Figure 3 X ray at 3 months showing absence of bones in the lower limbs.

1700 g. Systemic examination did not show any abnormality and neonatal reflexes were normal.

A radiograph showed the following radiological abnormalities (fig 2). In the upper limbs, there were short humeri, short, thick, bowed radii, absence of the ulna on the left and a rudimentary ulna on the right (speck of calcification), and absence of the carpal bones and phalanges. In the lower limbs there was total absence of all the bones. The chest was bell shaped and the skull, spine, and pelvis were normal. Skeletal survey of both parents showed no abnormalities.

An x ray of the lower limbs taken at 3 months of age (fig 3) showed total absence of bones in the lower limbs. This later x ray was taken to confirm our assertion that it was aplasia rather than delayed ossification.

Though the inheritance of this disorder has been considered to be autosomal recessive, the data suggest that the gene may have some effect on heterozygotes.⁴ The abnormalities reported in heterozygotes include absent phalanges, anatomical changes of the phalanges, talipes equinovarus, polydactyly, and double halluces.⁴ Neither of the parents of our case showed any abnormalities. The characteristic shortening noted in Grebe syndrome includes more severe involvement of the lower than the upper limbs and progressively increasing shortening from proximal to distal portions of the limb. The absence of the ulna and the phalanges is characteristic of Grebe syndrome.^{3,4} However, we are not aware of any case of Grebe syndrome with total absence of the bones in the lower limbs, as reported in the present case. When the gene for Grebe syndrome is expressed fully, it may result in total failure of bone formation.

1 Kumar D, Curtis D, Blank CE. Grebe chondrodysplasia and brachydactyly in a family. *Clin Genet* 1984;25:68-72.

2 Gracia-Castro JM, Perez-Comas A. Nonlethal achondrogenesis (Grebe-Quele-Salgado type) in two Puerto Rican sibships. *J Pediatr* 1975;87:948-52.

3 Kulkarni ML, Venkatesan G. Grebe syndrome. A family study. *Indian J Orthop* 1991;25:39-40.

4 Quele-Salgado A. A rare genetic syndrome. *Lancet* 1968;1:1430.

M L KULKARNI
BASANTH KUMAR
ABDUL NASSER
Department of Paediatrics,
JMM Medical College,
Davangere - 577 004,
Karnataka, India.

BHAGYAVATHI M KULKARNI
Department of Radiology,
CG Hospital,
Davangere - 577 004,
Karnataka, India.

BOOK REVIEWS

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Twins as a Tool of Behavioral Genetics
Editors T J Bouchard Jr, P Propping. (Pp 299; £60.00.) UK: Wiley Liss. 1993.

This book is based on a Dahlem workshop which was held in 1992. The book consists of four sections, on cognitive abilities/intelligence, personality, psychopathology in childhood, and adult psychopathology. Each section includes a series of background papers written by international experts and a group report from the workshop participants.

This is an excellent book which would be of interest to those involved in behavioural twin research. It would also be useful to those who are searching for ideas for future work. The chapters and discussions are particularly interesting as they focus on potential difficulties with twin studies, current thoughts, and ideas for future research rather than simply reviewing published findings. The main drawback is that although most chapters are well written, the contributions vary markedly in quality. Also some group reports may appear somewhat disjointed if they are not read in conjunction with the accompanying background papers.

In the first section on cognitive abilities, the question of how intelligence should be defined and the importance of a general ability factor is debated. The discussion focuses on the use of twin studies to design measures of intelligence and the incorporation of multivariate analyses to explore the covariation among abilities. The importance of longitudinal studies to investigate developmental mechanisms and the role of twin studies in identifying environmental influences are also highlighted.

The papers on personality cover the issue of how personality can be defined with particular reference to the five factor model. The evolutionary psychology of personality is considered and once again the importance of longitudinal studies is highlighted. The participants also emphasise the need for direct assessments of environmental factors and note that there has been insufficient research on the relationship between normal personality and psychopathology.

In the section of childhood psychopathology, the need for genetic research in this age group is highlighted. Most of the issues discussed are, however, relevant for all age groups. The comparability of twins and singletons and potential sources of bias in twin studies are covered in some detail. The potential uses of twin studies, for example,

in defining phenotypes and investigating comorbidity, are discussed and the issue of measurement is also raised.

The papers on adult psychopathology also highlight the difficulties in making valid diagnoses and point out the merits of twin studies in refining phenotypes. The group again highlight the role of discordant MZ twins in studying the contribution of environmental factors and the pathophysiology of disorders and the importance of twin studies is illustrated by findings for alcoholism.

Overall there are some general issues which emerge from all the groups. The importance of the assumptions of the twin method are repeatedly considered. The value of longitudinal studies and the importance of direct measures of environment are also highlighted. It is acknowledged that twin studies are particularly useful in defining phenotypes and finally there is a general agreement that the advent of molecular genetics research does not mean that there is no longer a place for twin research. It appears that there is still a need for twin studies which provide a different yet often complementary approach to molecular methods.

ANITA THAPAR

Functional Neural Transplantation. Editors S B Dunnett, A Bjorklund (Pp 603; \$183.00.) New York: Raven Press. 1994.

Clinical geneticists are often confronted by clients who are affected by, or have a family history of, an untreatable inherited neurological disorder and these people are well aware of the limitations of currently available therapy. They are often members of lay support associations and through their newsletters take particular interest in new therapeutic strategies targeting the relevant disorder. Indeed they are often aware of such strategies before their medical practitioners and can pose challenging questions at interview/counselling sessions.

Intracellular transplantation of tissues to alleviate the symptoms of neurological degeneration has a long history in experimental neurobiology. The editors of this impressive volume trace the first publication on the subject to 1890. In the 1980s this strategy was applied for the first time to humans: autologous adrenal medulla was transplanted into the caudate or putamen of people with advanced Parkinson's disease (PD). The results varied but the public attention has been caught; neural transplantation was in the public arena. The questions coming from patients were addressed to neurologists and, as the vast majority of cases of PD are not inherited, clinical geneticists escaped. The early studies of adrenal transplantation have been superseded by those using human embryonic mesencephalic tissue and few would now doubt the relative success of this strategy in alleviating the symptoms of advanced PD. This success has resulted in the proponents of neural transplantation widening the scope of the diseases to be targeted. Huntington's disease is now firmly on the agenda and indeed some transplantation has already been carried out and reported in abstract form. The first pan-European programme for recruitment towards transplantation of embryonic striatum into HD patients has been established and the topic is discussed by members of the lay associations for HD. So, where does the practising geneticist turn to

for the answers (if they exist) to the questions to come?

The answer depends on how much time you have available and how much you want to know about the background to the topic. If the answer to both is "a lot" then this volume is for you, but be warned, it does not make light reading.

The editors set out to "provide a critical assessment of the status of neural transplantation across the range of applications currently under consideration" (chapter 1, Introduction), limiting themselves (and the individual chapter authors) to central nervous system considerations. Understandably, a large proportion of the chapters deal with rodent models of neurodegenerative disease, especially Parkinson's disease, and the effects of grafting in these systems. These reviews are comprehensive and well written and provide a fascinating insight into the observations which have led to the human application of neural transplantation. The editors are to be congratulated for arranging the contributions in a manner which leads one from these initial rodent experiments (chapters 2 and 3) through non-human primate paradigms (chapter 4) to transplantation in humans (chapter 5). This chapter, by Lindvall, reviews the history, methodology, and results of the human trials of transplantation. It would serve admirably as a source for finding one's feet if this were one's first journey into the field, although it does, at times, seem a little dismissive of adrenal medulla transplantation.

Chapter 7 (Bjorklund *et al*) discusses functional aspects of striatal transplants in the rat HD model and presents a convincing argument for taking tentative steps towards human experimentation. In addition to reviewing the data on the improvements in aspects of motor behaviour after transplantation we are told that grafted human fetal striatal neurones can extend axonal projections (for up to 2cm) and that host dopaminergic afferents are capable of modulating the neuronal activity of the transplant. The authors conclude this chapter, however, with a caution on the need for further studies in non-human primates to validate the applicability of the rodent observations.

Chapters 9 to 13 review the status of transplantation to reverse cognitive impairment, discussing rodent and non-human primate model systems. The chapters are again well written, comprehensive and impressively referenced. The editors have again ensured that each contribution follows logically from those preceding.

Chapters 14 to 19 cover areas currently less advanced in their clinical potential including transplantation in ischaemia, grafts in epilepsy, modulation and restitution of circadian rhythms, and recovery after spinal cord injury.

The final chapter is a discussion of the proposed mechanisms by which neural grafts may restore function. The editors conclude that there is no single or simple answer to the question: How do grafts work? They and the

other contributors have, however, throughout this volume, provided us with a wonderful insight into the research which has shown that neural transplantation, in a variety of situations, does work and that it will have a place in clinical practice.

Although I have no reservations in recommending this volume, I doubt whether it would be purchased by a clinical geneticist without a particular interest in Huntington's disease. I think it equally unlikely that it will be found in most genetics departmental libraries. It is a volume, however, which it is useful to know exists and which one can turn to for a comprehensive account of the current status of neural transplantation.

JOHN C MACMILLAN

Inherited Disorders of the Thyroid System. G Medeiros-Neto, J B Stanbury. (Pp 221; £131.50.) UK: Times Mirror International Publishers/CRC Press. 1994.

Over the last 40 years an increasing number of inherited disorders affecting the thyroid system have been identified. These range from specific inborn errors of metabolism primarily involving iodide transport to subsequent organification to thyroglobulin expression and secretion. More recently specific receptor defects of the thyrotropin stimulatory hormone have been characterised. In addition, an inherited predisposition to thyroid disorders has been identified, particularly with regard to autoimmune thyroid disease.

It is therefore timely for a monograph to appear that has reviewed the genetic contribution to thyroid dysmorphogenesis and regulation.

Professor Stanbury has individually made an enormous contribution to this field. It is therefore appropriate that he should be associated with such a monograph which sets out in an ordered manner to cover the range of disorders that one may, albeit uncommonly, encounter within the practice of clinical genetics. Perhaps it is because of the infrequent exposure to such patients that the clinical geneticists would do well to have access to this monograph, at least as a ready source of additional references. However, on careful reading, the style of the monograph is somewhat uncomfortable in places and of course is specifically targeted to aspects of thyroid dysfunction. For example, in an otherwise excellent chapter reflecting the clinical variability in Pendred's syndrome (congenital deafness and sporadic goitre), the clinical studies are solely confined to aspects of thyroid pathology with little detail of the audiological findings that characterise this disorder. Descriptions of molecular genetic studies lack clarity and are unlikely to help the more general reader.

Overall the book is up to date and has been referenced from a wide source. Each of the

12 chapters carries a useful single page summary for rapid assessment of key points. I would consider this monograph to be a useful addition to the general medical library.

RICHARD TREMBATH

NOTICES

Inherited disorders and their genes in different European populations

This conference will be held in St Feliu de Guixols, Spain, on 11–15 November 1995. (Conference organiser: Peter Harper. Co-organisers: Jaume Bertranpetit, Albert de la Chapelle, Angus Clarke.) Applications are invited to participate in this meeting, the second in a series of European Research Conferences on the topic. The aim of the conference is to allow Clinical, Molecular, and Population Geneticists to share data and hypotheses, both with each other and with scientists from other disciplines, such as archaeology and anthropology. The number of participants will be limited to around 100 people. Younger research workers with relevant data to present and discuss will be especially welcome; specific financial support may be available for these and also for participants from Eastern Europe. In view of the wide interest in the subject and the success of the previous meeting in Strasbourg, it is likely that there will be considerably more applicants than can be accepted. Thus early application to the ESF Conference Office is advised; the latest date for applications is 1 July 1995. Applications to Caroline Grimont, Conference Manager, European Science Foundation, European Research Conferences, 1 Quai Lezay Marnésia, F-67080 Strasbourg Cedex, France. Fax: 33 88 36 69 87.

5th International Congress on Trace Elements in Medicine and Biology

Therapeutic Uses of Trace Elements Satellite Workshop: Molecular Basis of Copper Metabolic Disorders. This congress will be held in Méribel, France, on 4–7 February 1996. Further information from Madame Arlette Alcaraz, Laboratoire de Biochimie C-CHRU - BP 217, F-38043 Grenoble Cedex 9, France. Tel: (33) 76 76 54 84. Fax: (33) 76 76 56 64.