EXTRACORPOREAL HEMODIALYSIS*

MARIO BATTEZZATI, M.D. AND CARLO TADDEI, M.D.

Genoa, Italy

A. GENERAL

To understand the nature of extracorporeal dialysis, we believe that one should know the complex phenomena regulating the water exchange of a living being and the consequent electrolytic and protein equilibrium of the extracellular and intracellular liquids. The water of our body, representing 2/3rds of the body's weight, is the substance which transports the components of living matter and the substratum of every metabolic reaction. It is in continuous movement from one section of the organism to another, thus creating a perfect equilibrium of the so-called 'internal environment'.

We owe to Claude Bernard the conception of the 'internal environment'—with which the great physiologist succeeded in giving an exact biological definition of the essence of life in the living being. 'We must

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distinguish', he said, 'between the cosmic or outer environment, which completely surrounds the individual and the organic or inner environment, which is in immediate contact with the anatomical elements of which the living being is composed; every vital mechanism whatsoever has but one purpose, to maintain the unity of the conditions of life of the inner environment; this internal environment is composed of circulating liquid that surrounds and irrigates all the anatomical elements of the tissues; that is to say, it is the liquid part of the blood, which penetrates into the tissues and constitutes the whole of the interstitial liquids'. Later, Cannon called this dynamic equilibrium of the internal environment 'homeostasis'.

In the lowest order of living beings there is a situation of direct dependance of the internal environment upon the external environment, so that every variation of the later provokes a proportional variation of the internal equilibrium. Under such conditions, the life of the living being in relation to the external environment is a great deal easier, being reduced to the expression of elementary hydrosaline exchanges, surpassing by such an affirmation the philosophical concept of vital energy contained and outlined in matter. This hydrosaline flux and reflux between the environment and the living being (the internal environment of which is thus a part of the same environment), tends to level itself, just as a liquid tends to acquire the same level in two connecting jars. On the contrary, in living beings of the higher orders, the internal environment is independent of the external environment. This independence and liberty is dearly bought and maintained at any price, on pain of loss of life itself. The living being is thus in a continual struggle against the external environment to maintain its own physical individuality invariably, being inclined to favour its own independence and liberty.

And, as in the life-relationship the voluntary nervous system is the means by which man defends himself as a whole against the external, disintegrating elements, so in the life of the tissues and organs, neurovegetative and hormone factors preside in the equilibrium of the internal environment. This equilibrium is closely tied up to the hydrosaline exchange, meaning the variations in the amount of water and of the elements contained in it, in regard to the determining factors of osmotic pressure and acid-base equilibrium. Our organism may be imagined as a great lake of salt water in which the cellular elements are immersed. Into it are continually poured the most varied substances, which the organism disintegrates and modifies in order to make use of them if they are necessary to life or to eliminate them if they are superfluous or damaging. There are, therefore, some organs which have the very delicate and difficult function of maintaining at any cost the substances of the inner environment, eliminating the metabolic substances which would be damaging. Among these organs the most important and delicate is certainly the kidney.

This great lake-source of life is divided into various sections in which, on one hand, first consideration is given to the intracellular liquids, as water in vital combination and extracellular liquids make up the blood and interstitial liquids. The extracellular liquids play an extremely important role of defence and of balance between the cells on one side and the function of the emunctories and the kidney in particular, on the other, acting as a buffer for the variations coming from the outside.

There is, therefore, at one end of the cycle, the cell with a limiting membrane that functions as a dialyzing membrane but also has a secreting and discriminating power on the substances it gives up or acquires. At the other end of the cycle are the emunctory organs, first amongst them the kidney, which maintains the balance of the internal environment. Between the two end-pilasters of the system, cell and kidney, there is the bulk of extracellular liquid that is in continuous hydrosaline equilibrium, in which the vascular walls have, among other functions, the typical one of the dialyzing membrane. Also a part of this system is the glomerular filtrate which, later, is regulated and discriminated by the secretive activity of the renal tubules that recovers most of it according to plasmatic needs.

Summing up: In physiological conditions there are two fixed points with immutable laws; the cell on one side and consequently the renal excretory and secretive function on the other. Between these two extremes there are various communicating sections divided by dialyzing membranes which maintain an internal environment sufficiently balanced and consonant with the vital needs of the cell.

It should here be noted parenthetically that the interstitial liquids are practically an ultrafiltrate of the plasma as is the glomerular or preurine filtrate.

Two fundamental factors dominate the regulation of such a system of internal equilibrium, viz. *osmotic pressure* and *acid-base equilibrium*. The first is sustained by all the particles of the substances dissolved in the water, and consequently the smaller the particles (molecules or ions) the more they are proportionate to high osmotic pressure; thus the salts dissolved are largely responsible for the values of this pressure. The acid-base equilibrium has as substratum the ions dissolved with their electric charge, which may be negative or positive. Such equilibrium is regulated by the tampon system established by the relation between carbonic acid (H_2CO_3) and carbonates ($BHCO_3$), a relation that must remain fixed in physiological conditions (1 : 20).

We should like at this point to make it clear what is meant by osmotic pressure. If an aqueous solution is put in contact with water through a membrane of vegetable or animal origin (dialyzing membrane), the solution tends to penetrate the water (exosmosis) in order to balance itself, while the water tends to pass into the solution (endosmosis). This phenomenon is the fundamental element of the hydrosaline balance of our inner environment, conditioned by and closely connected with, the acid-base equilibrium. But what seems to us to need clarification, and what is surely essential to a large comprehension of the complexity of the problem, is the fact that to obtain osmotic balance the water shifts rapidly from one section to another (endosmosis) while the salts move more slowly in the opposite direction (exosmosis), so that the balance is more quickly obtained with the less damaging and more mobile element. And this, we repeat, seems to us a fundamental element in the mechanism of hydrosaline balance. It comes from the apparently paradoxical fact that the elements at highest osmotic pressure—for example chlorine and sodium in the extracellular liquids—penetrate more slowly into the cells while they draw water rapidly from them.

To the two factors in the play of the movements of water and salts thus expounded, must be added the *absorbent factor or oncotic pressure* exercised by the proteins on the water, through which this element becomes a part of the complex regulation of the going and coming of this same water. It might be said that the proteins exert on the water an action similar to inertia so as not to create excessive unbalance and displacements. They have, furthermore, great importance in recalling the water from the extracellular spaces in the venous capillary system where the hydrostatic pressure, which was high in the arterial region, has necessarily fallen.

Very briefly, and with only elementary and inadequate facts and imagery, we have tried to illustrate the complexity of the phenomena inherent in hydrosaline exchange and in the maintenance of homeostasis of the human organism. Impinging upon what we have said is a concept which is at the base of all these vital phenomena; that is, the *concept of dialysis*, which arises from a particular property already illustrated, of the vegetable and animal membranes. The concept of dialysis thus brings us back to this particular activity of the animal and vegetable membrane which governs in an elastic manner the equilibrium of the solutions placed in contact through it. In fact, with its special dialyzing properties, it performs the function of mixing up the two solutions, making them rapidly equal in the content of the particles of the solute. The rapid passage of the water from one section to the other through the membrane may remind us of the function of an agitator, which makes any solution whatsover uniform.

Dialysis in the Kidney

Such a dialyzing property is also a fundamental one of the kidney which, in its glomerular function and in the first tract of the tubule, carries on the formation of an ultrafiltrate plasma entirely similar to that of the interstitial liquids. This filtration in the glomerule is essentially subject to the action of the hydrostatic pressure of the blood in the same manner that, in the capillaries, hydrostatic pressure is the fundamental factor in the escape of the liquids into the interstitial spaces. Therefore, immediately afterwards, in the first part of the tubules, there is a phenomenon of dialysis through the difference of osmotic pressure between plasma and content of the tubules, by which a great quantity of water and salts (85% in water) is reabsorbed. This phenomenon is called iso-osmotic reabsorption. Finally, in the terminal tract of the tubules occurs a selective and discriminative action of the tubular cells, whose biological activity leads to an active reabsorption of liquids and substances against the same force of osmosis. There is thus formed a hypertonic liquid by which occurs the so-called phenomenon of concentration of the urine. This activity is dependent upon the antidiuretic hormone of the posterior lobe of the hypophysis.

The renal function is, therefore, one of the fundamental elements in the regulation of the interior environment of our organism, for which reason MacCullum (rightly stating that the establishing of a closed aqueous system has been the greatest victory in the history of animal organism) defined the kidney as the evolutionary organ *par excellence*. But what we should like to bring out at this point is that in the kidney, in as far as we have described it above, there occur in a brief space the same phenomena, dominated by the same forces, that we find in the various sections that we have described of our organism. That is to say, the glomerular function creates an ultrafiltrate of plasma as does the arterial capillary, and this phenomenon is controlled in both by hydrostatic pressure. A large part of the ultrafiltrate in the initial tract of the tubule passes into the blood, as from the interstitial spaces liquid re-enters into the venous capillaries, by a phenomenon pure and simple of dialysis controlled by osmotic pressure and by oncotic pressure. Finally there occurs in the distal tubule a biological activity of selection and discrimination with a well-defined finality, just as in the cells opposite the interstitial liquids there is manifested that complex of biological phenomena that gives consistency and reality to the life itself of the whole organism.

Summing up, therefore, whether in the various sections of the organism (vascular system, interstitial spaces, cell), or in the corresponding sections of the kidney, the hydrosaline exchanges occur in schematic line in the reciprocal and alternating play of 3 fundamental forces: *hydrostatic pressure or blood pressure, dialysis sustained by osmotic pressure, and the highly definitive biological activity of the cell.* Naturally other factors, which we have already acknowledged, impinge upon these various phenomena; i.e., the acid-base equilibrium, the oncotic pressure of the proteins, the gaseous exchanges, etc. We know fairly well how the hydrosaline exchanges of the plasmatic section and of the interstitial liquids (i.e. of all the extracellular section) occur; we are still very ignorant about what occurs through the cell membrane and in the cell proper, representing the biological entity of life itself. All that we know is given us by the complimentary image of the phenomenology of the extracellular liquids and of the true and proper renal functions. Research on the renal function, on the urine, and on the extracellular liquids with the physiological and pathological variations of their hydrosaline exchange can, in part, disclose or at least indicate what occurs in the mysterious forge of the cell.

Now, if we may easily study and vary the balance of the internal environment, that is, the extracellular liquids, using the same forces and exploiting the same physio-chemical laws, we shall have in our possession a formidable instrument that, like a mirror, reflects to us what occurs in such an internal section of our organism, and consequently the possibility of studying and varying for experimental purposes or of correcting for therapeutical ends, the so-called internal environment. Here according to us, is what should be the purpose and the value, the limits and the possibilities, of so-called extracorporeal dialysis. *Attempting a definition of what would be a perfect extracorporeal dialysis, we should say that it consists of the possibility of reproducing, outside of the organism, the same conditions of exchange which occur in the extracellular section of our organism, so that the maintenance of the constancy of the inner environment is in part transferred from the kidney to the dialyzer controlled and regulated by man himself.* Ideally, therefore, if we are sufficiently knowledgeable about it, the dialyzing apparatus should be the revealer and the regulator of the conditions of the internal environment. Here is why the problem, conceived in this manner, is no longer seen under the guise of an artificial kidney, which would be at the same time too much and too little, but as a simple extracorporeal hemodialysis.* The problem thus acquires not only a clinical and therapeutical value but certainly a high biological value.

What are the factors on which we may play in extracorporeal dialysis? Essentially two: hydrostatic pressure and osmotic pressure, and to these is added the oncotic pressure of the protein substance. By drawing off the blood of our organism in special tubes with a dialyzing wall having properties similar to that of the sanguineous vasa, tubes that are immersed in a saline solution, we reproduce the conditions existing in the extracellular liquids, which are dominated in large part, as we have already said, by the hydrostatic pressure of the blood, by osmotic pressure and by oncotic pressure of the proteins. Now, if we wish to confront the problem from a practical view-point, there are two determining factors for bringing about extracorporeal dialysis: *circulation* of the blood outside *of the organism* with all the related problems of hemodynamics, and *dialysis true and proper*, closely related to the property of the wall of the tube in which the blood runs, and to the composition of the bath.

B. HEMODIALYSIS

Up to now we have considered the problem of hemodialysis from a general view-point and we have explained how such a therapeutic instrument, according to us, might be used to restore a functionally regressive, altered electrolytic equilibrium. We shall now examine briefly, from a technical view-point, dialysis, extracorporeal circulation of the blood, the characteristics of our apparatus and our clinical experience.

In physiology *dialysis* means the process by which a colloidal solution (protein) frees itself from the salts dissolved in it. Dialysis through a cellophane membrane is governed by the same physical laws that control the passage of water and the substances dissolved in the plasma and in the interstitial liquids through the capillary wall on one side and the cellular membrane on the other. Naturally, however, both the capillary and the cell manifest a discriminative activity on the various substances that the cellophane membrane does not and cannot have.

The transportation of the water and the substances dissolved in the plasma is, therefore, in function with all those forces which act in liquid and on liquid. They are:

1. Hydrostatic pressure. By increasing or decreasing the pressure on the outside or on the inside of the filtrating membrane, the filtration increases in one direction or another.

2. Force of diffusion or osmotic pressure. The molecules of a substance dissolved in water are in continuous movement like the free molecules of a gas. Such movements generate the process of diffusion, performed through a membrane and proportional to the square root of the porosity of the membrane. Furthermore, every substance has its coefficient of diffusibility which varies in relation to (*a*) the temperature, (*b*) the percentage of the substance dissolved in the solution, and (*c*) permeability of the membrane.

3. Difference of electric potential. A difference in concentration between two solutions separated by a dialyzing membrane is caused by the shifting of ions, because a polarization is created and, therefore, a difference in the potential of the two sides of the membrane.

As in biology any cell presents in a functional sense a membrane which limits the protoplasm and which has different dialyzing properties, so in physiology there are different membranes.

There are two fundamental types of artificial membranes, viz. dialyzing membranes and semipermeable membranes:

1. Dialyzing membranes (parchment, cellophane, colloid) are permeable to water and crystalloids and impermeable to colloids (proteins). These are used in constructing dialyzers.

2. Semipermeable membranes (precipitated colloidals —ferrocyanide of copper) are permeable to water and more or less impermeable to all or part of the crystalloids, i.e., to the dissolved substances. Such membranes are used in making ultrafilters and are also commonly used to relieve the osmotic pressure exercized by a dissolved crystalloid. In fact, by not permitting the diffusion of this crystalloid towards the water, they oblige the water to pass into the solution and dilute the concentration of the crystalloid until the hydrostatic pressure produced counterbalances the osmotic pressure.

Between the type of dialyzing membrane that keeps back only proteins and the type of theoretical semipermeable membrane that keeps back also all the crystalloids, there is an entire intermediate range of membranes which behave in a special way with regard to one or more crystalloids.

In the artificial kidney dialyzing membranes are used which keep back only proteins, so that, wherever possible, either dialysis or osmotic and ionic equilibrium is obtained.

We will now examine those factors in whose function it is possible to modify dialysis. They are (1) the nature of the dialyzing membrane, (2) the shape of the dialyzing membrane (leaf or tubular), (3) the disposition of the membrane (in series or in parallel), (4) the output per minute of blood, (5) the dialyzing surface, (6) the composition, direction and temperature of the dialyzing bath, and (7) the means for maintaining or varying the water balance between the blood and the dialyzing

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* 'Hemo'-spelling retained in this article.

bath (hydrostatic pressure, ultrafiltration, oncotic pressure).

1. *Nature of the dialyzing membrane.* As a rule, membranes of cellophane without imperfections and, at the moment of use, free of the glycerine which normally covers them, are used. Dialysis varies in function with the thickness of the membrane and with its porosity, inasmuch as the diffusion of the molecules and ions through it is inversely proportional to the square root of its porosity.

2. *Shape of the dialyzing membrane.* The dialyzers may use two types of cellophane membranes, leaf or tubular. As a matter of principle it seems that all researchers have become orientated in the use of tubular membranes, since dialyzers made with this type of membrane offer a greater guarantee of use, ease in setting up, and the certainty of a good distribution of blood in the dialyzer itself.

3. *Disposition of the dialyzing membrane.* Each type of membrane may be disposed either in series or parallel. The dialyzer in series is the type in which all the blood discharges per minute are extracted from the patient through the same section of a dialyzer. The dialyzing surface then functions according to the length of the cellophane (if tubular membranes are used) or in the number of dialyzer elements (if dialyzers of cellophane leaves are used). In the parallel dialyzer, on the contrary, the blood discharge per minute extracted from the patient is divided into equal parts in the diverse dialyzer elements placed parallel (whether they are tubular or leaf) and the dialyzing surface depends exactly upon the number and the length of the single elements. Whether in the series or the parallel system, the discharge per minute at the entrance of the dialyzer system will be equal to the final discharge per minute, and therefore the output of the parallel or series systems will be nearly equal.

4, 5, 6. *Output per minute of the blood. Surface of dialysis and discharge per minute of the dialyzing bath.*

It would be interesting to establish the variations in the output of the artificial kidney in relation to the variations of the discharge per minute of the artificial kidney, of the dialyzing bath and of the dialyzing surface, in order to be able to vary these elements so as to obtain in the most opportune manner the maximum output from the artificial kidney with the minimum injury to the patient. One may conclude that:

(*a*) To evaluate the output of the artificial kidney in experimental and clinical practice, one would do well to make full use of the index of dialysis;

(*b*) To evaluate the work accomplished by the artificial kidney in a unit of time one might make use of the index of extraction and of clearance. Such indices may be utilized advantageously when one wishes to make comparisons of the output in the unit of time. In the artificial kidney the concept that a greater clearance corresponds to a greater output is not valid. To the increase of the discharges per minute of the artificial kidney there corresponds a contraction of the clearance and of the index of extraction, while the index of dialysis and the dialyzer total are increased.

(*c*) An increase in the index of the dialysis corresponds to the increase of the discharges per minute of the artificial kidney, of the surface of dialysis and of the discharges per minute of the dialyzing bath.

(*d*) In special clinical conditions, however, it would be advisable to make as much use as possible of those variants of technique which have no influence on the condition of the patient (as the discharges per minute of the dialyzing bath) and to select those values of the discharges per minute of the artificial kidney and of the surface of dialysis that express, in these special conditions, the optimum output of the artificial kidney.

(*e*) It is possible to increase the output of the artificial kidney by altering the discharge per minute of the artificial kidney or the surface of dialysis, but such alterations may, for various reasons and under special conditions, not conform to the conditions of the patient.

In every case it will always be expedient to increase the volume of the discharges per minute of the dialyzing bath.

7. *Means of maintaining or varying the water balance between the blood and the dialyzing bath.*

In the artificial kidney, the dialyzing bath and the blood which circulates in the dialyzer system are separated by a disposing, dialyzing membrane which prevents the escape of the plasmatic proteins and permits, instead, the passage of diffusable substances (water and electrolytes). There is, therefore, the possibility of ionic exchanges through the cellophane membrane and the setting up, through this membrane, of an electrolytic equilibrium brought about through the osmotic exchanges which cause movements of water and salts when they are exactly controlled by the differences in ionic concentration between the blood of the extracorporeal circuit and the dialyzing bath. For this reason the cellophane membrane behaves analogously to the capillary wall, it also being permeable to water and to the electrolytes and almost impermeable to the proteins.

The force of attraction of the water by the proteins, so important in the physiolgy of the exchanges between plasma and interstitial liquids (which occurs through the side of the capillaries), intervenes also in the exchanges which occur between blood and dialyzing bath in the artificial kidney. It is, therefore, necessary to insert into the study of the artificial kidney the concept of the measure of the force of attraction of the water by the proteins as they occur in the exchanges between the plasma and interstititał liquids. The force of attraction of the proteins as creators of oncotic pressure is about 25-30 mm. of Hg, i.e. 30-40 cm. of water.

In the human body the exchanges of water through the capillary wall depends upon two contrasting forces; on one side a hydrostatic force, arterial pressure, which tends to make the water go out from the vasa and pass into the interstitial liquids, and on the other side oncotic pressure, which tends to keep back the water in the same vas. The water escapes from the vasa into the interstitial spaces or passes from the interstitial spaces to the capillaries, according to which of these forces prevails over the other. From the finalistic view-point, these intense exchanges of water between the blood and the tissues are not as important as the ones which occur on the level of the cellular membrane and on the level of the renal tubule.

All the extracellular liquids have the same ionic concentration and the same composition of azotase substances (expression of cellular catabolism). They represent the indispensable hyphen between the life of the cell and the excretory function.

The precise division of the extracellular liquids into two sections, plasmatic liquids and interstitial liquids, is accounted for by an exclusively technical problem, a problem of hydraulic necessity and irrigation. Even nature may find it difficult to irrigate every cell with a capillary; evidently for this reason the submerging of the cells in a transporting liquid (total extracellular liquid) was made necessary, but this liquid would be too static if it were not continuously agitated by a strong and continuous movement provoked by the differences between oncotic pressure and hydraulic pressure which occur on the level of a vascular tree, very diffused, indeed, but limited in the number of cells served.

In the artificial kidney the blood present in the cellophane membranes is consequently found in contact with a saline solution which surrounds it. It is found, that is, in the same conditions as the blood in the venous capillaries. Except that a failure in the dialyzer does not cause artificially hydrostatic pressure and a failure in the dialyzing bath, oncotic pressure. There is, therefore, present in the blood only oncotic pressure of the plasmatic proteins and attraction of water from the dialyzing bath to the blood.

The water balance between the blood in the cellophane and the dialyzing bath may be obtained in the artificial kidney in two different ways, viz.: (*a*) by hydrostatic pressure or ultrafiltration and (*b*) by the increase of the oncotic pressure of the bath:

(*a*) *Regulation by hydrostatic pressure or ultrafiltration.* If a hydrostatic pressure equal to the oncotic pressure of the proteins in the blood itself is produced in the blood contained in the dialyzer system, a water equilibrium between blood and dialyzing bath is obtained. If the hydrostatic pressure of the blood contained in the dialyzer is superior to the oncotic pressure of the proteins, there might be a passage of water from the blood to the bath with consequent hemoconcentration, i.e. dehydration. By analogously decreasing the hydrostatic pressure, hemodilution, i.e. hydration, may be obtained.

Some types of artificial kidneys are based upon hydrostatic pressure to maintain water equilibrium and to hydrate or dehydrate the blood circulating in the dialyzer system. They have in fact succeeded in causing a passage of water from the dialyzing bath to the blood, varying the hydrostatic pressure of the blood contained in the dialyzer from 5 to 30 cm. of water, and from the blood to the dialyzing bath by varying the hydrostatic pressure of the blood from 39 to 55 cm. of water. With the hydrostatic pressure varying from 30 to 39 cm. of water, a perfect water balance between the blood contained in the dialyzer and the dialyzing bath may be obtained. In fact, the hydrostatic pressure of 30-39 cm. of water balances the oncotic pressure of the plasmatic proteins, which is 25-30 mm. Hg.

Another system utilizing hydrostatic pressure to control the balance between blood and dialyzing bath is ultrafiltration. A marked depression is effected, both in the blood and in the dialyzing bath, with ultrafiltration, so that a passage of water and salts (plasmatic ultrafilter) is caused from the blood to the dialyzing bath.

(*b*) *Osmotic and oncotic pressure in the dialyzing bath.* By varying the oncotic pressure in the dialyzing bath, the water balance between blood and dialyzing bath may be controlled so as to keep the hydremia unaltered, increased or diminished. Some authors have met the problem by adding gum arabic or soluble amylum, but such studies were abandoned because these colloids did not guarantee sufficient purity or practicality and control of the value of pH in the salt solution was difficult. The same objective was also sought by raising the osmotic pressure of the dialyzing bath with high concentrations of glucose, but such studies did not achieve satisfactory results because if the amount of glucose added to the bath was too little, the osmolarity of the bath was not sensibly increased (and therefore obtained no effect), and if the amount of glucose was too high, there was an increase of glycemia (the glucose passed in effect easily through the cellophane membrane).

C. HEMODYNAMICS IN EXTRACORPOREAL CIRCULATION

In the artificial kidney, the characteristic techniques of extracorporeal circulation are of tremendous importance. The techniques of derivation and re-deposit of the blood from and to the patient are numerous and may be summed up as follows:

Arteria-vena derivation. The blood is drawn out from an artery and after having been dialyzed it is redeposited in the patient through a vein. Under such conditions it is the patient's heart which pushes the blood in the extracorporeal circuit (e.g. Alwall's kidney).

Arteria-vena derivation with the aid of a pump. The blood is drawn out of an artery and after having been dialyzed it is redeposited in the patient through a vein with the aid of a pump. The patient's heart pushes the blood in the first section of the extracorporeal circuit, dialyzer included, while a mechanical pump moves the dialyzed blood from the dialyzer to the venous bed (e.g. Merril's kidney).

Vena-vena derivation. Both the drawing out and redepositing of the patient's blood is done through the venous passage. The extracorporeal circulation of the blood, both in the extraction and redepositing sections, is assured by one or more mechanical pumps. This extraction and redeposit may be effected by using one vein (rhythmic alternating flux) or two veins (e.g., Battezzati-Taddei kidney).

In the 1st type of derivation cited (arteria-vena) it is practically impossible to regulate independently of each other the discharges per minute of the flux of extraction and redeposit. In the 2nd type of derivation (arteria-vena with the aid of a pump) the regulation of the amount of blood drawn out and of the amount redeposited will depend upon the coordination of the discharge per minute of the mechanical pump with that of the cardiac pump, and for this reason it is not feasible to achieve and maintain hydraulic equilibrium in the extraction and redepositing sections. In the 3rd type of derivation (vena-vena), it will be necessary to coordinate properly the discharges per minute of the mechanical pumps to obtain hydraulic equilibrium.

D. TECHNICAL DESCRIPTION OF THE APPARATUS

On the basis of our direct experience with certain models of artificial kidneys made by us, and on the basis of studies by other authors who have been concerned with this subject, we have constructed in the last few months a new type of apparatus which corrects, according to our view-point, some of the characteristics in the preceding apparatus which did not satisfy us.

We shall observe some particular aspect of the problem, taking as standards of comparison some of the models of the artificial kidney most widely used today in clinical practice, viz. Kolff's kidney, achieved by the A.C.M.C., Alwall's kidney, and the third (1954) model of our artificial kidney. In the first place we shall examine *the problem of hemocirculation.*—Kolff's kidney is based principally on the coordination of the arterial flux of the patient with the discharges per minute of the mechanical pump designed for the re-introduction of the blood after dialysis. It seems clear to us that, although maintaining an extracorporeal hydraulic balance under such conditions is possible, it is somewhat questionable and delicate. In fact, a loss of control may easily be the cause—especially in a system like Kolff's, which uses a free dialyzer—of interference between the two circulatory divisions, corporeal and extracorporeal, with immediate repercussions on the circulatory hemodynamics of the patient. In any case,

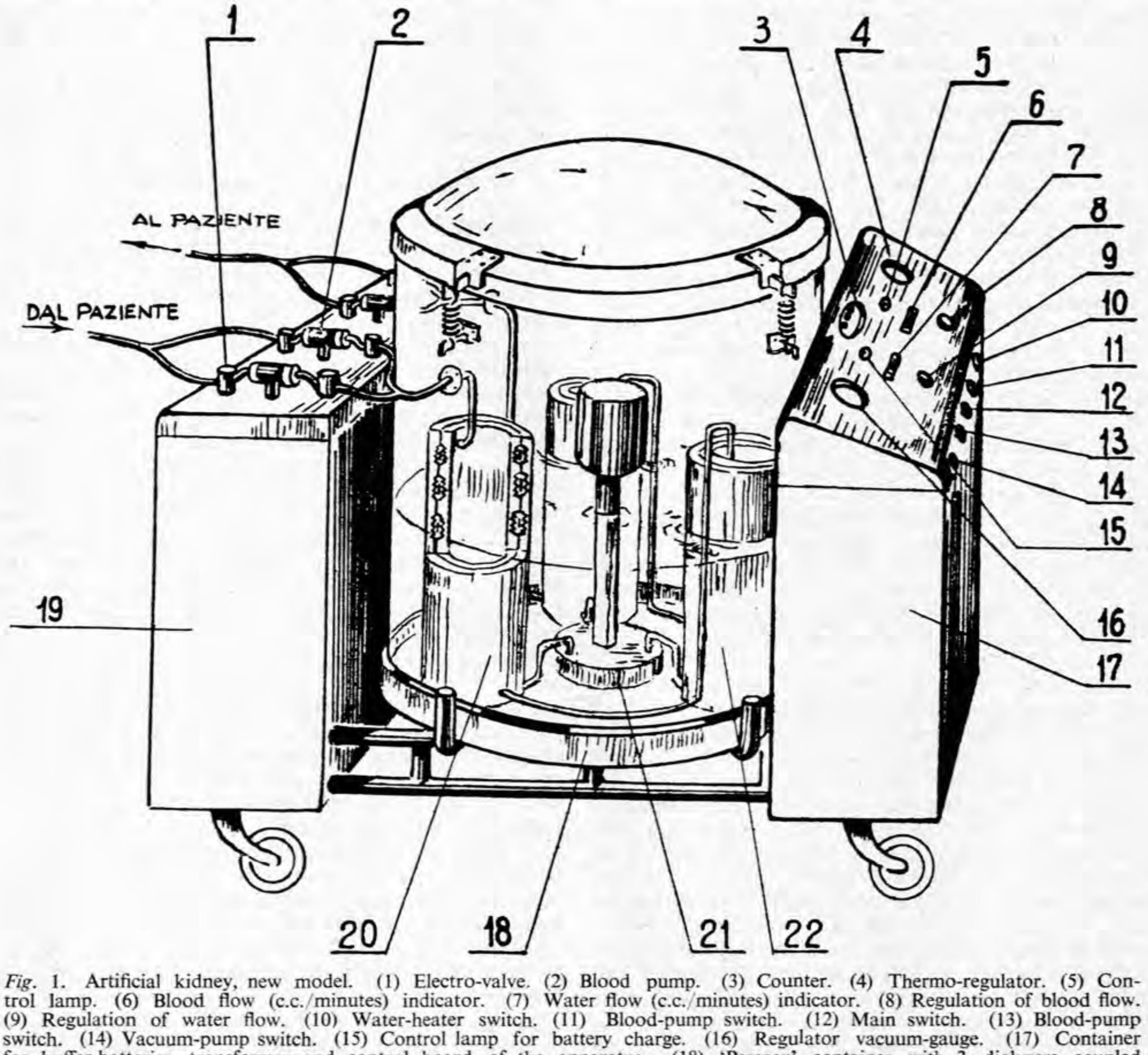

Fig. 1. Artificial kidney, new model. (1) Electro-valve. (2) Blood pump. (3) Counter. (4) Thermo-regulator. (5) Control lamp. (6) Blood flow (c.c./minutes) indicator. (7) Water flow (c.c./minutes) indicator. (8) Regulation of blood flow. (9) Regulation of water flow. (10) Water-heater switch. (11) Blood-pump switch. (12) Main switch. (13) Blood-pump switch. (14) Vacuum-pump switch. (15) Control lamp for battery charge. (16) Regulator vacuum-gauge. (17) Container for buffer-batteries, transformer and control board of the apparatus. (18) 'Perspex' container with 3 dialyzers coupled in series and pump for dialysis bath. (19) Container for the reducing motor and blood-pump engine. (20) Cross-section of the dialyzer. (21) Water pump. (22) Dialyzer.

by comparison with that of Alwall, Kolff's system presents some advantages which we consider rather important.

Alwall did not use any pump for the course of blood in the dialyzer, but only the arterial *vis a tergo*. Alwall's dialyzer differs notably from Kolff's in that the tubular cellophane membrane is compressed between two areas and, by not being able to dilate beyond given limits, prevents the setting up of a hemorrhage caused by the apparatus. Under such conditions the arterial blood circulates in all the closed circuit and returns to the venous circle of the patient. This method, however, does not allow a control of the amount of blood that passes in the dialyzer in unit time, or modification of the discharge per minute at will according to the circumstances.

Moreover both types of apparatus, Kolff's and Alwall's, present the serious inconvenience, according to us, of having to sacrifice an artery of considerable importance. Basing ourselves precisely on the total of these observations, we first achieved (model III 1954 artificial kidney Battezzati-Taddei) a system of hemocirculation which utilized, for taking out and putting back of blood, one or two venous passages. A rotating pump on rollers allowed a variation of discharges per minute varying from 10 to 200 c.cm. In such manner, with the extracorporeal circle filled with a donor's blood, the patient's circle is in a condition of complete independence from the extracorporeal circle. Many important advantages over the techniques described above were thus obtained. Clinical experiment conducted in the meantime has, however, shown us that it is possible to bring some important modifications to this system. Indeed, today we maintain that, in an extracorporeal circulation technique that is prolonged for several hours, any element whatsoever that may influence the cardiac dynamics, even in a limited way, must be eliminated. In line with this principle, we have today abandoned the system of rhythmic aspiration and reintroduction of the blood in the patient. With such a type of derivation, the patient's heart must, indeed, work in rhythmatically unstable conditions—in one period with a greater venous discharge and in the succeeding period with a diminished discharge.

The system achieved by us today (Fig. 1) allows a complete equalization of the amount of blood drawn out and put back contemporaneously through two different catheters or through one catheter with a double body. The control of the discharges per minute is absolutely secure since—the capacity of the blood contained in the small lungs (*a*), (*b*), (*c*) and (*d*) being constant—the variations of the discharge depend exclusively on the variations of the pulsating rhythm of the same. This indirect control of the discharges per minute is, we repeat, of very marked clinical interest.

Having examined the various types of derivations and propulsion of blood, we shall now examine *the problem of the dialyzer*. We shall take always as standards of comparison the dialyzers of the 3 artificial kidneys used the most in clinical practice (Kolff, Alwal, Battezzati-Taddei). All three of these dialyzers use the tubular cellophane as a dialyzing element. In Kolff's dialyzer the tubular membrane is used in one thickness (dialyzer in series) wound in close spirals on a horizontal rotating cylinder. The same is true of Alwall's dialyzer but, while in Kolff's the tubular membrane is free, in Alwall's it is compressed by a mantle in a section fixed beforehand so that it cannot dilate and, moreover, the cylinder is vertical and immovable. In the 1954 model of the Battezzati-Taddei dialyzer, the tubular membranes are placed parallel, free in a dialyzing bath.

Of these 3 dialyzers, the most rational from a practical view-point is surely Alwall's, since the fixed position of the cellophane tube has prevented hemorrhages caused by the apparatus, i.e., the excessive filling of the tubular membrane with the patient's blood that may be the cause, evidently, of the decompensation in the circulatory dynamics of the patient. On the contrary, in Allwall's dialyzer, again from our view-point, the circulation of the dialyzing bath is not satisfactory. This type of dialyzer, however, offers the advantage of being able to practice ultrafiltration inasmuch as it is closed in a perfectly air-tight container.

In Kolff's dialyzer it is not possible to effect ultrafiltration, and moreover the open system does not assure us of the constancy of the quantity of blood contained in the dialyzer itself. The rotation of the cylinder, however, in contrast to Alwall's dialyzer, assures a better utilization of the dialyzing bath since the blood runs against the current to the dialyzing bath itself.

In the dialyzer model 1954 Battezzati-Taddei it is not possible to effect ultrafiltration, and it is difficult to maintain constant the blood contained in the dialyzer itself. The utilization of the dialyzing bath is, on the contrary, excellent, since it runs against the current in the direction of the blood.

By considering all these elements, we have achieved a dialyzer which offers noteworthy guarantees of use and output. It utilizes as always the tubular cellophane membrane as dialyzing element, wound on 3 cylinders connected in series. All 3 of the cylinders are protected by a mantle which permits exact control of the amount of blood contained in the dialyzer. The dialyzing bath runs against the current for the entire length of the tubular membrane. The 3 cylinders are placed in a perfectly water-tight recipient so that it is possible to effect ultrafiltration (Fig. 1).

E. CLINICAL EXPERIENCE

In Table I we sum up the results achieved with hemodialysis. Even in its limitations, our experience may give some useful clinical indications. We realize, however, that it is incomplete. We have divided the morbid processes according to Allen's scheme into (1) glomerulonephritis, acute and subacute, (2) tubular nephrosis

TABLE I

	No. of cases	*No. survived*
Glomeruleonephritis, acute and subacute ..	6	4
Tubular Nephrosis:		
Lower nephron nephrosis	1	0
Nephrosis of the proximal nephron ..	3	1
Chronic glomerular nephritis	6	1
Nephrosclerosis	1	0
Polycystic kidney	1	0

of the lower nephron and (3) nephrosis of the proximal nephrons, (4) chronic glomerulonephritis, (5) nephrosclerosis and (6) polycystic kidney.

On the basis of our limited statistics we may affirm that, as a general rule, hemodialysis can be carried out in renal insufficiencies in which the lesion is prevailingly glomerular, and chiefly in the acute forms, while only negative results can be registered in the chronic forms, given irremediable irreversibility of the lesion. Renal insufficiencies attributable to alteration of the tubules may be greatly relieved. In a case of polycystic kidney or nephrosclerosis, no result can be expected from hemodialysis.

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Battezzati, M. and Taddei, C.

NATIONAL NUTRITION COUNCIL

RECOMMENDED MINIMUM DAILY DIETARY STANDARDS

COMPILED BY THE DIETARY STANDARDS COMMITTEE OF THE COUNCIL

1. In 1935, the League of Nations[1] made the first attempts to define man's daily requirements of specific nutrients in quantitative terms. The Committee on Foods and Nutrition of the United States National Research Council published a much more detailed table in 1941 which was adapted to South African conditions by the National Nutrition Council in the following year. The American figures were revised in 1945, 1948 and again in 1953. In 1953 the National Nutrition Council of South Africa decided to revise its own standards and in the present report the existing knowledge of the subject is applied to the somewhat unusual circumstances of a country with a mixed population that varies greatly in its dietary habits and occupations.

Existing Standards

2. The Dietary Standards of the Food and Nutrition Board of the National Research Council (NRC) of the USA are recommendations and not requirements 'since they represent, not merely minimal needs of average persons, but nutrient levels selected to cover individual variations in a substantial majority of the population. . . . The nutritive intakes recommended are, in general, higher than the average requirements and lower than the amounts which may be needed in pathologic states or in rehabilitation following depletion'.[2]

3. The figures given by the Committee on Nutrition of the British Medical Association, 1950[3] are intended to be adequate for the maintenance of a good nutritional standard for healthy persons. These standards also do not make provision for sickness or convalescence.

4. The standards of the Canadian Council on Nutrition (1950) are even lower than the British, and serve as a basis for determining food supplies of groups, and can also be used for judging the adequacy of the food intake of individuals, or groups. 'They also indicate a nutritional floor beneath which maintenance of health in people cannot be assumed'.[4]

5. In 1950 a Committee of the Food and Agriculture Organization FAO recommended methods that may be followed in assessing calorie requirements. Their recommendations are designed for application to countries or groups within countries. It is emphasized that the recommendations are not directly applicable to individuals and, even when applied to groups, local circumstances must be considered. The Committee considered requirements at the 'physiological level'; their recommendations represent the needs of healthy individuals and are 'set at such levels as to make possible an active life and a high degree of productivity in occupational pursuits'. They are based on a 'reference' man (weight 65 kg., 143 lb.) and woman (weight 55 kg., 121 lb.), aged 25 years living at a mean external annual temperature of 10°C (50°F). Suggestions are made for calculating the requirements of individuals differing from the 'reference' in respect of body size, age, activity and environmental temperature.[5]

General Principles

6. There is no evidence of racial differences in the requirements of nutrients; consequently no distinction between the standards proposed for Whites and non-Whites has been made in the table.

7. The nutrient requirements of individuals are influenced by sex, age, activity, ideal weight and other factors. If actual weight be taken as the basis, a corpulent person will gain weight owing to the higher calorie-allowance provided, whereas the needs of an underweight person will not be adequately met. If ideal weight for height, activity or body surface could be used as the criterion, the calorie requirements could be assessed more accurately; unfortunately adequate data for South Africa in this respect are lacking.

8. The close relationship or interaction of the different nutrients is a subject of much research. The intake of one nutrient probably affects the requirements of others. Thus the thiamin requirement is determined by the calorie content of the diet; both folacin and vitamin B_{12} play a part in the synthesis of choline, which is essential for the maintenance of liver morphology and function; vitamin D promotes the absorption and metabolism of calcium; a deficiency of niacin occurs particularly in diets low in complete proteins—such proteins provide the essential amino acid tryptophane, which is a niacin precursor.

Use and Limitation of Dietary Standards

9. It is most important to remember that dietary standards cannot be used as the only criterion for judging the nutritional state of a person or group, and that failure to comply with these standards will not necessarily lead to deficiency diseases.

10. In this connection the following quotations are of interest: 'Inasmuch as many persons who receive less than the recommended allowance of one or another nutrient may remain in health through long periods, it becomes apparent that these allowances are not to be used as the sole criterion for judging the state of nutrition of any population.'[6]

'If these allowances are used in dietary evaluation, it is essential to appreciate that, while most persons whose consumption equals or exceeds the goals are presumably adequately nourished, not all persons who fail to reach these goals are malnourished.'[2]

'It is important that standards should be correctly applied and their limitations recognized. In the past some of the conclusions drawn from the comparison of nutrition intake levels with the dietary standards have been far from valid. If the results of a dietary survey show that the diet has a very low calorie content, the conclusion that the group in question is suffering from undernutrition is perhaps a legitimate one. But the fact that the intake of certain nutrients falls below some recommended allowance does not justify the conclusion that a proportion of any group surveyed is suffering from malnutrition. In such circumstances the possible presence of malnutrition may be inferred, but the dietary survey *per se* provides no evidence of its existence.

The value of the information is that it indicates where further investigation may be needed and which dietary defects need most consideration in food and nutrition programmes.'[7]

Proposed Dietary Standards for South Africa

11. The standards proposed here should be regarded as adequate for the maintenance of health without allowing for a safety margin for ill-health, or for great individual differences in absorption and metabolism. The physical changes of the normal body with age and activity have been taken into consideration; for example, from the age of 10 years the requirements of boys and