BOOK REVIEWS

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Like Stephen Hawking, Barbara McClintock inspired as much by her existence as by what she discovered. Of course, high scientific achievement is an essential ingredient in the details don't matter. I am sure her papers on transposable elements are much more admired than read. As the subtitle suggests, her career spanned the history of genetics. She started when Mendel's ideas were still controversial, and she worked on well into the cloning era. She made her name as a virtuoso cytogeneticist, identifying each individual maize chromosome and physically assigning linkage groups. She went on to provide a classic proof that meiotic crossing over resulted in genetic recombination. Her later work on mobile genetic elements was a solitary march into unknown territory, which eventually won her the Nobel prize in 1983. As she approached her 90th birthday, her friends and admirers put together this Festschrift to celebrate her life and career. She lived to enjoy the celebration, dying on 2 September 1992.

It was a nice idea to reproduce several of her key papers as introductions to sections of related invited contributions. The reprints include her 1931 crossing over paper, a 1952 paper on Activator and Dissociator, and two papers (1956 and 1978) recording her growing belief in the wider role of 'controlling elements' in genome organisation. And of course her Nobel Prize lecture 'The significance of responses of the genome to challenge'. Between these meaty items, guest articles range from brief reminiscences to solid reviews. An excellent history by the late Marcus Rhoades of early maize genetics is reprinted from the 1984 Annual Review of Genetics, and Nina Fedoroff finishes the book with a fine updating on maize transposable elements. Even now they are all cloned and sequenced, their interactions are amazingly complicated. Other articles recount early investigations of transposable elements, which really took off once bacterial elements were discovered. Despite her reputation as a fierce and solitary person, McClintock was a valued mentor to many researchers, as we see from the fond accounts of lengthy, wide-ranging, and seminal conversations. Others came only in retrospect to appreciate McClintock's pioneering explorations and make amends here.

We often hear that McClintock's later work went 'out of the headlines of the time'. Indeed, she did have trouble with referees, and recorded the bulk of her results in the unreferred Carnegie Institute of Washington Year Book. Whether or not it was appreciated is less clear. Its experimental virtuality and validity in maize were not in question; the problem lay with deciding its significance. This work which did not fit into most people's mental maps, and it was not clear what to do with it. Was it an interesting but ultimately trivial feature of a few plant genes, or was it, as McClintock believed, evidence of a system parallel to the conventional genes, by which whole genomes adapted and restructured themselves, and through which evolution worked? Jumping genes now have joined mainstream genetics, but I think there would still be support for McClintock's more global ideas. At the moment it looks as if reductionism is triumphing over McClintock's holism. Perhaps she is still ahead of us – several of the contributors to this book think so.

Prophet in the wilderness or not, McClintock was widely admired, indeed almost deified, as a brilliant cytogeneticist, a deeply original thinker, and above all as a role model. How would we all love to work like her! – not just the Nobel prize, but the refusal to let committee meetings and paper work get between her and her science. She was a true free spirit. She constructed her own way of life and lived it supremely well for 90 years. Perhaps we would be less willing to make all the sacrifices which that freedom required. This handsomely produced book records the gratitude and affection of the people she influenced, and stands as a fine memorial to someone who exemplified what being a scientist is really about.

ANDREW P READ


Take an autosomal recessive condition with birth incidence of 1 in 4200 and a relatively predictable natural history (98% respiratory complications, over 99% pancreatic insufficiency, about 50% mortality by the age of 20). Evaluate genetic tests for the carrier state and find that sensitivity and specificity both exceed 99%, errors being the result of human factors not laboratory variation. Consider the cost-benefit equation for screening, including psychosocial costs. Why do 90% of people in the reproductive age group not respond to a letter inviting them to consider the offer of screening?

The condition is AF508 homozygous cystic fibrosis (CF), screening tests are based on the polymerase chain reaction, the setting is the educated UK middle class in 1992. Do the data suggest that the community is uninterested in a greater degree of individual informed choice? Or are we confused by the presence of CF resulting from other mutations, with or without AF508?

Cystic fibrosis research has burgeoned since the characterisation of the causative gene less than four years ago. That landmark, and a genome-wide search for the major mutations, influence many in North America and Europe (there are 1.9 million carriers of AF508 in the UK, 16.5 million in Europe, and 14 million in North America). The importance led the US Congress to require evaluation of the scientific, ethical, economic and social considerations of widespread carrier screening for CF. The resulting report from the US Office of Technology Assessment (OTA) was published in August 1992. It is an impressive document, ranging from a brief clinical development, to state of the art genetics and then educational, counselling, financial, and ethical issues. A brief chapter summarises Cf carrier screening in the UK, based on studies funded by the Cystic Fibrosis Trust and the Medical Research Council, some of which have now been published.1 The OTA investment was large: nine project and three administrative staff, 15 subcontractors, and over 120 advisors.

An initial summary chapter (also published separately for the lay reader) sets out the issues and examines the options open to the US Congress. No screening policy has emerged. The project director, John H Gibbons, concludes that the value of the Cf carrier test is the information it provides to the individual person – 'We believe that public understanding of this new knowledge and its implications is necessary for its wise and thoughtful application'.

The US health care systems do not facilitate early research or early development of carrier screening tests with such major implications. Also the US history of sickle cell carrier screening in the 1970s, which was in some states mandatory, has left painful memories which evoke thoughts of discrimination and stigmatisation. The reliance upon insurance as the vehicle for funding health care provision (often organised through employment schemes) has also inhibited any screening which might lead to the early recognition of families with high health care needs (and therefore high costs). The OTA's glance, therefore, at the UK CF programmes and at screening elsewhere (for example, in Cyprus and Sardinia where thalassemia carrier testing has evolved considerably) was quite essential. Where, therefore are we now?

In the UK the model for carrier screening in the antenatal clinics has been most studied in Edinburgh, where 73% of 4348 women chose to be tested, identifying 111 carriers and four partnerships which were at 1 in 4 risk of AF508 CF. Screening in primary care has the advantage over pregnancy testing of providing more choice for those identified as carriers. The disadvantage of the primary care approach is that people may see no relevance until they plan pregnancies. Thus the proportion who take up screening when invited by letter (9 to 12%) and by passive opportunistic offers from the GP (17%) are, in response terms, deep. Opportunistic carrier testing by the GP, with the test being available immediately, has a response of 70%, back to the pregnancy level, but are these high figures indicative of too
much pressure and directiveness? Other findings in primary care are similar with the addendum that offers to test women in family planning clinics can produce responses approaching 88%.

An attractive hybrid of the two screening models is CF carrier screening at first diagnosis of pregnancy in general practice. Harris et al. have shown that by this approach 96% of pregnant women could be offered tests before 14 weeks (average eight weeks) and that in a small pilot study women had a very positive attitude to testing and to the primary care approach. This is a paradigm of the closer relationship between the family doctor and the clinical geneticist which is to be desired. Further studies are essential.

All these studies have identified that the community's knowledge and education about CF must be increased. However, there are few who have set out to establish how such education is to be organised. This needs research in an arena unfamiliar to most doctors and scientists. Until this has been clarified the cautious attitude embodied in the OTA report will be more than justified.

J A RAEBURN


This volume is based on a symposium held in Fukui, Japan in 1990 to mark the 20th anniversary of the founding of the International Association of Human Biologists by scientists drawn from a variety of disciplines and working within the IUBS Decade of the Tropics Programme. There are 23 contributions from individual persons and research groups based in Asia, North America, Europe, and Oceania, and the populations investigated range in the geography and climate from northern Siberia to Polynesia. Studies conducted on Japanese populations, both home based and migrant, represent the largest single grouping and account for approximately 40% of the total content.

As with the majority of symposium volumes, there is considerable divergence in the nature and content of the subject matter and the presentational style of constituent chapters. However, the editors have ensured that the degree of variation is kept within acceptable limits and four main topics can be identified: population dynamics of human isolates, biogeography, and sociodemographic features of isolates, specific diseases associated with isolated populations, and the application of migration studies to epidemiological investigation. To a large extent, data presented on the first two topics were collected during and before the Decade of the Tropics Programme, and so the approaches adopted and studies discussed occasionally appear slightly dated. However, since much of the material relates to population isolates in India and Japan, and originally was published in those countries, this may well be the first opportunity for its appraisal by an international readership.

The global reduction in geographical isolation experienced by human populations during the last 40 years is a common theme. This transition usually, but by no means universally, has been accompanied by an increase in marriage distance and a concomitant reduction in marriages between close biological relatives. While a short to medium term local decline in the prevalence of recessive disease and less severe disorders might be expected to follow the establishment of agglomerated breeding pools, longer term changes are considerably more complex and difficult to predict. Manifestly, the accuracy of all such gene frequency predictions will be dependent on future trends with respect to isolation, whether based on geographical or other grounds. The recent reversion to ethnic and religious isolation in central and eastern Europe has shown the resilience of traditional intrapopulation marital boundaries. In a country such as India, comprising 880 million persons subdivided into tens of thousands of endogamous breeding groups, panmixia and its genetic sequelae must be regarded as an improbable prospect and effectively restricted to the realms of population genetic theory.

The prevalence and distribution patterns of infectious diseases are an important, if less obvious, area in which the study of isolates can contribute to an understanding of disease evolution and dissemination. An interesting example cited is the unique strain of HTLV-1 found among groups in Papua New Guinea, whose first contact with government and missionary workers was in the 1980s. More predictably, migrant populations have been extensively recruited in an attempt to examine the respective roles of genes and non-genetic factors as determinants of obesity and hypertension, and in the aetiology of common diseases of adulthood, including diabetes types 1 and 2 and ischaemic heart disease. But on the evidence presented, progress towards this goal has so far been limited.

Overall, the volume contains much information that will be of interest to workers in the general field of human variation. It is an interesting and topical, if somewhat eclectic, collection of papers which merits inclusion on the library shelf.


For aficionados, this could be the book you would choose if you were to be a castaway on a desert island. At any rate, such a sojourn would probably be the only chance you will have to read and digest such a massive tome. It is more than twice the size of its first edition. At first glance, it would seem to be simply an expanded version, accommodating the many relevant publications on neural tube defects which have arisen in more than a decade since the first edition appeared. Indeed, the chapter headings are remarkably similar. But much has happened in the field during that time and perspectives have changed. Our knowledge used to be mainly of an epidemiological nature; now, there are many different considerations: comprehensive screening and prenatal diagnosis, primipara prevention, ethical implications, and animal models. All this has led to the book being essentially rewritten. However, the authors have chosen to retain the old chapter headings and subheadings as the basis, and then to introduce some new ones to complete the contemporary picture. For instance, the section on 'Clustering in time and space' has been transformed. Four pages have become 58 and now include conceptual issues, an extensive review of statistical methods, and then the clustering of neural tube defects under three headings—a review of studies initiated when there was no known etiological factor, when clustering was suspected, and when there were specific environmental indications. For some chapters, the expertise of other eminent people has been called upon. The title too remains unchanged, and, as this suggests, the book is still largely a survey of epidemiological studies. As such it provides a unique wealth of information. But it is not just a review of previous publications: its strength lies in its analytical approach, which draws together the myriad lines of evidence and synthesises them, attempting to extract meaningful information.

Inevitably, one searches the text for mention of one's own work, justifying such action on the grounds that it will be a yardstick for the book as a whole. The initial gratification that one has been noticed soon gives way to critical appraisal of how the work has been summarised and what use has been made of it. My self-indulgence leads me to conclude that the coverage is both comprehensive and accurate. It is regrettable that this book, like so many others, is dated before it is published: there are references only up to the first quarter of 1991 and an observation could be speeded up. Nevertheless, the authors are to be congratulated on providing us with such a rich reservoir in which to delve. It is a pleasure to read and is a constant reminder that although much is known about neural tube defects there still remains much to be discovered.

A H BITTLIES

MARY J SELLER