Systemic capillary leak syndrome (SCLS) is a rare acquired disorder characterized by acute and severe recurrent attacks associated with a rapid fall in blood pressure. Attacks often last several days and require emergency care. They are sometimes fatal. SCLS occurs most often in adults and the disease is very rare in children. SCLS is not hereditary. More than one half of patients have a monoclonal or M protein detected in the blood. The level of M protein is usually low. The M protein is produced by what usually amount to small numbers of plasma cells in the marrow. The M protein itself does not appear to cause the attacks. Many possible explanations have been offered including an autoimmune mechanism. Recently it has been suggested that capillary lining cells may be damaged by a factor in the blood, which is produced during the acute attack. SCLS has been recognized in a range of racial backgrounds and nationalities. Although the cause of SCLS is not yet known, there appears to be no genetic predisposition to the disease. There are less than 100 patients reported in the world literature since its first description in 1960 by Clarkson. SCLS seems to occur more often in males and older adults. The disease may be more frequent than the literature suggests because the diagnosis is often missed or delayed. SCLS may be mistaken for a severe infection such as septic shock or toxic shock syndrome. Some features such as the swelling may lead one to suspect heart failure or kidney disease. C-1 esterase inhibitor deficiency syndrome may present with a type of recurring edema called angioedema and is often thought of in patients presenting with SCLS. In some cases the hemoconcentration and resulting high hematocrit and hemoglobin level have been mistaken for polycythemia.