

Clinical Reports

BURNELL R. BROWN, JR., M.D., PH.D., *Editor*

Anesthetic Management of the Prader-Willi Syndrome

SUSAN K. PALMER, M.D.,* AND JOHN L. ATLEE, III, M.D.†

In 1956, Prader and Willi¹ first described a clinical syndrome that included severe neonatal hypotonia, early childhood hyperphagia, obesity, diabetes, hypogonadism, cryptorchidism, dental caries, and mental deficiency. Since this initial report, more than 100 additional cases have been reported,²⁻⁶ and several reviews have appeared.^{7,8} Although the true incidence of the syndrome is not known, the Prader-Willi syndrome (PWS) may be at least as common as trisomy-21 (mongolism).⁹

Because diagnosis of this relatively new syndrome will be made with increasing frequency, and because PWS has several features of concern to the anesthesiologist, this case report and discussion are presented to aid others in planning anesthesia for these patients.

REPORT OF A CASE

An 8½-year-old Caucasian boy with PWS was scheduled for surgical correction of bilateral undescended testes. Past medical history revealed that the patient's mother had noticed markedly decreased intrauterine movements during her last four months of pregnancy. A normal spontaneous vaginal delivery at 43 weeks' gestation produced a small-for-age, hypotonic, cyanotic neonate who

required resuscitation with oxygen. Extreme hypotonia with difficulty in swallowing made nasogastric feedings necessary during the first three weeks of his life.

Documented recurrent episodes of hypoglycemia led to frequent feedings and an early excessive weight gain. Psychomotor development was retarded; the child remained hypoactive and manifested a labile affect punctuated with temper tantrums.

Previous surgical experience was limited to a single dental procedure, which had been complicated by an episode of severe postoperative hypoglycemia and grand mal seizure activity.

On the present admission, the child was obese (31 kg), his muscle tone was poor, his mouth was small and triangular, many of his teeth were carious, and he appeared hypoactive. The testicles were not palpable in the scrotum. The rest of the physical exam was not remarkable.

After preoperative medication with morphine sulfate (5 mg), pentobarbital (50 mg), and atropine (400 µg) im, the child was awake but calm. Induction of anesthesia was accomplished with halothane as the primary agent. An infusion of 5 per cent dextrose in 0.2 per cent NaCl was started during induction. Laryngoscopy disclosed a small glottis with a large, floppy, V-shaped epiglottis. A loose right canine tooth was removed prior to the intubation procedure.

Anesthesia was maintained with halothane (0.5-2.5 per cent) in nitrous oxide-oxygen (4-2 l), and ventilation was assisted throughout the three-hour inguinal exploration. Blood pressure remained stable, and arrhythmias were not detected during oscilloscopic monitoring of the ECG signal. At the conclusion of the operation, the patient breathed 100 per cent oxygen until he was well recovered from anesthesia and the trachea could be extubated. Both cough and airway maintenance appeared satisfactory following extubation.

The patient's condition was stable in the recovery room, where a blood glucose determination was reported as 74 mg/100 ml. Following discharge from the recovery room, the patient was returned to the ward, where the subsequent postoperative course was uneventful.

* Chief Resident.

† Assistant Professor.

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Address reprint requests to Dr. Palmer.

TABLE 1. Clinical Features that Distinguish the Prader-Willi Syndrome from Diabetes Mellitus and Simple Obesity

	Prader-Willi Syndrome	Insulin-dependent Diabetes	Diet-controlled Diabetes	Abnormal GTT or Simple Obesity
Severe hypotonia	+	-	-	-
Decreased reflexes	+	-	-	-
Hypoglycemias	+	+	-	+
Mental retardation	+	-	-	-
Dental caries	+	-	-	-

DISCUSSION

This child manifested several features typical of PWS, including his fetal inactivity, neonatal hypotonia, altered glucose-fat metabolism leading to early obesity, slight psychomotor retardation, hypogonadism with cryptorchidism, and dental caries. Because hypotonia and abnormal glucose metabolism may affect the anesthetic management of these patients, these features are reviewed in some detail. Miscellaneous features of PWS are mentioned because of their importance in the recognition of the syndrome.

Hypotonia is the first and most striking sign of PWS. Neonates with PWS have repeated aspirations and weak cough, and may develop pneumonia requiring intensive respiratory care. While the infants remain hypotonic, they often show some improvement in coughing, feeding, and crying during their first year.¹¹ In spite of severe muscle symptoms, there is no evidence of histologic, histochemical, or neurophysiologic disease localized to the muscles.¹² Electromyography and neural conduction-velocity studies have yielded normal results.¹³ Injections of edrophonium chloride fails to improve muscular function.¹⁴ The use of muscle relaxants in these patients has not been reported.

The relationships between obesity, hypothalamic appetite control, carbohydrate-fat metabolism, insulin receptor-release mechanisms, and hypoglycemia in normal individuals and in PWS are complex and still not are completely understood. Many patients who have PWS may be diagnosed as "diabetic" or "prediabetic"¹⁴ on the basis of an abnormal glucose-tolerance test (GTT). In fact, because PWS is a relatively recently defined entity, it is more likely that patients will carry the diagnosis of "diabetes" than PWS. As illustrated in table 1, however, PWS patients have several clinical features not

usually associated with either insulin-dependent or diet-controlled diabetes.

It has been suggested that PWS represents an inborn error of energy metabolism. Johnsen *et al.*²³ consider PWS patients to be defective in regulation of lipogenesis and lipolysis such that even during fasting PWS subjects utilize substrate for fat formation rather than to satisfy energy needs. This hypothesis is in keeping with the observed hypoglycemia the PWS child may develop if deprived of glucose for long periods, as might occur during a surgical and postoperative period.

Obesity in patients with PWS has been investigated.¹⁵⁻¹⁷ After the first year of life, these children are often more than two standard deviations above the mean weight appropriate for their age and height. If weight control is not instituted early in life, these patients may become morbidly obese.¹⁸ Jenab *et al.*¹⁹ reported a 6-year-old child with pickwickian features, who died of his cardiorespiratory symptoms. This patient, in retrospect, had many features typical of PWS.¹⁴

When overt diabetes does develop, it is usually nonketotic, non-insulin-dependent, and may well be a complication of the obesity.^{20,21} There may be an abnormality of insulin secretion or interference with insulin action in PWS as originally suggested by Evans.²² Defective insulin receptors or insulin antagonism at muscle, fat and/or hypothalamic sites may well explain the hypotonia, voracious appetite, and disturbed carbohydrate-fat metabolism.

Several additional features of PWS may be helpful in the recognition of the syndrome. The average I.Q. ranges from 50-60, and a labile temperament with temper tantrums is quite common. Hypogonadism and cryptorchidism often occur in males; however, precocious puberty has also been reported. Poor dentition and enamel hypoplasia,²⁴ a small

triangular-shaped upper lip,^{5,6} short stature and delayed bone age, narrow bifrontal cranial diameter, acromicria,²⁵ and strabismus²⁶ are also seen regularly.

In summary, the principal features of PWS of concern to the anesthesiologist are the hypotonia and the disturbed carbohydrate-fat metabolism. Extra attention should be given to airway protection and strength of cough, especially in the neonate. While not substantiated by our experience or reported by others yet, problems related to the use of muscle relaxants might be expected. The choice of anesthetic agent or technique should include consideration of the decreased muscle mass and greatly increased body fat content in these patients. Because these patients may continue to use circulating glucose to manufacture fat rather than to satisfy basal energy needs, the glucose level must be kept high enough during fasting states to allow vital organs to function properly even in the face of ongoing lipogenesis. Therefore, PWS patients should have glucose infusions during and after even brief surgical procedures; until oral intake is restarted, glucose levels should be monitored to prevent hypoglycemia and its possible complications.

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