Manual of Clinical Dialysis

Second Edition

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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.

Foreword (For First Edition)

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" $3^1/_2$ 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 $3^1/_2$ 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 $3^1/_2$ 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

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Contents

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

ESRD	End-stage renal disease
Epo	Erythropoietin
Eto	Ethylene oxide
FBV	Fiber bundle volume
GFR	Glomerular filtration rate
GU	Glucose uptake
HCO_3	Hydrogen bicarbonate
Hct	Hematocrit
HD	Hemodialysis
HDF	Hemodiafiltration
HDL	High-density lipoprotein
HF	Hemofiltration
ICF	Intracellular fluid
IHF	Intermittent hemofiltration
IDPN	Intradialytic parenteral nutrition
IJ	Internal jugular
IPD	Intermittent peritoneal dialysis
IUF	Intermittent ultrafiltration
K_{urea}	Urea clearance
(e)Kt / V	(Equilibrated) dose of dialysis
KoA	Mass transfer coefficient
K_{ru}	Residual renal urea clearance
K_{uf}	Ultrafiltration coefficient
kd	Kilodalton
LDL	Low-density lipoprotein
LMWH	Low molecular weight heparin
LVH	Left ventricular hypertrophy
MAK	Mechanical artificial kidney
MCV	Mean corpuscular volume
MM	Middle molecule
MMHD	Morbidity in Maintenance Hemodialysis Study
NCDS	National Co-operative Dialysis Study
NIPD	Nocturnal intermittent peritoneal dialysis
NKF	National Kidney Foundation
NO	Nitric oxide
NTx	Cross-linked N-terminal telopeptide of type I collagen
PAN	Polyacrylonitrile
(n)PCR	(Normalized) protein catabolic rate
pClCr	Peritoneal creatinine clearance
pCl_{urea}	Peritoneal urea clearance
PD	Peritoneal dialysis
PET	Peritoneal equilibration test
PGI_2	Prostacyclin
PICP	Procollagen type I C-terminal peptide
pKt	Peritoneal urea clearance rate

PMMA	Polymethylmethacrylate
(n)PNA	(Normalized) protein equivalent of nitrogen appearance rate
PO_4	Phosphate
PTFE	Polytetrafluoroethylene
PTH	Parathyroid hormone
PTT	Prothrombin time
PTX	Parathyroidectomy
pre-BUN	Predialysis concentration of blood urea nitrogen
post-BUN	Postdialysis concentration of blood urea nitrogen
PS	Polysulfone
PV	Plasma volume
Qb	Blood flow rate
Qd	Dialysate flow rate
RBC	Red blood cell
rClCr	Renal creatinine clearance
rClU	Renal urea clearance
RO	Reverse osmosis
ROD	Renal osteodystrophy
RRT	Renal replacement therapy
SCUF	Slow and continuous UF
SGA	Subjective global assessment
SLED	Slow low efficiency dialysis
SM	Small molecule
SUF	Sequential ultrafiltration and dialysis
t	Time
TBW	Total body water
TIBC	Total iron-binding capacity
TMP	Transmembrane pressure
TPN	Total parenteral nutrition
TPD	Tidal peritoneal dialysis
TPR	Total peripheral resistance
TSFT	Triceps skin fold thickness
UF(R)	Ultrafiltration (rate)
UKM	Urea kinetic modeling
UNA	Urea/nitrogen appearance
URR	Urea reduction ratio
V	Volume of distribution of body fluid
VDR	Vitamin D receptors
V_{urea}	Volume of distribution of urea
WBC	White blood cell
W(p)ClCr	Weekly (peritoneal) creatinine clearance

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 comatosed 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.

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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.

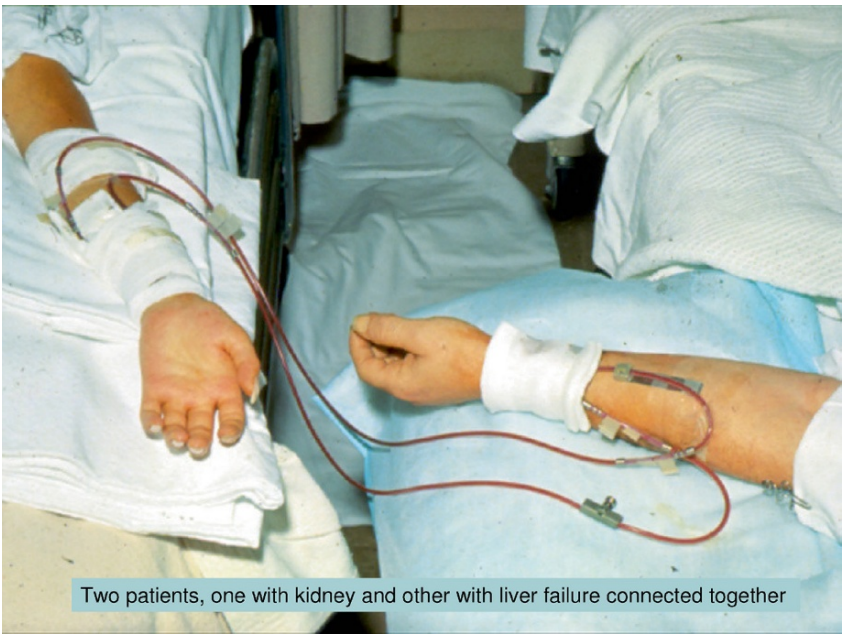
In early 1960s, Dr. Fred Boen joined the Seattle group and began treating a patient using peritoneal dialysis (PD), with a closed system containing 20-l (and later 40-l) bottles. Henry Tenckhoff, a research fellow with Dr. Boen, treated patients at home using Boen's repeated puncture technique. This 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.


Two patients, one with kidney and other with liver failure connected together

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).

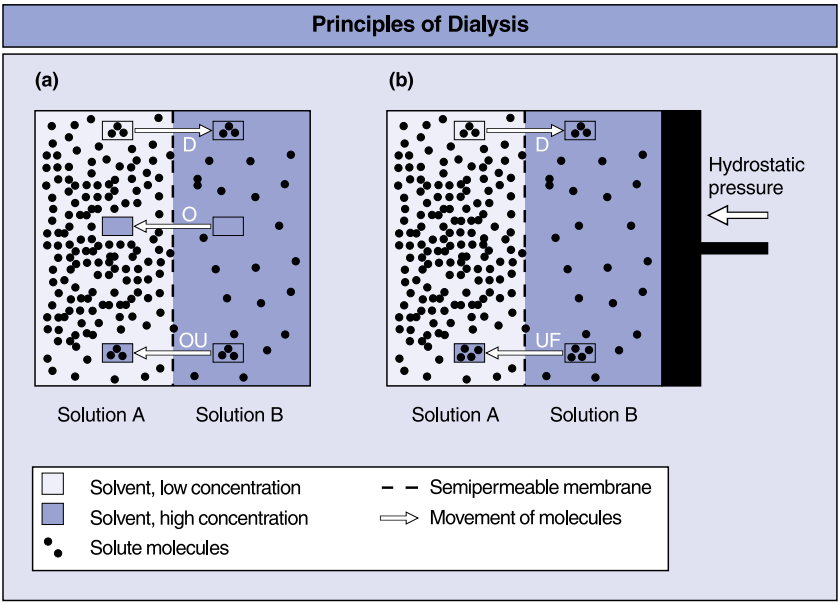


Fig. 1.1 **a** Diffusion, osmosis, and osmotic ultrafiltration by osmotic pressure. **b** Hydrostatic ultrafiltration. *D* diffusion, *O* osmosis, *OU* osmotic ultrafiltration, *UF* ultrafiltration by hydrostatic pressure, *C* convection

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

$Qb = 200\,ml/min, hematocrit = 35\%$
Plasma flow rate $= 200ml/min \times (1 - 0.35) = 130\,ml/min$
Plasma water flow rate $= 130\,ml/min \times 0.93$ (93% of plasma is water) $=$ 121 ml/min
Erythrocyte flow rate $= 200\,ml/min - 130\,ml/min = 70\,ml/min$
Erythrocyte water flow rate $= 70\,ml/min \times 0.80$ (about 80% of erythrocyte volume is water [containing diffusible urea]) $= 56$ 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 $= 177\,ml/min \times \{1-[(10\,mg/dl)/\,(100\,mg/dl)]\} = 159\,ml/min$
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

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Chapter 2
Hemodialysis Technique

As discussed in the previous chapter, the clearance of a solute is dependent on the Qb, Qd, 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 Qb and Qd.

2.1 Blood Flow Rate

Because clearance is calculated using Qb, it would be understandable to mistakenly assume that the relationship between urea clearance and Qb is linear. However, although urea clearance increases steadily as Qb 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 Qb multiplied by the fractional decline in urea) the clearance curve plateaus (see Fig. 2.1).

2.2 Dialysate Flow Rate

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

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