These are non-specific features and are present in the Prader-Willi syndrome (PWS) and many other conditions. The authors themselves state that their patients lack the typical features of PWS, which are low birth weight, neonatal hypotonia, narrow bifrontal diameter, hypogonadism, short stature, and feeding problems during the first year of life followed by hyperphagia and obesity in early childhood. In contrast, patients 1 and 2 developed severe obesity between the ages of 5 and 10 years without a change in diet. None of the patients fulfills the diagnostic criteria described by Holm et al.

Although we agree that obese and mentally retarded boys should be tested for the fragile X syndrome, we feel that this phenotype should not be described as "Prader-Willi-like." This description is misleading and confusing, because all of the typical features of PWS are absent in the patients described by de Vries et al.1 Careful use of the terms "Prader-Willi syndrome" and "Prader-Willi-like" is important, because the syndrome is overdiagnosed by geneticists and paediatricians who are not familiar with the specific features of PWS. Although PWS can be rapidly tested for at the DNA level,1 careful clinical distinction of this syndrome from other conditions is necessary.

In conclusion, we suggest that obesity should be included as an important feature in the fragile X syndrome and the term "Prader-Willi-like" should be avoided.

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Genetic studies of thymic carcinoids in multiple endocrine neoplasia type 1

Multiple endocrine neoplasia type 1 (MEN1) is an autosomal dominant disease characterised by hyperplasia or neoplasia of the parathyroids, anterior pituitary, and the endocrine pancreas.2 Genetic studies have identified several genetic variants associated with MEN1, including the MEN1 gene located on chromosome 11q13 and subsequently predictive testing using RFLP markers was developed.4 The two commonest MEN1 lesions, parathyroid and endocrine pancreatic neoplasia and their sporadic counterparts, have been shown to have loss of heterozygosity in the MEN1 region suggesting that the putative MEN1 gene is a tumour suppressor gene.5-7

The disease responsible for MEN1 was first mapped to chromosome 11q13 and subsequently predictive testing using RFLP markers was developed.8 The two commonest MEN1 lesions, parathyroid and endocrine pancreatic neoplasia and their sporadic counterparts, have been shown to have loss of heterozygosity in the MEN1 region suggesting that the putative MEN1 gene is a tumour suppressor gene.5-7

The aim of this study was to determine the region of genetic linkage in Tasmanian family 2 and thus the feasibility of using MEN1 linked markers for predictive testing in this family, and to elucidate the genetic defects of MEN1 related thymic carcinoids.

Subject II.1 was admitted for surgery for primary hyperparathyroidism. Prooperative chest x ray showed a shadow in the anterior mediastinum and CT scan identified a tumour mass arising in the thymus. An infiltrating mass of tumour and metastatic lymph node could not be dissected from the great vessels but were biopsied. Malignant thymic carcinoid was confirmed histologically. Patient II.5 had a history of insulinoma and multiple lipomatous and was found to have hypercalcaemia. CT scan showed a tumour in the anterior mediastinum arising from the thymus. Again a mass of tumour and lymph node extending around and infiltrating the great vessels was inoperable but was biopsied and malignant thymic carcinoid was confirmed. The other three sibs (I.1, I.7, II.9) and four children of the next generation (III.2, III.4, III.9, III.12) were all found to have hyperplastic parathyroid glands and an insulinoma was removed in addition from III.2. Lymphoblastoid cell lines were established from 24 family members.

Eleven DNA probes previously shown to be linked to the MEN1 locus and showing 14% meiotic recombination, were used. DNA from the cell lines and tumours was extracted, digested to completion with appropriate restriction enzymes, electrophoresed, blotted onto nylon membranes, and hybridised to radiolabelled probes as previously described.3 DNA from affected members using the program LIPEF with the criteria for scoring the disease state as described previously.4 Two malignant thymic carcinoids (II.1, II.5), five hyperplastic parathyroid glands (I.1, I.5, I.9, II.1, III.12), and one pancreatic tumour (III.2) were studied for loss of heterozygosity.

In linkage analysis, two markers, CL15 and CLG4, were uninformative in the pedigree. Meiotic recombinants were detected for markers telomeric of D11S427 (INT2 and D11S97), so negative lod scores (≤ 2.0) in both cases were obtained for these markers. However, peak positive lod scores were obtained at a recombination fraction of 0 for each of the other markers, ranging from 0.21 (CD20) to 1.85 (D11S19) and thus supporting linkage of this family to the MEN1 locus at 14q13 (results not shown). Genotypes of the family members are shown in the figure. In the youngest generation, four are evidently affected but the other 11, despite negative findings in biochemical and radiological screening, have been described as "unknown" as all were below 35 years of age.9 One of these "unknown" cases (III.6) was found to have inherited the mutant (hatched) chromosome and thus requires repeated follow up to detect early signs of disease.

The insulinomas (III.2) and one hyperplastic parathyroid gland (II.9) showed loss of heterozygosity for all informative markers from D11S288/D11S149 to INT2 (results not shown). In all cases the loss involved the allele derived from the consanguineous parent, that is, the putative wild type allele. The other four hyperplastic parathyroid glands and two malignant thymic carcinoids did not show any loss of heterozygosity in the MEN1 region. Although minute somatic deletions or point mutations, undetectable by the current method, cannot be excluded, this finding, together with the high incidence of thymic carcinoids in MEN1 patients, suggests that the genetic trigger for their tumorigenesis might be different from that of common MEN1 related tumours. Further studies in delineating specific genetic mutations in thymus tumours are required.

This work was supported by grants from the Tasmanian Cancer Committee, Queensland Cancer Fund, Australian Medical Association, Paul Bolton Foundation, Swedish Cancer Foundation, Swedish Medical Research Council, and the Magnus Bergwell Foundation. We would like to thank Dr John McArdle for performing the histopathology on all of the family members for their kind cooperation.

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Pedigree of Tasman family 2 showing segregation of chromosome haplotypes for the marker systems which are listed on the left. The chromosome carrying the mutant allele (hatched line) has been inherited by subject III.6, illustrating the usefulness of linkage studies in presymptomatic testing for MEN1. Meiotic crossovers, indicated by thin lines extending from the hatched lines, occurred in II.5, II.7, III.6, and III.9.

Letters to the Editor
leucodystrophy. Jennifer Puck (X linked immunodeficiencies) writes that none of the genes, apart from that for chronic granulomatosus disease, were cloned. Goddard and Solomon (Genetic aspects of cancer) discuss oncogenes and tumour suppressor genes but not microsatellite instability. Zannis, Kardas- sas, and Zanni discuss situation affecting lipoproteins, but only in connection with heart disease. The fifth chapter is by Gra- bowski on Gaucher disease. Each author, we are told, was given the opportunity at page proof to write a short addendum contain- ing the most up to date material, but only Moser took up the offer. The editorial hard was certainly not heavy.

Chapter 4: sonicimaging type of testing for multiple endocrine neoplasia type 1: a new method. Larsson C, Larsson Bystrom E, Wong YY, Santen RJ, Harris’s 1993;89:1344-8. These books appear to be aimed primarily at postgraduates, but their contents are also of interest to all readers. They bring together in one place a large number of references, and the authors’ efforts show that they have been willing to add to this list. They have also been willing to add to their own knowledge. This is a useful and practical book.