The Fiber Dialyzer

The search for an artificial device to clear the blood of poisons or toxins, and therefore to replace kidney function, is an old one. In 1913, Abel Rowntree and Turner developed a device consisting of collodion tubing and called the procedure they performed with it "dialysis."

Haas in 1923 tried to dialyze humans by using a modified device, but was unsuccessful because of lack of a suitable anticoagulant. His patient, a 23-year-old woman with post partum renal failure, died.

The use of small tubes or capillaries as dialysis devices was forgotten until 1964 when Stewart in his basic investigations showed that a small capillary system is an effective instrument for dialysis. We must consider this basic work as a new breakthrough in the development of artificial kidneys. At this point, two major problems were encountered:

1. Technical—The construction of a suitable capillary device required the assembling of at first 100,000 capillaries, and it was in this assembly step that difficulty arose. By constructing a machine assembly line, this problem could be overcome.

2. Clotting and fibrin deposits in the capillaries—Improving the inlet and outlet system solved this problem partially, but even today clotting is the only real problem encountered.

The ideal dialyzer for use in humans should:

1. Require no donor blood because of its small internal volume.
2. Operate at pressures sufficiently low so as not to require an external blood pump;
3. Be suitable for infant as well as adult use;
4. Increase the efficiency of transport of substances to and from the blood;
5. Be low in cost.

After a rather short period of development in the laboratory, a product was created suitable for hemodialysis in humans. In 1966 the hollow fiber artificial kidney was reported to be an effective dialyzer and the dialyzer, although it underwent some modifications, has basically the same design since this time.

The fibers (about 11,000 now) consist of regenerated cellulose. Their effective length is 13.5 cm, the inside diameter is 225 microns and the wall thickness is 30 microns. The effective surface area therefore is approximately 1.0 m². The tube sheet, which holds the fibers in position and forms a gasket between blood and dialysate chambers, is made of medical grade silicone rubber.

This sketch depicts the so-called "old cell". (Fig. 1) The average blood volume was 135 ml. The adaptors were not built-in. The latest model, here shown with the older one, has flat headers (Photo 1). This reduced the volume of the cell to about 95 ml. Both header volumes together were reduced from 50 ml to 10 ml. The FBV (fiber bundle volume) remained unchanged. As you can see, the adaptors are now built on, increasing the simplicity of setup and operation and making adapters for the Hansen quick connectors obsolete.

An experienced technician, using a glucose-free bath for easier checking of the formaldehyde content, needs about 8 to 10 minutes to set up the capillary kidney. I need not mention setup and operational procedures before this experienced audience. I only want to make one statement: I have seen no dialyzer so easy to handle with any kind of equipment, neither bedside proportioning systems nor central delivery systems, as the hollow fiber kidney.

The easiest mounting is with the IV pole. Perhaps it is worthwhile to mention an observation we made regarding mounting the cell: more clotted fibers were observed in the area of the arterial tube where air was trapped when the cell was not mounted in a strictly vertical position.

This half-moon shaped bundle of clotted fibers is found at the part of the tube where air bubbles get trapped and are in direct contact with the fibers. This evidently enhances clotting so much that the whole bundle becomes clotted at this point.

The whole cloting of such a cell is approximately 15%. Since we have been doing that, it means mounting the cell in a strictly upright position, the percentage of clotted fibers is less and more equally distributed over the whole fiber bundle. When we received the first cells for clinical evaluation, we were, as mentioned before, surprised by the simplicity of operation and insignificance of difficulties encountered.
The evaluation followed routine methods. Clearances and dialysance were measured one and six hours after beginning dialysis and after using the well-known formulas, the correlation of both was established. (Fig. 2)

Fig. 3 are the results of clearance evaluations at different blood levels, depicted as Mean ± SE. The drop in different clearances at a blood flow greater than 250 ml/min was at first a finding for which we had no explanation. But we soon found that it was probably related to the high transmembrane pressure used to ultrafilter the patients. The hypothesis is that probably fiber distortion increased under these conditions secondary to coning of the tube sheets and therefore the transverse section of the single fiber was changed from round to oval; both leading to increased clotting, loss of surface area and subsequently to drops in clearance.

The correlation between clearance and dialysance is linear with a correlation coefficient of 0.9. Comparing the results on the Dow with other commonly used dialyzers, we get the following curves. (Fig. 4) As you can see, the hollow fiber dialyzer compares favorably with all of the others—plate and coil kidneys. As a matter of fact, this dialyzer has a few advantages over the other dialyzers outside the field of clearance and fluid removal.

A further, very interesting point to us was the capacity of fluid removal. In our evaluations we could completely confirm the data given by the manufacturer. The ultrafiltration correlates directly to the transmembrane pressure and can be expressed by 1 ml/hr/mmHg of transmembrane pressure. This offers a great advantage: by knowing dialysis time and weight gain, we are able to predetermine weight loss and therefore the necessary negative pressure.

The maximal suggested transmembrane pressure should not exceed 500 mm Hg, but this allows fluid removal of about 400 cc/hr, or during an 8-hour dialysis, the removal of 3.2 kg of body water, an amount of weight gained only by undisciplined patients.

The flow resistance in the different compartments of the dialyzer characterizes it as a low-resistance dialyzer; the typical range in the blood compartment at approximately 200 ml blood flow is between 15 and 55 mmHg. This enables the use of the capillary kidney without a blood pump if an external shunt is present. The normal pressure drop on the blood side across the cell is in the range of 20-40 mmHg at a flow rate of 200 ml/min. Usually the pressure is monitored continuously at the arterial drip chamber and at hourly intervals at the venous drip chamber when no second pressure monitor is available. An increase in pressure—the so-called delta pressure—of more than 50-60 mmHg indicates clotting of fibers and ineffective dialysis, but at higher blood flow rates, higher delta pressures must be expected. Therefore, we measure the delta pressure at a given blood flow at the beginning of hemodialysis and set an upper limit, adding 40 mmHg to the measured value.

This brings us to the point of discussing what was once the main problem of the capillary kidney: clotting.

In the first reports, clotting was invariably the reason for early termination of dialysis. Dr. Gotch indicated that two factors are responsible for clotting—the patient and the dialyzer. In the latter, clotting problems were caused by tube sheet induced fiber distortion. Also, the surface of the header was in part responsible. Fiber distortion undoubtedly results in maldistribution of blood flow with unequal and prolonged residence time in partially obstructed fibers. This effect on residence time could be potentiated under conditions of high transmembrane pressure by both further obstruction of fibers and ultrafiltration in such fibers, leading to increased viscosity and further resistance to blood flow.
But the new developments led to much more uniform and stable tube sheet-fiber relationship under all conditions of transmembrane pressure so that other factors than these are now responsible for clotting. That factor is the patient and his heparinization.

Uremic patients unavoidably have clotting disturbances, i.e., prolonged bleeding time, decreased prothrombin consumption and abnormal platelet aggregation, all of which favor non-clotting. With initiation of treatment and adequate hemodialysis, these abnormalities reverse and all patterns, from completely normal to various partial abnormalities, can be found in the laboratory.

Heparinization followed standard procedures:

We use 1 mg heparin per kg of body weight as a priming dose. For example, 8000 units for a 70 kg patient, and continue with a constant infusion of 1500 units per hour by means of a syringe-infusion pump. We give protamine routinely in AV fistula patients at the end of the run, usually 25 mg. Patients with Scribner shunts receive no protamine.

Regional heparinization is no problem. In five dialyses done on three patients, regional heparinization was used. By keeping the clotting times of cell and patient at 1 hour and 10-15 minutes respectively, the clotting of all five cells was less than 5% of initial FBV.

Originally we observed three groups of patients:
1. Those who clotted no more than 7% of the fibers with the heparinization described above;
2. Those who clotted no more than 20% of the fibers during dialysis and were on oral anticoagulants between the hemodialysis procedures;
3. Two patients (of the original eleven) who clotted the cell in every run to an extent that the procedure had to be terminated.

The percentage of clotted fibers and therefore the efficiency of the dialyzer is of great importance if one intends to reuse the cell on the same patient.

Preparation for reuse is standardized. After flushing with normal saline and determining the fiber bundle volume at the end of the hemodialysis procedure, the cells are completely washed out with filtered tap water until the effluent is blood-free. This takes about 1/2 hour. Both compartments of the cell are then filled with 2% formaldehyde. All inlets and outlets are stoppered and the unit is stored for the next dialysis.

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Now the question arises: When is a cell reusable?

First, we decided arbitrarily to reuse cells with less than 20% of initial fiber bundle volume clotted. We disposed units with between 20% and 40% clotted. For the past three months we reuse every cell with a fiber bundle volume of 60 ml or more.

The next figure (Fig. 5) shows the average reuse of cells per patient. The explanation for the UP and DOWN is difficult to find; but we found correlation with the batch number. The clearances in 33 reused cells (average of second and third uses) were as follows: (Fig. 6) There was a slight drop, as expected with clotted fibers, but the absolute numbers were still very good. The percentages are 85% for urea, 90% for creatinine, 97% for phosphorus and 91% for uric acid, as compared to the original values.

So much for the characteristics of the cell. How do the patients tolerate it and what is the effect of long-term hemodialysis with this special kind of dialyzer?

Five patients have been dialyzed for more than a year and 11 others for at least six months. Central delivery systems are used: MAKs 300 or Drake-Willock and Centry systems. The delivery systems were modified by the manufacturer in order to adequately generate and monitor the required negative pressure.

Most patients are dialyzed 18-24 hours per week and their mean chemistries, usually drawn before hemodialysis, are shown on Table 1. Considering the liberal diet (largely unrestricted protein intake), the results must be considered satisfactory.

The control of phosphorus by dialysis alone is difficult to achieve. Not all of the eleven patients whose mean values are depicted on this slide were receiving phosphate binding agents. In patients taking aluminium hydroxide, the phosphorus values were below 5 mg%; in the other group they were between 7 and 8 mg%. In patients dialyzed for at least 21 hours a week, the creatinine never exceeded 9.5 mg%.

The desired control of water balance was achieved by controllable transmembrane pressures; the mechanical performance of the dialyzer is repeatable and highly dependable. The early problems of blood leaks, jacket leaks and high pressure drop across the dialysate compartments are eliminated by the current production. As a matter of fact, I know of only one blood leak during the past eight months with the hollow fiber kidney in our centers.

None of the patients developed polyneuropathy, nor did renal osteodystrophy, when present, worsen. As a matter of fact, the hematocrit rose an average of 2 points in our patients after two months on dialysis with this unit. The transfusion requirements were minimal; one patient received 2 units of blood in connection with shunt surgery. The values of hematocrit vary widely between 18% and 34%. This does not include patients with polycystic kidney disease. As a matter of fact, the patient with the highest hematocrit is a patient with chronic glomerulonephritis, dialyzed for 2½ years between 20 and 24 hours weekly.

In summary, the hollow fiber capillary dialyzer is highly efficient, constructed with a ratio of large surface area to a small volume. The small priming volume and the nearly nonexistent dynamic volume changes which are less than 5 ml minimize hypotensive tendencies especially when self-prime procedures are used. Pressure changes do not affect blood or dialysate compartment volumes.

The ease of handling, storing and shipping make it a favorite of our seven home dialysis patients who use this device. The simplicity of setup and operation save valuable technician time in the hospital.

Although I am not a psychologist or psychiatrist, I will not withhold an observation of our training staff: they feel that patients training for home dialysis on this small artificial kidney accept the idea of dialysis much better and encounter fewer psychological problems. There is no evidence of a rational explanation of this observation, but perhaps the small size of the device plays a major role in making the patient feel more comfortable and gives him a feeling of being competent to handle any situation.

We have dialyzed all kinds of patients—children and adults, chronic and short-term patients, those awaiting renal transplant—without medical problems. Although developed as a disposable dialyzer, the possibility of reuse is well established and in home dialysis programs this is a very welcome property, simply because it cuts costs considerably.

In my opinion, the fiber kidney has a very good chance to be the working horse in the field of hemodialysis in the future.

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