AAP issues guidelines on health supervision for children with Down syndrome - Committee on Genetics

The Committee on Genetics of the American Academy of Pediatrics (AAP) has issued guidelines designed to assist physicians in caring for a child with Down syndrome. In addition to a protocol concerning health supervision of children from birth to early childhood, the guidelines also address the need for ongoing medical surveillance.

Dr. Constant is right on the mark when he says in his preface that the fourth edition of this book is "designed for those who wish to balance the advances in technology by increasing their skills in diagnosing cardiovascular disorders through history.

This spiral-bound notebook is a comprehensive guide to the management of various types of snakebites. In the words of the author, it is "a merging of the methods of top experts into a guidebook for nurses and physicians, including comprehensive protocols.

Almost nothing is more frustrating to the practicing clinician than trying to justify charges for patient care to third-party payers. Although highly trained physicians deliver quality care for a reasonable fee, far too often (80 percent of the time), claims are denied or significantly reduced.

This book is a superb contribution to the pediatric and dermatologic literature. As Dr. Cohen notes in the preface, the book is designed for the pediatrician with an interest in dermatology and for the dermatologist who cares for children.

As discussed in Ebell's article, "Practical Guidelines for Do-Not-Resuscitate Orders," on page 1293 of this issue of AFP, the management of terminally ill patients is one of the most difficult problems physicians face. When patients are mentally competent and able to make decisions, the patient's wishes should be respected.

The American Academy of Family Physicians first carved a definition of primary care in 1975, and that definition served the discipline well for a decade and a half. With the national focus on the issue of health care reform, the political ramifications are significant.

Intoeing is common in newborn and children (Figure 1). Its importance resides in the large number of affected children, the frequency with which parents (and grandparents) seek medical advice about this problem and the large number of expensive and specialized consultations.

Early diagnosis of von Hippel-Lindau disease is critical because of the prognostic implications for both patients and their families. Unless the diagnosis is considered, the physician may incorrectly assume that the patient has an isolated lesion.

Cutaneous paraneoplastic syndromes are a group of dermatoses that may be associated with an underlying neoplastic condition. Recognition and management of these syndromes require a multidisciplinary approach.
A practical approach to hypercalcemia

Hypercalcemia is a disorder commonly encountered by primary care physicians. Approximately one in 500 patients who are treated in a general medicine clinic have undiagnosed primary hyperparathyroidism, the leading cause of hypercalcemia. The diagnosis of hypercalcemia most often is made incidentally when a high calcium level is detected in blood samples. The principal challenges in the management of hypercalcemia are distinguishing primary hyperparathyroidism from conditions that will not respond to parathyroidectomy and knowing when it is appropriate to refer the patient for surgery. It is essential that physicians know how to evaluate and optimally manage patients with hypercalcemia, because treatment and prognosis vary according to the underlying disorder.

Pathophysiology of Hypercalcemia

The skeleton contains 98 percent of total body calcium; the remaining 2 percent circulates throughout the body. One half of circulating calcium is free (ionized) calcium, the only form that has physiologic effects. The remainder is bound to albumin, globulin, and other inorganic molecules. Low albumin levels can affect the total serum calcium level. Directly measuring the free calcium level is more convenient and accurate, and the following formula can be used to calculate the corrected total serum calcium level:

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\text{Corrected calcium} = (4.0 \text{ g per dL} - \text{[plasma albumin]} ) \times 0.8 + \text{[serum calcium]}
\]

Parathyroid hormone (PTH), 1,25-dihydroxyvitamin D (sub.3), calcitriol, and calcitonin control calcium homeostasis in the body (Table 1). Increased bone resorption, increased gastrointestinal absorption of calcium, and decreased renal excretion of calcium cause hypercalcemia. Normal serum calcium levels are 8 to 10 mg per dL (2.0 to 2.5 mmol per L, Figure 1), although the exact range can vary among laboratories. Normal ionized calcium levels are 4 to 5.6 mg per dL (1.0 to 1.4 mmol per L). Hypercalcemia is considered mild if the total serum calcium level is between 10.5 and 12 mg per dL (2.63 and 3.07 mmol per L). Levels higher than 14 mg per dL (3.5 mmol per L) can be life threatening.

[FIGURE 1 OMITTED] PTH is an 84-amino acid hormone produced by the four pea-sized parathyroid glands posterior to the thyroid gland. In response to low serum calcium levels, PTH raises calcium levels by accelerating osteoclastic bone resorption and increasing renal tubular resorption of calcium. It also increases calcitriol, which indirectly raises serum calcium levels. PTH causes phosphate loss through the kidneys. Thus, in patients with PTH-mediated hypercalcemia, serum phosphate levels tend to be low.

Calcitriol, the active form of vitamin D, is derived from successive hydroxylation of the precursor cholecalciferol, first in the liver (25hydroxylation), then in the kidneys (1-hydroxylation). Adequate vitamin D is necessary for bone formation. However, the principal target for vitamin D is the gut, where it increases the absorption of calcium and phosphate. Thus, in vitamin D-mediated hypercalcemia, serum phosphate levels tend to be high.

Calcitonin is a 32-amino acid hormone produced by the parafollicular C cells of the thyroid. Calcitonin is a weak inhibitor of osteoclast activation and opposes the effects of PTH on the kidneys, thereby promoting calcium and phosphate excretion. Calcitonin levels might be elevated in pregnant patients and in patients with medullary carcinoma of the thyroid. However, there are no direct clinical sequelae, and serum calcium levels usually are normal.

PTH-related peptide (PTHrP) is the principal mediator in hypercalcemia associated with solid tumors. PTHrP is homologous with PTH at the amino terminus, the region that comprises the receptor-binding domain. PTHrP binds the PTH receptor and mimics the biologic effects of PTH on bones and the kidneys.

Clinical Manifestations of Hypercalcemia

The optimal concentration of serum ionized calcium is essential for normal cellular function. Hypercalcemia leads to hyperpolarization of cell membranes. Patients with levels of calcium between 10.5 and 12 mg per dL can be asymptomatic. When the serum calcium level rises above this stage, multisystem manifestations become apparent (Table 2). This constellation of symptoms has led to the mnemonic "Stones, bones, abdominal moans, and psychic groans," which is used to recall the signs and symptoms of hypercalcemia, particularly as a result of primary hyperparathyroidism.

Neuromuscular effects include impaired concentration, confusion, comatose calcification, fatigue, and muscle weakness. Nausea, abdominal pain, anorexia, constipation, and, rarely, peptic ulcer disease or pancreatitis are among the gastrointestinal manifestations. The most important renal effects are polydipsia and polyuria resulting from nephrogenic diabetes insipidus, and nephrolithiasis resulting from hypercalcuria. Other renal effects include dehydration and nephrocalcinosis. Cardiovascular effects include hypertension, vascular calcification, and a shortened QT interval on the electrocardiogram. Cardiac arrhythmias and osteoporosis of cortical bone, such as the wrist, are mainly associated with primary hyperparathyroidism. Excess PTH also can result in subperiosteal resorption, leading to osteitis fibrosa cystica with bone cysts and brown tumors of the long bones.

Differential Diagnosis for Hypercalcemia

Primary hyperparathyroidism and malignancy account for more than 90 percent of hypercalcemia cases. These conditions must be differentiated early to provide the patient with optimal treatment and accurate prognosis. Humoral hypercalcemia of malignancy implies a very limited life expectancy—often only a matter of weeks. On the other hand, primary hyperparathyroidism has a relatively benign course.

The causes of hypercalcemia can be divided into seven categories: hyperparathyroidism, vitamin D-related causes, malignancy, medications, other endocrine disorders, genetic disorders, and miscellaneous causes (Table 3). Evaluation of a patient with hypercalcemia (Figure 2) should include a careful history and physical examination focusing on clinical manifestations of hypercalcemia, risk factors for malignancy, causative medications, and a family history of hypercalcemia-associated conditions (e.g., kidney stones).
HYPERCALCEMIA OF MALIGNANCY

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REFERENCES


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Therefore, the diagnostic approach to hypercalcemia typically involves distinguishing between the two. It is usually not difficult to differentiate between them. Malignancy is often evident clinically by the time it causes hypercalcemia, and patients with hypercalcemia of malignancy usually have higher calcium concentrations and are more symptomatic from hypercalcemia than individuals with primary hyperparathyroidism. The first step in the evaluation of a patient with hypercalcemia is to verify with repeat measurement (total calcium corrected for albumin) that there is a true increase in the serum calcium concentration. If available, previous values for serum calcium should also be reviewed. A Practical Approach to Hypercalcemia

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Hypercalcemia is a disorder commonly encountered by primary care physicians. The diagnosis often is made incidentally in asymptomatic patients. Clinical manifestations affect the neuromuscular, gastrointestinal, renal, skeletal, and cardiovascular systems. The most common causes of hypercalcemia are primary hyperparathyroidism and malignancy. Some other important Hypercalcemia can have absent, few or nondifferential symptoms, but the condition can indicate the presence of major diseases such as breast cancer. Experts review how to quickly apply a high index of suspicion to make a diagnosis. Additional reading.