X chromosomes: Too few and too many

One to two infants per 1,000 have an abnormality in their number of sex chromosomes. These conditions, once thought to cause mental retardation, are now considered instead to have more subtle and variable psychological effects.

One child with a sex chromosome abnormality (SCA) may have numerous difficulties, while another with the same abnormality may appear quite normal, report scientists from the Denver-based National Jewish Center for Immunology and Respiratory Medicine. In Philadelphia last week, at the annual meeting of the American Association for the Advancement of Science, they described the development of 47 infants with sex chromosomal abnormalities identified in a newborn-screening program from 1964 to 1974. "Only now, as most subjects are in adolescence, are we in a position to understand the longitudinal importance of specific developmental findings," says researcher Bruce G. Bender.

Language, motor and learning deficits, report Bender and colleague Arthur Robinson, all occurred in about 30 percent of the males and almost 70 percent of the females in their SCA sample, but in none of the controls.

Bender and Robinson also found depressed IQ scores for some SCA groups. Girls with Turner's syndrome, who lack an X chromosome (XO), had an average score of about 85, a finding consistent with other studies of XO women. Women with Turner's syndrome are typically very short, reaching an average height of 4 feet 7 inches. Although some are indistinguishable from short women who are chromosomally normal, others have abnormal physical characteristics, including neck webbing and a broad chest.

Several research groups have reported that the low IQ scores of XO women are limited to the nonverbal, or spatial, portions of intelligence tests. However, Daniel B. Berch of the Univeristy of Cincinnati finds that only half of the XO children 5 to 9 years old he tested show a marked difference between verbal and nonverbal IQ scores. In some of these cases the nonverbal score was average and the verbal score was high. "Perhaps, then, the more extensive difficulties in spatial information processing do not typically emerge . . . until the adolescent period," Berch says.

Psychologists are now delving into the spatial deficiency. In independent studies, Berch and Joanne F. Rovet of Toronto's Hospital for Sick Children found that XO girls mentally transform (rotate, for example) spatial images at slower rates than do other children.

Some psychologists speculate that the source of this deficit is an altered use of the two brain hemispheres. Rovet says her data indicate that XO females use their left hemispheres to process both spatial and verbal information, instead of processing spatial information with the right hemisphere. She reports that the spatial ability of one XO woman improved after she developed epilepsy, damaging her left hemisphere.

Having an extra X chromosome, like lacking an X chromosome, can present difficulties. Bender reports that XXY males have a slight but statistically significant deficit in IQ, while XXX females have a larger deficit, similar to that in Turner's syndrome.

Shirley G. Ratcliffe of Western General Hospital in Edinburgh, Scotland, who has followed the development of 19 males and 16 females with extra X chromosomes, reports that XXX girls have an average IQ of 91, while XXY boys have an average IQ of 101. Ratcliffe finds, in addition, that speech development is delayed in both the males and females.

Men with the XXY condition, also called Klinefelter syndrome, show a disorder in language function but have normal spatial abilities, says Charles Netley of Toronto's Hospital for Sick Children. He suggests that, in contrast to the situation proposed for Turner's syndrome, in the XXY condition the right hemisphere takes over both verbal and nonverbal activities. "The degree of disturbance of right hemispheric functioning in extra-X males predicts the severity of their language deficit," Netley says.

Some other scientists are leery of these speculations. They say the sample sizes are small, the tests superficial and the data "soft."

"Hemispheric specialization is a very complex subject," says Julian Davidson of Stanford University. "It is very hard to make generalizations."

The critics say the biggest problem is to distinguish between biology and environment. According to Paula Caplan of the Toronto-based Ontario Institute for Studies in Education, "If children are chromosomally different, then all kinds of things may be different with the way they are raised." — *J. A. Miller*

'One man's poison': Genetic vulnerability

About a decade ago, in a Dupont plant in Deepwater, N.J., exposure to a chemical used in manufacturing caused 87 episodes of a potentially serious blood disorder in workers. But it wasn't a simple case of exposure equaling problems. Though many more workers were exposed, just 30 developed the disorder, and 30 of the episodes occurred in 8 workers. Now scientists are gathering tools to crack open the "black box" of why some people are predisposed to environmentally associated diseases. Some of those tools were described last week in Philadelphia at the annual meeting of the American Association for the Advancement of Science.

"Virtually all" of the common human-made compounds in the environment are metabolized by a complex group of enzymes called the cytochrome p-450 system, says Harry Gelboin of the National Cancer Institute in Bethesda, Md. These enzymes can convert a toxic chemical into a harmless metabolite — or a harmless chemical into a potent carcinogen. There is enormous individual variation in the amount and efficiency of the p-450s: The action of a given enzyme can vary three-fold among individuals, researchers say, affecting vulnerability to environmental toxins. But scientists have had trouble studying the system because of its complexity. Now, Gelboin says, his studies show that monoclonal antibodies are "a beautiful way of sorting out the multiplicity of forms and [of finding] which p-450 is responsible for which reaction."

Vulnerability may also stem from an inability to repair DNA damage. Lawrence Grossman of Johns Hopkins University in Baltimore and his colleagues have designed an assay for DNA repair potential. In the laboratory, Grossman damages an enzyme-coding gene in *Escherichia coli* bacteria; then he introduces the gene into human cells in culture. Because humans don't normally produce the enzyme, any enzyme found reflects the cells' ability to repair the genetic damage. According to Grossman, the technique will provide evidence about the relationship between variations in DNA repair potential and susceptibility to environmental mutagens, agents that cause changes in DNA.

Says Daphne Kamely, of the Environmental Protection Agency, "If we come up with good enough science, if we can really say only this fraction of the population is at risk, then [the regulatory agencies] may say, 'Maybe we shouldn't just ban this chemical entirely.' " Warnings could allow people to make choices about exposure, she says.

A number of ethical questions are tied like tin cans to the scientific advances. Some researchers note that the ability to profile individual vulnerability raises concerns — worries of workers about job discrimination, for example. But according to Gilbert Omenn of the University of Washington in Seattle, "There's an emerging consensus that you can deal with problems in the work place, if you do things stepwise. . . . And if a worker believes he or she is at higher risk, they might well be more motivated" to take self-protective measures. — *L. Davis*