2 Baraitser M, Patton M, Lam STS, Brett EM, Wilson J. The Angelman (happy puppet) syndrome: is it autosomal recessive? *Clin Genet* 1987;**31**:323–30.
3 Hagberg B, Goutieres F, Hanefeld F, Rett A, Wilson J. Rett syndrome: criteria for inclusion and exclusion. *Brain Dev* 1985;7:372–3.
4 Pembrey M, Fennell SJ, Van Den Berghe J, *et al*. The association of Angelman's syndrome with deletions within 15q11–13. *J Med Genet* 1989; **26**:73–7.

Recurrence of acheiria in a second cousin: extremely large pedigrees may include 'second cases' by chance

Lamont and Salisbury[1] report unilateral absence of the hand (acheiria) in an index case and in a second cousin. In their opinion the possibility that "both children could have been affected by chance . . . is too remote to be considered". They found no common environmental factor, and proposed a "common mutant dominant gene", transmitted from one of the shared grandparents, as "the most cogent explanation". While not denying the logic of their suggestion, nor the evidence from recurrences of acheiria in sibs and in second and third degree relatives, as mentioned in their paper, we wish to point out that if one records pedigrees so as to include second cousins (fifth degree relatives) of the index case one is potentially including data on a very large number of persons indeed, and 'recurrences', on a chance basis, are not as unlikely as may initially appear to be the case.

Assuming a simple family structure of two children for every pair of parents (that is, a steady state, non-expanding population), and the recording, in the genetics clinic, of families to include only sibs, parents, grandparents, uncles/aunts, and first cousins of the index case, one would record data on 1+2+4+2+4=13 other persons per family. Enlarging the pedigree to include second cousins, with the more recently born of their linking relatives, one would record four great uncles/aunts, eight first cousins once removed, and 16 second cousins, that is, a total of 41 relatives of the index case. Were one to include all first to fifth degree relatives in previous or contemporary generations (eight great grandparents, 16 great great grandparents, etc) one would obtain a total of 137 relatives per family, while still excluding generations younger than the index case.

Although we believe no families would possess information on all first to fifth degree relatives (that is, our estimate of 137 relatives is in that way unrealistic), our model of a family with only two children for each two parents underestimates family size. In our clinics we routinely record pedigrees to include grandparents, uncles/aunts, and first cousins, and examining the files of the first 25 families seen in Oxford in 1989 (referrals to a general genetics clinic) we found a total of 475 such relatives of the index cases, that is, an average of 19 per family (not 13, as would be expected on the 'simple' model). This suggests that our estimate of 41 relatives per family, if one extends to include second cousins, is also an underestimate. We found 4·68 uncles/aunts instead of the 'expected' two, and 7·32 first cousins instead of the 'expected' four, that is, each grandparental pair had on average 3·34 (4·68/2+1) offspring rather than two, and each of these persons had an average of 1·56 (7·32/4·68) live children at the time the pedigree was constructed. Assuming that fertility was no less in the previous (great grandparental) generation, we calculate an average of 9·36 great uncles/aunts, 31·26 first cousins once removed, and 48·89 second cousins, that is, a total of 108·51 relatives of the index case if families were to be recorded in this way (omitting all generations before the grandparental or after the index case).

Lamont and Salisbury give a birth prevalence for acheiria of 1 in 65 000. With about 600 000 live births in the UK per annum one would expect 92·3 births with acheiria within the last decade, and these would have a total of 10 015 relatives up to and including second cousins (92·3 × 108·51). The probability of acheiria, by chance, among these relatives would be 10 015/65 000=0·1541, and from the Poisson distribution the chance of one or more such families actually existing would be 14·28%.

However, Lamont and Salisbury quote an old reference for the birth prevalence of acheiria.[2] From the Edinburgh Register of the Newborn, Rogala *et al*[3] found birth prevalence of isolated transverse transcarpal absence defects to be 0·4 per 10 000, and this is in agreement with estimates one can make combining information from Birch-Jensen[2] and from Wynne-Davies and Lamb.[4] With this prevalence we would expect 240 UK cases in a decade, 26 042 extended family members, and a 64·7% chance of one or more families with recurrence on a chance basis. For all types of transverse forearm/hand defect the birth prevalence is much higher (5·8 per 10 000 from Wynne-Davies and Lamb[4]), and one would expect 3480 UK cases within a decade, with 377 614 extended family; about 6% of these cases would be 'familial'.

In conditions with a high birth prevalence the likelihood of chance recurrence within an extended family is considerable, and in general one should beware of arguing from such recurrences unless the necessary calculations have been made and a coincidence appears truly unlikely.

RICHARD LINDENBAUM,
HELEN FIRTH
Department of Medical Genetics, Churchill Hospital, Headington, Oxford OX3 7LJ.

1 Lamont M, Salisbury AJ. Unilateral absence of the hand in second cousins. *J Med Genet* 1989;**26**:190–2.
2 Birch-Jensen A. *Congenital deformities of the upper extremities*. Copenhagen: Munksgaard, 1949.
3 Rogala EJ, Wynne-Davies R, Littlejohn A, Gormley J. Congenital limb anomalies: frequency and aetiological factors. *J Med Genet* 1974;**11**:221–33.
4 Wynne-Davies R, Lamb DW. Congenital upper limb anomalies: an aetiologic grouping of clinical, genetic, and epidemiologic data from 387 patients with "absence" defects, constriction bands, polydactylies, and syndactylies. *J Hand Surg [Am]* 1985;**10A** (part 2): 958–64.

This letter was shown to Drs Lamont and Salisbury, who reply as follows.

While not disputing the logic of this comment by Drs Lindenbaum and Firth on the possibility of recurrence of acheiria within families when considering the entire United Kingdom population, we would point out that our case report referred to one family with 10 relatives, other than the proband, descended from the common grandparents. For our quoted prevalence rate of acheiria of 1 in 65 000, the probability of recurrence would be 0·00015, surely a low figure. With the prevalence rate of 1 in 25 000 from the survey by Wynne-Davies and Lamb, the probability of recurrence in our family would be 0·0004. From a total of 2833 relatives, including those of third degree, of 102 probands with

transverse limb defects in this study by Wynne-Davies and Lamb, there was one relative affected with a similar defect, a monozygotic twin. We feel that it would be a pity if the figures quoted by Drs Lindenbaum and Firth deterred other authors from reporting unusual recurrence of similar defects within a family.

M A LAMONT,
A J SALISBURY
Wessex Regional Counselling Service, Department of Child Health, Southampton General Hospital, Southampton SO9 4XY.

BOOK REVIEWS

100+ Principles of Genetics. Anthony J F Griffiths, Joan McPherson. (Pp 387; £9.95). New York, Oxford: W H Freeman. 1989.

The main text of the book is 120 principles of genetics, covering classical, molecular, and population genetics, set out in general groups of topics that include genes and inheritance, mutation, gene structure and function, recombinant DNA technology, organelle genes, and quantitative and population genetics.

The text itself is very easy to read with each principle in dark, bold type at the top of the page, a limited amount of explanatory text, and one or more excellent black and white line diagrams. There are also 78 problems with worked solutions with references to the relevant principles.

Although the authors indicate that the principles can be read in numerical sequence, each page has multiple cross references to other principles as appropriate. If one followed these without adhering to the numerical sequence, reading this text could be like some children's books currently in vogue where each page offers a number of alternative choices making it difficult to know when one has or will finish the book!

The most serious drawback of this textbook, to my mind, is when difficulties of understanding might be encountered. For example, the mathematical formulae in the principles dealing with population genetics are, in some instances, merely stated without demonstration of their derivation. In this eventuality, the reader would have to refer back to their basic genetics textbook. I feel the text would be greatly enhanced by cross references to standard textbooks or journals that lucidly explain particular topics to assist in this situation.

The authors indicate in the introduction that this book could be useful as a supplement to textbook(s) in fundamental genetics and might be used to update or review a basic understanding of genetics. I would accept that this book might be useful for the latter purpose but would not expect many students of genetics to purchase it for that purpose alone, even if it were also used for the former. A genetics textbook with a good summary at the end of each chapter or the liberal use of a highlight pen might suffice.

R F MUELLER

Genetics of Neuropsychiatric Disease. Ed L Wetterberg. (Pp 363; £50.00.) New York: Stockton Press. 1989.

This book presents the Proceedings of a symposium held in Stockholm in 1988 which focused on the application of genetics, particularly molecular genetics, to neuropsychiatric disorders. It is divided into four sections: on research methods, research models, applications to particular diseases, and the likely directions of future research.

Most of the contributors are well known in this field and have provided brief and to-the-point coverage of quite a wide range of topics, which will be of interest to psychiatrists, neuroscientists, and to geneticists who have a particular interest in disorders of the nervous system.

The first section of the book on methods contains very useful brief accounts of techniques of DNA analysis and linkage analysis, as well as presenting a gene map of diseases, enzymes, and proteins that may be of relevance to the understanding of neuropsychiatric disease. The same author, Wahlstrom, also contributes an informative chapter on the potential use of chromosome aberrations in mapping mental disorders. Other chapters, such as that on the molecular genetics of PKU, are interesting but of less immediate relevance to general neuropsychiatry where the bulk of the work consists of far commoner conditions, such as schizophrenia and manic depressive illness. If the book has a principal weakness it is that these topics and classical approaches are not more extensively covered. The time honoured methods of family, twin, and adoption studies still provide the strongest evidence that abnormal genes are involved in the aetiology of abnormal behaviour. Therefore, it is a pity that, in the understandable enthusiasm for the 'new genetics', the more classic methodologies that have driven psychiatric genetics so far, and are still good for a few more miles yet, are largely overlooked.

Aside from this criticism, and the fact that collections of 'photoready' chapters are never quite as pleasing to the eye as a book set in uniform type, this volume is a useful addition to the literature and should have a definite place in the libraries of all departments and research units interested in this field.

PETER McGUFFIN

Molecular Genetics of Muscle Disease: Duchenne and Other Dystrophies. British Medical Bulletin, July 1989, volume 45, number 3. Ed A J Buller, J Goodfellow, J M Newsom-Davies. (Pp 828; £25.00.) Edinburgh: Churchill Livingstone. 1989.

In his introduction to this second issue of the *British Medical Bulletin* devoted to muscular dystrophy, A J Buller observes that the magnificent advances in muscle research that have occurred in the last nine years have been partly the result of the support of applied research by the muscular dystrophy charities. It is not surprising that many chapters in this volume deal with recent advances concerning the Duchenne/Becker gene and with methods of examining gene transcription in muscle. M E Buckingham describes the enormous variety of muscle proteins, some owing to multiple genes, and others owing to differences in splicing the same gene. The current function, or evolutionary importance, of such diversity is unclear. The development of the primitive muscle cell, or myoblast, to