Heparin reduces glomerulosclerosis without altering hemodynamics. However, the benefit of heparin may not be due entirely to anticoagulant activity. Evidence for this derives from experiments in which N-desulfated heparin, which is devoid of anticoagulant effects, also reduces glomerular lesions in rats with a remnant kidney.

This beneficial effect of heparin may result from its known antiproliferative effect. This may be of importance because several forms of renal disease have associated *mesangial hypercellularity*. Such mesangial cellularity could be mediated by growth factor enhancing peptides (interleukins), by the physical effects of enhanced glomerular mesangial flows, or from mesangial migration of monocytes with release of monokines (interleukin I) locally.

HYPERLIPIDEMIA

High serum lipid levels, frequently present in various renal diseases, may contribute to progressive sclerosis. Mechanisms include: an effect of lipoproteins upon mesangial cell proliferation and collagen production, lipid-induced adherence of monocytes to endothelial cells, and lipid-induced changes in basement membrane permeability as a result of neutralizing the negative charge on the membrane.

Reduction of cholesterol by drugs (mevinolin or clofibrate) in rats with subtotal nephrectomy and obese Zucker rats decreases focal glomerulosclerosis (Keane WF et al. Am J Clin Nutr 1988; 47:157–160). Dietary protein restriction results in lower serum lipids. Thus, protein restriction may mediate protection against progressive sclerosis via its lipid-lowering effects.

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IDENTIFY MALIGNANT HYPERTHERMIA SUSCEPTIBILITY TO AVERT LIFE-THREATENING EPISODES

Malignant hyperthermia became well known in 1960 when Australian physicians described a 21-year-old student who survived an episode. Ten of his relatives had died as a direct consequence of ether anesthesia. The mortality rate for malignant hyperthermia was more than 60% until intravenous dantrolene sodium therapy became available for widespread use in 1979 and drastically reduced mortality. However, some mortality does occur if malignant hyperthermia susceptibility is not detected before surgery. Thus, the key is to detect susceptible patients prior to surgery so that an episode can be prevented or aborted with proper treatment.

CHARACTERISTICS

Malignant hyperthermia is an autosomal dominant muscle disease that manifests in susceptible persons when they are exposed to general anesthesia. Potent volatile anesthetics (eg, halogenated agents) or succinylcholine produce increased aerobic and anaerobic metabolism, rapidly increasing temperature, systemic acidosis, and frequently muscle rigidity in susceptible persons. This metabolic storm usually includes tachycardia, signs of general circulatory and metabolic stress, and increased muscle permeability that leads to increases in serum electrolytes, creatine kinase, and myoglobin. The mechanisms of metabolic storm are not fully understood, but abnormal calcium control may trigger the event in both excitable and nonexcitable cells.

INCIDENCE

The estimated frequency of susceptibility is 1 of 15,000 children and 1 of 50,000 adults who undergo general anesthesia. Surprisingly, 23% of malignant hyperthermia-susceptible patients have a history of previous uneventful general anesthesia. Susceptibility in the black population is only one-tenth that of the Caucasian population.

DIAGNOSIS AND TREATMENT

The best treatment is prevention. Genetic counseling and diagnostic tests are crucial for those who have had unusual anesthetic complications or who have one or more family members with a history of malignant hyperthermia. All susceptible people should wear a medical alert bracelet. The diagnostic test for malignant hyper-

thermia susceptibility is an in vitro halothane/caffeine contracture test, which is now standardized and is 90% accurate.

PATHOPHYSIOLOGY

Certain neuromuscular diseases predispose patients to malignant hyperthermia, including central core disease, Duchenne muscular dystrophy, myotonic dystrophy, myotonia congenital, and idiopathic chronic elevation of creatine kinase. Others who are susceptible to malignant hyperthermia may complain of nonspecific muscle aches and cramps or may have subclinical myopathy characterized by creatine kinase elevation, nonspecific abnormalities in muscle histology, and sometimes abnormal electromyographic changes.

STRESS-INDUCED MALIGNANT HYPERTHERMIA

Although human malignant hyperthermia is considered a pharmacogenetic disease, physical and perhaps mental stress alone can trigger a malignant hyperthermia episode. This phenomenon is similar to porcine stress syndrome, known in veterinary medicine, which is characterized by sudden malignant hyperthermia in pigs, and is triggered by fright, transportation, or other stress. A study of 634 members of a Nebraska family appears to support the theory that stress can trigger malignant hyperthermia; of 31 deaths or near deaths among the family members, nine deaths and two near-deaths occurred with anesthesia. Twenty other family members died outside the hospital of unusual or unexplained causes associated with stress.

Recurrent episodes of unexplained high fever, aching joints, muscle spasm, and severe malaise that follow extreme physical or emotional stress or fatigue are also related to malignant hyperthermia. If screening is positive in these patients, episodes may be treated with oral dantrolene sodium.

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