But let us not adopt a decision rule for genetic screening, as Nelson et al. seem to do, simply because we can easily collect the numbers. The technical and ethical issues inherent in population screening are just too subtle and the need for a continued searching debate too critical for me to accept the Nelson benefit-cost decision model as a helpful guide to a sound public policy towards genetic illness.

ROBERT P. INMAN

Departments of Finance and Economics
University of Pennsylvania
Philadelphia, Pennsylvania

REFERENCES

1. NELSON WB, SWINT JM, CASKEY CT: An economic evaluation of a genetic screening program for Tay-Sachs disease. *Am J Hum Genet* 30:160–166, 1978
2. ACTON JP: *Evaluating Public Programs to Save Lives: The Case of Heart Attacks*. Santa Monica, Calif., The Rand Corporation, R-950-RC, 1973
3. MISHAN EJ: Evaluation of life and limb: a theoretical approach. *J Polit Econ* 79:687–705, 1971
4. ZECHAUSER R: Procedures for valuing lives. *Public Policy* 4:419–464, 1975
5. BUSH JW, CHEN MM, PATRICK DL: Health status index in cost effectiveness: analysis of PKU program, in *Health Status Indexes*, edited by BERG R, Chicago, Hospital Research and Educational Trust, 1973, pp 172–194
6. FOOT P: Euthanasia. *Philos Public Affairs* 6:85–112, 1977
7. COHEN M, NAGEL T, SCALON T: *The Rights and Wrongs of Abortion*. Princeton, N.J., Princeton Univ. Press, 1976
8. LYONS D: Human rights and general welfare. *Philos and Public Affairs* 6:113–129, 1977

LATERAL ASYMMETRY OF HUMAN CHROMOSOMES

In this issue of the *Journal,* the papers of Angell and Jacobs [1] and Emanuel [2] on lateral asymmetry at various sites on human chromosomes have a number of interesting implications.

The use of electron microscopy or computerized microdensitometry has often been advocated as a means of increasing the resolution of chromosome banding or the speed of karyotyping. However, once again simple techniques available in all cytogenetic laboratories have kept a jump ahead of the expensive machines. Just as the computerized karyotyping has begun to standardize Giemsa stained chromosomes, chromosome banding threw them into disarray because of the high frequency of touching chromosomes and greater complexity of banded preparations. Just as these problems began to be partially solved, the increased resolution provided by prometaphase chromosomes [3] found use in more and more laboratories. If computers had trouble with touching chromosomes, the tangle of prometaphase preparations will drive them into the machine-land version of the looney house. The report of Angell and Jacobs [1], showing the high degree of polymorphism in the C-band region of

chromosome 1 due to variations in lateral asymmetry, further illustrates the great sensitivity available with straightforward light microscope techniques. Densitometry scans of C-banded no. 1 chromosomes give about five subclasses, while the technique of lateral asymmetry utilizing chromosomes exposed to BrdU for one S period has the potential of dividing each of these into nine subclasses for a theoretical possibility of 35–45 types of no. 1 C-bands.

The virtue of this increased range of variability of the no. 1 C-band in linkage is obvious. Of 44 unrelated individuals tested, 20 were clearly heterozygotes for the no. 1 C-band [1]. This degree of heterozygosity could also be useful in amniocentesis, where comparison of the C-bands in XX amniotic cells with those in maternal lymphocytes should rule out accidental culturing of maternal cells in most cases.

Uniform satellite polarity has been observed in organisms with a single satellite DNA, such as the mouse [4–6]. Here lateral asymmetry in relation to the centromere is the same in all chromosome arms. This satellite polarity is also preserved in interstitial C-bands [5, 6]. The results of Angell and Jacobs could mean that (1) satellite polarity is not always preserved, or (2) more likely, that switches in lateral asymmetry are reflections of the presence of two or more different satellites in the C-bands of chromosome no. 1 and no. 9. If the latter is correct, why do only chromosomes 1 and 9 show such switches when in situ hybridization suggests that many C-bands contain several different satellites [7]? By combining the methods of growing cells in Hoechst 33258 that greatly extend C-band regions with staining for lateral asymmetry and high resolution in situ hybridization with human satellites purified to 100% by cloning techniques, a team of molecular cytogeneticists could be kept busy for years with the fine mapping of the distribution of human satellites.

The polymorphism in lateral asymmetry in chromosome no. 1 is probably due to unequal crossing over in repetitious DNA. Smith [9] has proposed that satellite DNA evolved through a long series of unequal crossing over events. This raises the question of the extent to which this process is still going on. Given the frequency with which such events must occur for the evolution of satellites and the implied frequency necessary to produce the degree of variability in chromosome no. 1, it was a little surprising that there were no de novo events observed in the 10 families examined [1]. More extensive family studies should provide information on this interesting question.

The observation of Emanuel of lateral asymmetry in the 6q12 C-band negative region also has a number of interesting implications. Since the initial observation of Arrighi and Hsu [10], C-bands have often been thought of as synonymous with sites of repetitious DNA. However, studies of the Chinese hamster have shown that some C-band regions do not contain satellite DNA [11, 12]. Thus most C-bands are repetitious DNA + C+, while some are repetitious DNA − C+. Since lateral asymmetry is most likely to be observed only in regions containing repetitious DNA, the observation of Emanuel seems to add the category of repetitious DNA + C−. It has been clear for sometime that C-banding is not due to its content of repetitious DNA; the association of repetitious DNA with proteins has been implicated [13, 14]. When and if the mapping of human chromosomes with antibodies against nonhistone proteins approaches that possible with *Drosophila* polytene chromosomes [15, 16], it will be interesting to see if 6q12 is complexed with different proteins than C-band + regions.

Two conditions are necessary to produce lateral asymmetry: (1) a segment of DNA which has a disproportionate number of adenines in the Watson strand and a corresponding deficiency in the Crick strand; and (2) this occurrence in a sufficiently long stretch to be cytologically usable. Since these would never occur by pure chance, a segment of repetitious DNA must be involved. It does not have to be AT-rich as long as those that are present are asymmetrically distributed in the two strands. Although the presence of lateral asymmetry implies the presence of some repetitious DNA, it is interesting that the 6q12 region not only does not hybridize to any of the four major human satellite DNAs [7], it also shows no hybridization to whole unfractionated highly repetitious sequences [17], making it unlikely that this site simply contains an unstudied minor satellite.

Excluding an unexpected trivial explanation of the results of Emanuel, we should keep an open mind to the possibility that the sensitivity of some of the BrdU techniques may be great enough to detect the location of long segments of moderately repetitious DNA that have been missed by the in situ hybridization done to date.

DAVID E. COMINGS

City of Hope National Medical Center
Duarte, California

REFERENCES

1. ANGELL GA, JACOBS PA: Lateral asymmetry in human constitutive heterochromatin: frequency and inheritance. *Am J Hum Genet* 30:144–152, 1978
2. EMANUEL BS: Compound lateral asymmetry in human chromosome 6:BrdU-dye studies of 6q12→6q14. *Am J Hum Genet* 30:153–159, 1978
3. YUNIS JJ: High resolution of human chromosomes. *Science* 191:1268–1270, 1976
4. LIN MS, DAVIDSON RL: Centric fusion, satellite DNA, and DNA polarity in mouse chromosomes. *Science* 185:1179–1181, 1974
5. LIN MS, DAVIDSON RL: Centromeric asymmetry and induction of translocations and sister chromatid exchanges in mouse chromosomes. *Nature* 254:354–356, 1975
6. HOLMQUIST GP, COMINGS DE: Sister chromatid exchange and chromosome organization based on a bromodeoxyuridine Giemsa-C-banding technique (TC-banding). *Chromosoma* 52:245–259, 1975
7. GOSDEN JR, MITCHELL AR, BUCKLAND RA, CLAYTON RP, EVANS HJ: The location of four human satellite DNAs on human chromosomes. *Exp Cell Res* 92:138–147, 1975
8. HILWIG I, GROPP A: Decondensation of constitutive heterochromatin in L cell chromosomes by a benzimidazole compound (''33258 Hoechst''). *Exp Cell Res* 81:474–477, 1973
9. SMITH GP: Evolution of repeated DNA sequences by unequal crossover. *Science* 191:528–535, 1976
10. ARRIGHI FE, HSU TC: Localization of heterochromatin in human chromosomes. *Cytogenetics* 10:81–86, 1971
11. COMINGS DE, MATTOCHIA E: DNA of mammalian and avian heterochromatin. *Exp Cell Res* 71:113–131, 1972
12. ARRIGHI TF, HSU TC, PATHAK S, SAWADA H: The sex chromosomes of the Chinese hamster: constitutive heterochromatin deficient in repetitive DNA sequences. *Cytogenet Cell Genet* 13:268–274, 1974
13. COMINGS DE: Heterochromatin of the Indian Muntjac. replication, condensation, DNA ultracentrifugation, fluorescent and heterochromatin staining. *Exp Cell Res* 67:441–460, 1971

14. COMINGS DE, AVELINO E, OKADA TA, WYANDT HE: The mechanism of C- and G-banding of chromosomes *Exp Cell Res* 77:469–493, 1973
15. SILVER LM ELGIN SCR: A method for determination of the in situ distribution of chromosomal proteins. *Proc Natl Acad Sci USA* 73:423–427, 1976
16. ALFAGEME CR, RUDKIN GT, COHEN LH: Locations of chromosomal proteins in polytene chromosomes. *Proc Natl Acad Sci USA* 73:2038–2042, 1976
17. GOSDEN JR, BUSKLAND RA, CLAYTON RP, EVANS HJ: Chromosomal localization of DNA sequences in condensed and dispersed human chromatin. *Exp Cell Res* 92:138–147, 1975