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Progress in treating kidney failure

Growing knowledge of the immune system is benefiting patients on dialysis and improving transplant prospects.

Patients with kidney failure are continuing to benefit from our growing knowledge of the function of the immune system, not only in the more obvious area of improvements in renal transplantation, but also in our ability to deal with the impaired immunity of patients on chronic dialysis. Two articles in the Jan. 7 issue of the British medical journal *The Lancet* report on developments which affect both transplant and chronic dialysis patients.

Kidney failure is the end-product of numerous causes, but, once it occurs, there are only two treatment options, dialysis or transplantation. Regardless of the underlying cause of the loss of kidney function, the end-result is a condition known as the uremic syndrome. The uremic syndrome consists of signs and symptoms of impaired function of many systems of the body. This is because the primary function of the kidney is not simply to produce urine, but in fact to maintain the internal physiologic balance necessary to the optimum functioning of all systems.

One system which is particularly affected in renal failure is the immune system. To begin with, renal failure is associated with problems in what is known as cell-mediated immunity. This is the part of the immune system which is primarily affected in AIDS. As in AIDS, there are defects in both the number and function of cells, such as T-lymphocytes. In fact, the opportunistic infections which characterize AIDS, such as Pneumocystis carinii pneumonia, have been well known problems in dialysis and transplant patients for years.

In addition to the primary effects of uremia, the immune system can also be affected by the treatment of the uremia. In particular blood transfusions, either given for anemia or in the course of dialysis, can result in exposure to such agents as hepatitis virus or HIV, or can cause sensitization of the recipient to blood cell antigens resulting in rapid (hyperacute) rejection of a transplanted kidney.

Researchers from the renal unit of Dulwich Hospital and King's College Hospital Medical School in London published an article entitled "Removal of anti-HLA antibodies by extracorporeal immunoadsorption to enable renal transplantation" in the issue of *Lancet* cited above.

Anti-HLA antibodies are antibodies to tissue surface molecules (antigens) produced by a cluster of genes known as the major histocompatability locus. The A and B antigens which determine the blood "type" are an example of such surface molecules. The antibodies themselves are molecules of a protein, immunoglobulin-G, which specifically react with the target molecule and which float around in the bloodstream, awaiting an opportunity to do their thing. In Britain, approximately 20-30% of patients awaiting kidney transplants have such antibodies, and since these antibodies are a major bar to receiving a transplant, this is a serious and growing problem.

If the level of circulating antibodies is reduced, and kept down, it is possible to have a successful transplant. The British team used a technique known as plasmapheresis in which blood is removed from a patient and the red cells and plasma are separated. The red cells are then returned to the patient, and the plasma is percolated through a column containing a substance which binds immunoglobulin-G. The treated plasma is then returned to the patient. To prevent resynthesis of new antibodies, chemotherapy is given.

All nine patients in the study are alive, and seven have received transplants. Of these, five are functioning well and only one patient, who rejected his kidney, has had a serious infection.

In patients undergoing hemodialysis there is constant risk of exposure to hepatitis-B virus, and ultimately one-third of such patients will become chronic carriers of that virus. As such they are at risk of ultimately developing severe liver disease as well as a potential source of infection to other patients and workers in dialysis units. Thus they are prime candidates for prophylactic vaccination against hepatitis-B.

Unfortunately, many hemodialysis patients fail to mount an immune response to the vaccine. This defect results from failure of a group of cells, known as macrophages, to produce a chemical, interleukin-2, which activates a second group of cells involved in processing the vaccine. Now a group of West German researchers has shown that this defect can be overcome by administering low doses of interleukin-2, along with the vaccine.

Once again, knowledge and techniques developed in one area improve therapy in another area, and show the potential for improving the quality and quantity of life. It is ironic that such progress continues, despite an inadequate epistemology and the current virulent hostility to the very concept of progress.