Manual of Clinical Dialysis

Second Edition

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Springer
Grateful thanks to my family, Vimli, Saba, and Zeba, and friends for their strong support and to Arlene for all of her help. This work is dedicated to my teachers, namely Dr. Scribner, and all of my patients.
As the next millennium begins, we hope that in the years ahead the need for dialysis will be decreased by better preventive care, especially the control of hypertension during the early stages of chronic renal disease. An increase in the number of donated kidneys and a decrease in their rejection rate also seems possible. In the meantime, it is our goal as dialysis professionals to do the very best job we can to make dialysis treatments as effective as possible in terms of patient survival and rehabilitation.

Despite the excellence of this manual, in terms of dialysis dose, one conclusion is inescapable: the current recommendation for dialysis dose, although recently revised upward, is still too low to support the well-being needed for rehabilitation. Indeed, at a urea reduction ratio of 65%, which is the current minimum set by Medicare, patients remain chronically uremic. The author does not say this, but if you read between the lines, he is trying to tell the reader that it is true. Furthermore, this dosage is based on observed (often malnourished) body weight, whereas it should be based on ideal body weight to reflect more accurately the needed dose.

Equally bad for patient well-being is the fact that there is no margin of safety built into this minimum. I believe a margin of safety is essential since the delivered dose is not checked with every dialysis; yet every aspect of dialysis procedures works against delivering the prescribed dialysis dose. For example, if adverse intradialytic events occur during a session, the time lost is seldom made up.

It is important to point out that the higher the weekly dose of dialysis the better. No adverse effects have been encountered no matter how high the dose. Pierratos has shown, with seven nights per week of home dialysis, a marked improvement in well-being, using a dose so large that phosphate had to be added to the dialysate.

Access to the circulation still is the “Achilles heel” of hemodialysis, and recirculation is a major cause of under-dialysis. The native Cimino fistula remains the gold standard. Vein grafts should never be used in patients in whom any natural vein is usable.

In the case of peritoneal dialysis, the danger of under-dialysis is ever present. Since the contribution by the native kidney in controlling uremia is more important in this group of patients, loss of residual renal function puts patients at risk for
severe under-dialysis. In this group the close monitoring of the dose, including that supplied by residual renal function, is particularly critical to avoid adverse patient outcome.

The basic constraint that Dr. Ahmad has to live with in order to be realistic in his dosage recommendations is the “standard” 3½ h, three times a week dialysis schedule. Both dialysis professionals and their patients must come to understand the basic fact that it is not possible, except in small patients, to give enough dialysis in 3½ h, three times a week, to support rehabilitation. The current dismally low rehabilitation rate supports this contention. As suggested in the text, there are many ways to get beyond this session time constraint, and I hope these suggestions will increase interest in pursuing them according to the needs of the individual patient because under-dialysis is a major cause of failure to rehabilitate dialysis patients.

Of course, as soon as ways are found to break through this 3½ h, three times a week session time barrier, other benefits begin to fall into place, such as correction of chronic acidosis and especially the ability to control blood pressure. It is my opinion, which is based on a huge amount of practical experience and published material, that antihypertensive medications are totally ineffective in controlling blood pressure in the dialysis population. In addition, their use increases the incidence of hypotensive episodes, especially during short dialyses. Indeed, antihypertensive medications must be discontinued before the patient’s extracellular volume can be reduced to the level of dry weight. I define dry weight as that which reflects an extracellular volume small enough to render the dialysis patient normotensive and unable to tolerate antihypertensive medications. However, all this important information cannot be applied unless at least 12–15 h per week are devoted to being on dialysis.

Even if professional staff optimize every aspect of dialysis according to the guidelines in this manual, there still remains a key task. Staff must convince the patients of the vital importance to their well-being of receiving the highest possible dose of dialysis. Physicians in particular have proven to be poor advocates and teachers of this crucial objective. Patients must be made to understand that the higher the weekly dialysis dose, the better they will feel. Then it is up to the patients to decide whether it is a worthwhile trade off to spend extra time on dialysis in exchange for better sense of well-being, without which rehabilitation is very difficult if not impossible.

Seattle, Washington, USA

Belding H. Scribner, MD

July, 1999
Acknowledgements

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Abbreviations

AII  Angiotensin II
AAMI  Association for the Advancement of Medical Instrumentation
ACE  Angiotensin-converting enzyme
ACT  Activated clotting time
AMAC  Arm muscle area circumference
AN6  Acrylonitrile-6
ARB  Angiotensin (II) receptor blockers
AV  Arteriovenous
AVP  Arginine-vasopressin
BIA  Bioelectric impedance analysis
BP  Blood pressure
BSA  Body surface area
BUN  Blood urea nitrogen
(i)Ca  (Ionized) calcium
CAAPD  Continuous automated ambulatory peritoneal dialysis
CAPD  Continuous ambulatory peritoneal dialysis
CAVH  Continuous arteriovenous hemofiltration
CAVHD  Continuous arteriovenous hemodiafiltration
CCB  Calcium channel blocker
CCPD  Continuous cycling peritoneal dialysis
CHF  (Slow and) continuous hemofiltration
CTS  Carpal tunnel syndrome
CVVH  Continuous venovenous hemofiltration
CVVHD  Continuous venovenous hemodiafiltration
DDS  Dialysis disequilibrium syndrome
DEXA  Dual-energy X-ray absorptiometry
DFO  Deferoxamine
DI  Dialysis index
DOQI  Dialysis Outcome Quality Initiative
DPI  Dietary protein intake
ECF  Extracellular fluid
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>ESRD</td>
<td>End-stage renal disease</td>
</tr>
<tr>
<td>Epo</td>
<td>Erythropoietin</td>
</tr>
<tr>
<td>Eto</td>
<td>Ethylene oxide</td>
</tr>
<tr>
<td>FBV</td>
<td>Fiber bundle volume</td>
</tr>
<tr>
<td>GFR</td>
<td>Glomerular filtration rate</td>
</tr>
<tr>
<td>GU</td>
<td>Glucose uptake</td>
</tr>
<tr>
<td>HCO$_3$</td>
<td>Hydrogen bicarbonate</td>
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<tr>
<td>Hct</td>
<td>Hematocrit</td>
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<tr>
<td>HD</td>
<td>Hemodialysis</td>
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<tr>
<td>HDF</td>
<td>Hemodiafiltration</td>
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<tr>
<td>HDL</td>
<td>High-density lipoprotein</td>
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<td>HF</td>
<td>Hemofiltration</td>
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<tr>
<td>ICF</td>
<td>Intracellular fluid</td>
</tr>
<tr>
<td>IHF</td>
<td>Intermittent hemofiltration</td>
</tr>
<tr>
<td>IDPN</td>
<td>Intradialytic parenteral nutrition</td>
</tr>
<tr>
<td>IJ</td>
<td>Internal jugular</td>
</tr>
<tr>
<td>IPD</td>
<td>Intermittent peritoneal dialysis</td>
</tr>
<tr>
<td>IUF</td>
<td>Intermittent ultrafiltration</td>
</tr>
<tr>
<td>K$_{urea}$</td>
<td>Urea clearance</td>
</tr>
<tr>
<td>(e)Kt/V</td>
<td>(Equilibrated) dose of dialysis</td>
</tr>
<tr>
<td>KoA</td>
<td>Mass transfer coefficient</td>
</tr>
<tr>
<td>K$_{ru}$</td>
<td>Residual renal urea clearance</td>
</tr>
<tr>
<td>K$_{uf}$</td>
<td>Ultrafiltration coefficient</td>
</tr>
<tr>
<td>kd</td>
<td>Kilodalton</td>
</tr>
<tr>
<td>LDL</td>
<td>Low-density lipoprotein</td>
</tr>
<tr>
<td>LMWH</td>
<td>Low molecular weight heparin</td>
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<tr>
<td>LVH</td>
<td>Left ventricular hypertrophy</td>
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<tr>
<td>MAK</td>
<td>Mechanical artificial kidney</td>
</tr>
<tr>
<td>MCV</td>
<td>Mean corpuscular volume</td>
</tr>
<tr>
<td>MM</td>
<td>Middle molecule</td>
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<tr>
<td>MMHD</td>
<td>Morbidity in Maintenance Hemodialysis Study</td>
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<tr>
<td>NCDS</td>
<td>National Co-operative Dialysis Study</td>
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<tr>
<td>NIPD</td>
<td>Nocturnal intermittent peritoneal dialysis</td>
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<td>NKF</td>
<td>National Kidney Foundation</td>
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<tr>
<td>NO</td>
<td>Nitric oxide</td>
</tr>
<tr>
<td>NTx</td>
<td>Cross-linked N-terminal telopeptide of type I collagen</td>
</tr>
<tr>
<td>PAN</td>
<td>Polyacrylonitrile</td>
</tr>
<tr>
<td>(n)PCR</td>
<td>(Normalized) protein catabolic rate</td>
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<tr>
<td>pClCr</td>
<td>Peritoneal creatinine clearance</td>
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<td>pCl$_{urea}$</td>
<td>Peritoneal urea clearance</td>
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<td>PD</td>
<td>Peritoneal dialysis</td>
</tr>
<tr>
<td>PET</td>
<td>Peritoneal equilibration test</td>
</tr>
<tr>
<td>PGI$_2$</td>
<td>Prostacyclin</td>
</tr>
<tr>
<td>PICP</td>
<td>Procollagen type I C-terminal peptide</td>
</tr>
<tr>
<td>pKt</td>
<td>Peritoneal urea clearance rate</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
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<td>--------------</td>
<td>-------------</td>
</tr>
<tr>
<td>PMMA</td>
<td>Polymethylmethacrylate</td>
</tr>
<tr>
<td>(n)PNA</td>
<td>(Normalized) protein equivalent of nitrogen appearance rate</td>
</tr>
<tr>
<td>PO₄</td>
<td>Phosphate</td>
</tr>
<tr>
<td>PTFE</td>
<td>Polytetrafluoroethylene</td>
</tr>
<tr>
<td>PTH</td>
<td>Parathyroid hormone</td>
</tr>
<tr>
<td>PTT</td>
<td>Prothrombin time</td>
</tr>
<tr>
<td>PTX</td>
<td>Parathyroidectomy</td>
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<tr>
<td>pre-BUN</td>
<td>Predialysis concentration of blood urea nitrogen</td>
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<tr>
<td>post-BUN</td>
<td>Postdialysis concentration of blood urea nitrogen</td>
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<td>Polysulfone</td>
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<td>PV</td>
<td>Plasma volume</td>
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<tr>
<td>Qb</td>
<td>Blood flow rate</td>
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<tr>
<td>Qd</td>
<td>Dialysate flow rate</td>
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<tr>
<td>RBC</td>
<td>Red blood cell</td>
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<tr>
<td>rClCr</td>
<td>Renal creatinine clearance</td>
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<tr>
<td>rClU</td>
<td>Renal urea clearance</td>
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<tr>
<td>RO</td>
<td>Reverse osmosis</td>
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<tr>
<td>ROD</td>
<td>Renal osteodystrophy</td>
</tr>
<tr>
<td>RRT</td>
<td>Renal replacement therapy</td>
</tr>
<tr>
<td>SCUF</td>
<td>Slow and continuous UF</td>
</tr>
<tr>
<td>SGA</td>
<td>Subjective global assessment</td>
</tr>
<tr>
<td>SLED</td>
<td>Slow low efficiency dialysis</td>
</tr>
<tr>
<td>SM</td>
<td>Small molecule</td>
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<tr>
<td>SUF</td>
<td>Sequential ultrafiltration and dialysis</td>
</tr>
<tr>
<td>t</td>
<td>Time</td>
</tr>
<tr>
<td>TBW</td>
<td>Total body water</td>
</tr>
<tr>
<td>TIBC</td>
<td>Total iron-binding capacity</td>
</tr>
<tr>
<td>TMP</td>
<td>Transmembrane pressure</td>
</tr>
<tr>
<td>TPN</td>
<td>Total parenteral nutrition</td>
</tr>
<tr>
<td>TPD</td>
<td>Tidal peritoneal dialysis</td>
</tr>
<tr>
<td>TPR</td>
<td>Total peripheral resistance</td>
</tr>
<tr>
<td>TSFT</td>
<td>Triceps skin fold thickness</td>
</tr>
<tr>
<td>UF(R)</td>
<td>Ultrafiltration (rate)</td>
</tr>
<tr>
<td>UKM</td>
<td>Urea kinetic modeling</td>
</tr>
<tr>
<td>UNA</td>
<td>Urea/nitrogen appearance</td>
</tr>
<tr>
<td>URR</td>
<td>Urea reduction ratio</td>
</tr>
<tr>
<td>V</td>
<td>Volume of distribution of body fluid</td>
</tr>
<tr>
<td>VDR</td>
<td>Vitamin D receptors</td>
</tr>
<tr>
<td>V_{urea}</td>
<td>Volume of distribution of urea</td>
</tr>
<tr>
<td>WBC</td>
<td>White blood cell</td>
</tr>
<tr>
<td>W(p)ClCr</td>
<td>Weekly (peritoneal) creatinine clearance</td>
</tr>
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Chapter 1
Brief History of Clinical Dialysis: The Seattle Experience

Although it was not until the 1960s that long-term dialysis in a clinical setting became a reality, dialysis as a treatment for renal failure had been the focus of interest for some time. By the end of the 1950s, Dr. B. H. Scribner had established an acute dialysis program at the University of Washington. In 1960, a uremic comatose man who was thought to have acute renal failure was brought back to almost normal active life with intermittent hemodialysis. However, he was found to have chronic irreversible renal disease and had to be sent home to die; it became clear to the Seattle team that if long-term vascular access could be maintained, long-term dialysis would become a reality. This led to the development of the Scribner Shunt and the advent of chronic hemodialysis.

The Seattle team developed an entire program to care for a population of patients who had a chronic disease and who were being kept alive on a new form of treatment. New equipment and systems were developed and refined and solutions for unexpected problems had to be devised—specifically, treatment of hyperphosphatemia, renal osteodystrophy, and hypertension. To make the treatment more practical, by reducing the bulk of the dialysate through the use of concentrated dialysate, a proportioning system had to be developed and a substitute for bicarbonate was used to prevent the precipitation of calcium carbonate. This was achieved by using acetate. However, when acetate-related problems started to appear (due to the use of more efficient dialyzers, in the mid-1970s), a double proportioning system was developed to enable the use of bicarbonate again. As is often the case, the resolution of one problem often led to other unexpected difficulties. The commitment and ingenuity of the pioneers of dialysis treatment, however, meant that these hurdles were overcome and the success of dialysis as a treatment for end-stage renal disease (ESRD) was assured. Later in the 1980s, another Scribner fellow, Joseph Eschbach, developed and used recombinant erythropoietin, and anemia-related issues became history. The pioneering work continues today; the most recent modification in dialysate was the development of a citric acid-based acid concentrate for dialysate. This is proving to be more beneficial to the patients than the currently used acetic acid-based acid concentrate.
The shortage of resources in the early days of dialysis necessitated the founding of a patient selection committee to decide which of the needy patients would be accepted into the program. This committee (thought by many to be the foundation for the development of medical ethics) forced several actions with far-reaching consequences, one of which was the development of home dialysis.

A young high-school student was found to have ESRD but was not accepted for dialysis by the patient selection committee. The team decided that home dialysis was a viable alternative if they could develop a smaller hemodialysis machine that could be used at home. The collaborative effort of Dr. Scribner’s clinical team and the engineering team of Dr. Albert L. Babb succeeded in building a home hemodialysis machine in only 3 months. This home machine became the prototype of machines in use currently.

In early 1960s, Dr. Fred Boen joined the Seattle group and began treating a patient using peritoneal dialysis (PD), with a closed system containing 20-l (and later 40-l) bottles. Henry Tenckhoff, a research fellow with Dr. Boen, treated patients at home using Boen’s repeated puncture technique. This technique, however, required aseptic access to the peritoneal cavity with a catheter each time dialysis was needed, and meant that Dr. Tenckhoff had to visit each patient’s home at least three times a week to insert the access device. Eventually, Dr. Tenckhoff developed the indwelling peritoneal catheter and a sterile technique for its insertion, which made it possible to use the new form of dialysis on a larger scale.

A detailed analysis of the Seattle experience with intermittent PD (IPD) revealed the potential risk of under-dialysis and poor “technique survival rates” [1], suggesting that the dialysis dose needed to be increased. In 1965, Dr. Robert Popovich while in Seattle had become involved in the kinetics of the “middle molecule” across the peritoneal membrane before moving to Texas and becoming a pioneer of the continuous ambulatory PD (CAPD) technique. This continuous therapy improved the dialysis dose and made PD a viable technique of renal replacement therapy (RRT).

Encountering a patient who was dying of malnutrition due to bowel disease, Dr. Scribner saw an opportunity to apply the group’s expertise in vascular access to another area of medicine. The development of Broviac (and later on Hickman) catheters and the “total parenteral nutrition” (TPN) program (operated by the nephrology team at the University of Washington) was a result of the vision and dedication of Dr. Scribner and his co-workers.

This very brief account of the Seattle experience shows that the commitment of Dr. Scribner, his team, their collaborators, and community members accomplished more than the development of a dialysis access device. Their efforts led to the development of systems for dialysis, central venous catheters, parenteral nutrition, long-term care of ESRD patients, community-based dialysis centers, home dialysis programs, an early concept of dialysis dose calculation, and continued technological improvement. The development of the dialysis program established nephrology as a subspecialty and has also had far-reaching implications in the fields of bowel disease, organ transplantation, oncology, and for all acutely ill patients. It is now
difficult to imagine that less than 50 years ago, patients with ESRD had only one prognosis—death—and that patients with renal failure were connected to patients with liver failure so that each could be kept alive by the healthy organ of the other.

1.1 Definition of Dialysis

In broad terms, the process of dialysis involves bidirectional movement of molecules across a semipermeable membrane. Clinically, this movement takes place in and out of blood, across a semipermeable membrane. If the blood is exposed to an artificial membrane outside of the body, the process is called hemodialysis (HD) or hemofiltration (HF). If the exchange of molecules occurs across the peritoneal membrane, the process is called peritoneal dialysis (PD).

1.2 Mechanisms Involved in Molecular Movement

The movement of molecules follows certain physiological and physicochemical principles that are outlined below (see Fig. 1.1a).
1.2.1 Diffusion

If two solutions of different concentrations are separated by a semipermeable membrane, solute will move from the side of higher to the side of lower solute concentration. This process of solute movement on a concentration gradient is called diffusion and is caused by the random movement of the solute molecules striking and moving across the membrane. Several factors influence this random movement and thus the rate of diffusion. The transport of any solute or solvent molecule is dependent on the physical size of the molecule relative to the size of the pores in the membrane. Any molecules larger than the pores of the membrane cannot pass through. Similarly, the electrical charge and the shape of the molecule also determine the rate of transport across the membrane. If the membrane has a negative charge, particles with a like charge will have limited transport as compared with those with a positive or a neutral charge.

1.2.2 Ultrafiltration

A solvent such as water can be forced across a semipermeable membrane on a pressure gradient, from higher to lower pressures (see Fig. 1.1). The pressure could be a result of osmotic force (see below) or of mechanical hydrostatic pressure. The
solvent carries with it the dissolved solute molecules small enough to pass through the membrane pores (see below). This movement of molecules across a semipermeable membrane, caused by a pressure difference, is called ultrafiltration (UF). If the pressure is hydrostatic, the process is called “hydrostatic UF.” Conversely, the UF caused by osmotic pressure is called “osmotic UF.”

1.2.3 Osmosis

As solute concentration increases, solvent concentration correspondingly decreases and vice versa. If a semipermeable membrane separates solutions of different concentrations, solvent along with dissolved small solutes will flow from the side with the higher solvent concentration to the side with the lower solvent concentration. This process is called osmosis (see Fig. 1.1).

1.2.4 Convection

As solvent molecules move on a pressure gradient, the dissolved solute molecules are dragged along (solvent drag); this process of solute movement is called convection. The ease with which the solute is dragged along is determined by the size of the solute molecule relative to the size of the membrane pores. Smaller solutes are transported easily and the entire solution can sieve across the membrane without any change in concentration. In contrast, larger solutes move more slowly and the rate of convective transport is slower. Thus, the convective transport of a solute depends on the porosity of the membrane. This porosity, known as the “sieving coefficient of the membrane,” can be calculated by dividing the concentration of solute on side A by the concentration on side B.

1.3 Clearance

In a clinical setting, the removal of a solute is measured in terms of clearance, the term being defined as the volume of blood or plasma from which the solute is completely removed in unit time. Let us assume that the blood urea concentration across a hemodialyzer drops from 100 mg/dl at the inlet to 10 mg/dl at the outlet. This 90% decline represents the diffusion of urea from blood into the dialysate and depends largely on the concentration gradient between these fluids. However, the magnitude of the “cleaning” of blood also depends on blood flow rates (Qb). Thus, in the above example, a blood flow rate of 100 ml/min means that 90 ml of the blood was cleared of urea. However, for a blood flow of 200 ml/min, 180 ml of blood is cleared of urea each minute (see the example below for a more accurate calculation). Clearance measures the magnitude of blood cleaning, independent of the concentration of the solute entering the dialyzer.
1.3.1 Blood vs Plasma Clearance

During transit across the dialyzer, most solutes are removed from plasma water (about 93% of blood volume, depending on plasma protein concentration). If the solute is not in the blood cells or if the movement of solute out of these cells is slow, the clearance of the solute decreases as the hematocrit increases (since the plasma volume decreases). Urea is often used as a solute to measure dialysis efficiency (it is present in plasma water as well as in erythrocytes), and the flux of urea across the erythrocyte membrane is reasonably fast. This means that urea is cleared from whole blood during dialysis and is not affected greatly by the hematocrit. The following example clarifies these concepts:

Example

\[ Q_b = 200 \text{ml/min}, \text{hematocrit} = 35\% \]
\[ \text{Plasma flow rate} = 200 \text{ml/min} \times (1 - 0.35) = 130 \text{ml/min} \]
\[ \text{Plasma water flow rate} = 130 \text{ml/min} \times 0.93 \text{ (93\% of plasma is water)} = 121 \text{ml/min} \]
\[ \text{Erythrocyte flow rate} = 200 \text{ml/min} - 130 \text{ml/min} = 70 \text{ml/min} \]
\[ \text{Erythrocyte water flow rate} = 70 \text{ml/min} \times 0.80 \text{ (about 80\% of erythrocyte volume is water containing diffusible urea)} = 56 \text{ml/min} \]

Thus, the whole blood water flow rate effective for urea clearance = 121 ml/min + 56 ml/min = 177 ml/min

If the blood water concentration of urea = 100 mg/dl at dialyzer inlet and 10 mg/dl at outlet, the urea clearance of whole blood = 177 ml/min \times \{1 - [(10 \text{mg/dl})/ (100 \text{mg/dl})]\} = 159 ml/min

This means that 159 ml of blood is cleared of urea each minute.

1.3.2 Clinical Factors Influencing Dialysis Urea Clearance

The three major determinants of urea clearance during hemodialysis are:

- Blood flow rate (Qb)
- Dialysate flow rate (Qd)
- Membrane (dialyzer/peritoneal membrane) efficiency

Reference

As discussed in the previous chapter, the clearance of a solute is dependent on the $Q_b$, $Q_d$, and membrane efficiency. The dialyzer membranes have different pore sizes that are variably distributed, larger pores being fewer than smaller pores. Small solutes like urea can be transported through all pore sizes whereas the larger molecules such as vitamin B12 or beta-2-microglobulin can only pass through the larger pores. Thus the clearance of the larger solutes, unlike urea, is more influenced by the membrane and less by $Q_b$ and $Q_d$.

### 2.1 Blood Flow Rate

Because clearance is calculated using $Q_b$, it would be understandable to mistakenly assume that the relationship between urea clearance and $Q_b$ is linear. However, although urea clearance increases steadily as $Q_b$ is increased from zero, at faster flow rates, the dialyzer is unable to continue to transport urea with the same efficiency and the urea concentration at the dialyzer outlet increases. In other words, the urea removed as a percentage of urea inflow into the dialyzer decreases and (as clearance is $Q_b$ multiplied by the fractional decline in urea) the clearance curve plateaus (see Fig. 2.1).

### 2.2 Dialysate Flow Rate

An increase in $Q_d$ generally increases the urea clearance. This effect is negligible, however, as long as $Q_d$ is 150–250 ml/min faster than $Q_b$. With high-efficiency dialyzers, there is little ($<10\%$) increase in urea clearance if $Q_d$ is increased from 500 ml/min to 800 ml/min, provided that $Q_b$ remains 350 ml/min.