Management of Acute Glomerulonephritis

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Glomerulonephritis is responsible for over one half of all cases of end-stage chronic renal failure and, in its most fulminant form, is a cause of acute, irreversible renal failure. Electron microscopy and immunofluorescent studies together with newly recognized clinical associations have revealed a wide variety of histologic subgroups and myriad etiologies for what was once regarded as a single, simple entity. The addition of electron microscopy has lent an entirely new dimension to the delineation of glomerulonephritis subtypes and offers a more reasonable approach to the search for treatment of these subtypes. It is, after all, not unreasonable to suppose that different etiologic factors and host responses are involved in the various pathologic lesions so clearly defined on electron microscopy. Immunofluorescent studies identify the presence of immune globulins and complement components in glomerular lesions and aid in recognition of their localization sites; they may reveal the contribution of fibrin deposition or specific antigens in the pathogenesis of glomerular involvement.

Most, if not all, forms of glomerulonephritis are acknowledged to be the result of immunologic processes, and many can be mimicked by immunologic manipulations in laboratory animals. A growing body of research data has incriminated circulating immune complexes, activation of the complement cascade and the coagulation system, antibodies directed specifically against the glomerular basement membrane, proteolytic activity of leukocytes, and other phenomena in the mediation of particular types of glomerular injury. In experimental animals, at least, manipulation of the antigen:antibody ratio or depletion of complement and/or polynuclear leukocytes may blunt the severity of, or prevent entirely, lesions which are otherwise inevitable and severe. In the rabbit, the prophylactic administration of anticoagulants has marked beneficial effects on the development of glomerulopathy. Unfortunately, comparable benefit is not observed when these maneuvers are performed after glomerular abnormalities are already established.

Most experimentally induced glomerulopathies are self-limiting and of brief duration. Aside from the maneuvers mentioned in the previous paragraph, therapy which would be considered suitable for use in man appears for the most part to be of little benefit in the laboratory. In man, the value of currently available treatments intended to halt or reverse the progression of glomerular abnormalities is no more impressive. Corticosteroids, immunosuppressive agents, and anticoagulants are of proven value in only a minority of histologically specific lesions (for example, hypersensitivity angiitis, Wegener granulomatosis, minimal lesion nephrotic syndrome), and their efficacy in other forms of glomerulonephritis is strongly debated. The very existence of such debate, over 25 years after the introduction of steroid therapy and 15 years after azathioprine (Imuran) became available, should indicate that current treatment modes are less than optimally effective. New forms of treatment must be developed.

Working on the assumption that immunologic mechanisms are the key to the appearance of glomerular injury, one would ideally search for new

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means of turning off or minimizing the impact of those mechanisms, an approach which meets with considerable success in the prevention of renal transplant rejection. Having been largely unsuccessful in achieving suitable manipulation of immune mechanisms with our present knowledge, we can at least attempt to minimize the impact of the immune system on the kidney. In that regard, a new approach to the problem is under study here at the Medical College of Virginia and elsewhere—plasmapheresis. This technique involves the removal of the patient's plasma and replacing it with donor's plasma so as to remove circulating immune complexes and/or preformed antikidney antibodies. Preliminary data indicate that, in selected cases, significant improvement in renal function may follow such treatment. The overall value of plasmapheresis is still under review, however, and will not be known until suitable numbers of patients have received this treatment.

Use of the "Melbourne cocktail"—a combination of dipyridamole, corticosteroid and heparin therapy—has been reported to reverse the most fulminating and devastating form of acute glomerular disease termed "rapidly progressive glomerulonephritis." While the clinical presentation of oligoanuria with virtually complete cessation of glomerular filtration in children is often completely reversible, it is rarely so in adults. Fibrin deposition, formation of luxuriant epithelial crescents, and marked cellular proliferation of the glomerular tuft typify this subgroup of patients. Employing a treatment which affects platelet aggregation and intracapillary coagulation seems entirely rational but is not without hazard to the patient. Once this particular form of fulminating glomerulonephritis is recognized, however, the prognosis for return of renal function is so poor that the cocktail is being investigated in several centers. Evaluation of such treatment requires experience, ideal patient management and careful patient selection, and should be undertaken only under the most stringent precautions if we are to establish its efficacy in a controlled fashion.