grams. Intervention for kidney disease depends on the structural and/or functional natures of the problem. Hormonal supplementation in males for hypogonadism requires confirmation of low testosterone levels.

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Bloom Syndrome

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DEFINITION: Bloom syndrome (BS) is a genetically determined form of dwarfism characterized clinically by proportional smallness at all ages and, at maturity, infertility. It usually is accompanied by sun-sensitive facial erythema and immunodeficiency, with or without additional less constant features. The genetic material in BS somatic cells is abnormally unstable; a wide variety of neoplasms arise unusually frequently and at exceptionally early ages.

DIFFERENTIAL DIAGNOSIS: Russell-Silver dwarfism.

SYMPTOMS AND SIGNS: The predominating and constant clinical feature of BS is small body size, both pre- and postnatally, proportioning being fairly normal except for a slightly disproportionately small brain/head and dolichocephaly. Subcutaneous fat is conspicuously scanty. The facies is characteristic, somewhat keel shaped because of malar and mandibular hypoplasia, and a prominent nose. The ears are often unusually prominent. Facial erythema, characteristically limited to the butterfly area of the face, usually appears in infancy following sun exposure. This lesion sometimes extends to other areas of the face, ears, and neck and may affect the dorsa of the hands and forearms. It is variable in severity and sometimes is absent, especially in dark-complexioned individuals. The skin in other areas is not hypersensitive to sunlight. Another dermal feature is an excessive number of circumscribed areas of hyper- and hypopigmentation. The voice is characteristically high pitched, and of somewhat coarse timbre. During infancy, vomiting and diarrhea are increased in many patients; severe gastroesophageal reflux has been diagnosed in some. Typically, affected infants and young children show relatively little interest in eating; in a few cases, surgically placed tubes into the stomach for supplementary feeding have permitted weight gain due to an increase in fat depo-

sition. Immunodeficiency is demonstrable in most affected individuals, and most are prone to respiratory infections complicated by otitis media and pneumonia. Several adults have had bronchiectasis and fatal chronic lung disease. Intelligence usually is average to low average, although several persons with BS have been mentally defective. Generally, affected individuals are infertile, although some women have had normal children. Diabetes mellitus develops in more than 10% of adults with BS. Both benign and malignant neoplasms arise unusually frequently. During infancy and childhood, acute leukemia and lymphoma predominate; carcinomata predominate in adulthood.

ETIOLOGY/Epidemiology: BS is transmitted as an autosomal-recessive trait. More than 60 mutations causing BS have been identified, but all at a single locus, BLM, in chromosome band 15q26.1.

DIAGNOSIS: The appearance of persons with BS is striking, which facilitates their recognition. The clinical diagnosis can be confirmed cytogenetically: dividing BS cells have excessive numbers of gaps, breaks, and rearrangements in their chromosomes. A uniquely increased tendency for exchange to take place between DNA strands is demonstrable as an increase in sister-chromatid exchanges (SCEs); an SCE analysis is the standard way to confirm the diagnosis, including prenatally. Molecular methods are applicable when the BS-causing mutation segregating in a given family has been identified.

TREATMENT
Standard Therapies: Measures to increase height in BS, including administration of growth hormone, have not been found effective. The skin lesion requires protection of the face from the sun. Increased surveillance for carcinoma is advisable in adults. Cancer chemotherapy in BS is un-
usually challenging because of hypersensitivity to many DNA-damaging agents; reduced dosage is often required to avoid fatal ablation of enteric tract mucosae and bone marrow. Potential HLA-matched bone marrow donors (usually unaffected siblings) can be identified.

REFERENCES


RESOURCES
78, 188, 299