

### DETECTING HYPOTHYROIDISM

SIR,—The scheme described by Dr. Philp and his colleagues<sup>1</sup> for the detection of hypothyroidism in thyrotoxic patients treated with radioiodine is admirable and imaginative in permitting identification of these patients at risk. While admitting that the smaller number of clinical features to be sought does provide greater simplicity than the diagnostic index for hypothyroidism previously described,<sup>2</sup> I am surprised that their index does not appear to include the muscle complaints of cramps, "heaviness", or "tightness" so common in these individuals. In a study some years ago in Sir Edward Wayne's department, I found that, whereas only 36% of 100 patients with primary hypothyroidism had these complaints, "muscle pain" was present in 71% of 35 individuals with iatrogenic hypothyroidism. Conversely, paræsthesiæ, which are included in this index, were present in 56% of the primary group but in only 46% of the iatrogenic group. These were small numbers but later experience has fully confirmed that muscle pain is extremely common in patients rendered hypothyroid by radioiodine therapy and indeed is often the premonitory complaint. This, of course, is not a new observation, since Kocher was particularly impressed by this complaint in patients after thyroidectomy in his classic paper in 1883 on "cachexia struipriva".<sup>3</sup>

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### HAND-FOOT-UTERUS SYNDROME

SIR,—We have recently investigated a family in which 12 living members of 4 generations have mild hypoplasia and dysplasia of the hands and feet. The hand shows mild clinodactyly, especially of the fifth digit, with shortening and malposition of the thumb. The feet are strikingly small. An undersized forefoot causes the ankle, which is normal, to appear thick and heavy by contrast. A shortened first metatarsal causes the great toe to come short of the line of the other toes. In addition, at least 4 affected females in 3 consecutive generations have duplication anomalies of the müllerian-duct derivatives, including double uterus, double cervix, and septate vagina.

The propositus was at first thought to have Holt-Oram syndrome,<sup>4</sup> because he had a ventricular septal defect as well as malformed thumbs. However, he also had the aforementioned foot changes, and did not have the shoulder-girdle abnormalities or atrioventricular-conduction defect usually found in persons with Holt-Oram syndrome. The other living affected members did not have congenital heart-disease. Two structurally variant chromosomes (one each in the D and E groups) were observed in cultured peripheral leucocytes of the propositus; several other family members, unaffected as well as affected, had one or the other but not both marker chromosomes. We suggest that the "structural load"<sup>5</sup> of two variant chromosomes, in association with the trait for small hands and feet, may have been sufficient to exceed a critical threshold, resulting in congenital heart-disease in the propositus.

Dermatoglyphic studies showed striking departures from the usual. Of 8 tested affected family members, all had a distally placed axial triradius, and 7 had low arches on both thumbs. No whorls were present on any finger. Loops were exclusively ulnar-directed and very thin, averaging only 3 or 4 ridges from triradius to core. Total fingerprint-ridge count was drastically reduced from normal, averaging about 24 ridges for all 10 fingers. Unaffected family members had normal fingerprint and palm patterns.

This syndrome has in common with Holt-Oram syndrome malformation of the hand, with the thumb showing most

pronounced involvement. However, the bony involvement in Holt-Oram syndrome includes the entire upper appendicular skeleton, often with severe degrees of malformation, while the hand anomaly in this family was mild and easily missed if not looked for, and with no involvement beyond the wrist. Fingerprints in Holt-Oram syndrome are fairly normal. In addition, the feet are never involved in the Holt-Oram syndrome. Duplication anomalies of the uterus have not been reported in Holt-Oram syndrome, nor indeed, so far as we have been able to discover, in any other regularly inherited entity.<sup>6,7</sup> In view of the fairly mild clinical manifestations of this syndrome, it should not be excessively rare.

A complete report is being prepared for publication. Partial support for the study of this family has been provided by National Institutes of Health research grant HD 02083.

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### BRADYARRHYTHMIA COMPLICATING MYOCARDIAL INFARCTION

SIR,—Dr. Pantridge<sup>8</sup> reiterates, in reply to Dr. Pentecost and his colleagues,<sup>9</sup> that the bradycardia in patients with myocardial infarction is an important feature related to serious complications (e.g., fatal arrhythmia), and that the bradycardia "sensitises" the heart to ventricular fibrillation. The bradycardia early in infarction may be due to release of adenosine-type compounds,<sup>10</sup> and this in itself may seriously impair an already weakened myocardium. Adenosine produces bradycardia, which may be severe (thereby impairing coronary flow), and even asystole, and its action is not reversed by atropine. There may be immediate death from asystole or ventricular fibrillation, later death from hormonal release (adenosine with asystole, adrenaline with ventricular fibrillation), or delayed death from gradual failure.

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### CHLORPROPAMIDE IN DIABETES INSIPIDUS

SIR,—The antidiuretic action of chlorpropamide in diabetes insipidus was described by Arduino et al. in 1966.<sup>11</sup> The usefulness of this agent has since been confirmed by Meinders et al.<sup>12</sup> and Reforzo-Membrives et al.<sup>13</sup> Reforzo-Membrives et al.<sup>13</sup> have also shown that the primary effect of chlorpropamide, both in normal subjects and in patients with diabetes insipidus, is a decrease in the renal free-water clearance. This effect is specific for chlorpropamide, for none of the other commonly used sulphonylureas were found to be active. We describe here our experience with the drug at this hospital in the past year.

A 5-year-old girl, known to have histiocytosis X since the age of 2 years (diagnosed by biopsy of a swelling in relation to right parietal bone), had developed diabetes insipidus at the age of 3 years, and had required 'Pitressin' (vasopressin injection) for its control. She was taken off pitressin on Sept. 1, 1968; on Oct. 1 her urine volume was 6360 ml. Her urine specific gravity stayed at 1001. She was started on chlorpropamide 100 mg. daily. No change in urine volume or specific gravity occurred. The dose was increased to 150 mg.

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