The Prevalence of the 47, XYY Chromosome Abnormality in Selected Human Populations[1]

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Abstract

Quinacrine mustard fluorescence staining of buccal smears was used to survey 1,646 males constituting five populations in an attempt to identify individuals possessing the 47, XYY chromosome constitution. Although on the average, 25 per cent of the cells examined revealed the presence of one fluorescing Y chromosome, no individuals were found whose cells revealed the two fluorescing bodies indicative of the 47, XYY chromosome aberration.

As a result of this study, an impressive decrease can be reported in the prevalence rate of the 47, XYY chromosome complement among the mentally ill. The sample of 1,017 mental patients permits the reduction of the prevalence rate from 0.305 per cent to 0.12 per cent, a figure comparable to that reported for normal males when neither group is restricted by height.

The 47, XYY chromosome abnormality received considerable public attention in 1968 in three murder trials, and popular opinion or misapprehension instantly linked the genetic aberration with biologically induced criminal behavior. The premature public dissemination of information on the 47, XYY abnormality was based largely on a single study which reported a remarkable concentration of 47, XYY males in a special maximum security institution, Carstairs, in Scotland. Initially, these 47, XYY males were characterized as violent, dangerous or criminal, and as having borderline to mild mental subnormality (4).

More recent research has considerably moderated these early speculations; however, many writers speak of the 47, XYY syndrome as if it were an accepted fact that the afflicted individuals had anatomical, physiological, psychological, and mental characteristics in common. The National Conference on the XYY Chromosome Abnormality sponsored by the Center for Studies of Crime and Delinquency, National Institute of Mental Health, in June, 1969, accepted the following statement (7):

> 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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[1] This paper is based on a portion of a doctoral dissertation completed by Dr. Exley under Dr. Mertens' direction.

In addition, the Conference participants denied the existence of a 47, XYY syndrome by citing the wide range of variation in behavioral, physical, and psychological information tabulated for the known XYY individuals (7).

Numerous studies on the prevalence of the 47, XYY chromosome abnormality have been reported in the literature. A recent review article by Baker (1) examines each of these and discusses the several numerical chromosome disorders and associated antisocial behavior. The data presented in these studies are perplexing and often contradictory, to the extent that it is not possible to establish accurate prevalence rates for the normal male population or the various institutionalized populations. Obviously, establishing these prevalence rates must precede social, legal, or medical conclusions about the behavior of the 47, XYY male.

The Study

In this study, several different populations were examined to determine the prevalence of the 47, XYY chromosome abnormality among juvenile and adult males. The mentally ill patients were located in two institutions and numbered 1,017. Richmond State Hospital, a general psychiatric facility, provided 301 subjects. The patients ranged from 162.5 cm to 193 cm in height. Age or infirmity prevented accurate height measurement in many patients, but 54% of the patients were less than 180.3 cm in height.

The second general psychiatric facility, the Veterans Administration Hospital, Marion, Indiana, is an 1,100 bed hospital, and 716 patients were obtained here for the study. The selection procedure ensured that representative groups from the entire institution would be included in the population sampled.

Bethel Home Place for Boys, Inc., is a private, church supported institution which receives its admissions through the courts. Seventy-one of the 79 boys currently enrolled were included in this study. The boys ranged in age from 9 to 17 years. Accurate height records were available and with three exceptions, the boys were within two standard deviations of the United States mean for their age.

Male college students who were taller than 180.3 cm comprised a group of 498 subjects. These students were enrolled in introductory biology courses at Ball State University. Sections of these classes were visited, the purpose of the study explained, and volunteers who were taller than 180.3 cm were accepted. No tall students refused.

The term "aggressive" is linked so consistently to the 47, XYY abnormality that one group was selected specifically to test this putative relationship. The group consisted of college students who could be considered to be aggressive by virtue of their voluntary participation in the contact sports of wrestling and football. Seventeen members of the wrestling team, with an average height of 175 cm, and 43 members of the football team, with an average height of 183 cm participated in the study.

The study was considered to be of significance in that the mentally ill population surveyed is the largest reported; the collection of prevalence data for a population of tall normal male college students is unique; the putative relationship between aggressive behavior and the 47, XYY aberration is tested; and the study is the first reported using the quinacrine mustard staining technique for fluoromicroscopy of buccal smears.

Methodology

Pearson (6) reported a technique using fluorescence microscopy for identifying the Y chromosome in interphase nuclei obtained by buccal smear. The method was suggested as complementary to the Barr body procedure in its ability to identify numerical sex chromosome abnormalities.

Casperson *et al.* (2) initially reported the use of fluorescent acridine derivatives in staining mitotic chromosomes of various organisms. Fluorescent substances bind to well-defined regions on each chromosome, and this is accepted as evidence of chemical differentiation along the chromosomes. Quinacrine mustard is an effective fluorochrome for selective labeling of DNA. It seems probable that the highly fluorescent bands observed correspond to areas previously identified as constitutitive heterochromatin.

The quinacrine mustard staining technique for epithelial cells obtained by buccal smear used in this study is a modification of the procedure described in the workbook provided participants at the Fourth Tutorial on Clinical Cytology (3). Two buccal smears, left and right, were obtained from each subject using a wooden tongue blade and scraping forcefully across the buccal mucosa. The resultant material was immediately transferred to a clean microscope slide and sprayed with a commercial aerosol fixative (Spray-cyte, Clay-Adams). The slides were refrigerated until staining could be accomplished.

Quinacrine mustard was obtained commercially from Poly-Sciences, Inc., Paul Valley Industrial Park, Warrington, Pennsylvania. A 0.005% aqueous solution was prepared using 0.0025 g of quinacrine mustard in two ml of distilled water. McIlvanie's buffer, pH 5.6, was prepared using 378 ml of 0.1 M citric acid and 522 ml of 0.2 M disodium hydrogen phosphate. The 2 ml of aqueous quinacrine mustard were added to 48 ml of the buffer.

Slides were immersed in the staining solution of quinacrine mustard for 10 min and then rinsed in a gentle stream of tap water for 3 min. The slides were then placed in McIlvanie's buffer for 5 min and mounted in buffer. Coverslip edges were sealed with clear nail polish. Slides were refrigerated and read within 24 hours using a fluorescence microscope and darkfield illumination.

An American Optical fluorescence microscope and Fluorolume illuminator were used. A 200-watt mercury arc vapor lamp provided the source of ultraviolet light. A Schott No. B-G 12 primary (excitor) filter 3 mm thick was used to pass selectively exciting wavelengths through

the condenser and into the specimen to stimulate the specific fluorescent characteristics. Various secondary (barrier) filters were used to block transmission of undesired wavelengths and pass only the fluorescing wavelength emitted by the chromosome. Generally, a 20 mm light yellow-green barrier filter (Schott C-G 9) provided the best visualization; however, the EK 2A colorless barrier filter was more effective on occasion. Slides were observed using the oil immersion objective and immersion oil (Cargill's Type A) having very low fluorescence.

Fifty cells per slide, totaling 100 cells per subject, were examined and recorded as to the presence of a fluorescing body presumed to be the Y chromosome. Records were maintained on the height and location of each subject and the number of cells which contained the fluorescing body.

A slide from a known 47, XYY male was prepared using this technique and viewed by the investigator. The two brightly fluorescing Y chromosomes were readily apparent.

Results and Discussion

No individuals having the 47, XYY chromosome abnormality were identified in any of the populations tested. However, if the data obtained in this study were added to those which were previously available (1), the following prevalence rate decreases would occur:

1) The XYY percentage among institutionalized juveniles, not restricted by height, decreases from 0.341% to 0.332%.
2) The XYY percentage in tall normal males decreases from 0.304% to 0.237%.
3) The XYY percentage in the mentally ill, not restricted by height, decreases from 0.305% to 0.12%. This decrease reduces the prevalence rate among the mentally ill to that which is found among normal males, not restricted by height (0.125%).

Negative findings, such as obtained in this study, are not unique in the research reports relating to the prevalence of the 47, XYY chromosomes abnormality, but such studies are less frequent than those which do identify individuals with this aberration. Many authors have speculated on the extreme variation that has been observed in reported prevalence ratios. Jacobs *et al.* (5), whose study at Carstairs initiated this new area of genetic research, has questioned the fact that the rate found in her original Scottish study was not equaled in later English studies. Availability of mental hospital beds, admission and discharge policies of institutions, and the polygenic inheritance of mental disorders have all been used in an attempt to explain the diversity of XYY data.

When it became apparent that the 47, XYY individual was exceedingly rare, the original proposal for this study was enlarged to in-

clude a prison population. The necessary approval was secured from the Department of Correction, State of Indiana, to examine a minimum of 200 tall inmates incarcerated at the Pendleton Reformatory. Apparently, the popular view of this disorder is so strong and so negative that the Inmate Council of the Reformatory overwhelmingly rejected participation in the study. Even though the Council was assured of the anonymity of research findings, they felt it necessary to refuse cooperation, believing that if the published study contained a report of any 47, XYY individuals in the prison, the prison officials might institute their own laboratory tests and identify the person(s). The Inmate Council members believed that the parole board would never consider an XYY individual for parole, and that their refusal to participate was a necessary and desirable protection of their rights.

As this is the first known study employing the quinacrine mustard staining of buccal smears for fluorescence microscopy, some attention should be paid to the method itself. A single, brightly fluorescing spot presumed to be the Y chromosome was observed, randomly located, within the cell nucleus in an average of 25% of the cells examined. A striking variation occurred among the different populations tested. The slides from the patients at Richmond State Hospital averaged 13% of the cells displaying the Y chromosome; those from the Veterans Administration Hospital averaged 16% Y visualization. Thirty-one per cent of the cells were positive for Y fluorescence among Ball State University students and 42% among the juveniles at Bethel Home.

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