amount of antigen. This diminishes the possibility that the results could be explained by some unique quality of the absorbed antiserum.

The role played by low affinity antibody in immunopathologic lesions may be considerable. In serum sickness the antibody responsible is without much doubt of relatively low affinity. In this disease alone such diverse lesions as endothelial proliferation, increased glomerular permeability, vascular necrosis and anaphylactic alterations in vessels take place. Anaphylactic reactions bringing about an increase in vascular permeability may be of special importance in causing circulating antigen-antibody complexes to localize in vessel walls to produce the lesions. Anaphylaxis may thus act as a trigger mechanism in initiating the development of the disease(11-13). The extent to which low affinity antibody may influence the development of related lesions has not been determined. These studies, along with those of Osler(1), indicate that low affinity antibody may be less efficient in precipitating anaphylactic responses under conditions of low concentrations of antigen. However, when an optimum of antigen is present such antibody is fully reactive.

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Massive Diuresis Following Renal Homotransplantation.* (29284)

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With awareness that massive diuresis must be added to severe oliguria as a potential hazard following sudden relief of urinary tract obstruction, it has become apparent that observed large urine volumes may be the common expression of diverse pathogenetic mechanisms. Wilson, Riseman and Moyer reported acute shocking salt loss following prolonged diuresis(1), and persistence of a salt wasting defect over many months was meticulously characterized by Bricker and coworkers(2). However, a vasopressin resistant water diuresis was responsible for polyuria in the case studied by Earley(3), while solute diuresis principally due to urea has recently been recorded by Maher, Schreiner and Waters(4). In this case, urea comprised 37-56% of urine osmolality during an 8-hour period of observation in which concentrations of serum urea nitrogen (SUN) and serum creatinine (SCr) fell from 175 to 75 and from 17.8 to 7.4 mg per 100 ml respectively. The authors speculated that a similar phenomenon might account for the sometimes massive diuresis seen following renal homotransplantation into azotemic subjects.

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TABLE I.

No. of patients	Pre-operative SUN Mean	Pre-operative SUN Range	Initial day's urine vol
6	56	26– 77	78–2574 ml*
12	64	24–104	803–3040 "
8	56	21– 80	Exceeding 4500 ml

* Ishemic tubular necrosis, as manifested by rising SUN, with or without oliguria.

In 20 of 26 recipients of renal homotransplants at this institution there has been immediate urine formation by the transplant, with the initial day's urine volume averaging 3968 ml. The average preoperative SUN in these 20 patients has been 59 mg per 100 ml (range 21-104) as compared to 56 mg per 100 ml (range 26-77) in the 6 subjects in whom initial copious urine flow did not occur due to presumed ischemic tubular necrosis of some degree. In 8 of the 20 patients who had good initial function, urine volume exceeded 4500 ml/day (Table I), exceeding 7000 ml/day in only one.

Methods. The most pronounced diuresis (15,925 ml/day) occurred in a 19-year-old girl who had become oliguric (75 ml urine per day) as a consequence of bilateral chronic pyelonephritis. Following this development, she had been maintained by intermittent peritoneal dialysis by Dr. Alan Kanter (Michael Reese Hospital, Chicago, Ill.). In a 72-hour dialysis immediately preceding transplantation, SUN fell from 162 to 57 mg per 100 ml and SCr from 8.9 to 6.6 mg per 100 ml. On November 12, 1962, she received a renal homotransplant from her sister; details of the operation have been published(5).

Urine was collected in the recovery room, *via* a Foley catheter into polyethylene jugs, sent to the Renal Laboratory, measured into graduated cylinders, and aliquots saved and frozen. Total solute activity was determined by cryoscopy (Fiske Associates), sodium and potassium by internal standard flame photometry (Baird Associates), chloride by electrometric titration (Aminco-Cotlove), inorganic phosphorus by the method of Fiske and Subbarow(6), creatinine by the method of Peters(7), urea N by the method of Marsh, Fingerhut and Kirsch(8), and glucose (performed by Dr. William R. Harlan, Jr.) by the method of Salomon and Johnson(9).

Results. In the immediate post-operative period urine volume exceeded 600 ml per hour for 19 hours, during which time SUN fell from 61 to 14 mg per 100 ml; subsequent urine volumes did not exceed 300 ml per hour. Urine flow rate during this period ranged from 10.6 to 14.2 ml per minute, and urine solute activity from 258 to 348 milliosmols per kilogram water. Urea comprised 19.6, 19.6, 19.3, 17.3, 14.1, and 13.5% of urine osmolality in successive periods. Intravenous fluid (6-9 ml per minute) was administered at approximately half the urine flow rate throughout the 19-hour period, containing glucose at a rate of 1375 micromols per minute, and sodium and chloride each at rates of 400 micromols per minute. Average glucuresis was 182 micromols per minute and average creatinine excretion 142 micromols per minute. The combined contribution of urea, glucose, and creatinine to urine osmolality was 40.4, 37.9, 40.6, 38.6, 28.3 and 26.8% in successive periods. The principal solutes contributing to urine osmolality were sodium and chloride, excreted at average rates of 1278 and 1210 micromols per minute; average excretion rates of potassium and phosphate were 139 and 60 microequivalents per minute. Observation on the initial 19 hours are summarized in Table II.

Discussion. The possible mechanisms of diuresis in the present case included water diuresis, due to physiologic suppression of antidiuretic hormone by body fluid hypotonicity, or to tubular unresponsiveness to this hormone. However, urine osmolality in successive periods was 258, 285, 300, 315, 348 and 348 milliosmols per kilogram water. Alternative possibilities, consistent with the observed isosthenuria, were osmotic diuresis, due to inclusion in the glomerular filtrate of unreabsorbable particles or to tubular rejection of normally reabsorbable particles, or filtration diuresis ("third type of diuresis" of Borst(10)), here associated with assumption of filtration function by the transplant.

When osmotic diuresis is induced by exogenous urea or mannitol administration, the loading solute comprises approximately two-thirds of the osmotically active particles. The

TABLE II. Excretion Rate of Urine Solutes in Successive Periods Following Renal Homotransplantation.

1	2	3*	4†	5‡	6§	7‡
	Urine flow rate	Total solutes	Non-electrolyte solutes		Electrolyte solutes	
Hr	ml per min.	milliosmoles per min.	micromoles per min.	% of total	micro-equivalents per min.	% of total
1-3	10.6	2.735	839	40.4	2079	59.6
4-6	11.7	3.335	934	37.9	2467	62.1
7-9	14.2	4.270	1148	40.6	2828	59.4
10-11	13.9	4.379	1027	38.6	2660	61.4
12-16	12.6	4.385	848	28.3	2996	71.7
17-19	12.3	4.280	825	26.8	3083	73.2
Mean	12.6	3.897	937	35.4	2686	64.6

* Total solute (activity) per minute, determined by freezing point depression (Fiske osomometer). Calculated as milliosmoles per gram water × urine flow rate.

† Non-electrolyte (concentration) per minute, determined by sum of concentrations of urea, glucose, and creatinine. Calculated as micromoles per ml urine × urine flow rate.

‡ % of total: non-electrolyte solutes/non-electrolyte + electrolyte solutes; electrolyte solutes/non-electrolyte + electrolyte solutes.

§ Electrolyte (concentration) per min., determined by sum of concentrations of sodium, potassium, chloride, and phosphate. Calculated as microequivalents per ml urine × urine flow rate.

remaining osmotic activity is principally due to unreabsorbed sodium and attendant anions, attributed to restraint by the unreabsorbable particles upon water reabsorption and consequent dilution of the filtered sodium, in the proximal tubule, where its reabsorption is subject to limiting concentration gradients(11). Since the analogous gradients are inoperative in restricting glucose and phosphate reabsorption, the contribution of these solutes, where not themselves filtered in excess, is not great in osmotic diuresis(12). Creatinine, using loads comparable to those obtaining in renal disease, has been used to induce experimental osmotic diuresis in subjects whose filtration function was normal (13). In the present case, however, initially high SUN and SCr levels had been appreciably reduced by preoperative dialysis; mannitol was not administered to donor or patient.

When osmotic diuresis is induced pathophysiologically or pharmacologically, by inadequate tubular recovery of normally reabsorbable solutes at normal or reduced filtered loads, electrolytes account for a major share of the urine osmolality and, depending upon the sites of tubular involvement, potassium may constitute a significant portion of the excreted cation. In filtration diuresis, the preponderant contribution to urine osmolality is also made by sodium and chloride, without significant kaliuresis(10).

The principal solutes contributing to urine osmolality in the present case were sodium and chloride. This pattern of electrolyte loss is similar to that noted in the subjects of Bricker and associates, studied at a time when SUN concentrations ranged 50 to 80 mg per 100 ml and filtration rates (inulin clearance) 19.6 to 44.1 ml per minute. Evidence was adduced in these patients for a probable proximal tubular defect in sodium reabsorption, persisting for as long as 3 months. In the present case a greatly enhanced filtration rate may have contributed to incomplete sodium reabsorption during the initial diuresis, without the necessity of implicating impaired tubular reabsorptive capacity. The kidney of a 24-year-old sister (surface area 1.8 square meters) was transplanted into the patient (1.4 square meters), whose body fluids were greatly expanded at time of operation, as evidenced by a 17-lb weight loss during the post-operative diuresis. However, with the institution of prednisone immunosuppressive therapy, restricted dietary sodium intakes were necessary to prevent a tendency to fluid reaccumulation, and 24-hour sodium excretions were as low as 10 milliequivalents per day.

Urine to plasma creatinine concentration ratios in the present case, averaging 26.7 during the first 9 hours of diuresis, are apparently best interpreted as indicating creatinine secretion into tubular lumina, rather than as an effect of distal water abstraction in increasing the concentration of filtered creatinine. At the onset of diuresis creatinine clearance (ml per minute per 1.73 square meters) was 270; 8 weeks later it was 134, and 3 months postoperatively 170. Simultaneous inulin clearance at the time of the last cited value was, however, 97 ml per minute per 1.73 square meters, a ratio of creatinine to inulin clearance of 1.75. High creatinine to inulin clearance ratios were noted in the recipient of a transplant previously performed by one of us (D.M.H.)(14). Assuming the true initial filtration rate of the transplant to have been 90 ml per minute, filtered loads of sodium, potassium, and creatinine would have been: 12,600; 605; and 45 micromols per minute. Average urine excretions of these substances were 1280, 139, and 142 micromols per minute, or excretion fractions of 10.2, 23, and 315% of filtered load. The kaliuresis (urine potassium concentrations 8.5-18.9 millimoles per liter) of the order of magnitude recorded by Bricker and associates(2), was modest in comparison with the case of Maher and associates(4), where potassium excretion equalled or exceeded the filtered load.

Summary. Characterization of the diuresis experienced by a 19-year-old recipient of a renal homotransplant revealed certain features in common with the diuresis seen in experimental osmotic diuresis in normal subjects, and with the diuresis seen following relief of urinary tract obstruction and in other salt-wasting syndromes. The preponderant unreabsorbed solutes were sodium and chloride rather than urea. Since the salt wasting state did not persist, it may have been due to volume expansion and to an enhanced filtration rate, rather than to a tubular reabsorptive defect.

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