.

Overall, from the evidence at hand at the time of the conference, the participants concluded that some association between XYY and atypical

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[1]A glossary for key technical terms underlined in the report is provided at the end of Appendix B, pages 41-42.

socialization appeared to have been established only for excessively tall inmates of penal and related institutions. However, extensive research will be necessary to determine whether there is a similar association in some or most of the XYY individuals who have not been detained in such institutions. If research reveals that XYY men on the "outside" are either not overly aggressive or more adequately channel aggressive tendencies into socially acceptable behavior, then the popular notion that an extra Y chromosome in some way compulsively drives a person to deviant and aggressive behavior will very clearly have been disproved.

On the basis of available studies, a general statement which could be made is that the individual with an XYY chromosomal anomaly in comparison to XY males, appears to incur some increased risk of developing behavioral problems.[1] However, there is no reason to believe that an XYY male is inexorably bound to develop antisocial traits or behavioral problems.

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[1]The increased risk of developing behavioral problems is possibly more clearly substantiated for individuals with the 47,XXY chromosomal constitution (Klinefelter's syndrome), even though many such persons make quite satisfactory social adjustments.

III

THE XYY KARYOTYPE AND CRIMINAL RESPONSIBILITY

As described in the introduction to this report, rather wide publicity has been given in the news media to several criminal trials in which the XYY chromosome constitution was either considered or was actually included as a defense against criminal responsibility. These events have led to much discussion in legal and scientific circles as to the validity of basing an insanity defense on the presence of the XYY karyotype in the accused (see, e.g., 5, 6, 8, 9, 14, 19, 20, 21, 30, 31, 32, 33, 38, 41, 55, 61, 69, 84 & 85).

The problem is an extremely complex issue because the concepts of mental disease and mental disorder are vague and ill defined and have been undergoing important changes. Furthermore, the terms "mental disease" or "mental disorder", are not used by the law in an exclusively medical or psychiatric sense. As used in reference to tests for determining criminal responsibility, they become legal terms. Thus, the findings of "mental disease" in a defendant constitutes a determination by judge and jury of a legal rather than a medical or psychiatric fact.

The criminal law is basically concerned with moral and social value judgments. In the insanity defense, the determination is whether the accused is so different from the average individual, because of mental disease or defect, that he ought not to be held accountable and blameworthy, i.e., criminally guilty, for his act.

The basic issue is not simply whether an accused does or does not have an XYY or other abnormal chromosomal constitution and whether such abnormality might be classified as a mental disease or defect, but rather the precise manner and degree to which his psychopathology impairs his cognition of what is right or wrong or his capacity to regulate and thus be responsible for his behavior. At this point in our state of knowledge we cannot say how far the XYY complement of any given individual is causally linked with possible behavioral pathology.

On this specific issue, viz., the legal questions pertaining to determining an individual's criminal responsibility, the conferees arrived at a formal consensus:

> "The demonstration of the XYY karyotype in an individual does not, in our present state of knowledge, permit any definite conclusions to be drawn about the presence of mental disease or mental defect in that individual. A great deal of further scientific evidence is needed."[1]

[1]For further discussions of this particular issue the reader may wish to see Bartholomew (5), Burke (14), Fox (38), Money (55), Russell and Bender (69), and several comments and editorials in scientific and legal journals (19, 20, 30, 31 & 61), in order to study a variety of views on the subject.

In reference to the above statement, a recent appellate court ruling concerning a defense of insanity based on the XYY aberration is very pertinent.[1] The defendant, charged with robbery with a deadly weapon, contended that he suffered from a mental disease or defect and lacked the capacity to appreciate the criminality of his conduct or to conform his conduct to the requirements of the law (41). Convicted of the charge, the defendant appealed his conviction. In its ruling the Maryland Court of Special Appeals stated:

> "We do not intend to hold as a matter of law that a defense of insanity based upon the so-called XYY genetic defect is beyond the pale of proof under the insanity statute. We only conclude that in the record before us the trial judge properly declined to permit the case to go to the jury - a determination which, contrary to the defendant's further contention, is not violative of any of his constitutional rights, state or federal."

The conference participants indicated their view that increasing knowledge concerning the genetic and other hereditary contributions to behavior make it obvious that all persons are not equally endowed biologically in terms of regulating and controlling their behavior. Further, it was emphasized that the heredity versus environment or nature versus nurture issue is grossly simplistic and outdated. Modern genetic thinking in no way views genetic or other hereditary influences in an absolute or fatalistic manner. Rather, as noted earlier, very complex and continuous interactions among hereditary, social and environmental factors determine or influence human behavior. This point has very cogently been expressed by Money in a recent article (56):

> "The fact is that the genotype cannot express itself except in interaction with the environment, whether it be the environment created by neighboring cells in the embryo, the environment provided by the mother in the uterus, the perinatal environment, or the environment encountered in the home and community."

In a similar vein the conferees expressed much criticism of the notion that problem behaviors associated with a chromosomal abnormality are untreatable and unchangeable, and that the individual is doomed to remain the way he is. Not only is such a view entirely inconsistent with the above-stated interactions of hereditary and environmental influences, but it also misses some other important points. In reference to deviant behaviors the treatment needs are indicated by the particular patterns of problem behaviors manifested, not by the chromosomal abnormality itself. Treatment and remedial efforts would need to be directed, therefore, at specific behavioral problems and not at the chromosomes.

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[1] Millard v State, 38 LW 2401, Md. Court of Special Appeals, 1.12.70

IV

MAJOR GAPS IN KNOWLEDGE AND SOME RESEARCH NEEDS

Earlier discussion has already pointed to various deficits in our current knowledge concerning the XYY chromosome constitution. This section will address itself to the major gaps in knowledge and will indicate some of the outstanding needs for further research. Technical aspects which would be of interest to professionals in the field have been placed in Appendices C and D.

More Accurate Incidence and Prevalence Data

Many of the currently available studies pertaining to incidence and prevalence of the XYY complement suffer from deficiencies because of their selective and biased nature. It is essential that more systematic, unbiased and representative surveys of newborns, adults in the general population, and also of various institutional populations be undertaken. Lacking such data it is most difficult to make meaningful comparisons among the varying prevalence rates thus far reported among a variety of institutional groups, and the rough prevalence estimates for males in the general population.

Incidence and prevalence studies need adequate representation from various geographic, ethnic, social and economic groups, as well as of environmental factors that may be related to these groups. In addition, these studies should be supplemented by inquiries into the hereditary and environmental backgrounds and socio-medical histories of the parents.

Several discussants felt that it was very important to look for other chromosomal abnormalities during the course of XYY surveys; they also highlighted the importance of avoiding the kinds of conscious or inadvertent selectivity which may impair the accuracy of the survey data. As an example of how bias may effect the interpretation of a study, one neonatal survey was described in which only physically "normal" infants were karyotyped. However, recent evidence suggests that at least some XYY infants tend to display mild abnormalities, including prematurity.

The question of attrition in the proportion of XYY cases in the population as a function of age was also raised. Whether or not the XYY infant has a less than average chance of reaching adulthood is not known. The possibility was discussed whether the XYY karyotype in some infants might change to another abnormal pattern or even to a normal chromosomal complement during the maturation process.

Effects of Various Environmental Influences

As an example of possible influences of environmental agents, x-rays and other ionizing radiation of the gonadal area of either parent prior to fertilization have the potentiality of affecting the chromosomes of

either egg and sperm. The possibility that chemicals, including medicinal drugs, may affect the chromosomes of germinal cells before fertilization has already been demonstrated in animals. It was brought out during the conference discussions that viral infections of the mother immediately prior to and during pregnancy may also have an effect on the chromosomal constitution of the child. Conclusions about the role of prenatal x-rays, drugs, smoking, or virus infections require more complete data on exposure to all of these factors than have been available in most of the past studies.

The participants repeatedly stressed that knowledge concerning the influence of social and environmental factors on the behavior patterns of XYY individuals was as much needed as better incidence and prevalence data. For example, since the age of the mother at conception is known to affect the incidence of some other chromosomal aberrations, viz., Down's Syndrome, which is associated with Mongolism, the factor of parental age should be included among the information obtained during incidence studies.[1]

The XYY Anomaly and Social Behavior

Before reliable conclusions can be drawn as to the direct causal influence of the XYY chromosomal constitution on behavior, a solid base must be established regarding the frequency of occurrence of this anomaly in the general male population, adult as well as infant.

It was emphasized several times during the conference that if one studies the frequency of XYY anomalies among tall males detained in institutions because of mental illness, criminal or violent behavior, then quite obviously all that would be determined would be the prevalence of that anomaly among tall mentally ill, criminal or violent institutionalized males.

The conferees generally agreed that the institutional surveys had probably established tallness as a common characteristic of the extra Y chromosome. However, some participants were of the view that, in light of the selective nature of most institutional surveys (i.e., screening only of tall males), the trait of tallness as associated with the XYY complement should remain an hypothesis until more thoroughly tested in general population surveys.

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[1] Since non-disjunction in the case of XYY anomalies probably takes place at the second meiotic division in the spermatogenesis of the father, Borgaonkar and Mules (13) have tried to ascertain paternal age at birth of the XYY individual. They find that the very slight tendency toward increased paternal age (about a year more than average) in XYY cases is not significant.

It was also noted that we do not presently know whether or not there is a similar frequency of XYY complements in those tall and socially aggressive persons who have attained economic success and made outstanding social adjustments and contributions. Likewise, the aforementioned studies of tall, incarcerated offenders tell us nothing about the tall, aggressive men whose antisocial behavior has escaped official notice and action by the various social control systems in the community.

There was general agreement that even in the case of the many XYY males found in institutions for the mentally disordered or criminals, the question of how the chromosome anomaly exerted its influence upon the individual's behavior was at present unknown. There was information from available studies that many XYY persons have displayed a variety of physical abnormalities including those of the endocrine and central nervous system. Very important questions are raised concerning the role of the chromosomal aberration in terms of influencing physical and psychological development, personality and behavior.[1]

The discussants felt that carefully controlled studies were needed of children and adults possessing the XYY and other chromosomal aberrations (e.g. XXY) to ascertain specific behavioral and response characteristics. For example, one might initially compare the frequency of deviant aggressive behavior among XYY males with carefully matched groups of males without such karyotypes. If such gross comparisons indicated that XYY males had a significantly higher frequency of antisocial aggressive behavior, then a variety of systematic laboratory studies could be undertaken to compare XYY males and matched controls in regard to their threshold for response to modeling cues and the adequacy of inhibiting capacities for controlling aggressive and other behaviors. (See Appendix D for further information about such studies as outlined by Dr. Albert Bandura.)

The XYY Syndrome?

Numerous reports have appeared in the scientific literature which suggest that there is a syndrome having certain common features which describes XYY males. In regard to behavioral features, it has often been stated that persons with an XYY chromosomal constitution are inclined to be aggressive, antisocial, and to suffer from personality disorders.

However, an extremely wide range of physical and behavioral traits have been found for the more than 200 persons with 47,XYY chromosome complements so far described in the scientific literature. For example, there have been reports of cases with a variety of physical abnormalities involving the genitalia, central nervous system, congenital heart disease, webbing of the neck, and other aberrations (see, e.g., 15, 23, 27, 28, 34, 39, 78 & 79). On the other hand, there have also been some

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[1] See Appendix C for some of the physiological, biochemical, and related factors which need to be investigated in connection with the XYY aberration.

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reports of physically normal males who have average and even superior intelligence (e.g., 12 & 75). While much of the discussion of the XYY aberration refers to phenotypic males, and there may be a general belief that this anomaly is found only among men, there have been several reports of phenotypic females with a 47,XYY chromosome complement (23 & 79).[1]

From his review of almost 100 cases of males with the XYY complement, Hienz (43) reports that there appear to be at least four clinical manifestations of this anomaly. On the basis of the five cardinal symptoms which appear to dominate the clinical picture, Hienz suggests the following classification:

1. Overgrowth; normal intelligence; no criminal history; no somatic malformations; normal sexual development.
2. Overgrowth; mental deficiency; criminal history (eventually psychosexual disorders); no somatic malformations; normal sexual development. Most published cases of the XYY karyotype appear to fall into this group, which consists almost exclusively of inmates of mental and maximum security hospitals, and of prisons.
3. Overgrowth; normal intelligence or slight mental retardation; no criminal history; no somatic malformations; hypogonadism and other genital disorders.
4. Overgrowth; normal intelligence or mental retardation; no criminal history; various somatic malformations (resembling in part well-known syndromes which usually are not associated with chromosomal aberrations); genital malformations.

Hienz also notes that it remains to be determined whether the different clinical manifestations of the XYY complement represent varieties of a uniform aberration of sex chromosomes or whether they are caused by underlying structural differences between the two chromosomes (43).

In light of the rather wide range of physical, psychological, and behavioral variations found among persons possessing a 47,XYY chromosome constitution, it seems somewhat premature and indeed misleading to speak at the present time of an "XYY syndrome."

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[1] Most of the cases described in the literature of phenotypic females with XYY chromosome complements are demonstrable mosaics (45,XO/47,XYY). In such cases, the XO line of cells dominates and provides the female phenotype. Court Brown (23) reports on a case of a fertile and normally developed male with a 45,XO/47,XYY complement in whom the XYY line dominated. However, Court Brown also refers to a report of a mentally retarded female where extensive chromosome studies on lymphocytes, marrow cells, and fibroblasts from the skin showed a single line of cells with a 47,XYY complement.

V. SOME METHODOLOGICAL CONCERNS

Lack of Information About Study Populations and Procedures

During the conference several questions were raised concerning the scientific quality of some of the research which has been done in this area. The conferees were generally critical of the lack of information in many of the reported institutional and neonatal surveys about the characteristics of the populations, details of study procedures, various selection criteria utilized, and related items of information.

1. Karyotyping procedures. Some important questions were raised concerning the technical reliability of the XYY karyotyping procedures. Information generally is lacking on the methodology of the examinations or the experience and training of those who did the microscopic analysis. The experience of those doing the microscopic work apparently ranged from students to highly skilled cytogeneticists.

It was concluded that most of the karyotype determinations were based solely on identification of the extra Y chromosome by its size and shape, that is, by examination of the morphology of the chromosomes. (See Appendix C-3, "Characteristics for Identifying the Y Chromosome," page 46.) This procedure makes the criteria followed for identification and experience and skill of the person doing the microscopic analysis matters of crucial importance. (See also Appendix C-4, page 47.)

There was also the problem that in a few instances other types of chromosomal anomalies may well have been identified as XYY complements. Because of the very low base rates for the occurrence of the XYY aberration, an error in the identification of even one XYY case (in a total, say, of five, seven or even ten) would markedly change the incidence or prevalence rates estimated for the particular group. One discussant pointed out that in his experience several individuals with syndromes associated with chromosomal conditions other than XYY had exhibited extra chromosomes morphologically similar to, even though not identical with, an extra Y chromosome.[1]

Published reports in many instances have not been explicit concerning the number of cells (metaphases) examined. Likewise, seldom have the investigators stated whether preliminary screening for excess X chromosomes by the buccal smear method had been performed. On the basis of their personal knowledge, some of the conferees indicated that the number of cells examined generally ranged from two to 30, with most karyotyping probably limited to one cell. The discussants noted that by using only one or two cells there was the possibility of missing cases of mosaics as well as of reduced reliability.

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[1] Trisomy 22 (47, 22+)
Trisomy 21 (47, 21+)

2. Information about the characteristics of the population studied. In most of the published reports concerning chromosome surveys, relatively little information has been provided about the populations screened and about the nature of the institution in which groups have been confined. The tabulation of various populations surveyed into categories such as "adult criminals," "mentally disordered offenders," "mentally subnormal," "criminally insane," "juvenile delinquents," and the like, is not very helpful. While these designations may reflect the official or legal classification of the persons or the particular institutions, the terms are somewhat arbitrary and not very helpful in describing those given such labels. Terms such as "mentally disordered" or "mentally subnormal" tend to be both vague and unreliable; they do not clearly distinguish persons so labelled from many others with very similar characteristics and behaviors who do not receive such official designations.

Furthermore, the selection factors and admission criteria which influence and determine the kinds of persons found in various institutions and their social class status and characteristics have typically not been described in any detail.

3. Screening criteria. It has already been noted in previous sections of this report that a variety of screening criteria have been used in survey studies in order to facilitate the discovery of persons with extra Y chromosome complements, e.g., height of six feet (183 cm.) and above. However, as indicated in Table I (page 8), the height limitations used by various investigators vary from 175.3 cm. to 185.4 cm. In addition, screening criteria pertaining to intelligence and/or aggressive behavior have also been used. Of particular concern is the fact that in many instances the investigators have not explicitly stated or described all their screening criteria.

4. Variations in sample size. As Table I indicates, the variations in sample size among the several surveys have been considerable. It may be noted, for example, that the size of samples in the studies listed in Table I range from 11 to 607. In view, however, of the expected frequency of the XYY chromosome anomaly in the general population of one or two per 1000, or even the very rough prevalence estimate of one in 140 for certain institutionalized groups (cf. page 7), the sizes of the samples studied have often been rather small.

The lack of detailed information about selection criteria, characteristics of the populations studied, and technical procedures utilized in many of the studies thus far reported, makes comparison and drawing of even tentative conclusions very difficult.

One proposal at the conference was that a special study be initiated for the specific purpose of obtaining information on the aforementioned items directly from the various investigators. Another suggestion was that during an international cytogenetic meeting scheduled to be held late in

1970, leading investigators in the XYY chromosome area should agree among themselves to observe certain standard criteria in their methodologies and reporting procedures.

It was also suggested that data presented in the scientific journals should provide more details of the populations studied, the screening criteria, the number of cells and culturing techniques utilized, the precise ascertainment procedures, and other such information. Without such information it becomes very difficult to compare and evaluate published reports, the value of which is thus decreased.

Some Methodological Issues and Problems

A review and analysis of the various reports in the scientific literature reveals a number of problems pertaining to methodological requirements for such research. These issues are discussed under a few broad categories.

1. Need for "double-blind" studies. Several studies have compared persons with XYY chromosome complements with control subjects (46,XY complements) drawn from the same populations, e.g., institutionalized mentally disordered offenders. It is noteworthy that most of these studies have not used "double-blind" procedures. A double-blind research design requires that during the course of the study neither the person being studied nor parents nor investigators can know which persons are the primary research subjects (viz., the XYY cases) and which are the matched controls. In this way the research is protected against the influence of various psychological biases which are known to enter otherwise into the evaluation and which could confound the comparison. In comparative studies involving XYY subjects, the persons doing the laboratory studies, clinical observations, neurological, psychiatric, psychological or social examinations, should not know about the chromosomal complement of the various persons being studied.

Similarly, double-blind procedures are of great importance in conducting longitudinal studies of children detected as having chromosomal anomalies during surveys of newborns. The possible effects of experimenter and observer expectations and bias are well known in the behavioral and social science literature and need diligently to be avoided whenever it is possible to do so.

Although the scientific desirability of double-blind studies was generally acknowledged there were questions about the feasibility of intensive longitudinal follow-up of infants. It was pointed out that parental apprehensions and concerns about the possible existence of an abnormality could also negatively influence their care and handling of the child.

There was general consensus that the requirements of scientific rigor in such research needed carefully to be balanced with proper concern for and

protection of the rights and welfare of the research subjects as well as those of the parents of the infants studied.

Important questions also concern the extent to which parents should be informed about chromosomal abnormalities in their children when the medical and behavioral effects of such anomalies are still largely unknown. While there are some critical ethical and legal issues in regard to informing parents about the chromosomal complements of their children when follow-up studies are to be undertaken, it must be remembered that parental expectations and apprehensions about possible - but as yet unknown or even non-existent - problems, may well create certain difficulties and lead unwittingly to self-fulfilling prophecies.

One participant expressed the view that in some situations follow-up studies of infants and children may well require that careful information and skillful counseling be provided the parents concerning the chromosomal anomaly. (These matters are further discussed in Section VI, "Legal and Ethical Issues.")

2. Need for careful matching. Earlier discussion has noted that in some of the institutional studies reported thus far the inmates used as control subjects have been randomly, or sometimes haphazardly, selected from the same population. In view of the potential significance attached to obtained differences between such groups, viz., 47,XYY cases and 46,XY controls, it is rather essential that more rigorous and sophisticated matching procedures be utilized.

For example, in reference to studies of institutionalized XYY males, it seems important that matching consider variables such as intelligence, height, social class, previous criminal record, and length of institutionalization. A desirable approach would be to utilize more than one set of control subjects for purposes of matching in order to be able to compare the XYY persons on a number of different variables.

3. Need for accurate prevalence data. It has previously been emphasized that as a result of selective screening of various institutional populations, the biases thereby introduced into such surveys do not allow such data to be used for purposes of obtaining general prevalence rates for the institutional populations being studied. While selective screening has led to the discovery of relatively large numbers of individuals with chromosome anomalies, such procedures do not provide meaningful estimates of prevalence rates. It is essential, therefore, that sound prevalence studies be undertaken and that they systematically sample the full range of height both in institutional groups as well as in the general population.

The dangers of using the aforementioned types of incomplete or inadequate data on the occurrence of the XYY chromosomal constitution as a basis for making crucial decisions involving the welfare of individuals and groups

or for social policy decisions was a recurrent theme during the conference. It was emphasized that the information needed for such decisions can be obtained only through properly designed and carefully conducted prevalence studies of non-institutionalized as well as institutionalized populations in sufficient numbers as to have statistical validity. The groups studied must, in total, fairly represent the ethnic, geographic and socioeconomic subgroups which compose a national male population.

Furthermore, methodologies for study should be standardized and must meet criteria sufficiently rigorous as to permit valid scientific inferences as well as meaningful comparison and pooling of data.

VI

LEGAL AND ETHICAL ISSUES

The various ethical and medico-legal issues surrounding many aspects of research pertaining to chromosomal anomalies are by no means unique. Such problems are inherent in much of biomedical and behavioral research, as well as in medical diagnosis and treatment. The several legal and ethical issues discussed can be reduced to two distinct but interrelated categories.

The Issue of Informed Consent

In screening, diagnostic and related situations it is necessary to obtain informed consent of the individuals to be involved in the research. As the Public Health Service (U.S. Department of Health, Education, and Welfare) regulations guiding research involving human subjects clearly spell out[1], and also in keeping with general legal opinions on the issue, a person cannot be assumed to have given informed consent unless he was given proper information and explanation about the study procedures. The Public Health Service guidelines state:

> "An individual should generally be accepted as a research subject only after he, or his legally authorized guardian or next of kin, has consented to his participation in the research. Such consent is valid, however, only if the individual is first given a fair explanation of the procedures to be followed, their possible benefits and attendant hazards and discomforts, and the reasons for pursuing the research and its general objectives." (Page 3)[1]

Viewed in full perspective, the need for consent poses a vexing dilemma for researchers involved in sex chromosome surveys or in-depth studies of persons with XYY and related anomalies. On the one hand, important medical and behavioral problems need better understanding for both individual and social benefit. This would be impossible without extensive and thorough research. For example, in order to obtain accurate incidence and prevalence data on particular chromosomal variations it is essential to have total ascertainment of the study population. However, when informed consent is to be obtained some unrepresentative fraction of the study population may refuse to participate in the study, thereby seriously complicating total ascertainment and biasing the results obtained. Even if a large random sample of the population were to be used, similar problems would arise in reference to those who are unwilling to participate since there would be no way of determining or even accurately estimating the kinds of biases thus introduced into the study.

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[1] "Protection of the Individual as a Research Subject." Grants, Awards, Contracts, U.S. Department of Health, Education, and Welfare. Public Health Service. Washington, D.C. May 1, 1969.

Confidentiality, Privacy, and Welfare of Research Subjects

Another major issue pertains to protecting the confidentiality, privacy and welfare of persons involved as research subjects. In view of the widespread and often sensationalized publicity concerning the XYY chromosome and aggressive, violent behavior, it is crucial that the identities of the XYY cases in research on institutionalized groups should be kept strictly confidential. Even though the precise nature and extent of a causal link of the XYY chromosome constitution to antisocial behavior has yet to be established, institutional and parole authorities may be inclined to use such information in making various decisions. To the extent that the length of a person's confinement or his chances for parole may be influenced by his XYY - or even XXY - karyotype, such premature reliance upon this type of information might be quite prejudicial to the individual. Hence, information of this nature should not be displayed as a by-product of activities labelled as "research." Moreover, presumptions that a person's chromosome pattern clearly disposes him toward aggressive and antisocial behavior could lead to further stigmatization of that individual. Responses from others interacting with him might then be of a form that would tend to promote aggressive behavior, thereby making a possibly unwarranted assumption become a self-fulfilling prophecy.

For the above reasons there was consensus among the conferees that classification of various institutionalized subjects by XYY karyotype would be a premature and indeed problematic innovation.

Protecting the rights of the research subject also entails the maintenance of confidential records and protecting access to such information. It was pointed out, for example, that the statutory privilege which in many states protects the physicians' or psychiatrists' patient and the psychologists' client from having confidential information revealed from a witness stand, does not apply to information obtained in research. A recent article[1] indicates that only 11 states presently have statutes that recognize in broad terms the confidentiality of general research information of a public health nature. The researcher thus faces serious difficulties if he seeks to protect such information from a subpoena.

To the extent that the confidentiality of the research data in relation to the identity of the research subject cannot be fully protected -- because of a court order compelling such information to be revealed -- the privacy and welfare of the individual as well as the feasibility of

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[1] Schwitzgebel, R.K. Confidentiality of research information in public health studies. Harvard Legal Commentary, 1969, 6, 187-197. (The 11 states mentioned by this author are: California, Florida, Illinois, Maryland, Massachusetts, Michigan, Minnesota, New Jersey, New Mexico, South Dakota and Texas.)
See, also, Shah (74).

such research would seriously be jeopardized. Thus, even though professional and scientific standards of ethics and research regulations (e.g., those of the U.S. Public Health Service) can safeguard confidentiality in most instances, the lack of appropriate statutory privilege is a serious gap in the researcher's ability to guarantee a confidential relationship with his subjects.

In view of the foregoing considerations, it was urged that legal advisors in close cooperation with the research community should formulate model legislation to safeguard the confidentiality of certain types of research information. Such legislation should carefully balance competing societal values as well as provide appropriate safeguards for privacy and confidentiality for research subjects.

Chromosome Surveys of Newborns

Among the issues discussed in reference to planning or conducting chromosome surveys of newborns in medical facilities was the question of whether information concerning a positive XYY karyotype should be placed in the official hospital record, made available to patients, or given to the physician having medical responsibility for the patient.

There were conflicting views on these matters. Some felt that the information should be part of the person's medical record and that the responsible physician should be informed. Several other discussants, however, felt that in view of the uncertain scientific status of the causal relationship between the XYY chromosome constitution and behavior, and also because of the widespread and misleading publicity, such information should be kept separate from the medical record in order to guard against disclosure of stigmatizing information. Similarly since the precise medical hazards of the XYY condition were not yet scientifically established, and again in view of apprehension-arousing publicity on this matter, disclosure of such information even to parents might lead to undesirable consequences (see previous discussion on pages 25-26). However, there was complete agreement that as soon as problems were detected skillful briefing and counseling of the parents should be provided to assist them in their care and handling of the child.

It should be emphasized that the above discussion and views were specifically in reference to neonatal surveys and related research studies. Whenever a chromosome diagnosis was sought by the family physician, or when it might have some bearing on the usual clinical care of a patient, the information should be given to the physician and entered in medical records like any other item of medical information in such a context.

Disclosure of information about the identity of XYY cases to the subjects, parents or physicians, or even to the researchers actually doing follow-up studies, could not be made when double-blind research design is used. Several conference participants indicated a definite preference

for the double-blind approach in order to have more rigorous research methodology and also to prevent problems relating to disclosure of information about XYY cases at this stage of uncertain scientific knowledge about the condition.

Others expressed the view that in any close and long-term follow-up studies it would be most difficult not to disclose such information to parents. In addition, closer and detailed follow-up studies could more readily be undertaken when such information has been disclosed and carefully explained to the parents. Various techniques for such disclosure and counseling were discussed. It was emphasized that professionals working with the parents should desirably combine knowledge of human behavioral genetics and psychological counseling techniques.

When follow-up was not intended, and when there was an attending physician having continuing responsibility for the child, the occurrence of a chromosome anomaly should be explained to him as being of possible benefit in his management of the patient. Thereafter, it would be the physician's responsibility to inform or not inform the parents, according to specific circumstances and his best professional judgment. There was consensus that in all instances where a physical or behavioral abnormality is detected which posed a known or likely medical hazard, the physician should indeed be informed. In view of the fact that family physicians may in many instances not have sufficient knowledge of behavioral genetics and counseling techniques, one participant suggested that every research team should include a knowledgeable and skilled counselor to provide appropriate assistance to parents and also to consult with family physicians.

Underlying this particular discussion and, in fact, the whole topic of the need for more information about the biomedical and behavioral aspects of the XYY condition was the question of whether treatment is now possible or desirable or will become so in the future. This concern is particularly applicable in the case of infants and children.

In response to a question raised about the need for prophylactic measures in the case of XYY children, a participant emphasized that such concerns were clearly premature at this time since it was not yet known whether indeed there was any future problem to be prevented. In fact, some discussants felt that more harm than good might be done in terms of arousing false expectations in the parents, which expectations and apprehensions could lead to negative influences on the child's behavior and increase the possibility of the stigmatizing label leading to self-fulfilling prophecies. If, however, the individual manifested behavioral or medical problems, treatment appropriate to those problems should be promptly undertaken just as would be done if he did not have the XYY condition.

Reference was made to recent developments pertaining to amniocentesis and their implications for early detection and preventive therapeutic interventions in regard to certain chromosomal abnormalities.[1] The general view expressed at the conference was that such a discussion must be postponed until more adequate data are available concerning the incidence and prognosis for the chromosomal abnormalities in question.[2]

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[1] Amniocentesis is a procedure developed within the last couple of years which allows ascertainment of abnormalities (including genetic disorders) in the fetus after the third month of pregnancy. In this procedure amniotic fluid is obtained by direct trans-abdominal needle puncture of the womb. The procedure is comparable to that typically used for drawing blood from the veins. Presently available studies indicate that the risk to the unborn child is less than one in 600. No complications for the mother have been described.

For more information about amniocentesis in reference to this issue see:

Nadler, H.L. Role of amniocentesis in the intrauterine detection of genetic disorders. New England Journal of Medicine, 1970, 288, 596-600.

Littlefield, J. Editorial: The pregnancy at risk for a genetic disorder. New England Journal of Medicine, 1970, 288, 627-628.

See also: Lubs, H.A. & Ruddle, F.H. Chromosomal abnormalities in the human population: estimation of rates based on New Haven newborn study. Science, 1970, 169, 495-497.

[2] Two conferences relating very much to these issues have recently been held:

Conference on "Ethical Problems in Human Genetics: Early diagnosis of Genetic Defects." May 18-19, 1970. Fogarty International Center for Advanced Studies in Health Sciences, Bethesda, Md. Proceedings to be published.

Conference on Antenatal Diagnosis. June 11-12, 1970. Sponsored by the National Institute of Child Health and Human Development and the Department of Pediatrics, School of Medicine, University of Chicago. Proceedings to be published.

VII

CONCLUSION

Studies conducted thus far on limited and often selected groups of inmates of penal and mental institutions indicate that the prevalence rates for the XYY chromosome anomaly are much higher among such persons than in the general population. Available data, as well as theoretical considerations, suggest that tallness appears to be a fairly common characteristic of XYY males. However, lacking rigorous prevalence studies in the general population, definite causal links between the XYY chromosome complement and deviant, criminal or violent behavior cannot be established.

Several XYY cases studied in institutions for criminal law violators do demonstrate a variety of endocrinological, neurological and other abnormalities which appear related to their deviant behavior. However, many XYY individuals display no such abnormalities. Indeed, it is not yet known whether these persons have a higher frequency of such abnormalities than matched non-XYY cases also drawn from institutionalized populations. Moreover, the widespread publicity notwithstanding, individuals with the XYY anomaly have not been found to be more aggressive than matched offenders with normal chromosome constitutions. In this respect, it appears that premature and incautious speculations may have led to XYY persons being falsely stigmatized as unusually aggressive and violent compared to other offenders.

Further research is clearly needed to confirm whether the trait of excess body height is a genotypic consequence of an XYY constitution and to determine if there are other inherited markers, such as neurological or endocrinological departures from the norm. Such additional information on a wide range of XYY males would help to characterize the phenotype and also to indicate the various pathways (e.g., central nervous system, hormonal, etc.) through which the extra Y chromosome exercises influence on behavior. There is also a critical need for appropriate legislation to protect the confidentiality of certain types of research data in order that the rights and welfare of subjects in such studies suitably be safeguarded.

The preponderant opinion among the Conference participants was that the behavioral aberrations implied or documented thus far do not indicate a direct cause and effect relationship with the XYY chromosome constitution. Thus, it would not be possible to say at the present time that the XYY complement is definitely or invariably associated with behavioral abnormalities. Quite clearly, very complex and varied interactions between hereditary and social and environmental influences appear to be involved. Further, it seems unlikely that such variable and socially defined and determined problems as delinquency and crime, are primarily and directly linked with possession of an extra Y chromosome. Under certain conditions, the trait of non-conformity and aggressiveness hypothetically ascribed to XYY individuals might earn social acclaim; under other conditions and in other

social contexts, such behavior might be judged totally unacceptable by society. It is quite possible, however, that in particular cases this and other chromosomal aberrations (e.g., XXY) and their related genotypic traits can increase vulnerability to the development of socially maladaptive patterns of behavior.

It would be highly questionable logic and poor science, in our present state of knowledge, to assume either that this particular interaction of genotype and highly variable external influences constitutes a preordained, inflexible and irremediable hereditary determinant of a particular behavioral pattern or, that the XYY genotype does not constitute a factor contributing to particular patterns of behavior.

A pervasive note struck throughout the Conference was the need for more knowledge obtained through extensive and meticulous research. Until more precise knowledge is available, social judgments about the XYY individual based on his chromosomal constitution are unjustified.

APPENDIX A

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Appendix B

BACKGROUND INFORMATION ON GENETICS[1]

The second half of the nineteenth century saw rapid advances in the biological sciences. Included in those advances was much new knowledge in the field of genetics -- that branch of biology which is concerned with the mechanisms by which traits and characteristics are passed on from one generation of living organisms to the next.

In addition to the landmark observations of Mendel on the inheritance of observable traits in the garden pea, important clues were found concerning the specific mechanisms by which living cells divide and reproduce themselves. Utilizing technological advances in microscopy, and with the application of appropriate staining techniques, the fine structures of cells could be observed at various stages of cell division and reproduction, a process termed mitosis.

Very briefly, the following events occur within the cell, more specifically, within the nucleus, during mitosis: (1) The basic genetic material known as genes is duplicated; (2) The chromosomes, long filaments on which the genes are located, are also duplicated; (3) The chromosome filaments grow shorter and thicker and become segregated into roughly paired segments; (4) The nucleus and the entire cell split into two "daughter" cells, each of which contains within its nucleus one set of the paired chromosomes. In normal circumstances, the entire process now begins all over again.

Early in the 1900s the growing science of cytogenetics (microscopic and biochemical study of cells, chromosomes and genes in particular) found that an association existed between the mitotic transfer of chromosomes and the transmission of cell form and function. Working with plants, fruit flies, mice and other animals, cytogeneticists were able to identify many specific inherited traits with specific genes and to locate their grouping on the same chromosomes.

Sex chromosomes

In 1891 a German biologist found that during formation of the sperm in certain insects half received a particular structure and half did not. He named it the X structure. Subsequently, other investigators found that the X structure existed also in the egg cells of all females of an insect species. They determined further that eggs fertilized with X-carrying sperm developed into females (XX), and that eggs receiving sperm without the X developed into males.

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[1] Readers interested in more information about the fundamentals of genetics may wish to consult some of the references provided in Footnote 1 of the Foreword, page 1.

Soon thereafter, studies made on other insect species showed that a distinctive structure, designated as the Y chromosome, usually occurred in half of the mature sperm and that the familiar X chromosome turned up in the other half. Occasionally, however, a sperm might have neither; this was designated as an O sperm. Further, it was determined that the combination in the fertilized egg of either XX or XO chromosomes produced females, while the XY combination produced males. In other words, both X and Y were sex chromosomes, X being the female determinant and Y the male.

The normal individual in each species of living organisms has the same basic number of paired chromosomes. Man, for example has matched pairs of 23, totalling 46. The rhesus monkey has 42; horses have 32. Chromosomes are of two kinds: autosomes (body forming), and the two sex-determining chromosomes. In the normal individual each parent furnishes one half of the usual complement of 46 chromosomes -- 22 autosomes plus one sex chromosome (X) contributed by the egg and 22 autosomes plus one sex chromosome (X or Y) from the sperm, thus forming the normal complement of 46 chromosomes.

Obviously, a form of cell division different from mitosis must be required to insure that only one-half of the chromosomes originally in the egg or sperm are present when fertilization takes place. This special form of cell division in the earlier stages of sexual reproduction is known as meiosis.

In meiosis, two cell divisions are required to achieve duplication of the chromosomes in the egg and sperm, which are, of course, the highly specialized cells required for sexual reproduction. This is in contrast to the single stage process by which all other cells are divided. The second division of the egg and sperm results in a reduction by one-half of the 46 chromosomes originally present in the primary stage of the sex cells. In this way, not only the doubling of chromosomes in each new generation is avoided, but also each parent is enabled to contribute 23 -- one half -- of the required 46 chromosomes.

However, meiosis does not always proceed normally, and either the egg or the sperm may contain more or less than the normal 23 chromosomes prior to fertilization. Perhaps the most frequent cause of this abnormality is non-disjunction, or improper separation of the chromosome pairs during the egg or sperm meiotic processes. When such an abnormal egg or sperm is joined with a normal egg or sperm at fertilization, the resulting individual will have one or more chromosomes in addition to or less than the customary 46.

When the 44 autosomal chromosomes are affected by such errors as non-disjunction, serious and often lethal results can arise. For example, in the condition known as Mongolism, or Down's syndrome, the 21st group of the 23 pairs of chromosomes is composed of three instead of the usual two chromosomes. This anomaly occurs in about one of each 700 live births and accounts

for about 10 percent of hospitalized cases of mental retardation in the U.S. Other, usually lethal, excess autosomal abnormalities have been noted, leading to the conclusion that the human organism can accommodate excess genetic material only within very limited ranges. A deficiency of genetic material is even more harmful.

In still other individuals, sometimes apparently quite normal, two different kinds of cells may be found in the body - one with the normal complement of chromosomes and one with excess chromosomes. This chromosome pattern is known as mosaicism. Generally, the "mosaic" individual is less affected physically than a person having excess chromosomes in all cells.

Non-disjunction involving the sex chromosomes is more germane to this discussion than autosomal non-disjunction. More is known about it, because study of a single pair of chromosomes is easier than of the 22 pairs of autosomes.

In normal meiosis the mature egg cells each receive one X chromosome. However, non-disjunction can result in either none (0) or a two X complement (XX). When fertilized by a normal X or Y-bearing sperm, these abnormal eggs can give rise to individuals having chromosomal constitutions and conditions as follows:

45,XO - "Turner's syndrome": females with defective development of the reproductive system, short stature, broad chest, and other physical anomalies.

47,XXX - Females, normal physically, but generally believed to have a moderately depressed intelligence.

45,XO - This condition is presumed to be lethal and has never been reported in the scientific literature.

47,XXX - "Klinefelter's syndrome": males with late onset of puberty, underdeveloped testes, possible breast development, increased frequency of mental retardation, and also believed to be more vulnerable to social and psychological problems.

Similarly, non-disjunction can give rise to mature sperm with: an O complement, that is, neither X nor Y chromosomes; an XX complement; and the YY complement. Fertilization of the normal egg with these sperm can result in the following chromosomal constitutions: 45,XO (Turner's syndrome); 47,XXX; 47,XXY (Klinefelter's syndrome); and 47,XYY (males who are taller than average and who, according to recent studies, may be prone to antisocial or other behavioral problems).

Identifying the XYY

Several procedures are helpful to the cytogeneticist and the physician in identifying individuals with sex chromosome defects. By far the most important is karyotyping, which is the characterization of the size and shape of the chromosomes within stained cells at the stage of mitosis during which the chromosomes divide longitudinally and double in number. The stains used have an affinity for chromatin, a material rich in DNA (deoxyribonucleic acid), the chemical substance of the genes which carries the hereditary information.

The cells to be examined generally are obtained from gentle scraping of the lining of the mouth (buccal smears) or by culturing lymphocytes (white blood cells) which have been isolated from a tiny sample of the subject's blood. The latter method is more informative and is necessary for enumerating and identifying the individual chromosomes but is more expensive and time consuming. For preliminary screening and rapid identification of excess X chromosomes, buccal smears are used more often. Promising work is under way to develop electronic, computerized methods for karyotyping from lymphocytes.

GLOSSARY

Autosomes	Chromosomes other than the sex chromosomes.
Buccal Smear	Material obtained from the inner surface of the cheek for microscopic examination.
Chromosomes	Microscopic bodies within cell nuclei, rich in a substance called deoxyribonucleic acid (DNA), and carriers of the genes.
Cytogenetics	Study of the contributions to heredity of structures and phenomena within the cells.
DNA	Deoxyribonucleic acid, the chemical composing the information-carrying substance of genes.
Gene	The basic unit of inheritance; a portion of a DNA molecule within or attached to a chromosome.
Genotype	The totality of the genes in the chromosomes of an individual; thus the total of inherited characteristics and predispositions.
Incidence	The rate at which new cases of a certain condition occur within a given population over a given period of time; i.e., the annual incidence per 100,000 of TB, or the incidence of XYY at birth per 1000 live births.
Karyotype	An array of the cell's entire chromosome complement to display their comparative size and shape.
Lymphocyte	A form of white blood cell which has a relatively large nucleus.
Meiosis	The total cell division process of the germinal cells (egg and sperm), also called reduction division.
Mitosis	The total cell division process of an autosome.
Morphology	That branch of biological science which deals with structure and form. As used herein, the size, shape and location of chromosomes.

Mosaic	An organism in which the cells of some tissues have chromosomes differing from those in other tissue cells.
Non-disjunction	Improper separation of chromosomes during cell division.
Prevalence	The number of cases of a disease or other condition existing in a population at a given time.
Phenotype	A discernible trait in an individual, such as exceptional height or a particular blood group type.
Syndrome	A group of symptoms which characterize a certain disease or abnormality.

APPENDIX C-1

Some Physiological, Biochemical and Familial Factors Requiring Study in Reference to the XYY Anomaly

1. Endocrine Function: (a) evidence seems to be accumulating that the luteinizing hormone may be elevated in some cases of the XYY complement; (b) androgens appear to show an unduly large variation above and below normal levels in XYY individuals; (c) growth hormones need to be studied since it has been hypothesized that a major role of the Y chromosome is production of some kind of growth regulator.

2. Size and body proportions associated with size.

3. Abnormal muscle movements.

4. Electroencephalographic abnormalities.

5. Electrocardiographic abnormalities.

6. Abnormally short Y chromosomes; if these are found, a very careful search should be made for minor hypospadias.

7. Twinning; there has been a history of twins in some reported cases of sex chromosome anomalies. Also, cases have been reported of identical twins who are nonidentical in terms of their chromosomal constitution.[1]

8. Ascertainment of the medical, social and behavioral status of the parents of XYY individuals. For example, a study reported that all of one group of XYY prisoners came from broken homes.

9. Thyroid function and disease.

10. Sense of taste and smell. This was judged to be fundamental since taste and smell acuity appear to be genetically determined to a greater extent than is presently realized.

11. Dermatoglyphics; preliminary evidence suggests that the XYY subject may have characteristic finger, palm and footprint patterns, as do persons with other sex chromosome abnormalities.

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[1] Money (56).

APPENDIX C-2

Some Specific Suggestions Regarding Further Research

1. In view of their many points of similarity, including techniques for karyotyping, and because of the basic need for every bit of potentially useful information, wherever feasible screening for other sex chromosome abnormalities should also be done while conducting XYY surveys. Specifically, additional light would be focused on the role of chromosomes in influencing organic and behavioral development, as well as on the individual and social impact of these chromosomal variations.

2. The feasibility and desirability of establishing a central registry of XYY and other sex chromosome karyotypes uncovered in unpublished studies or during clinical work with individual patients was extensively discussed. While the value to researchers of having access to such pooled data was obvious, a number of problems and difficulties were also anticipated. It was urged that case histories and other relevant information concerning chromosome anomalies should be published in suitable journals.

3. Techniques and apparatus are now available which permit rapid and accurate measurement of aggressivity in adolescents and adults under experimental conditions. These laboratory procedures may be employed wherever feasible to obtain objective information on this behavioral characteristic in XYY subjects and carefully matched controls. (See, Appendix D, "Measurement Procedures for Investigating the Correlates of the XYY Syndrome.")

4. A critical issue in research methodology is the dichotomy between the need for long-term follow-up of XYY infants to study physical and behavioral development and the need to obtain answers to these questions as quickly as possible. One partial solution proposed was to conduct simultaneous karyotype surveys and developmental studies on XYY children and suitably matched controls at four age levels: first grade, fourth grade, and the first and last years of high school. Such a study might also have the interesting outcome of showing an attrition in the frequency of XYY cases with increasing age from infancy onward, thereby raising the possibility that persons with such a chromosome constitution disappear progressively from the population, either because of death or perhaps because they are drawn off to institutions for the physically, psychologically or socially handicapped.

5. Also in the area of survey methodology was the question as to the best and most economical way to fill the critical gap in our knowledge about the baseline prevalence rate for the XYY complement in normal male populations, i.e., the non-institutionalized. Coherent groups in which ready access could be had to blood samples and background social, medical and familial data would be a prerequisite. Among the groups which might meet these criteria would be industrial and wider-based prepaid medical care groups and Selective Service inductees.

It was concluded that firm recommendations on various study possibilities should not be made by the Conferees. However, it was felt that very valuable results might be achieved if a smaller group with representatives from all appropriate disciplines, including epidemiologists and population statisticians, were to be convened for this purpose.

Concern was expressed about the high cost of the karyotyping procedures now available. Optimistic reports were heard about the likelihood of faster, cheaper and more accurate biochemical techniques being developed within the next ten years. (See, for example, Appendix C-4, Quinacrine Fluorescence Technique for Identifying the Y Chromosome.)

In this regard the question was raised whether major surveys should be deferred, because of their cost, until new and more efficient karyotyping technologies became available. The sense of the group was that the social demands for early clarification of the XYY issue were such that needed studies should not be deferred.

APPENDIX C-3

Characteristics for Identifying the Y Chromosome

Morphological Characteristics[1]

1. Absence of a satellite region as compared with the G group autosomes and thus not connected with satellite association.

2. The long arms of the Y tend to be more aligned than those of the G autosomes.

3. The short arms of the Y are forked in comparison with other autosomes.

4. In some cases it is possible to see a secondary constriction in the middle of the long arm of the Y chromosome.

5. The Y is usually on the periphery of a cell spread and is fuzzy in appearance.

In addition to the aforementioned morphological features, the Y chromosome may also be identified in terms of its DNA replication pattern and, in the case of persons with extra Y chromosomes, there are fairly distinctive dermatoglyphic patterns. There is some evidence that the DNA replication pattern of the Y chromosome may be heavier as compared to the G autosomes.[2] The dermatoglyphic changes related to the presence of an extra Y chromosome are significantly different when compared to an extra G autosome in both XYY as well as XXYY males.[3]

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[1]Patau, K. Identification of chromosomes. In, J.J. Yunis (Ed.) Human chromosome methodology. New York: Academic Press, 1965.

[2]Borgaonkar, D.S., Herr, H.M., and Nissim, J. DNA replication pattern of the Y chromosome in XYY males and XXYY males. Journal of Heredity, 1970, 61, 35-36.

[3]Borgaonkar and Mules (13).

APPENDIX C-4

Quinacrine Fluorescence Technique for Identifying the Y Chromosome

Based upon some work done two years ago showing that certain fluorescent derivatives of acridine stain the chromosomes of various organisms, a recent report by Pearson et al (62) has demonstrated that the quinacrine staining test shows up the number of Y chromosomes in a human interphase (non-dividing) cell. This new technique has been hailed as an important time saver for those interested in screening human populations for XYY males. The quinacrine test (using quinacrine mustard and quinacrine hydrochloride) is viewed as the exact counterpart of the simple stain for the Barr body which reveals the presence of extra X chromosomes.[1]

More recently, the quinacrine stain has been used on human spermatozoa and it has been possible to distinguish the male-determining spermatozoa from the female ones.[1]

However, even more recent studies suggest that while the aforementioned developments are indeed promising, certain reasons for caution need to be kept in mind. Thus, Borgaonkar and Hollander[2] have found that while the distal portion of the long arm of normal Y chromosomes fluoresced clearly and distinctly in metaphase plates and a corresponding fluorescent particle was present in many interphase nuclei, no comparable fluorescence was detected in preparations from patients with small Y chromosomes.

Hence, caution may well have to be exercised in using the quinacrine fluorescent technique for identification of Y chromosomes since, in light of the above findings, there is a possibility at the present time of not being able to identify small Y chromosomes with this technique.

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[1]Editorial. In pursuit of the Y chromosome. Nature, 1970, 226,897.

[2]Borgaonkar, D.S. & Hollander, D.H. Quinacrine fluorescence of the human Y chromosome. (Submitted for publication, 1970)

APPENDIX D

Measurement Procedures for Investigating the Correlates of the XYY Syndrome

Albert Bandura, Ph.D.

The types of assessment procedures selected to investigate the psychological correlates of the XYY syndrome should depend upon the nature and specificity of the hypotheses being tested. At the most general level, the major research question may be concerned with whether any personality characteristics are consistently associated with this particular chromosome abnormality. In a study of this type, investigators would be advised to measure a wide range of psychological characteristics, including intellectual and other cognitive functions, social behavior, sexual functioning, emotional responsivity, and capacity to form and to maintain satisfying interpersonal relationships. These functions can be measured by interview techniques, by standardized examinations, by situational tests, and by behavior observation methods.

At a more specific level, it has been hypothesized that males with an XYY sex chromosome complement are predisposed to impulsive aggressiveness. A gross test of this hypothesis would require a study in which baserates of deviant aggressive behavior among XYY males are compared with matched groups of males without the abnormal karyotype. Unless the groups are carefully matched on variables that are known to be correlated with antisocial aggression, a comparative study may result in highly misleading conclusions. It has been reported, for example, that XYY males are, on the average, six inches taller than men with a single Y chromosome. Given evidence that tall youngsters tend to be arrested at earlier ages than short ones, it would be important to match the two samples with respect to height. Investigators also report an unusually high evidence of broken homes in the history of XYY samples. Since familial conditions associated with broken homes tend to promote antisocial aggression, it would be essential to include family stability as another matching variable.

If comparative studies demonstrate significantly higher baserates of antisocial aggression then systematic laboratory studies are required to establish the mechanisms through which aggression-promoting influences have relatively strong effects in XYY males. Do they have a lower threshold for aggressive arousal? Are they excessively responsive to aggressive modeling cues and reinforcement feedback? Do they have defective inhibitory capacities? Existing laboratory procedures that measure ease of aggression arousal, modeling of aggressive behavior, rate of operant conditioning of aggressive behavior, and strength of aggressive response inhibition could be employed for this purpose.

It is conceivable that baserate studies relying on legal records of antisocial behavior may yield negative results because such dependent measures are unreliable or confounded by many extraneous factors. The question of whether XYY predisposes one toward antisocial aggression, therefore, can be best answered through a longitudinal study in which the form, intensity, and periodicity of aggressive behavior is assessed at periodic intervals for matched XYY and genetically normal samples. A time-sample behavior observation procedure would provide the best measure of aggressive tendencies. Systematic observation of familial interactions, which is being increasingly employed in child psychology, would be essential for elucidating how social influences interact with genetic characteristics to produce aggressive and other personality characteristics.

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