The Artificial Kidney

A. V. Wolf

Department of Physiology and Pharmacology, Albany Medical College, Albany, New York

IN PRINCIPLE AN ARTIFICIAL KIDNEY is a differential dialyzer. Thirty-eight years ago a small one was first described by Abel, Rowntree, and Turner (*1–3*). Their device, connected to an artery of an animal, permitted blood to traverse celloidin tubes surrounded by a bath of salt solution and to return to the animal through a vein. Through hemodialysis, crystalloids present in the blood plasma but not in the bath fluid diffused into the bath. Subsequent attempts at "vividiffusion" were made by others, but technical difficulties lying between hemodialytic principle and widespread application were so forbidding that the whole matter remained quietly confined to academic circles until about seven years ago. At that time W. J. Kolff (*4, 5*), of Holland, cut the Gordian knot and put the principle of the lecture room to work in the hospital. Since then artificial kidneys have multiplied in design and number (*6–17*), and their clinical status is becoming clear even though unforeseen developments may change conditions at any time. At present they hold singular promise as experimental tools; but, if technique can be highly perfected, there is no discernible limit to the novelty, wealth, and importance of hemodialytic explorations.

Fig. 1 shows one kind of modern artificial kidney. Its distinctive features—the use of the quasi-Archimedean screw to move blood through the cellophane dialyzing tubing, and the 100-liter bath—are derived from the original Kolff kidney, but it embodies extensive improvements over the latter, in consequence of the painstaking efforts of investigators at Peter Bent Brigham Hospital in Boston (*13, 14*). These machines, properly used, are thoroughly reliable.

Two cannulas are placed by a surgeon, one in the radial (wrist) artery and one in a vein on the inner aspect of the same arm at the elbow. A sterile cellophane "sausage casing" about 115 feet in length has previously been wrapped about the wire mesh drum in a closely coiled helix, and its ends adapted to terminal couplings ("arterial" and "venous"). These devices permit the drum and cellophane to be rotated by a motor without disturbing the tubes leading blood to the arterial and from the venous coupling. Banked blood, perhaps 400 ml, and some physiological saline are used to "fill" the machine initially, and heparin is administered through the venous cannula so that the patient's blood will not clot in its passage through the artificial kidney. Arterial pressure drives blood through the arterial coupling into the flattened cellophane tubing, where it sinks to the lowest portion of the loops during the rotation of the helix. This blood, the pressure of which is now negligible, is literally rolled to the venous coupling. From this point it is pumped through a pair of plastic valves by an air piston (minimizing the trauma to which the blood cells are subjected) and raised several feet above the bed level of the patient. It is led into a buret from which, by gravity, it drains through a protective clot-catching funnel containing glass beads, and then back to the patient's vein. One of the important responsibilities of the operating hemodialyst is to prevent the blood content of the patient from fluctuating widely during treatment, and he is attentive to the blood balance, seeing that nearly equal quantities of blood are lost to and gained from the machine per unit time.

Just before the extracorporeal circulation is started, the bath, prepared with 100 liters of a solution containing major electrolytes of the plasma, is motor-hoisted so as to immerse the lower portion of the dialyzing coils. All parts of the system in contact with blood are sterilized before operation, except for the bath fluid, since microorganisms do not, and viruses apparently do not, penetrate the cellophane. The concentrations in the bath fluid of electrolytes such as sodium, potassium, calcium, magnesium, bicarbonate, and chloride approximate their concentrations in normal plasma, although for particular purposes fluid of any desired composition can be used. A mixture of 5 per cent carbon dioxide and 95 per cent oxygen is passed steadily through the space between the surface of the fluid and the plastic cover of the bath. The carbon dioxide, equilibrating with bath fluid, enables calcium to remain in solution with bicarbonate. Metabolites such as urea and creatinine are, of course, absent from the virgin bath. This permits a differential dialysis with, for example, little net change of sodium, while urea and creatinine move from blood to bath readily along their blood-bath concentration gradients. A 6-hour hemodialysis produces striking changes in the chemical composition of body fluids. An abnormally high blood level of urea, reflecting essentially an abnormally large quantity of urea dissolved throughout body water, may be reduced to one half or one third (Table 1). Excesses of potassium, deficits in bicarbonate, and, in general, almost any aberrations of electrolyte concentration in the plasma are sharply reduced.

There is some control of water balance, but this remains to be improved. Since there is no appreciable hydrostatic pressure gradient across the wall of the cellophane casing and no colloidal material in the bath fluid, the osmotic pressure of the plasma colloids

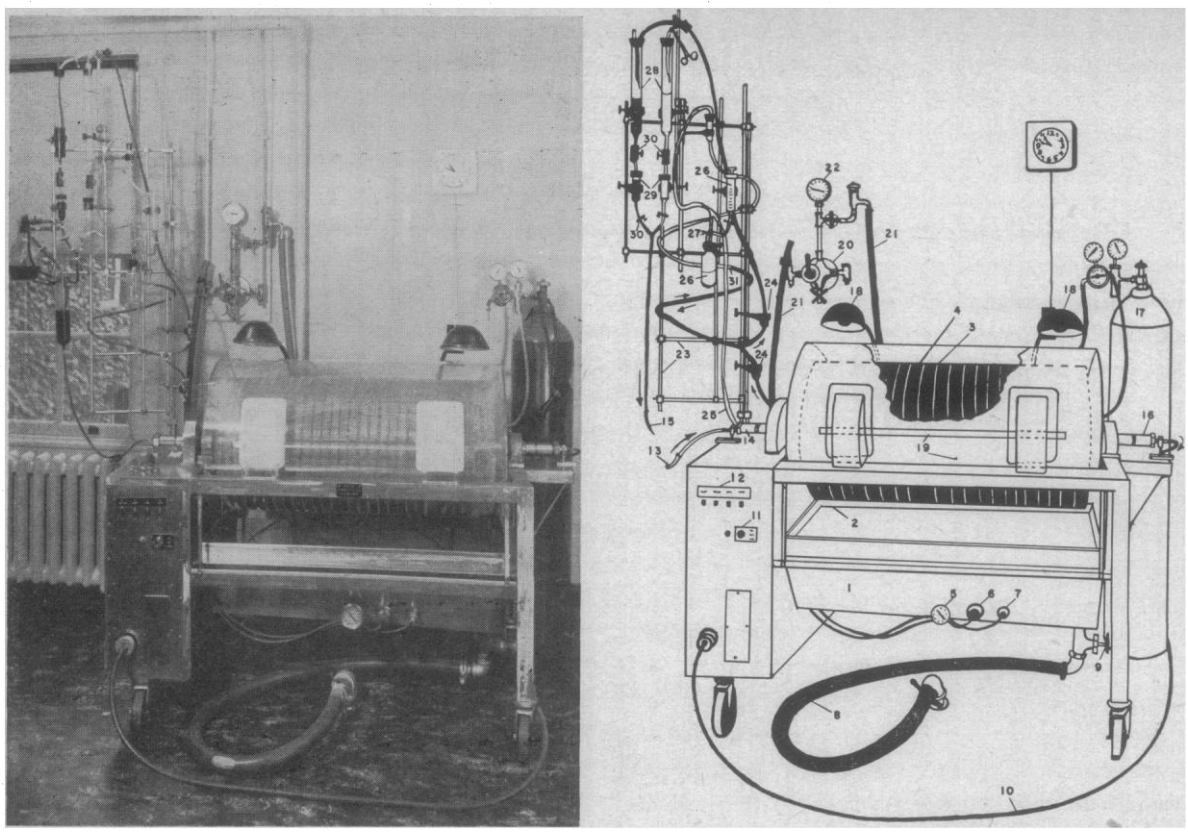

FIG. 1. Artificial kidney at Albany Hospital. For demonstration, the flask (extreme left) and large buret below and to the right of it are partly filled with blood, simulating patient. These are omitted from line drawing of the photograph at right. The cellophane coils about the wire mesh drum are seen behind and below the transparent plastic cover of the bath. The bath itself is in the DOWN position, and its fluid level is visible. Only one of the pair of air-trap burets with attached clot catcher is used at a time. The other set is in reserve.

Right: Diagram of machine in photograph. 1, bath pan; 2, bath fluid level; 3, wire mesh drum; 4, cellophane tubing; 5, thermometer; 6, bath light socket; 7, thermoswitch set to maintain bath fluid at 100° F; 8, drain for bath; 9, drain faucet; 10, electric cable supplying lights, motor-hoist for bath, bath fluid heater, rotation drive for wire mesh drum, and pump for air piston; 11, UP-DOWN switch for bath; 12, HEATER, LIGHTS, and ROTATION-DRIVE switches; 13, arterial cannula; 14, arterial coupling; 15, venous cannula; 16, venous coupling (blood goes from here through the tube passing behind the machine to the lower of the pair of valves); 17, tank of 5% CO_2 and 95% O_2; 18, gooseneck lamp; 19, transparent plastic cover of bath and handle for raising; 20, mixing valve for providing water at body temperature to fill bath; 21, water hose; 22, thermometer of mixing valve; 23, supporting rods; 24, plastic valve; 25, rubber tube from air compressor (pump) in housing to blood flow control apparatus; 26, blood flow control apparatus; 27, petcock for adjusting rate of blood flow from venous coupling; 28, plastic air-trap buret; 29, clot catcher; 30, adjustable clamp; 31, interface of blood and air (piston), which oscillates up and down in the winding plastic tubing during pumping.

promotes a tendency for fluid from the bath to enter the blood. If unchecked, the resulting hydration could have serious clinical consequences, such as pulmonary edema. The movement of fluid into the blood is retarded or reversed by adding glucose to the bath. However, precise regulation of fluid exchange cannot be obtained in this manner, because glucose passes across the cellophane (Table 2), changing the glucose gradient,[1] and because osmosis under these conditions is a function of blood flow, which is changeable. Moreover, the protein content of plasma is variable. Ordinarily 0.7 per cent glucose in the bath fluid seems clinically satisfactory, but considerably higher concentrations have been used to dehydrate patients (*5, 17, 18*). If enough glucose is added to the bath, the fugacity, or escaping tendency, of the bath fluid becomes less than that of the plasma (*19*). The plasma consequently loses protein-free fluid to the bath, its oncotic pressure rises, and its fugacity with respect to interstitial accumulations of fluid is lowered. Thus, an osmotic siphon is started in which the plasma assumes the role of a conductor of fluid. Interstitial (edema) fluid moves "uphill" to the higher hydrostatic pressure of the blood stream, through the plasma fluid, and then "downhill" to the lower hydrostatic pressure of the bath fluid. In the hemodialyzer of Alwall (Fig. 2) water balance is controlled by regulating directly the hydrostatic pressure of the bath fluid relative to that of the blood (*7, 8*); and the ultrafiltration principle has been used in other forms (*15, 20*), as in Figs. 3 and 4.

An interesting phenomenon results from the fact that, as dialysis proceeds, concentration gradients between blood and bath tend to decrease, diminishing the rate of transfer of certain solutes. In order to aug-

[1] Other osmotically effective materials have been considered or used—e.g., gelatin, Carbowax, sucrose, etc.

TABLE 1

COMPARISON BETWEEN ARTIFICIAL AND NATURAL KIDNEYS

Feature	Artificial kidney*	Human kidneys (normal)
1. Number of nephrons	1	2,000,000
2. Surface area for exchange or excretion	21,000 sq cm (cellophane)	8,000 sq cm (glomerular capillaries) 60,000 sq cm (tubules)
3. Blood pressure	Less than osmotic pressure of plasma colloids	Greater than osmotic pressure of plasma colloids
4. Blood flow	100–500 ml/min	1200 ml/min
5. Time required for blood to pass through kidney	4–1.8 min	0.02 min
6. Quantity of blood in kidney	400–1040 ml	24 ml
7. Principles of excretion and regulation	Diffusion primarily, some filtration	Filtration, reabsorption, secretion
8. Urea (at plasma level of 300 mg %)†		
a, Excretion	68%/6 hr (2 bath changes) 102 g/6 hr (2 " ") 57%/6 hr (no bath change) 85 g/6 hr (" " ")	42%/6 hr‡ 63 g/6 hr‡
b, Clearance	Falls with time—e.g., 175 ml/min at zero time, 135 ml/min at 2 hr	Independent of time, e.g., 75 ml/min
c, Half-life	3.7 hr (1 bath change after 2 hr)§ 4.4 hr (no bath change)§	7.7 hr
9. Weight	> 400 kg	0.3 kg

* Shown in Fig. 1.
† Ignoring rate of urea formation.
‡ A diseased kidney would put out much less and might be responsible for the high plasma urea.
§ See qualification in text.

ment their exchange, the bath can be drained and refilled with fresh fluid one or more times during a run. It has been shown (*18, 21*) that maximal augmentation occurs if the time intervals between n changes of bath fluid in a total dialytic operating time t are equal to $t/(n+1)$. If one optimal change is thus made at 3 hours in a total operating time of 6 hours, urea removal under specified conditions might be augmented 16 per cent above what would have occurred with no bath change. For the same conditions, but with two changes at 2 and 4 hours, the increment would be 20 per cent. Similarly, for an infinite number of changes the increment would be 31 per cent. This indicates how close to the dialyzing limit of the cellophane it is possible to work with only two changes. It points up further the limits of counterflow dialyzers, which approach in varying degree, but never equal, the efficiency obtained with "an infinite number of changes."

It is of interest to assess the operation of artificial

TABLE 2*

Substance	*D*	*d*	*E*
Chloride	310	1.03	0.61
Urea	300	*1.00*	.60
Potassium	300	1.00	.60
Sodium	235	0.78	.47
Creatinine	169	.56	.34
Bicarbonate	168	.56	.34
Alanine	148	.49	.30
Glucose	120	.40	.24
Magnesium	100	.33	.20
Inorganic phosphate	92	.31	.18
Sucrose	67	.22	.13
Phenol red	33	0.11	0.07

* Average dialysances (D) and relative dialysances (d) obtained at a "plasma flow" (a) of 500 ml/min. The extraction fraction (E) given here is the fraction of solute removed from arterial plasma in one passage through the cellophane casing by a virgin bath containing none of the solute. For a substance x, $E_x = D_x/a$. As blood flow approaches zero, all these extraction fractions and relative dialysances approach 1.0 (*18*).

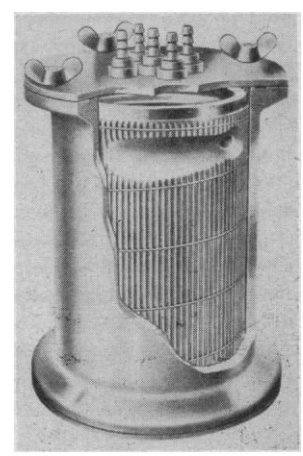

FIG. 2. A hemodialyzer-ultrafilter, intended for rabbits. Cellophane tubing (700 sq cm, not shown here) is wound helically around the inner fluted cylinder, which is provided with a bottom, fitting in the narrow space between inner and outer cylinders. The small volume of bath fluid contained in the apparatus is steadily replaced, entering one of the taps in the top-plate and passing through a rubber tube connected to another tube in the bottom of the inner cylinder. From there it flows over the surfaces of the cylinders and in thin layers around the cellophane, leaving the apparatus through a tap on the top-plate. With a controlled bath fluid inflow, the effluent is allowed to pass through a long rubber tube, discharging at a variable but lower level than the apparatus. The degree of negative pressure of the bath fluid on the outer surface of the cellophane tubing (and, consequently, the filtration pressure) can thus be regulated (*8*).

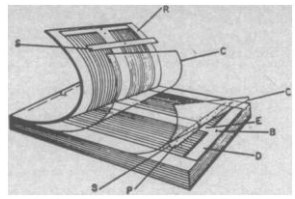

FIG. 3. An assembly of 4 units of a counterflow hemodialyzer in parallel. Two such assemblies in series have 12,000 sq cm of cellophane sheet and contain 400 ml blood. The top rubber pad has been bent back to show the relative positions of the inner parts. *R*, grooved rubber pads; *C*, cellophane sheets; *S*, stainless steel plates between the two sheets of cellophane—these plates are separated 1 mm by projections (*P*) in one of the plates; *D*, depression in rubber pads to accommodate the steel plates; *B*, interconnecting tubes for blood—the holes in the steel plates fit exactly over *B*; *E*, interconnecting tubes for dialyzing solution. Several units may be used in series and/or in parallel (*10*).

kidneys against an elementary background of natural kidney function. One human kidney contains about 1,000,000 units called nephrons, each having an intimate blood supply for its two major portions, the glomerular capsule and the tubule. A tiny ball of capillaries, the glomerulus, invaginates the dilated tip of the tubule so as to be almost surrounded by a double-walled capsule. The combined capillary-capsule barrier is relatively impermeable to colloidal constituents of the plasma such as proteins but rather freely permeable to its water and crystalloids. Largely because the hydrostatic pressure of the blood within the glomerular capillaries exceeds the colloid or effective osmotic pressure of the plasma, there occurs a filtration of essentially protein-free fluid from the plasma, across the barrier, into the tubule. As this filtrate courses along the tubule, its dissolved materials may be selectively reabsorbed in whole or part, or added to by tubular secretion; or, they may suffer no change in quantity. About 120 ml of glomerular filtrate are thought to form each minute in the collective 2,000,000 glomeruli of an adult, and the tubular cells ordinarily reabsorb about 99 per cent of the filtered water, returning it to the blood stream. The remaining fluid, whose composition is now qualitatively similar to, but quantitatively different from, the glomerular filtrate is called urine and ultimately enters the bladder. Ever since the discovery that the major, normal constituents

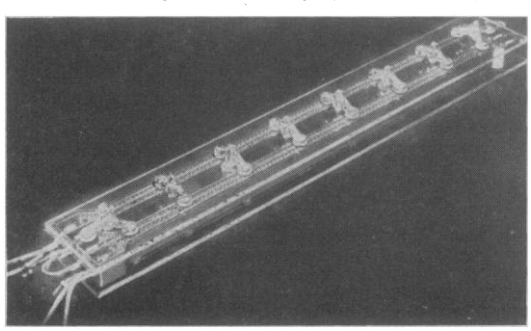

FIG. 4. An assembled 4-channel counterflow hemodialyzer unit using 4,000 sq cm cellophane tubing compressed to a slitted lumen about 1 mm deep. Several units may be used in parallel. Blood volume per unit is 300 ml at 50 mm Hg differential pressure (*15*).

in the urine are derived from the blood by ultrafiltration at the glomerular capsule, there has been a rationale for basing an artificial kidney on the principle of hemodialysis.

The urinary function is complex. A metabolic waste such as urea is merely excreted. There can be no quantity of this material in the blood so small that some is not found in the urine. Glucose, on the other hand, is not usually detected in the urine by ordinary tests unless it is present in abnormally great quantity in the blood, as in certain diabetics. Thus, the kidneys regulate concentrations in body fluids by retention as well as by excretion. In the case of water and ions such as sodium and chloride, the regulatory faculty is highly developed. Sodium, for example, taken in such excess as to elevate the plasma sodium concentration above normal, leads to the excretion of a urine more concentrated in sodium than the concurrent plasma. This output, removing from the plasma relatively more sodium than water, tends to depress the plasma sodium concentration toward normal. If water is taken, diluting the plasma sodium below normal, the renal response is the production of a urine more dilute in sodium than the concurrent plasma. In this case, elimination of relatively more water and less sodium tends to pull the plasma concentration of sodium up toward normal.

In renal disease excretory power is reduced, resulting in an accumulation of materials in the body which should have been eliminated in the urine. Urea, creatinine, uric acid, phenols, guanidine, acids, and potassium are among these materials. Curiously, the regulatory function for other ions such as sodium is not strikingly impaired, and aberrant concentrations of this ion are less commonly seen. Uremia—nausea, vomiting, vertigo, coma, and death—may accompany these retentions, but the substances responsible are not specifically known. Urea and creatinine, for example, are relatively nontoxic. Known or not, offending material is apparently removed from the body readily by hemodialysis, to judge from the prompt alleviation of symptoms following this treatment.

Some renal disabilities appear to be intrinsically temporary since, given time, they disappear. Such impairments are called "reversible." If the kidneys are badly injured by inhalation of carbon tetrachloride fumes, or by mercuric chloride poisoning, renal excretion of toxic metabolites declines. The patient becomes uremic and, for a period, worsens steadily. If he does not run out of time, his kidneys eventually recover sufficient function so that he gets well. Reversible renal dysfunctions are also found following a patient's reaction to the transfusion of blood of the wrong type, following severe burns, and in other conditions. Treated conservatively, such individuals have been known to show spontaneous return of renal function after one, two, or three weeks, or even longer. Conservative treatment aims at preserving the *status quo* of the patient in as many dimensions of regulation as possible, as long as possible, using the usual hospital armamentarium. Although little can be done to

prevent completely, or to reverse, the steady rise of urea or more toxic metabolites in the body fluids in renal failure, the amount of water lost through cutaneous and pulmonary channels can be replaced almost quantitatively, and it is helpful similarly to replace the salt that may be lost in sweat, vomitus, and other excretions. Where acidosis sets in, akalinizing agents may be administered, and so on. Despite careful management, a sudden rise in the plasma concentration of potassium, released from cells that contain it in relatively high concentration, may early snuff out heart action and preclude further recovery.

How can one say that such patients, given time, might have recovered, when in fact they died? Actually the belief in potential reversibility of renal function is strongly supported by observations following hemodialysis. We now know of numerous instances in which conservative treatment has no meaning for survival. Consider a patient approaching terminal uremia: he has been steadily deteriorating, has become moribund, and by sober clinical judgement will probably die in a matter of hours or, at best, days. After several hours of hemodialysis an accumulation of toxic material is removed from his body. Coma becomes consciousness, then alertness. Where there were nausea and vomiting, there are appetite and hunger, and the patient's condition is now as it was perhaps a week previously in the course of his uremia. Or consider a woman, dialytically awakened from what should have been her final sleep, who can effortlessly, skillfully, and promptly lie about her age. If the underlying kidney defect persists, the patient's downhill course is renewed, but there are now several more days available to the recovery processes going on in, or in behalf of, the kidneys. If no renal improvement is manifest, the patient again passes into a highly critical condition, and a second hemodialysis can be performed with effect similar to the first. Even a third run might be considered, but by this time there will usually be some indication as to whether restoration of kidney function is likely.

Some who have observed clinical effects obtained with one or another of the various artificial kidneys will fairly protest these heart-warming clinical pictures. They have seen only indifferent results, or worse. If patients recovered, so much for coincidence. But those who have seen patients slip away and be pulled back once or twice, ultimately to recover, believe that critical, life-saving time is borrowed from hemodialysis. If this therapy is more effective than conservative treatment, one should expect to find a significant increase in the percentage of renal disabilities that ultimately reverse, where hemodialysis is undertaken. A statistical demonstration will have to wait until studies have been made in a larger number of more carefully screened candidates. Whether it is humane for the physician to yield to family pressure to "do everything possible" for the patient whose kidney tissue is almost assuredly irreparably damaged, and for him to bring such patients to the artificial kidney in the hope, but not the expectation, of giving lasting aid, is a moot question. Perhaps valuable information toward future developments is so provided. Nevertheless, there is little doubt that this practice mars the statistical record of hemodialysis. It is natural, meantime, that believers should be more articulate than skeptics, and that controversy as to the merit of this therapy should abound. There are evidences that not all hemodialyzers can provide the hoped-for statistics: On the one hand it seems clear that the dialytic capacity of some machines is less than that of others; but, on the other, there is testimony that indifferent or poor results may accompany "chemical cure."

Chronic renal disease, progressing slowly toward a degree of dysfunction incompatible with life, cannot usually be helped except transiently by the artificial kidney. Yet the sense of well-being that may result improves the prospect of instituting proper medical management which, emphasizing a low protein diet to minimize the production of toxic metabolites, is often effectively palliative (*22*).

Before leaving eristic matters, let us note additional treatments claimed of value in kidney disease. The most important of these are exsanguinotransfusion, or repeated withdrawal of uremic blood followed by replacement with normal blood, and lavage of the abdominal or intestinal cavities (*23*). Whatever their merit, they bring with them new and often trying procedural problems. They are usually less effective per unit time of therapy than hemodialysis, and time may be of the essence. Kolff (*5*) has studied in a man perfusion of a 1-meter intestinal loop, the ends of which were brought through the abdominal wall. Five grams of urea were removed in one 10-hour period. On another occasion (*24*) larger amounts were removed by way of a 2.5-meter loop. Concluding a lecture in 1947 (*25*), Kolff expressed the hope that in time he might see a patient "who is doing his work in the daytime and who is dialyzing himself through his intestinal loop during the night and in whom both kidneys will have been removed as useless, superfluous, and even dangerous organs."

At some point in thinking of uremia one wonders about operatively exchanging diseased kidneys for healthy ones. Even if there were no obstacle to setting up "kidney banks" or obtaining relatives, friends, or others willing to give up one of their own valued emunctories, the transplantation problem is fundamentally formidable. It is not too difficult surgically to autotransplant a kidney—i.e., to dissever it from its given vascular and other connections in an animal and suitably reconnect it in another site, say, in the neck of the same individual. Here it may carry on the urinary function successfully indefinitely. But homotransplants—i.e., transplants from one animal to another of the same species—behave as foreign bodies, provoke tissue reactions, and atrophy in a relatively short time. Such transplants have been found successfully to "take" and function adequately for some months (*26*), but greater success than this is unlikely in the present state of knowledge of tissue types. Heterotransplants—i.e., transplants from one to an-

other species—are even shorter-lived. A goat kidney connected to the circulation of a dog can kill the host promptly. It is supposed that the graded reactions to transplants vary with genetic relationship, antagonism being less the closer the donor's gene totality is to that of the host. If so, transplantation cannot now be considered the therapy of choice, except possibly in the case of identical twins.

"Natural kidney" physiologists frequently use a concept of "clearance." The renal clearance of a substance from the plasma is its rate of excretion per minute per unit plasma concentration. Dimensionally, clearance has the units of ml/min and represents the number of ml of plasma virtually cleared of the substance in one minute. In another way, it is the volume of plasma which contains that quantity of the substance excreted in the urine in one minute. Where the clearance remains constant at varying plasma concentrations, it may indicate that a load of the substance in the body disappears according to the law of exponential decay, much as a lump of radioactive material disintegrates. The kinetically related concept for the artificial kidney is that of "dialysance" (*18, 27*), defined as the net rate of exchange of a substance between blood (plasma) and bath per minute per unit blood-bath concentration gradient. At the beginning of hemodialysis (zero time), if a dialyzable substance is present in the plasma but not in the bath, the dialysance and the dialytic clearance are equal. With time, the dialytic clearance falls off, whereas the dialysance tends to remain constant. Thus, with natural renal excretion at constant clearance, we may speak of the half-life of a load of material; but not so with a bath type of artificial kidney. Here it is the concentration gradient that has a half-life. Table 1, which dilates upon a scheme of comparative nephrology proposed by Kolff (*5*), may be misleading unless this fact is kept in mind.

Moreover, it is not easy to generalize upon the relative excretory efficiencies of artificial and natural kidneys. Comparisons for urea are creditable but do not hint at the fact that in the excretion of a substance such as bromide, the artificial kidney can be distinctly superior to natural kidneys, whereas with *p*-aminohippurate the reverse may be the case. Occasionally a devotee of a bromide-containing proprietary remedy will ingest an amount of bromide causing an appreciable blood level of this material (normally not present except in traces), and bringing on a train of unpleasant or dangerous symptoms. As his natural kidneys view it, the rare and foreign bromide is not very different from the ubiquitous and natural chloride. These two ionic species possess a kind of "congruence" which causes them to be excreted similarly, and therefore competitively, by the natural kidney. This means that the rate of excretion of bromide is only in proportion (which may be small) to its fraction of the total halide, and that the natural bromide clearance is of the same small order of magnitude as that of chloride (1–2 ml/min). The artificial kidney, however, is largely oblivious to ionic mimicry. It permits bromide to be excreted at a rate proportional to its blood-bath gradient which, at zero time at least, implies a rate proportional to its own amount in the body without regard to total halide. And, as might be expected, its dialysance (and dialytic clearance) is large (*28*). In the case of *p*-aminohippurate, natural kidneys couple tubular secretion of this material to its filtration, giving, at least at low plasma concentrations, a natural clearance of some 650 ml plasma/min, which is far in excess of the present operational capacity of artificial kidneys.

Dialysances of different materials vary considerably, presumably reflecting different diffusibilities, permeabilities, and electric charges, among other things. With constant dialyzing surface, dialysances increase with blood flow, but when this is high, they take up relative values more or less characteristic of the particular molecular or ionic species. The ratio of the dialysance of a substance to that of urea measured simultaneously at any given flow is called the relative dialysance. *In vitro* experiments (*18*) at a flow of 500 ml/min have yielded the values shown in Table 2. The remarkable thing is that these hemodialyzers separate not merely colloidal from crystalloidal material but separate the different crystalloidal species. Fuller implications and applications of this phenomenon have yet to be discovered.

One looks to the future of artificial kidneys and hopes they will become smaller in bulk and weight, and still more effective. Some counterflow dialyzers (Figs. 3, 4) are at present quite small, but they remain with an irreducible bulk of dialysis fluid (and container) necessary to effect a desired degree of solute exchange in a given time, not to mention the bulk of thermostats and other appurtenances. It seems logical to advocate that increases be made in the dialyzing surface, the membrane permeability, and the blood flow in future hemodialyzers to improve their efficiency. Yet he who attempts to implement these disarmingly simple suggestions—incorporating the other desiderata as well—must live with some obstinate if not ineluctable facts of physiological engineering. Of course, some entirely different principle than differential dialysis for artificial kidneys may eventually be exploited; exchange resins have been tested (*29*), for example. This is the more credible inasmuch as natural kidneys do not themselves use the hemodialytic principle described here, so far as we know. In any event, it improves one's perspective to remember that the artificial kidney is merely another of the multifarious products of an engineering that gives us artificial eyes, teeth, breasts, limbs, and brains. The prosthetists are busy even now polishing their artificial heart valves, and it is not so difficult (for those who are not biochemists) to envisage the day of the factitious liver.

References

1. ABEL, J. J., ROWNTREE, L. G., and TURNER, B. B. *Trans. Acad. Am. Physicians*, **28**, 51 (1913).
2. ———. *J. Pharmacol. Exptl. Therap.*, **5**, 275 (1914).
3. ———. *Ibid.*, 611.

4. KOLFF, W. J., and BERK, H. TH. J. *Acta Med. Scand.*, **117**, 121 (1944).
5. KOLFF, W. J. *New Ways of Treating Uraemia.* London: Churchill (1947).
6. MURRAY, G., DELORME, E., and THOMAS, N. *Arch. Surg.*, **55**, 505 (1947).
7. ALWALL, N. *Acta Med. Scand.*, **128**, 317 (1947).
8. ———. *Ibid.*, **133**, (Suppl. 229), 20, 22, 30 (1949).
9. SKEGGS, L. T., JR., and LEONARDS, J. R. *Science*, **108**, 212 (1948).
10. SKEGGS, L. T., JR., LEONARDS, J. R., and HEISLER, C. R. *Proc. Soc. Exptl. Biol. Med.*, **72**, 539 (1949).
11. STERLING, J. A., and DOANE, J. C. *Urol. and Cutaneous Rev.*, **53**, 385 (1949).
12. VANATTA, J., MUIRHEAD, E. E., and GROLLMAN, A. *Am. J. Physiol.*, **156**, 443 (1949).
13. MERRILL, J. P., *et al. J. Clin. Invest.*, **29**, 412 (1950).
14. MERRILL, J. P., *et al. Ibid.*, 425.
15. ROSENAK, S. S., and SALTZMAN, A. *Proc. Soc. Exptl. Biol. Med.*, **76**, 471 (1951).
16. LOWSLEY, O. S., and KIRWIN, T. J. *J. Urol.*, **65**, 163 (1951).
17. MERRILL, J. P. *New Engl. J. Med.*, **246**, 17 (1952).
18. WOLF, A. V., *et al. J. Clin. Invest.*, **30**, 1062 (1951).
19. WOLF, A. V. *The Urinary Function of the Kidney.* New York: Grune & Stratton (1950).
20. LEONARDS, J. R., SKEGGS, L. T., JR., and KAHN, J. R. *Federation Proc.*, **10**, 214 (1951).
21. WOLF, A. V., KILEY, J. E., and CURRIE, G. D. *Ibid.*, 148.
22. MERRILL, J. P. *Ann. Internal Med.*, **33**, 100 (1950).
23. SNAPPER, I. *Bull. N. Y. Acad. Med.*, **25**, 199 (1948).
24. TWISS, E. E., and KOLFF, W. J. *J. Am. Med. Assoc.*, **146**, 1019 (1951).
25. KOLFF, W. J. *J. Mt. Sinai Hosp. N. Y.*, **14**, 71 (1947).
26. LAWLER, R. H., *et al. J. Am. Med. Assoc.*, **144**, 844 (1950); *ibid.*, **147**, 45 (1951).
27. WOLF, A. V., *et al. J. Clin. Invest.*, **30**, 683 (1951).
28. MERRILL, J. P. Personal communication.
29. MUIRHEAD, E. E., and REID, A. F. *J. Lab. Clin. Med.*, **33**, 841 (1948).

News and Notes

University of Illinois Conference on Physics of Ionic Crystals

ABOUT 70 physicists and physical chemists met at the University of Illinois Oct. 29–30 to discuss recent developments in research on the thermal, electrical, and optical properties of ionic crystals. Occasioned by the presence in this country of Robert W. Pohl, of the University of Göttingen, pioneer investigator in this field, and sponsored by the University of Illinois in cooperation with the Office of Naval Research, the conference was under the joint chairmanship of F. Seitz and R. J. Maurer. The formal program consisted of 19 invited papers, primarily on the alkali halides, of which about one third were theoretical in nature.

There seem to be two main reasons for the current interest in ionic crystals, particularly the alkali halides: (1) Many types of electrical, optical, and thermal measurements can be made on ionic crystals that cannot be performed, for example, on the more obviously interesting metals, but which nevertheless are related to phenomena occurring in all crystals. (2) The general properties of the alkali halides are probably better understood than are those of most other solids, so that new effects can be isolated and interpreted with relatively great confidence in the alkali halides and then generalized and applied to other crystals. For example, the effects of crystal imperfections, such as dislocations, vacancies, and impurities, are of first-order importance in the strength of structural materials, and these imperfections can be investigated in the alkali halides by a number of methods not available for metals.

One of the best ways of obtaining information about vacancies is through study of F-centers in the alkali halides. The F-center, almost certainly consisting of an electron trapped in a negative ion vacancy, is perhaps the most thoroughly investigated phenomenon in ionic crystals. Nevertheless, new experiments continue to be performed, and many new and significant data were presented on this subject. Burstein (NRL) described experiments demonstrating the effects of temperature and pressure in the width and position of the F-band in KCl, and showed that the results were in qualitative agreement with the simple particle-in-a-box model for the F-center. Scott (Oregon State College) discussed experiments on the optical and thermal coagulation of F-centers into larger aggregates, and determined activation energies for these processes.

Dutton and Maurer (University of Illinois) described electrical and optical measurements on KCl crystals which were allowed to heat up slowly from low temperatures. Associated with the disappearance of the V_1 absorption band and a diminution of the F and F' bands, they observed a large burst of thermally released charge and a flash of luminescence. These experiments indicate that positive holes are thermally released from positive ion vacancies at about $-130°$ C, wander to F-centers, and combine optically with the F-center electrons. When KCl crystals were irradiated with x-rays at liquid He temperatures, negligible production of F'-centers was observed, but there was normal darkenability in the F-band. This is somewhat surprising, since one expects a totally negligible number of isolated vacancies at these temperatures and insufficient thermal energy for appreciable diffusion of ions or vacancies. Markham and Duerig (Johns Hopkins Applied Physics Laboratory) also observed this large darkenability by x-rays at He temperatures, and it seems necessary to infer that the local heating arising from absorption of an x-ray photon is sufficient to allow the diffusion of vacancies. These experiments point out the extreme desirability of investigations designed to create F-centers at He temperatures by the relatively gentle means of irradiating in the tail of the first fundamental band. According to current ideas, the only negative ion vacancies present at He temperatures should be attached to dislocations