Genetic Disorders of Endocrine Neoplasia
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Preface

Genetic syndromes have always fascinated endocrinologists, but in the face of their apparent rarity and obscure manifestations they remained somewhat of a minority interest. Then, in 1993, with the identification of the molecular defect in the Sipple syndrome, now referred to as multiple endocrine neoplasia type 2 (MEN 2), the whole field became massively transformed. In the first place, it became possible to screen directly for mutations for MEN 2 as well as familial medullary carcinoma of the thyroid and other related conditions, thus considerably simplifying the accurate prediction of risk and the follow-up of such patients.

In particular, the presence of 'hot-spots' identifying with some precision genotype-phenotype correlations, for the first time gave the clinician the means to forecast and advise. Not only were patients given accurate predictive information, but many other unaffected relatives were spared the investigation and anxiety by knowing that they were mutation-free. This has also impacted directly on treatment, as certain knowledge of the affected relative has allowed for prophylactic thyroidectomy in early childhood in order to avoid later neoplasia. By contrast, the positional cloning of the MEN 1 gene took much longer than many expected, with many false starts, and then the eventual discovery of a gene which even now is only poorly characterised from a functional point of view. In addition, the huge number of scattered mutations, albeit with occasional 'warm-spots', and the lack of a close genotype-phenotype correlation, has meant that its clinical usefulness is presently limited. In spite of these caveats, there is no doubt that the recent molecular discovery of these and other genes such as those associated with von Hippel-Lindau syndrome, Cowden syndrome, and, very recently, one variant of the Carney complex, has led to an enormous increase in interest in these diseases. It is becoming increasingly clear that they are much more common than
previously recognised, and that the genes involved may well be involved in the more frequent sporadic tumours. Most importantly, they are adding considerably to our understanding of cancer in general, similar to the hereditary disorders of the colon, and indubitably will add to more effective clinical management and eventually therapy.

Patricia Dahia and Charis Eng have assembled an impressive group of authors in this volume, covering all of the major hereditary endocrine neoplasia syndromes: most, if not all, of these contributors were intimately involved in the initial discovery of the relevant genetic pathology. I am most grateful to the editors for putting together this review, which just a new years ago would have consisted of advisory clinical guidelines and genetic uncertainty. It is a tribute to all the workers in this field how far we have come in so short a time.

Ashley Grossman, London