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FINAL TECHNICAL REPORT

Period Covered by Report:

January 1, 1953 - August 31, 1962

Principal Investigator:

John P. Merrill, M.D.
Associate Clinical Professor of Medicine, Harvard Medical School
Physician, Peter Bent Brigham Hospital

Title of Report:

Metabolic Disorders and Therapeutic Approaches to Renal Failure

Contract Number:

DA-49-007-MD-429

ASTIA AVAILABILITY STATEMENT:

Qualified requestors may obtain copies of this report from ASTIA.

Security Classification:

NONE

COMPREHENSIVE REPORT

A. Consolidated Summary

During the course of 10 years' work, we have demonstrated a number of effects of uremia upon metabolism. Rats with chronic uremia show a decrease in glucose uptake from the intestine and a marked decrease in liver glycogen as well as impairment of glucose utilization following a glucose load. Urea does not appear to be dispersed equally throughout the body but may have a higher intracellular concentration in some cells. The half-life of red blood cells infused into uremic patients is decreased and this increased destruction may be reversed by hemodialysis. The neurologic manifestations of uremia appear to be due to the generalized metabolic defect rather than to hypocalcemia. Cardiac arrhythmias are frequent in patients with uremia and may be produced by rapid changes of extracellular pH or levels of sodium and potassium. Patients with both acute and chronic renal failure have high serum citrate levels.

Patients deprived of all renal tissue do not develop hypertension unless they are overhydrated. This type of hypertension related to overhydration may be corrected by salt and water deprivation.

A technique has been devised for the management of chronic renal failure by periodic peritoneal irrigation through an inlying peritoneal conduit. An apparatus which will automatically cycle dialyzing fluid has been devised and is currently undergoing clinical trial. Four patients, so treated, have been maintained at home by peritoneal dialysis.

During the course of this work achievements in the field of clinical renal homotransplantation in man have been as follows: In 1954, the first successful transplantation of the kidney of identical twins. In 1959, the first successful transplantation of the kidney between nonidentical twins. In 1962,

the first successful transplantation of a totally unrelated cadaver kidney which has survived at the present for 15 months. More than 60 human renal homografts have been performed to date. Current techniques of immuno-suppressive therapy use drugs rather than radiation. With these techniques we have demonstrated that partial tolerance for a transplanted kidney may be obtained and that rejection once again may be aborted by drug therapy. At the present time, five patients are alive and in good health with kidneys transplanted from other than twins.

A technique has been evolved for the demonstration of degrees of histocompatibility between humans based on the degree of accelerated rejection of skin placed on different donors following prior transplantation of the skin from the first member of the pair to be tested.

It has been possible to elute antibody from a rejecting kidney and to reject this with soluble antigen from donor platelets in an in vitro system, employing complement fixation.

B. Significance of these results:

The results referred to above have led to better understanding of the metabolic abnormalities in uremia and have enabled us to proceed with more effective techniques for therapy. Ultimately, we believe the most satisfactory solution to the problem of chronic renal failure will be transplantation of the kidney. The work discussed above represents the progress in some of the fields which must be thoroughly explored before this can be generally feasible. However, it is now possible in certain instances to restore an individual with terminal uremia to full activity for periods as long as 15 months by the transplantation of unrelated kidney.

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