INTRODUCTION

Many of the symptoms that make up the complex clinical picture of Prader-Willi syndrome (PWS) point at derangements in hypothalamic function: short stature, hypogonadism, loss of appetite control, diminished pain sensitivity, excess sleepiness. Most of these symptoms were described in the original report of nine patients by Prader et al (1956), and confirmed by others (Jeffcoate et al, 1980; Bray et al, 1983). However, it has become evident that diabetes mellitus is not as common as was originally thought, and it has been argued that many of the endocrine problems are merely secondary to obesity. This chapter will give a brief review of the endocrine manifestations of PWS, against the background of our own comparison of PWS patients with a group of children and adolescents with "simple" obesity.

PATIENTS AND PROCEDURES

The patients are described in Tables I and II. They were all referred to the Departments of Pediatrics at the Karolinska or Huddinge Hospitals in 1978-1981. The protocol on admission included one week of laboratory investigations during which time the patients were allowed to eat the regular hospital meals.

The endocrine work-up included an arginine-insulin tolerance
test (only in PWS patients), a combined i.v. gonadotrophin releasing hormone/adrenocorticotropic hormone/thyroid releasing hormone (GnRH/ACTH/TRH) test (100 µg GnRH, 0.25 mg tetracosactide, 200 µg TRH per 1.73 m² body surface) and an overnight blood sampling every four hours. All blood samples were obtained after overnight fasting. A glucose infusion tolerance test (Grill and Efendic, 1987) was performed by a bolus injection of glucose, calculated to give a blood glucose concentration of 18-20 mmol/l followed by a 1 hour infusion of glucose to maintain the blood concentration at about 20 mmol/l. The hormones were measured by standard radioimmunoassay (RIA) techniques. Insulin-like growth factor-1 (IGF-1) was determined by both radioimmunoassay and radioligand methods (Hall et al, 1980). Insulin-like growth factor binding protein-1 (IGFBP-1) was determined by radioimmunoassay (Povoa et al, 1984). Melatonin measurements were kindly done by Dr. L. Wetterberg, Department of Psychiatry, St. Goran's Hospital, Stockholm.

The study was approved by the Karolinska Institute Ethics Committee.

RESULTS

Growth

The control obese patients were of average height but markedly overweight (+4.2 SDS, Table I). The short stature of the PWS patients became more pronounced with advancing age; the three children between 7 and 10 years of age had a mean height of -1.4 SDS, while the four above 16 years averaged -3.8 SDS. The same was true for overweight; while the body mass index of the youngest three averaged 25.7 (± SD 4.0), it was 43.3 (± SD 13.2) for the four above 16 years.

Evaluation of growth hormone secretory capacity was done in three different ways; in blood samples drawn before and one hour after falling asleep, before and after 20 minutes of exercise on