along their axis. On the right side only absence of the thumb was observed.

Radiographs obtained at 4 months showed left humeroradioulnar synostosis, two meta-
carpophalangeal bones (probable fusion of a third metacarpal bone), and the middle phalanx of the 5th finger was absent. On the right, there was humeroradial synostosis and thumb ossification was absent (figure). Lower limb radiographs disclosed no abnormality. Skull x ray failed to show craniosynostosis as reported by Edwards et al. 2

An abdominal ultrasound scan showed hydroureteronephrosis of the left kidney, with a pyelogram suggestive of left pyeloureteral stenosis. This finding, however, could be coincidental, but should be searched for in similar cases.

This case represents an example of the possible variability of this condition, the pathogenesis of which still remains obscure. 2

X rays of the upper limbs showing (top) humeroradioulnar synostosis and (below) humeroradial synostosis and absent thumb ossification.

BOOK REVIEW

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In the excitement of the rapid developments of today, it is easy for readers of this journal to be unaware of the debt that they owe to J B S Haldane, for much of the theory on which clinical genetics is founded originated with his work. His influence, great in all fields of genetics human and non-human, was equally great in physiology and biochemistry. He wrote some 400 scientific articles, 20 books, and numerous essays, and at least 20 of his pupils were elected Fellows of the Royal Society. It was therefore fitting to commemorate the centenary of his birth, and the same idea occurred to several. Thus a one day sym-

postium was organised at University College London on behalf of the Biometric Society, by Professor C A B Smith, and there seven of Haldane's friends and colleagues spoke on aspects of his work and ideas, essentially a personal tribute. A much more ambitious celebration, a full conference, was organised in December 1992 at the Indian Statistical Institute in Calcutta, to which Haldane re-
tired. The proceedings of that conference form the subject of this book. Its object was to evaluate the effect of Haldane's con-

tributions in various areas of human genetics, in the light of the more recent developments.

C R Rao, a former Director of the Research and Training School of the Indian Statistical Institute, and jointly responsible (with Mahal-
anobis) for attracting haldane there, gave the opening address of which a condensed version opens this book, illustrating with examples the scientific method followed and advocated by Haldane. The technical papers are then grouped in five sections.

The first, devoted to population genetics and evolution, opens with a highly pro-

vocative paper by W J Ewens, criticising se-

eral aspects of Haldane's thought and work. The very readable style of this criticism con-

tinues in Ewen's discussion of key de-

velopments in population genetics post 1955, in which flesh has been added to the Fisher-

Haldane-Wright skeleton, for example, the incorporation of multilocus systems and the development of stochastic theory appropriate for the situation of infinitely many alleles that is emerging from recent molecular work. Other noteworthy contributions in this section are those by N Takahata on the evolution of the immune system, and by T Gojobori and T Imanishi which draws together a great deal of MHC gene frequency data, and the phylogenetic trees based on them show the importance of the major racial groupings in contributing to variation at these loci.

The second part concerns the formal ge-

netics of man, and the papers here are out-

standing, though not easy reading for the mathematically fearful. C C Li reviews the several methods of segregation analysis that have been developed in the post Haldane period. They are essentially applicable for cases of complete ascertainment, which is much more attainable today with modern computerisation of records than at the time of Haldane's pioneer work in the early thirties.

Li notes that the segregation models involving varying values of ascertainment probabilities are somewhat arbitrary and inadequate, largely on account of complex social factors that contribute to the completeness or incompleteness of ascertainment. To overcome these difficulties he recommends striving for complete ascertainment by establishing ade-
quate systems of registration and reporting by health agencies. R Elston to oxeamines recent developments in the theory of seg-

regation analysis. He describes the two well established multiparameter models available for performing likelihood based analyses (the transmission probability and the mixed model). P P Majumder's chapter, also on segregation analysis is complementary, for he concentrates on a multilocus epistatic model with or without variable age of onset, but finally provides a reminder of the value of a
simpler way of investigating mode of inheritance without segregation analysis. The chapter by J Edwards on Haldane and the analysis of linkage is lighter reading, characteristically interspersed with short historical anecdotes. In it Edwards discusses Haldane's contributions against the background of the mendelian controversy and recent foreground of "shotgun linkage". Jurg Ott, whose work has done more to bring about the widespread practice of linkage analysis today than that of anybody else, concludes this section with a discussion of recent developments in linkage analysis, covering likelihood formulation, simulation methods, data errors, approximate methods, and models for complex traits.

In the next section, genetic structure and diversity of human populations, R Chakraborty shows that the presence of strucluting within any natural population is a biological reality, and it can be defined and evaluated from genetic data. He concludes that though this substructuring is important for evolutionary understanding, its omission in calculating probabilities in forensic work is not as great as was claimed in the recent public controversy (Science 1991; 294). D Roberts enquires why Haldane ignored what is to us so obvious, that human breeding populations are not large and are not homogeneous, and is glad that he did so. In this section also there are two papers on genetic diversity in India and one on European populations, discussing the data in relation to social, geographical, and ethnic variables.

In the next section, on genetic epidemiology, Newton Morton reviews developments in the past decade and, like Chakraborty, reminds us of the importance of valid genetic considerations in forensic cases; this is a masterly, thoughtful, and in places hard hitting chapter. The second paper in this section by G Volger and D C Rao summarises path analysis in genetic epidemiology, particularly as applied to complex quantitative phenotypes. They argue that it reaches parts that other methods, and particularly molecular studies, alone cannot reach, and look forward to the coupling of molecular studies with population based epidemiological approaches to provide more realistic models of familial resemblance. R Chakraborty and C Plato discuss neurodegenerative disorders in the Chamorro isolate.

In the last two chapters in the book there is a report of the panel discussion on genes, environment, and disease, in which six panelists were prompted to discuss the challenge of deciphering the mechanisms and processes of gene manifestation in disease. Much of this discussion was forward looking, for example, Elston's thoughts on the future of determining the genetic and environmental determinants of common diseases (those that are not single mendelian). In this context much of the chapter relates to topics that could be usefully explored in India, taking advantage of the unique opportunity that exists in the great variation in environment, culture, and particularly mating systems and gene pools of the numerous populations. The final chapter contains the text of a special lecture by J V Neel, enquiring how Haldane would have viewed the societal implications of today's genetic knowledge. He argues that geneticists have misplaced the emphasis on the issues facing the public. The genetic threat of increasing radiation and chemical pollutants assumed an importance inconsistent with the risks. Similarly, recent public attention has been focused on the promise of gene therapy, again probably far out of proportion to the societal significance of this development. Yet geneticists have been singularly uninvolved in the most pressing problems of today, the clash between the needs of a rapidly expanding human gene pool and a rapidly shrinking resource base to support it.

This is an interesting book. The papers fall into four types: the historically oriented, for those interested in past developments in the subject; those concerning recent developments in methods, which should be consulted by all those wishing to use them; compilations of data on particular characters; and the frankly provocative. This combination means that parts of the book are extremely enjoyable reading, others are most useful for reference and consultation. The division into sections is not clear cut and some papers in one could easily have fitted into a different section. But each section features a critical assessment of Haldane's work in the given area; a discussion of current approaches, theoretical principles, techniques, and practical applications. With its expert analyses and full documentation, this book will be a useful supplement to advanced courses in human genetics and for advanced courses on genetic methods to be applied in analyses of human disease.

D F ROBERTS