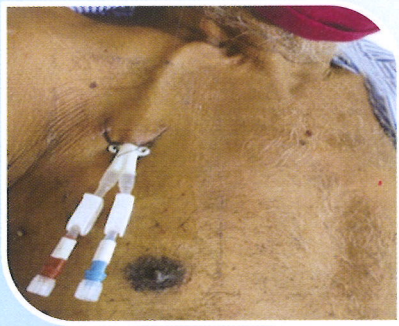
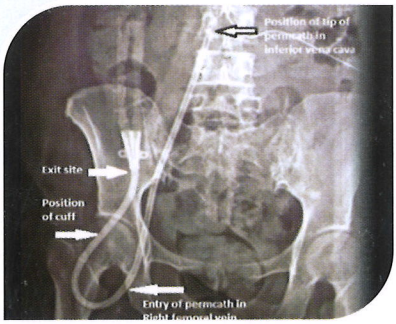
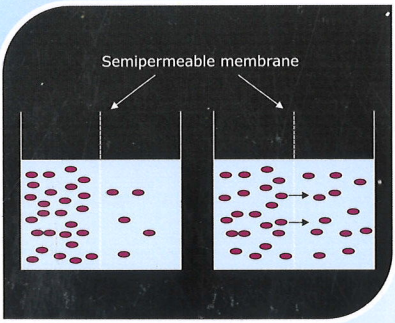
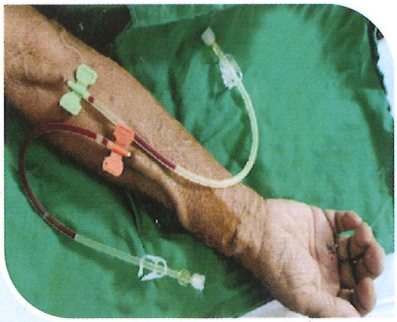
Handbook of Dialysis Technology









R. Kasi Visweswaran
Umesh B. Khanna
Girish Narayen

BHALANI

About the Authors

Dr. R. Kasi Visweswaran

Dr. R. Kasi Visweswaran has over 40 years' experience as a nephrologist and retired from medical college, Trivandrum as Professor of Nephrology and Vice Principal of the college. He has been a gifted teacher throughout his professional career spanning 5 decades, having been involved in teaching doctors, nurses, and dialysis staff. He had the opportunity to set up many new dialysis centers in government and private institutions. He has been awarded numerous Fellowships, orations, invited lectures in international/national conferences, and Life time achievement awards. He has been the president/chairman of local, regional and national societies of Nephrology in India. He has contributed chapters in international textbooks in Nephrology and the popular on-line platform "up-to-date". He has authored and edited numerous books in nephrology for nurses, doctors, physicians and Nephrologists in India and neighboring countries.

Dr. Umesh B. Khanna

Dr. Umesh B. Khanna is a practicing Nephrologist in Mumbai since the last 35 years. He has been a pioneer in establishing the concept of Satellite dialysis units in Mumbai, and has setup more than 20 such centers. He was one of the first ones to establish Nephrologist owned dialysis centers and NGO managed charitable dialysis setups instrumental in giving good quality subsidised dialysis in Mumbai.

He runs an NGO called Mumbai Kidney Foundation which is at the forefront of teaching and training Dialysis technicians, Nurses, Dieticians, and Transplant coordinators. He has been a great academician and a good teacher involved in teaching Nephrology students, physicians, GPs, dialysis technicians, and paramedicals.

He has organized national conferences in Nephrology and Dialysis and presented and written on various nephrology topics.

He has been on various national committees in ISN, IMA, etc.

Dr. Girish Narayen

Retired as Professor and HOD Nephrology in Osmania General Hospital/ Osmania Medical College, Hyderabad. Presently working as Chief of nephrology division in Udai Omni Hospital, Chapel road, Hyderabad. He continues to be involved in academic activities and is teaching DNB students of Medicine and Nephrology. He has presented several papers in National and International conferences, gave guest lectures, and CME talks. Delivered orations at meetings organized by Association of Physicians of India, Indian Medical Association, Gynecology Society of Andhra Pradesh, Nephrology Society of Nagpur, and Nizam's Institute of Medical Sciences, Hyderabad.

Dr. Girish Narayen has written chapters in several books and authored articles in Journals. He has been examiner for DM and DNB Nephrology exams at various Universities of India and National Board of Examinations, Delhi. He has been vice president of the Indian Society of Nephrology and Chairman of the Southern Chapter of the Nephrology Society.

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R. Kasi Visweswaran
MD, DM (Nephrology)
Consultant Nephrologist
Ananthapuri Hospitals and Research Institute
Trivandrum
Formerly, Professor of Nephrology and Vice Principal,
Medical College, Trivandrum

Umesh B. Khanna
MD, DNB (Nephrology)
Director, Kidney Associates, Mumbai
Honorary Nephrologist, Karuna Hospital, Mumbai
Chairman, Mumbai Kidney Foundation

Girish Narayen
MD, DM, MNAMS (Nephrology)
Chief Nephrologist
Udai Omni Hospital
Hyderabad
Formerly, Professor of Nephrology, Superintendent,
Osmania General Hospital, Hyderabad

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to
OUR PARENTS
and
OUR TEACHERS
Prof. Kirpal Singh Chugh [Chandigarh]
Prof. Vidya N. Acharya [Mumbai]

Foreword

Chronic kidney disease has emerged as a major public health problem globally. Its growth is fastest in the developing resource-poor countries, including India. The most obvious and best recognized consequence of chronic kidney disease is kidney failure, a state in which life is not possible without kidney replacement therapy, viz., dialysis or transplantation. While the latter is the preferred treatment, it is available only to a minority of patients. Most patients with kidney failure need to undergo dialysis, either hemodialysis or peritoneal dialysis, including those who eventually get a kidney transplantation. Between the two modalities, hemodialysis is by far the more common—95 out of 100 patients with kidney failure in India receive hemodialysis.

An important myth around dialysis is that this treatment is provided by nephrologists. Nothing could be further from truth—the central players in dialysis delivery are the non-physician professionals who work in dialysis units, the technicians and the nurses. They are the ones who the patients meet and greet at every visit, they start the dialysis procedure, supervise the entire process and deal with complications if they arise, close the procedure and bid the patients goodbye until they meet for the next session. In many centers, these professionals carry out tasks that would normally be conducted by physicians including dialysis catheter insertion. In many instances our patients may not see a nephrologist for weeks or months.

The success of dialysis—measured in terms of survival, freedom from morbidity (both infectious and non-infectious) and quality of life is largely determined by how our non-physician health worker colleagues manage the procedure. Despite the centrality of this workforce, relatively little attention has been paid to provide them with practical education and training beyond just the basic procedural issues. They can provide holistic care only when they understand what this treatment is about, its physiology, why things are done the way they are, the importance of safety, infection control, nutrition, physical activity, and management of

other complications that complement the process of dialysis and make it kidney replacement therapy in true sense.

This book addresses that important knowledge gap. This is the most comprehensive resource for dialysis technicians and nurses which aims to provide them with the required knowledge in a way that they would be able to understand. The book covers almost all aspects of dialysis delivery in a language that is shorn of jargon and provides information in a way which is relatable.

It is a fact that we are grossly short of dialysis technicians and nurses. There are a number of training programmes, but the fact is that large number of dialysis centers are managed by staff that has learnt on the job rather than through a formal training program. It is important to recognize this reality. Any healthcare delivery that is conducted without recognizing the available resources is likely to be unsuccessful.

This laudable effort will be certainly of immense value to our technician and nurse colleagues. They will be able to enrich themselves with fundamentals of the function of the kidney, the manifestations of kidney failure, and the technical aspect of not only dialysis and water treatment, but also other extracorporeal techniques that are commonly undertaken by the same workforce. They will also learn about other components of kidney replacement therapy including kidney transplantation and peritoneal dialysis. This will allow them to provide integrated care to patients with kidney failure. There is even a chapter on possible future of dialysis such as the wearable artificial kidney, which will increase their interest in innovations.

The editors and the authors need to be congratulated for producing this much-needed resource. I do hope that the community for whom this resource is intended will find value and provide feedback to the editors and authors so that the next editions are even more to their liking. One hopes that the book will be expanded to include issues about quality control, outcome monitoring, how to measure success and aspects of reporting, and comparison of data so that our non-physician colleague grow into leadership and contribute to improvement in the way we manage

and support our patients with kidney failure. Given that they are the main ones that our patients talk to most often, technicians and nurses would also benefit from learning about the principles and tools for shared decision-making so that they can help the patients and their families make informed the choices about their kidney replacement therapy options in line with their values and preferences, such as choice of dialysis modality and supportive care.

New Delhi
2nd December 2021

Vivekanand Jha, MD DM FRCP FAMS

Executive Director, George Institute, India
Chair of Global Kidney Health, Faculty of Medicine, Imperial College, London
Conjoint Professor of Medicine, University of New South Wales, Sydney
Immediate Past President (2019–21), International Society of Nephrology.
vjha@georgeinstitute.org.in

Preface

Kidney disease is an important non-communicable disease and the number of cases of kidney failure are increasing at a fast rate. It is estimated that there will be 2,00,000–3,00,000 new cases requiring dialysis in the country in the near future. There are limitations to cater to such a huge patient load through a few thousand dialysis centers throughout the country now. Facilities for dialysis are now available in major towns throughout the country and are expanding to smaller towns. In due course, satellite dialysis centers will be available in smaller towns and villages. Home dialysis will also become more prevalent.

Among the procedures undertaken as renal replacement therapy, hemodialysis accounts for >90%. About 5% each is contributed through peritoneal dialysis and renal transplantation. Any renal replacement therapy is expensive. Considering the increasing number of patients, the central and state Governments have taken steps to further expand the network and support the patients through various schemes.

The dialysis technicians and nurses play a key role in the success of the program. They perform and monitor the various steps in the process and medical help is available "on call" in most units. For the success of the program, the technicians/nurses should have sound knowledge of the fundamentals and have to perform the procedure based on a set of guidelines and "standing orders" provided by the institution. Receiving and monitoring the patient before, during and after the procedure, providing emotional support to patient and family are some of their important responsibilities. Good communication skills and maintaining rapport with patients, colleagues, and doctors are important in their work ethics. Hemodialysis is one of the important service which must continue without any interruption.

Good understanding of the preventive maintenance of dialysis machine and water treatment system will ensure long life for the costly equipment. Proper maintenance of reusable items and disposal of single use items are important aspects in the running

of a good dialysis unit. The technician/nurse should be aware of and be competent to participate in the various procedures done in a hemodialysis unit and also involve in preparation of a patient for kidney transplantation.

Some principles and guidelines regarding modifications of dialysis, which are likely to involve dialysis technitian/nurse, are also highlighted in the respective chapters. This book is prepared with a view to address these issues and presented in simple English so that a student or junior technician whose mother tongue is not English can easily understand the subject. Good knowledge of fundamentals helps to lay a firm foundation which is necessary to understand newer developments/advances, more sophisticated techniques in hemodialysis, and related procedures.

Three of us with inputs from junior colleagues and dialysis technologists have compiled this volume for the benefit of junior dialysis technologists, nurses, and students and we hope, it will be well received, useful, and appropriate for clear understanding of the subject.

R. Kasi Visweswaran (Trivandrum)
Umesh B. Khanna (Mumbai)
Girish Narayen (Hyderabad)

Acknowledgements

Mumbai Kidney Foundation (MKF), is an NGO endeavoring to brighten the lives of chronic kidney disease patients. This initiative was launched by Dr Umesh Khanna as the founder chairman, on the auspicious occasion of the first World Kidney Day (9th March), with the aim of disseminating information about kidney diseases in the community, promoting education, training, initiating measures for prevention, systematic treatment of kidney diseases and rehabilitation of patients. The foundation has been successfully conducting educational programs for patients, staff nurses, dietitians, technicians and doctors relating to prevention, and treatment of kidney diseases.

The mission statement of MKF is "SHARING THE BURDEN".

It aims at creating awareness of kidney disease and works towards its goal, by controlling non communicable diseases. The twin signature campaigns—

1) "Know your numbers" and
2) "Ek Chammach Kum"

initiated by MKF have been appreciated by the society.

The activities have helped in spreading awareness about prevention and early treatment of kidney diseases. In addition, MKF financially supports some CKD patients and also promotes scientific and lawful organ donation.

It has been the endeavor at the MKF to train and educate dialysis technicians making them knowledgeable and up-to-date in the art and science of dialysis. MKF is in the forefront of organizing CMEs and conferences for the healthcare workers especially, dietitians, dialysis technicians, and nurses. This book is written by 3 Nephrologists, from different parts of the country with wide experience in starting and running dialysis units. They have tried to simplify the procedure with an aim to deliver good quality dialysis.

The authors are thankful to MKF for their effort to promote the book among dialysis units in the country. The authors have decided to

donate amount receivable from the publisher as "Royalty" to Mumbai Kidney Foundation for furthering their activities.

We are thankful to Mr. Himanshu H. Bhalani and Mr. Hemant S. Bhalani of Bhalani Publishing House, the publisher of this hand book, who have taken keen interest and much pain for publishing this hand-book in a short time. The publisher has promised to price the volume at affordable levels for the students and junior technicians/nurses for whom this book is meant.

R. Kasi Visweswaran
Umesh B. Khanna
Girish Narayen

List of Contributors

Amit Jain
Consultant Nephrologist
Mumbai

Ankit Mody
Consultant Nephrologist
Mumbai

Chintan Shah
Consultant Nephrologist
Mumbai

Hemant Chougule
Consultant Nephrologist
Mumbai

Rajesh Kumar
Consultant Nephrologist
Mumbai

Shruti Tapiawala
Consultant Nephrologist
Mumbai

Mohammed Althaf
Dialysis Technician
Ananthapuri Hospital and
Research Institute
Trivandrum

Kamal Shah
Director
NephroPlus
Hyderabad

Priya J.
Dialysis Technician
Ananthapuri Hospital and
Research Institute
Trivandrum

Rachna Jasnani
Dietitian
Mumbai

Reshma T.
Dialysis Technician
Ananthapuri Hospital and
Research Institute
Trivandrum

Revathy G.
Dialysis Technician
Ananthapuri Hospital and
Research Institute
Trivandrum

Sreedevi P. A.
[Formerly Chief Dialysis Technician]
Ananthapuri Hospital and
Research Institute
Trivandrum

Supin Vijayan
Dialysis Technician
Ananthapuri Hospital and
Research Institute
Trivandrum

Contents

1 Kidney Functions and Symptoms in Kidney Diseases

R. Kasi Visweswaran

Kidneys are the main excretory organs of the body and are part of the urinary system. The urinary system consists of a pair of kidneys, ureters, urinary bladder and urethra. The kidneys are situated on either side of the vertebral column in the back of the abdominal wall. Each kidney is made up of nearly 1,000,000 nephrons. The nephrons form the functioning unit of the kidney and consist of the glomerulus, proximal tubule, loop of Henle, distal tubule and collecting duct. The glomeruli filter the blood and the ultrafiltrate that is formed contains substances essential for the body, as well as waste products. The tubules re-absorb the water, glucose, bicarbonate, sodium and all other substances essential for the body. The tubules also help in excreting more waste products. Waste products like urea, creatinine, uric acid, ammonia and other substances are excreted through urine. The urine formed by the nephrons is carried from the kidneys to the urinary bladder through the pelvis and ureter. The pelvis of the kidney is a funnel-shaped expansion of the upper part of the ureter. The urine travels from the pelvis to the bladder through the ureter. The urine is stored in the bladder and the person empties the bladder periodically depending on the circumstances. In addition to the excretion of waste products, kidneys regulate the water content, chemical composition (electrolytes like sodium, potassium, bicarbonate, calcium, magnesium, chloride and phosphate) and content of acids and alkalis in the blood and body fluids. The kidneys also perform the following endocrine functions:

a. ***Renin***: Renin is an enzyme which activates renin-angiotensin-aldosterone axis which helps in the long-term regulation of blood pressure. Thus, the kidneys play an important role in the regulation of blood pressure. Hypertension can be caused by kidney disease and hypertension causes damage to kidney as well. Medicines acting on the renin-angiotensin-aldosterone axis

are used in patients for treatment of high blood pressure.

b. ***Erythropoietin:*** Erythropoietin is a protein secreted by the kidney and stimulates the RBC forming (erythropoietic) stem cells in the bone marrow. This results in an increase in the number of RBCs in blood. Kidney diseases are associated with anaemia which is related to deficiency of iron and erythropoietin. Erythropoietin is commonly used in patients undergoing dialysis for correction of anaemia. It should be used only after correcting iron and vitamin deficiencies.

c. ***Active vitamin D*** (1, 25-dihydroxycholecalciferol): Kidneys secrete an enzyme [1-alpha hydroxylase] which converts inactive Vit D [25-hydroxycholecalciferol] to the active form of vitamin D [calcitriol [1, 25-dihydroxycholecalciferol]. This is an important hormone in the regulation of calcium homeostasis, development of bones and also has numerous other functions. Deficiency of active vitamin D may cause bone deformities (rickets) in children and bone disease in adults. Vitamin D deficiency is common in patients with kidney disorders. It must be used cautiously in patients undergoing dialysis, because excess Vitamin D can cause calcium deposition in the blood vessels.

d. ***Prostaglandins***: Prostaglandins are produced in the kidney, and they are involved in protecting the kidneys (self-protection) by a process called "autoregulation". Non-steroidal anti-inflammatory drugs (NSAIDs) suppress the activity of prostaglandins. Since the autoregulation is lost, such patients may develop acute and chronic damage to the kidneys. These drugs are commonly used by patients, even without prescription.

e. ***Kinins:*** *Kinins* like bradykinin are released in small quantity from kidneys which help to decrease blood pressure by causing dilatation of arteries.

Symptoms and Signs of Kidney Disease

The symptoms of kidney disease can vary from no symptoms to those of severe kidney failure. It is important to determine whether the symptom is harmless or suggest a serious kidney disease. Some

of the signs and symptoms of kidney disease may be non-specific and may not appear until the advanced stage of kidney failure. A patient may present with no symptom, abnormality detected on urine examination, routine blood tests, imaging or with characteristic symptoms and signs of kidney disease. Kidney involvement is common in other diseases or may be part of a multi-system illness. Since the symptoms due to kidney diseases are extremely variable, the patient may present to any specialty. Some symptoms which point directly to kidney disease are:

a. Edema: Accumulation of excessive fluid in the interstitial compartment of the body gives rise to edema. Other diseases like congestive heart failure, cirrhosis of liver, nutritional deficiency or side effect of drugs (non-steroidal anti-inflammatory drugs and some blood pressure medications) can cause edema. In kidney diseases, the patient is unable to excrete water from the body. Edema is an important sign of kidney disease. Common kidney diseases causing edema are nephrotic syndrome, acute nephritis, chronic kidney disease and acute kidney injury. The edema usually occurs initially around the eyelids (puffiness of eyelids) and later may become generalized.

b. Hypertension: Hypertension is very common in kidney diseases. Kidney diseases can cause hypertension, and hypertension can result in kidney disease. When a child or young person develops hypertension, kidney disease should be strongly suspected.

c. Pain: The pain due to diseases of the kidney or urinary tract has some characteristic features. There are pain-sensitive nerve fibres in the capsule and "collecting system" in the kidney (calyces, pelvis, ureter, bladder and urethra). Pain due to stretching of capsule (covering) of the kidney is a dull aching pain in the loin area. "Renal colic" is due to stone in the kidney or upper urinary tract, and the pain is sharp and severe and radiates from the loin to the inguinal region, inner side of upper thigh, scrotum or vulva. The patient is often in distress and is not comfortable in any position. Bladder tumors or stones cause pain in the suprapubic region.

d. Abnormalities in micturition (changes in urination).

i. **Oliguria**: (Decreased urine output) Oliguria is defined as a urine output less than 400 ml in 24 hours in adults.

ii. **Anuria:** (Patient passes less than 100 ml of urine per day). The causes are the failure in the function of kidneys and/or obstruction to the flow of urine. If the patient does not pass even a drop of urine, then total obstruction should be suspected.

iii. **Polyuria:** (Excessive urine output) It is defined as urine output greater than 3000 ml over 24 hours in adults.

iv. **Nocturia**: (Need to wake up at night to pass urine many times). In normal persons, the urine formed during sleeping hours is less than when the person is awake. When kidneys are chronically damaged and the strength to concentrate the urine during sleep is lost.

v. **Burning micturition/Dysuria/Strangury** are the terms used for various grades of pain during passing urine. They suggest infection or irritation in the urinary tract.

vi. **Frequency of micturition:** In this condition, the patient has to go for urination more frequently. (This can be due to reduced bladder capacity or inflammation in the bladder or urethra.)

vii. **Hesitancy:** It is a condition where the patient has difficulty in starting micturition. (This occurs usually in older men with prostatic enlargement.)

viii. **Precipitancy:** It is the term used when the patient is forced to pass urine as soon as he feels the sensation in the bladder.

ix. **Incontinence:** It is a condition where the patient passes urine without control. There are many types of incontinence:

- *Continuous dribbling*
- *Stress incontinence (passing urine while coughing/laughing, etc.)*

- *Urge incontinence (passing urine as soon as the feeling occurs)*
- *Postvoid dribbling (passing a small quantity of urine after completing the urination)*
- *Overflow incontinence (bladder is full and leakage of urine occurs).*

e. Changes in urine color. (Normal—light yellow/amber color)

i. Deep yellow: Concentrated urine (dehydration/exercise/jaundice).

ii. Red/pink color: Blood/haemoglobin/beetroot consumption/menstrual contamination, Drugs—pyridium/warfarin/rifampicin.

iii. "Cola" color: Hematuria (nephritis)/hemoglobinuria (hemolysis)/myoglobinuria (muscle damage).

iv. Brown/black: Phenylketonuria (inborn error of metabolism – rare), Drugs—nitrofurantoin, metronidazole, iron sorbitol.

f. Changes in composition of urine.

i. Proteins in urine: Some proteins like Tamm Horsfall glycoprotein, beta 2 microglobulin, albumin and immunoglobulins are present in urine in small quantities. The excretion of all types of protein is called proteinuria. The excretion of albumin in urine is called albuminuria. The daily albumin excretion in a normal person is <30 mg, whereas the normal daily urinary protein excretion is <150 mg.

In microalbuminuria (now referred to as moderately increased albuminuria), the urinary albumin excretion is between 30 and 300 mg daily. It can be detected by special albumin-specific urine dipstick test or simple radioimmunoassay test. It is an important test as it finds out if the kidney is already affected due to diabetes in a patient with prolonged diabetes. This test is also useful in patients with cardiovascular disease and hypertension. If it is more than 300 mg in 24 hours, it can be measured by a simple dipstick test.

If proteinuria is >500 mg in 24 hours, it can also be detected by a simple dipstick examination. It causes the urine to become frothy or foamy. Proteinuria can be divided into three categories: transient (intermittent), orthostatic (proteinuria occurs only when the patient is in an erect position) and persistent (always present). Proteinuria may be due to glomerular/tubular diseases, due to overproduction (myeloma/leukemia) of different types and severity.

a. >500 mg to <3.5 gm/day: Subnephrotic proteinuria

b. >3.5 gm/day: Nephrotic syndrome

c. >20 gm/day: Massive proteinuria

ii. Hematuria (blood in urine): Hematuria is defined as the presence of three or more RBCs per high power field in centrifuged urine specimen. If the urine is bright red with blood clots, it may suggest injury, tumor or stones in the urinary system.

iii. Casts (cylindrical mould of the lumen of the distal tubule): Casts are formed from Tamm Horsfall glycoprotein in the distal tubule. Sometimes different types of cells, like RBCs, WBCs or fat globules, may be incorporated into the cast forming RBC/WBC/fatty casts. The presence of cast suggests involvement of parenchyma of the kidney.

g. As mentioned earlier, clinical features of poor kidney function are very variable and may affect any system of the body. The usual features are:

i. Hypertension: Blood pressure above 140/90 mmHg in adults.

ii. Gastrointestinal system: Anorexia (poor appetite), Nausea, vomiting or abdominal distension.

iii. Nervous system: Numbness of legs, peripheral neuropathy, tremor and myoclonic jerks (sudden contraction of muscles). They may also have dementia, depression, convulsions or coma.

iv. Heart: Cardiac failure, pericarditis, cardiac muscle dysfunction, arrhythmias or ischemic heart disease (heart attacks).

v. Respiratory: Dyspnoea (difficulty in breathing) due to water inside the lung, pleurisy and "air hunger" (Kussmaul's breathing—deep sighing breathing) observed in persons with metabolic acidosis.

vi. Skin: Pale skin, peculiar dull yellow color (sallow complexion), itching (pruritus), calcium deposits in skin and tissue, and nail changes.

vii. Bones: Bone pain, deformities in children (rickets) and fractures.

viii. Anaemia

ix. Reproductive system: Abnormalities in male and female hormonal functions.

2 Common Kidney Diseases and Renal Replacement Therapies

R. Kasi Visweswaran

When a patient presents with suspected renal disease, history, physical examination and preliminary investigations are done first. On the basis of the results, the disease is classified and a provisional diagnosis is made. There are 10 important syndromes in nephrology. Once the syndrome is identified correctly, the correct diagnosis can be made by further analysis and investigations. The 10 syndromes are:

1. **Acute nephritic syndrome**: Nephritis is due to inflammation of the glomerulus (glomerulonephritis). There are numerous causes. It may present rather suddenly with oliguria, hematuria, hypertension and renal failure. In children, most cases recover. In adults, they may have progression or complications.
2. **Nephrotic syndrome**: In this condition, there is leakage of protein in urine (>3.5 gm/day) which results in edema, low serum albumin level (hypoalbuminemia), high blood levels of cholesterol and other lipids (hyperlipidaemia). The causes have to be identified by investigations and appropriate treatment should be instituted.
3. **Acute kidney injury (AKI):** It is a common condition occurring in patients admitted to the intensive care units of hospitals. The kidney function decreases rapidly and accumulation of waste products occurs. There is often a reduction in urine output and the blood levels of urea and creatinine starts increasing rather suddenly (few hours to days). Many patients may need dialysis or other 'renal replacement' therapies.
4. **Chronic kidney disease (CKD)**: If any type of kidney disorder persists for >3 months, the condition is called chronic kidney disease (CKD). The disorder can be due to abnormalities in urine, blood, or X-ray and/or ultrasound examination. It may also occur after diseases like diarrhoea, infections, and use of toxic substances. It

is classified into five stages. (See section CKD below). Almost all patients undergoing dialysis for CKD will be in Stage 5.

5. **Urinary tract infections (UTI):** The urinary tract is usually sterile. When bacteria invade the urinary system, the condition is called urinary tract infection (UTI). Bacteria often enter the urinary system through the urethra. Sometimes, it may enter through the bloodstream.
6. **Urinary tract obstructions:** Whenever the free flow of urine is obstructed, there will be an accumulation (retention) of urine and development of urinary infection or even renal failure. The treatment is to correct the obstruction. If the ureter is obstructed, there will be collection of urine in the ureter, renal pelvis and calyces. The kidney will be enlarged (hydronephrosis). When the urethra is blocked, the bladder will enlarge and later, the "back pressure" will be transferred to the ureter and kidneys on both sides (lower urinary tract obstruction).
7. **Renal tubular defects:** Structural tubular defects are various types of renal cysts or tumors while functional tubular defects are mainly renal tubular acidosis and AKI.
8. **Urolithiasis**: Otherwise known as stone diseases. Stones can form in any part of the urinary system. Most stones contain calcium and are radio-opaque (visible in X-ray).
9. **Hypertension:** Kidney disorder can cause hypertension, and uncontrolled hypertension can damage the kidneys.
10. **Asymptomatic urinary abnormalities**: Sometimes abnormalities in the urine may be detected in a person who has no symptoms and undergoes a medical check-up. Sometimes, these abnormalities may be harmless but it may also indicate some underlying illness. Therefore, such patients should undergo necessary investigations and remain under periodic follow-up.

The common renal diseases which may require renal replacement therapies (RRTs) are AKI and Stage 5 of CKD. Hemodialysis, peritoneal dialysis, and renal transplantation are the main forms of RRT. There are, however, a few non-renal failure indications and related

procedures. A dialysis technologist should be aware of this, which will be discussed in subsequent chapters.

Acute Kidney Injury (AKI)

AKI means sudden onset of impairment of the renal function (occurring within hours to weeks), resulting the accumulation of substances in the blood that are normally excreted by the kidneys. As a result, there can be an increase in the level of blood urea, creatinine, uric acid, potassium and reduction in bicarbonate. All these are detrimental to the body and even cause death. There are two main types of AKI: community-acquired and hospital-acquired.

Community-acquired AKI occurs due to diseases like gastroenteritis, dehydration, blood loss, snake envenomation, leptospirosis, or use of nephrotoxic toxins or drugs. The causes for the common hospital-acquired AKI are sepsis, low blood pressure (hypotension), loss of water from the body (dehydration), imbalance of chemistry of body fluids, use of many drugs or a combination of these. If the kidneys alone are affected, the treatments may be favorable. However, if a number of other organs are affected/failing (multiorgan involvement/failure), the prognosis may be poor.

There are many systems of classification of AKI. We will follow the classification based on the kidney disease improving global outcome (KDIGO) guidelines. In this, the AKI is divided into three stages.

Stage 1	= Serum creatinine increase 1.5–1.9 times baseline or >0.3 mg% in 24 hours or urine output <0.5 mL/kg/hour for 6 hours
Stage 2	= Serum creatinine increase 2–2.9 times baseline or urine output <0.5 mL/kg/hour for 12 hours
Stage 3	= Serum creatinine increase 3 times baseline or creatinine >4 mg% or initiation of dialysis or output <0.3 mL/kg/hour for 12 hours or no urine output [anuria] for 12 hours

The causes of AKI can be broadly divided as follows:

1. Pre-renal causes: Important pre-renal causes are dehydration (loss of blood/body fluids/water), low blood pressure (hypotension/shock) or rarely liver disease (cirrhosis). Shock may occur due to heart failure (cardiogenic shock), infections (septic shock), obstruction to blood flow (pulmonary embolism—blood clot blocking blood flow in the lungs).
2. Intrinsic renal causes: The most important cause is damage to the renal tubules if the "pre-renal cause" persists for a long time and deprives the tubules of their blood supply and oxygen (ischemia). This results in necrosis of tubules. The damaged tubules often recover in due course. In such cases, if the kidney functions are supported by dialysis, near-complete recovery can be expected.
3. Post-renal causes: Obstruction of urine flow is the most important post-renal cause and can result in AKI. Although the treatment is to correct the obstruction or draining the urine, if the AKI is in Stage 3, the patient may need to undergo dialysis before attempting correction of the abnormality.

A patient with AKI often has oliguric phase (low urine output), diuretic phase (early recovery phase with uncontrolled high urine output) and recovery. During the oliguric phase, the excretion of water and waste products (urea, creatinine, potassium and acids produced from the body) do not occur. Thus, accumulation of water (fluid overload/edema), and high urea/creatinine in blood (uremia), potassium accumulation (hyperkalemia) and acids (acidemia) takes place. Fluid overload, pulmonary edema and hyperkalemia are life-threatening complications and require emergency treatment. Severe uremia and acidosis are also life-threatening and should be treated early. In about 20% patients with AKI, there may not be oliguria (non-oliguric AKI).

Chronic Kidney Disease (CKD)

CKD is a common problem worldwide. Nearly 10% of adults may have CKD although many may not have any symptoms. The kidney function is measured by estimating the glomerular filtration rate (GFR). The

normal range is 120 +/− 20 mL/min. Patients develop symptoms only when the kidney function is less than 20% of normal. A diagnosis of CKD can be made even though the kidney function is within normal range, if any of the following abnormalities are present for more than 3 months.

i. Albuminuria >30 mg/day
ii. Abnormalities in urine microscopy
iii. Abnormalities in renal function tests
iv. Abnormalities in renal imaging (X-ray/scan)
v. Abnormalities in renal pathology
vi. After renal transplantation

CKD is staged as follows depending on the kidney abnormalities and GFR (See BOX).

Criteria for staging CKD

CKD 1	GFR >90 mL/min [normal kidney function], one or more of the above abnormalities present	
CKD 2	GFR 60–89 mL/min [normal kidney function], one or more of the above abnormalities present	
[If GFR <60, it is CKD even if markers of kidney damage are absent.]		
CKD 3a	GFR 45–59 mL/min [	**-do-**]
CKD 3b	GFR 30–44 mL/min [	**-do-**]
CKD 4	GFR 15–29 mL/min [	**-do-**]
CKD 5	GFR <15 mL/min [	**-do-**]

D = Indicates patient on dialysis

A = Indicates patient has Albuminuria—severity denoted as A1, A2 and A3

A1 = Albuminuria <30 mg/day (normal range of urinary albumin excretion)

A2 = Albuminuria 30–299 mg/day moderate increase (but not detected by simple lab tests)

A3 = Albuminuria >300 mg/day detected by simple lab tests

Stages of CKD and symptoms are shown as a cartoon below.

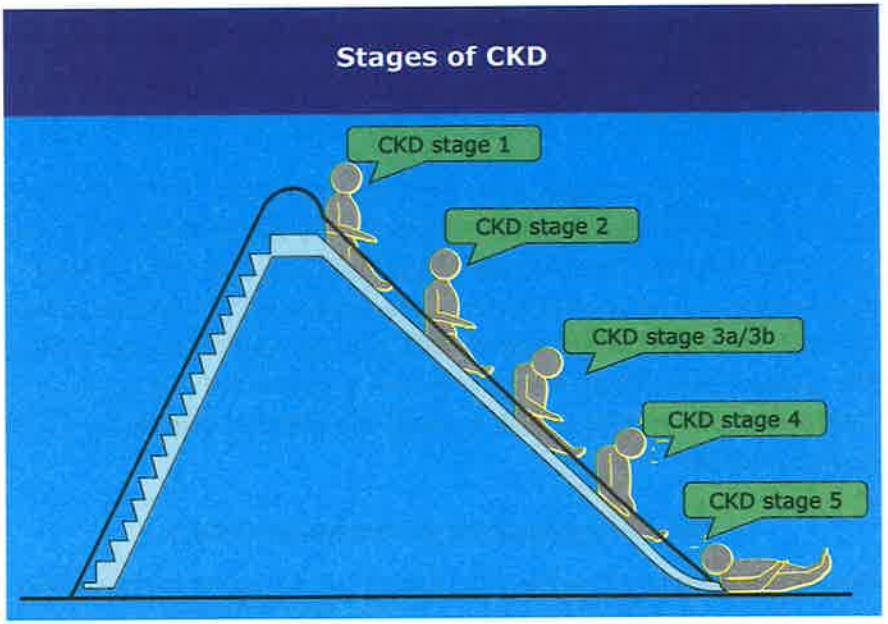


Fig. 2.1: Patient is feeling quite well in Stages 1 and 2, slightly unwell in Stages 3 and 4, and quite unwell in Stage 5.

There are many causes of CKD. Long-standing uncontrolled diabetes and high blood pressure (hypertension) are the two leading causes. Chronic glomerulonephritis (inflammation of the glomeruli) with kidney damage and shrunken kidneys is another important cause. Polycystic kidney disease is an inherited kidney disease which is characterized by the formation of thousands of cysts throughout the kidneys. These cysts may enlarge, develop infection, bleeding, form stones or even become cancerous. Other conditions like congenital diseases, kidney stones, UTI, drugs and toxins can also cause CKD. Unknown factors may lead to a condition called CKDu.

The clinical features of CKD in earlier stages may be insignificant and the patient may not have any symptom. The findings in CKD Stages 4 and 5 are extremely variable and may affect any part/system of the body. Gastrointestinal symptoms (poor food intake, nausea, vomiting) are common. Hypertension, difficulty in breathing,

anaemia, bone pain, tremors, sudden muscular contractions (myoclonic jerks), drowsiness, disorientation or even coma may occur. Sometimes, CKD Stages 4 or 5 is diagnosed when the patient comes for treatment for anaemia, sterility, visual complaints or for medical check-up.

Treatment in CKD Stages 4 and 5 is symptomatic and correction of the body's internal environment is very much necessary. Any correctable factor (uncontrolled hypertension, diabetes, infection, obstruction, active primary disease leading to CKD) should be looked for and corrected. Planning for RRT should start with counselling the patient from Stage 4 onwards and prepare the patient for the treatment. Depending on the available facilities and resources, RRT can be initiated.

Renal Replacement Therapies (RRT)

Renal replacement therapies include dialysis and renal transplantation. Most often, patients undergoing transplantation will have to undergo some form of dialysis during the preparation and waiting time for the transplantation. Sometimes, children are taken up for transplantation earlier (in CKD Stage 4) even before the need for dialysis occurs. This is called "Pre-emptive" transplantation. We will discuss the various types of dialysis later in this book.

Hemodialysis: This is the commonest form of dialysis therapy followed all over the world. An artificial membrane is used as "semipermeable" membrane to separate the waste products from blood. Today, the Hemodialysis machines are electronically controlled with many safety systems and alarms. The procedure has now become relatively simple, safe and painless. The three main requirements for Hemodialysis are as follows:

i. Vascular access: To continuously draw the blood from the body and return the blood after dialysis.

ii. Artificial kidney: Semipermeable membrane separates blood and dialysis fluid in two watertight separate compartments and enables dialysis to take place.

iii. Dialysis monitor (machine): This machine helps to—

a. Prepare, check and deliver the dialysis fluid.

b. Circulate the blood to the artificial kidney and back.

c. Give alarm and stop dialysis if the safety is compromised.

The other requirements are anticoagulation, immunization protocols, diet, universal precautions, patient education, assessing adequacy of dialysis, and identifying and management of complications.

There are many modifications of conventional Hemodialysis. (These will be discussed in detail in the respective chapters.)

i. SLED – Sustained low efficiency dialysis

ii. SCUF – Slow continuous ultrafiltration

iii. CRRT – Continuous renal replacement therapy

iv. HF – Hemofiltration

v. HDF – Hemodiafiltration

vi. CVVHD – Continuous venovenous Hemodialysis

vii. CAVHDF – Continuous arteriovenous hemodia-filtration

viii. NDD – Nocturnal Daily dialysis.

- The term CAV represents continuous arteriovenous (the blood flow is from patient's artery to machine and returned to the vein). (This is not practiced now.)
- The term CVV represents continuous venovenous (a double lumen catheter in the vein is used and the blood flow is from the patient's vein to machine and back).

Peritoneal dialysis: In this form of dialysis, the peritoneal membrane covering the abdominal cavity is used as the semipermeable membrane and the waste products are removed by repeatedly filling the peritoneal cavity with sterile dialysis fluid and draining it after a specified time. Machines which can be programmed to perform the repeated filling and emptying the peritoneal cavity (exchanges) are

available and called "Cyclers". The following are the three main types of peritoneal dialysis:

i. Intermittent peritoneal dialysis (IPD)

ii. Continuous ambulatory peritoneal dialysis (CAPD)

iii. Continuous cyclical peritoneal dialysis (CCPD)

Gastrointestinal dialysis: In this procedure, the patient is administered water and medicines to cause diarrhoea. The waste materials are excreted through the large volume of diarrhoeal fluid. Since the loss of water and chemicals through diarrhoea is unpredictable, and the patients do not tolerate such procedures, this is not practiced. Some modifications using gut microorganisms are being tried.

3 Understanding Body's Chemistry

R. Kasi Visweswaran

The cells in the body are surrounded by the body fluids which forms the "internal environment" or "milieu interior". The internal environment should be maintained within normal limits for the cells to function normally. The extracellular fluid is the "internal environment". The body contains approximately 60% water (varies from 45–70% depending on age, sex and fat content). This is distributed in the body in different compartments **(Fig. 3.1)**.

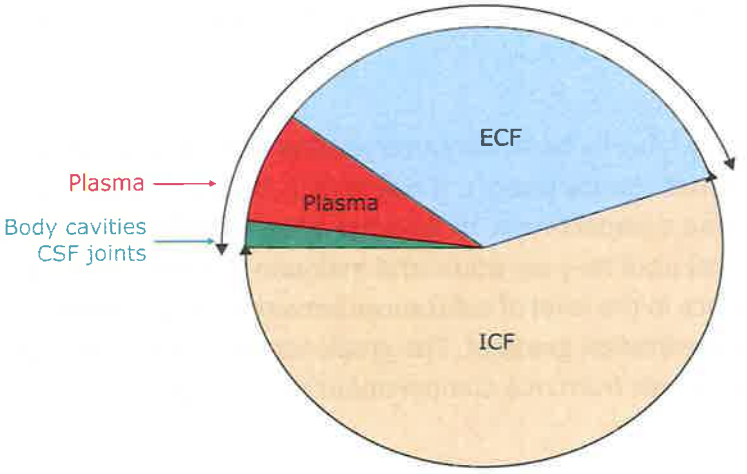


Fig. 3.1: Showing the distribution of water in the body.
ICF: Intracellular, ECF: Extracellular fluid.

Body Fluid Compartments

There is constant movement of fluids between the body fluid compartments. The fluid inside the cell is called intracellular fluid (ICF, about 66% of all fluids) and the body fluid outside the cell is called extracellular (ECF, about 34% of all body fluids). The ECF compartment is further divided into—

i. Interstitial (surrounding the cells): 74% of ECF

ii. Intravascular (in the blood): 25% of ECF and

iii. Transcellular: Fluid covering brain (CSF), in joints, eyes, and lymph about: 1% of ECF

The chemical composition of the fluid (water) in the different fluids is different. The chemicals can be positively charged or negatively charged ions. The positively charged ions are called cations (e.g., sodium [Na^+], potassium [K^+], calcium [Ca^{++}], magnesium [$Mg2^{++}$], and ammonium [NH_4^+]. The negatively charged ions are denoted by – sign and are called anions (e.g. chlorine [Cl^-], bicarbonate [HCO_3^-], and phosphate [PO_4^-]). The ICF contains mainly potassium, magnesium and phosphate, and calcium and bicarbonate are very low. In the extracellular fluid, sodium, chloride, calcium, and bicarbonate are high.

The body tries to have the same level of osmotically active solutes in all three compartments. If the level is different, water will move from one compartment to another (due to difference in osmotic pressure) until they are equal and maintain the osmotic equilibrium. Difference in the level of substances between compartments is called the concentration gradient. The gradients cause movement of water or substances from one compartment to another.

The movement of water due to pressure gradient is called ultrafiltration.

The movement of water due to osmotic gradient is called osmosis. If the concentration of osmotically active solutes is different, the osmotic forces across the cell membrane will cause the movement of water from an area of low osmotic pressure to higher osmotic pressure.

The movement of solute particles due to concentration gradient between two solutes is called diffusion.

During dialysis, only fluid and solutes in the bloodstream (intravascular compartment) can be removed. Other changes between the compartments occur because of the shift of water and electrolytes according to the concentration gradient.

For example, urea is present throughout all the three body compartments equally. The dialysis fluid does not contain urea. Therefore, there is a steep concentration gradient for urea across the semipermeable membrane in the artificial kidney. During dialysis, urea diffuses from the blood (intravascular compartment) to the dialysis fluid. As the urea level in blood comes down, more urea diffuses from ECF to the bloodstream because of the concentration gradient. Later, when the ECF urea is lower, urea from the ICF diffuses to ECF and later to blood. Finally, it is removed by dialysis. The movement from ICF to ECF and ECF to blood will be slower than the removal through the dialysis membrane.

The body tries to maintain equilibrium with the help of kidneys and other organs. To maintain sodium and water balance, the intake of fluids and output from the body must be nearly equal. The intake includes food, liquids and volume of intravenous fluids (if any). The output from the body includes urine, vomitus and diarrhoea. Insensible water production occurs from the metabolism of foods and insensible water loss occurs through breath and sweating.

Water: The thirst mechanism regulates water intake. In a normal person, when the body loses water, the thirst mechanism is stimulated and the person consumes water. Simultaneously, anti-diuretic hormone is secreted by the posterior pituitary gland and the urine volume decreases and the deficiency is corrected. If the normal person consumes water excessively, the kidneys excrete the water as urine and the excess water is removed from the body.

Sodium: The average normal salt intake is about 6 grams. Depending on the need of the body, the salt is excreted or retained by the kidney. In conditions of dehydration, more salt is reabsorbed in the kidney and the urinary sodium is lower. Otherwise, the excess sodium is excreted by the kidneys.

Potassium: Potassium is mainly inside the cell and the blood level should be maintained in a narrow range of 3.5–5.0 millimoles/L. Fruits, fruit juices, tender coconut water, meat and vegetables contain potassium. The potassium in the body is also excreted mainly in the urine. The hormone aldosterone regulates the potassium level in the blood. Aldosterone causes loss of potassium through urine. Some potassium is lost through the gastrointestinal system in the form of stools.

Calcium: Calcium in the body is deposited mainly in the bones. The blood level of calcium must be maintained in the narrow range of 9–11 mg%. Calcium has important roles to play in functions of heart, contraction of muscles and function of nerves. The intestines, Vitamin D, parathyroid and other hormones, bones, and kidneys interact with each other and maintain the calcium level.

Phosphorus: Like calcium, phosphorus in the body is found mainly in the bones and teeth. It is also present in the intracellular compartment and is important for regulating the function of enzymes in the body. The blood level is maintained in the range of 2.8–4.5 mg% by the kidneys with the help of hormones like the parathyroid hormone, fibroblast growth factor 23 [FGF 23], insulin and Vitamin D. The daily intake is excreted by the gastrointestinal system (about 30%) and kidneys (about 70%). In renal failure, when retention of phosphorus occurs in blood, a series of changes will lead to bone disease and calcium deposits all over the body including blood vessels. So, early diagnosis and prompt treatment helps to prevent such complications.

Magnesium: Major part of magnesium (about 60%) in the body is in the bones. The remaining is in the intracellular fluid compartment. The blood level is between 1.4 and 2.2 mg%. It is very important for many enzymatic reactions in the cells, in addition to the functioning of heart, muscles and nerves. The kidneys excrete the magnesium from diet and help to maintain the blood level. When kidney function is poor, higher blood levels of magnesium may occur. Therefore, magnesium-containing diet and drugs should be avoided in patients with renal failure.

Acid-Base Balance

The pH represents the amount of acid or alkali ions in the body. The pH of pure water is 7.0. If the pH is more than 7, the solution is in the alkaline range and if below 7, it is in the acidic range. The pH of blood is maintained in a narrow range of 7.35–7.45. If pH is below 7.35, the condition is called academia and if >7.45, alkalemia. The terms acidosis and alkalosis are used to specify the condition causing academia and alkalemia, respectively. The blood pH is maintained in the normal range with the help of "buffers". The buffers in the blood and body (e.g., bicarbonate, phosphate, proteins, hemoglobin, bone) either give away or accept hydrogen ions depending on the situation and maintain the pH within the normal range. The body gets hydrogen ions from food and these are excreted by the kidney. Many conditions including chronic kidney disease can cause acidosis. Carbon dioxide is derived from carbonic acid and is excreted by the lung.

Acidosis occurs when acids are added to or when alkalis are removed from the body:

a. Acids are added to the body from outside (diet, drugs)

b. More acids are formed within the body (shock)

c. Alkalis are lost from the body (diarrhoea, drainage of bile, or pancreatic fluid)

d. Failure to produce bicarbonate by the body

e. Accumulation of carbon dioxide in the body (respiratory failure)

Alkalosis may occur in the following circumstances:

a. Administration of sodium bicarbonate/alkalis

b. Alkalis added to blood from inside (endogenous)

c. Loss of acid from the body (excessive vomiting – loss of hydrochloric acid)

d. Excessive removal of carbon dioxide (over-breathing can cause excessive removal of carbon dioxide)

There are four primary disorders of acid base balance. If the primary problem can be respiratory or metabolic, the disorder can be acidosis or alkalosis. Therefore, the four primary disorders of acid base balance are as follows (See BOX):

a. Metabolic acidosis	→ [Primary fall in blood bicarbonate level]
b. Metabolic alkalosis	→ [Primary rise in blood bicarbonate level]
c. Respiratory acidosis	→ [Primary rise in carbon dioxide - pCO_2]
d. Respiratory alkalosis	→ [Primary fall in carbon dioxide - pCO_2]

When there is a metabolic abnormality, the respiratory system will try and compensate so that the pH is not altered significantly. For example, the compensation for metabolic acidosis is by respiratory alkalosis, metabolic alkalosis is by respiratory acidosis and so on. In some illnesses, more than one acid base abnormalities may coexist.

Arterial blood gas (ABG) is done to assess the acid base status of a patient. The blood sample should be taken from an artery with great care. There should be no air in the syringe and the sample must be analyzed with no delay. The main data obtained from ABG are pH, partial pressure of carbon dioxide (PCO_2) and bicarbonate (HCO_3).

The normal values are:

pH = 7.4 (range 7.35–7.45)

pCO_2 = 40 mmHg (range 35–45)

HCO_3 = 24 mmol/L (range 22–26)

Other data like Na, K, Cl, and anion gap (AG) are also available in the report for interpretation.

Study of acid base balance is important in patients undergoing dialysis since renal failure may cause acidosis and alkalosis may be a complication of inappropriate treatment.

4 Introduction, Principles and Understanding Terms

R. Kasi Visweswaran • Sreedevi P. A.

Introduction

The word "dialysis" is derived from the Greek terms – "DIA" meaning "through" and "LYSIS" meaning "separate and remove". Hemodialysis, therefore, means to separate and remove waste materials from the blood through a membrane. Accumulation of waste materials can cause discomfort and illness. Crude forms of removal of waste products through sweat by hot water bath or steam bath had been practiced for centuries. Modern dialysis has its foundations in the 19th century. The important landmarks are:

1854: **Thomas Graham** (1805–1869) described the nature of diffusion, osmotic forces in fluids and behaviour of biologic fluids across a semi-permeable membrane. He used Ox bladder as the semi-permeable membrane.

1913: **Abel, Rowntree and Turner** working in John Hopkins Medical School, Baltimore, USA, invented an apparatus and dialyzed a living animal injected with salicylic acid. They used hirudin (obtained from leaches) to prevent blood clotting. Blood from the artery was circulated through celloidin tubes immersed in saline and returned through a vein. They showed successful removal of salicylates from the blood.

1924: **Georg Haas** (1886–1971) performed the first human dialysis in the University of Gissen, Germany, using collodion tubes. However, he could continue the procedure for only 15 minutes.

1945: **Willheim Johan Kolff** (1911–2009) performed the **first successful human dialysis**. He was working in the University of Grohigen in the Netherlands and is considered the "Father of Hemodialysis". He invented the "rotating drum" artificial kidney. The dialysis membrane was a cellophane and wound around the wooden drum. As the drum rotates in a tank filled with dialysis

solution, movement of materials across the membrane and dialysis occurred. The drum and tank were large and occupied a lot of space.

Improvements in dialysis membranes and technology have resulted in the modern-day hollow fibre artificial kidney which is used throughout the world today.

Understanding Common Terms

Water: Water found in earth is the life-giver for all living things. It is a colorless odourless liquid composed of hydrogen (11.8%) and oxygen (88.2%) by weight. Water is an important ingredient for preparing the dialysis fluid, and the importance of water and water treatment for dialysis is discussed in a separate chapter.

Electrolytes: Substances (like sodium [Na^+], potassium [K^+], calcium [Ca^{++}], magnesium [Mg^{++}], phosphate [PO_4^{++}], chloride [Cl^-] and bicarbonate [$HCO3^-$] are some examples of common electrolytes. They dissolve and disperse uniformly in water. If electric potential is applied to the water containing electrolytes, the positively charged ions travel to the negative pole of the terminal (cathode) and are called cations. The negatively charged ions travel to the +ve pole (anode) and are called anions. Electrolytes are important for the body, and the kidney helps to maintain the concentration of electrolytes in the body within the normal range. In patients with kidney failure on dialysis, the correct concentration of electrolytes in the dialysis solution is very important.

Solution: We get a solution when any substance is dissolved in a liquid. The liquid is called the solvent and the substance dissolved is the solute. For example, if salt and water are mixed in a glass, we get a solution of salt water. Here, the salt is the solute and water is the solvent. Although sugar is not an electrolyte, water with dissolved sugar is also a solution.

Solubility: Solubility is the property of a chemical substance to dissolve in liquid. The chemical substance or the solute can be solid,

liquid or gas, and the solvent can be any substance in liquid form. The solubility depends not only on the chemical properties but also on other factors like temperature, pressure, pH and presence of other chemicals.

Unsaturated solution: In a solution containing solvent and some solute, if more solute is added, it will dissolve. This solution is unsaturated.

Saturated solution: If you keep on adding solute to the same solution, after a point, the solute will not be able to dissolve and remain undissolved. The solution is now "saturated" with the solute and cannot dissolve anymore.

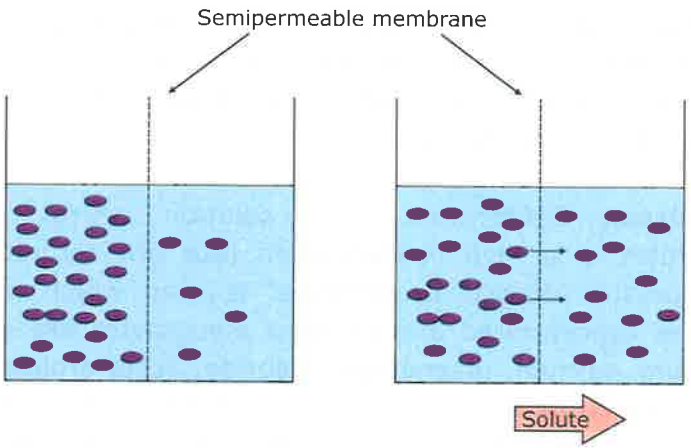
Concentrate: Concentrate is a solution which contains the solutes in a high concentration (but not saturated). In Hemodialysis, "dialysis concentrate" is used which is about 34 times concentrated and contains electrolytes like sodium, potassium, calcium, magnesium, chloride, acetate/bicarbonate and non-electrolytes like glucose dissolved in water. When the Hemodialysis concentrate is diluted with treated water in a proportion of approximately 34:1 to get acetate dialysis fluid. The dialysis fluid will contain the electrolytes that are almost similar as blood. (Refer chapter on dialysis fluid.)

Permeability: It is the ability of a substance to pass through a barrier. If a substance can pass through a membrane, the membrane is permeable to the substance.

Semi-permeable membrane: It is a natural or synthetic membrane which allows certain ions and molecules to pass through them. Dialysis membranes are semi-permeable membranes. There are very small (sub-microscopic) openings called pores. Solutes which are larger than the pore size cannot pass through the pores. Various types of membranes have been synthesised with different properties for use in different situations. (Refer chapter on membranes and artificial kidney.)

Principles of Dialysis

Diffusion: It is defined as the spontaneous movement of a **solute** from a solution with higher solute concentration to a solution with lower solute concentration across a semi-permeable membrane. For example, if a spoon of sugar is added to water, the sugar sinks to the bottom, and gradually, the sugar molecules diffuse and dissolve in water. There is no movement of water in diffusion **(Fig. 4.1)**.



Note: Only **solute moves** from higher concentration to lower concentration. There is no movement of water.

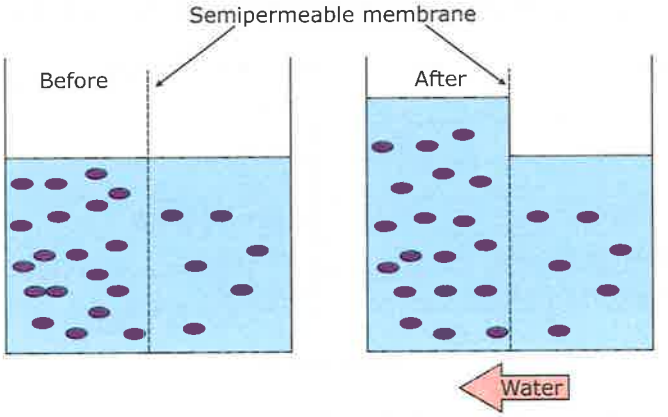
Fig. 4.1: Diffusion across a semi-permeable membrane.

Ultra-filtration: It is defined as the **movement of water** molecules across a semi-permeable membrane from an area of higher hydrostatic pressure to an area of lower hydrostatic pressure.

Convection/(advection/solvent drag): When there is movement of water across the membrane, dissolved and smaller solute particles are also "dragged" with the water to the other side of the membrane. This is called advection/convection or solvent drag.

Osmosis: It is defined as the spontaneous movement of **solvent** (water) from a solution of lower solute concentration to a solution with higher solute concentration across a semi-permeable membrane.

If two solutions with different salt (solute) concentrations are separated by a semi-permeable membrane, water (solvent) moves spontaneously (passively) from the solution with lower solute concentration to an area of higher solute concentration. The principle of osmosis is used mainly in peritoneal dialysis **(Fig. 4.2).**



Note: There is no movement of solutes. Only **water moves.** Note the higher water level.

Fig. 4.2: Osmosis.

Understanding More Terms in Hemodialysis

Molecular cut-off: Molecular cut-off is the molecular weight (MW) above which the substance will be unable to cross the membrane. Red blood cells, white blood cells, platelets and most plasma proteins are too large to pass through the pores in dialysis membranes. Water and substances dissolved in water pass through the membranes freely. MW is represented as Daltons (D). MW determines whether the molecule can go through the pores in the membrane. The pore size of different types of membranes is different. Cuprophane membrane permits small molecules up to MW <3000 D to pass through. High cut-off membranes permit larger molecules up to 65,000 D to pass through. Plasmapheresis membrane has MW cut-off of about 3,000,000 D and allows plasma with proteins and immunoglobulins to pass through. The blood cells like RBCs, WBCs and platelets are prevented from going through.

Certain substances known as middle molecules are not removed by conventional dialysis membranes and the accumulation of such middle molecules is harmful. Special membranes are now available to remove middle molecules.

The MW of some common substances is given in **Table 4.1**.

Table 4.1: Molecular weight of some common substances

Substance	Molecular weight
Urea	60 D
Creatinine	113 D
Glucose	184 D
"Middle molecules"	3,000–60,000 D
Immunoglobulin G (IgG)	160,000 D
Immunoglobulin M (IgM)	900,000

Clearance

Clearance is the amount of blood that is completely cleared of a certain solute in 1 minute. It is a measure of membrane's permeability to small solute substances such as urea and creatinine. It is related to the rate of blood flow through the dialyzer.

$$\text{Clearance} = \frac{(\text{Arterial Concentration} - \text{Venous Concentration}) \times Q_B}{\text{Arterial Concentration}}$$

(Q_B = blood flow rate)

Example: If the level of urea entering the artificial kidney and leaving are respectively 250 mg% and 100 mg% and the blood flow rate is 300 mL/min, the urea clearance for the dialyzer is calculated as follows.

$$\text{Urea clearance} = \frac{(250 - 100) * 300}{250} = 180 \text{ mL/min @ 300 } Q_B$$

Urea clearance of 180 mL/min at 300 Q_B means that at a blood flow rate of 300 mL per minute, the membrane in the dialyzer should totally clear all the urea from 180 of the 300 mL of blood passing through it every minute.

Flux and Convective Transport

The term "flux" refers to the permeability of the membrane. Flux determines the quantity of solutes that pass through the membrane.

Smaller solutes like urea (MW 60) can move freely across most semi-permeable membranes. But larger solutes move more slowly and the rate of convective transport is also lower. In the case of "High flux" membranes, substances with higher MW also pass through the membrane easily.

Sieving Coefficient (SC)

Sieving coefficient (SC) is a mathematical expression which describes the percentage of a solute, which passes through the membrane from the blood into the dialysate by convection. Sieving coefficient is expressed as a decimal from 0.1 to 1.0. SC = 1 means that the membrane allows 100% of the given solute to pass through whereas SC of 0.4% means only 40% of the solute could pass through. (If the number is higher, more of the solute passes through.) The convective transport of the solute depends on the SC of the membrane.

$$\textbf{Sieving coefficient (SC)} = \frac{\textbf{Solute concentration in Ultrafiltrate}}{\textbf{Solute concentration in blood}}$$

Example:

1. If solute concentration in ultrafiltrate is 100 mg% and blood concentration is 150 mg%, the **SC** = 100/150 = 0.66.
2. If the solute concentration in ultrafiltrate is 25 mg% and blood concentration is 150 mg%, the **SC** = 25/150 = 0.17.

The SC for larger molecules like Beta 2 microglobulin (Mol Wt – 12,000) in low flux membranes will be only around 0.2, whereas it will be nearly 0.7 in high flux membranes.

Surface Area

Surface area is the area of a membrane which is in direct contact with blood, on one side, and dialysate, on the other side, and is expressed in square meters (m^2). The dialyzer with larger surface area is required for patients with higher body weight. The efficiency of dialysis increases with higher surface area dialyzers. In conventional dialyzers, the surface area varies from 0.5 to 1.3 m^2.

Mass Transfer Coefficient (KOA)

Mass transfer coefficient (KOA) is a number which represents solute transport efficiency of a dialyzer. It will be proportional to the surface area of the membrane.

i. Dialyzer with KOA values <500 mL/min are used for low-efficiency dialysis or for small patients.

ii. Dialyzer with KOA values of 500–800 mL/min are moderately efficient and are used for routine therapy.

iii. Dialyzers with KOA values >800 mL/min are used for "high efficiency" dialysis.

Transmembrane Pressure (TMP)

Transmembrane pressure (TMP) is the pressure difference across the membrane. In the present models of dialysis machines, it is possible to apply negative pressure on the dialysis side which will help to increase the pressure across the membrane. This will enable fluid removal from the blood. Most membranes can withstand TMP of 300 mmHg, beyond which the membrane may rupture resulting in leak of blood from blood compartment to dialysate compartment.

Transmembrane pressure (TMP) = VP – DP

VP = Venous pressure (pressure in venous drip chamber)

DP = Dialysate (negative) pressure

Example:

If the pressure in the venous drip chamber is + 50 and pressure in dialysate compartment is (negative) – 200 mmHg, TMP is calculated as follows.

TMP = 50 – (-200) = 50 + 200 = 250 mmHg

Co-Efficient of Ultra-Filtration (KUF)

Co-efficient of ultra-filtration (KUF) is the volume of fluid removed from blood in each hour for each millimeter of mercury (Hg) pressure difference across the membrane. If the KUF of a dialyzer is 4, it means 4.0 mL of water will be removed from the blood in each hour for every 1 mm Hg TMP. So, it is possible to find out the amount of

ultra-filtration every hour and plan for the total fluid removal during the dialysis schedule.

Ultra-filtration hour (UFR) = KUF X TMP

Example:

If KUF is 4 and TMP is 300, UFR will be 1200 mL/hour.

Dialyzer membrane can be classified into low flux, middle flux and high flux depending on the KUF **(Table 4.2)**.

Table 4.2: Showing the Ultrafiltration coefficient of different membranes

Type of dialyzer	KUF in mL/min per mmHg
Low-Flux dialyzers	<8
Intermediate/Middle-Flux	8–20
High-Flux	>20 mL

Biocompatibility

The dialysis membrane is a foreign body. Some materials used in the manufacture of dialysis membranes are associated with the interaction between the blood and membrane. As a result, discomfort to the patient and other complications may occur. During the passage of blood through the membrane, proteins adhere (adsorb) to the membrane and "isolate" the blood from direct contact with the membrane. The ability to adsorb the protein on the membrane surfaces improves biocompatibility. Although biocompatibility improves, the clearance and overall efficiency may decrease with repeated reuse. Poly acrylonitrile (PAN) membrane has the greatest adsorptive capacity and is more biocompatible compared to cellulose or semi-synthetic membranes.

The membranes used for procedures are different and will be discussed in the respective chapters.

5 Infection-control Precautions and Vaccinations in the Dialysis Room

R. Kasi Visweswaran • Priya J.

It is necessary to take steps to prevent the spread of infection to the patient and also protect the staff. Bacteria and viruses are present in the body, as well as the surroundings. All normal persons carry bacteria in the nose, mouth, intestinal tract and skin. They may not cause disease, and some of the bacteria are essential for the body. Pathogenic organisms (bacteria, viruses and fungi) are capable of causing diseases. Bacteria can spread from person to person through coughing, sneezing or touching. In the case of medical personnel, it can also spread through injections, needle stick injuries, performing nursing or other procedures or by handling blood and body fluids. Thus, the staff who are exposed to contact with blood and body fluids must be very careful and follow the suggested precautions strictly. Protecting the staff from infection is as important as preventing the spread of infection to the patient. The universal precautions were introduced in the United States after the AIDS epidemic, to protect healthcare workers from HIV and other blood-borne pathogens. In 1987, body fluid isolation was advised to prevent transmission of disease through handling blood and body fluids. Later, standard precautions were made applicable to all. With the advent of newer viral diseases like avian flu, SARS, H1N1/H5N1 influenza and SARS – COVID19 pandemics, special isolation precautions are practiced. Since none of these organisms can be seen through the naked eye, extreme care should be taken by all healthcare workers to protect themselves, as well as the patients.

Infection can spread from person to person through air, close physical contact, injection with contaminated needles, use of blood or blood products or "needle stick injury". The common methods of transmission of infection are:

i. Air-borne transmission – e.g., tuberculosis

ii. Droplet transmission – e.g., mumps, measles, rubella, viruses like COVID 19, etc.

iii. Physical contact – e.g., staphylococcus and other skin bacteria

iv. Through food – e.g., cholera, typhoid

v. Through contaminated syringes/injections/needle stick injury/ use of blood products – e.g., Hepatitis B, Hepatitis C, human immunodeficiency virus (HIV), etc.

Standard precautions are very important for all healthcare workers and patients. Any worker exposed to body fluids, such as blood, urine, faeces, semen, vaginal secretions, synovial/amniotic/cerebrospinal/ pleural/pericardial/peritoneal fluid is at higher risk.

It is now advised to take "standard precautions" under all circumstances by **considering every patient as a potential risk** to each other. Standard precautions are a set of infection-control practices that healthcare personnel (HCP) use to reduce the transmission of microorganisms in healthcare settings. It protects both HCP and patients from contact with infectious agents. Thus, the health giver and the patient are protected from the risk of transmission of infection. The important methods practiced as part of infection-control techniques are:

i. Good personal hygiene habits and education

ii. Hand washing

iii. Use of personal protective equipment (PPE) (gloves/face mask/ goggles/disposable impermeable aprons/shoe cover)

iv. Correct handling of syringes, needles, sharp objects/other equipments (no recapping of used needle)

v. Aseptic techniques

vi. Cleaning of contaminated surfaces/surface of dialysis machines and all other equipments with liquid bleach (1% sodium hypochlorite solution)

vii. Managing spillage of contaminated body fluids

viii. Safe handling/disposal of contaminated material (linen/sharps/waste)

ix. Screening and monitoring for Hepatitis B (HbsAg test), Hepatitis C (anti-HCV antibody) and HIV periodically (as per hospital policy)

Hand Hygiene

This is the most important simple precaution to stop the spread of infection. The hands as well as the equipment/instruments used by the hand are very important in spreading the infection. In the hospital, the HCP should wash hands with soap and water before and after touching the patient or bed **(Fig. 5.1)**.

Proper washing time is at least 20–30 seconds and includes the following eight steps which should be correctly followed.

1. Wet both hands and apply enough soap (liquid soap preferred).
2. Rub the palms together in circular motion (clockwise and counterclockwise) to form good lather (foam).
3. Rub the backside and fingers of each hand with the palm of the other hand and the fingers.
4. Keep both palms together, interlink the fingers and rub against each other (to clean the side of fingers and the web between fingers).
5. Cup the fingers of both hands and interlock them. Rub the back of fingers and nails against the palm. Perform for each hand.
6. Clean thumb by holding the thumb with the other hand and clean in circular movement for each side.
7. Rub palm with the fingers of the other hand on each side.
8. Hold the wrist with opposite palm and clean with twisting movement on each side.

Once washing is completed, wash off the soap in running water. Most dialysis rooms have "elbow tap" which can be closed with the

elbow or automatic taps. If the tap has to be closed manually, it is done by using the paper towel to close the tap and discarding the paper towel. A fresh paper towel (or unused fresh sterilized towel) is used to dry hands. It is not advisable to use reusable cloth towel, since it can be heavily contaminated **(Fig. 5.1)**.

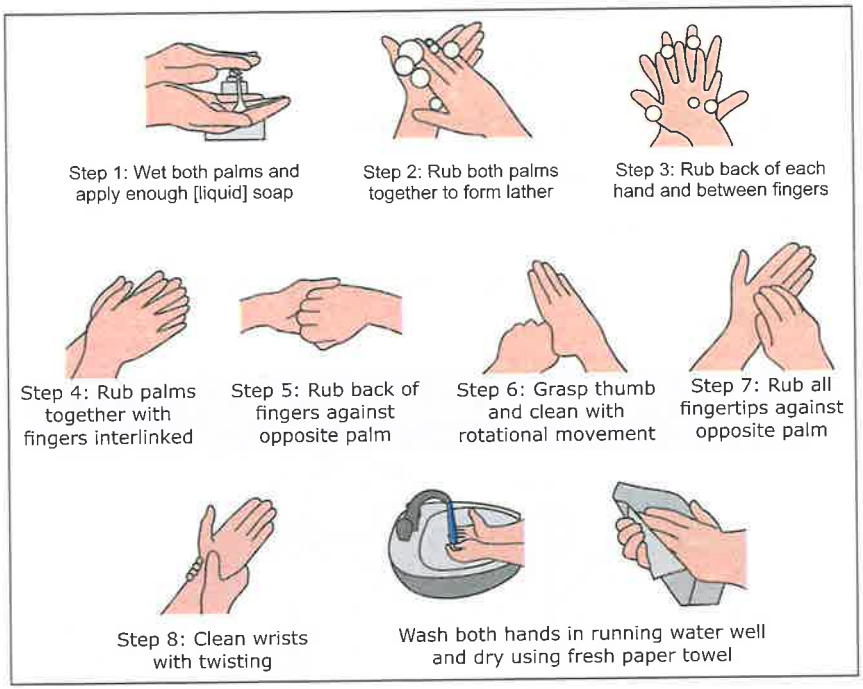


Fig. 5.1: Eight steps in hand washing.

Hand washing is a very important step in preventing the spread of infection, particularly in a hospital. Illnesses like food poisoning can be prevented by taking precautions, such as hand washing, by the food handlers and consumers. The dialysis staff should be more careful because the infection can spread not only from the staff to patient but also from patient to staff. Therefore, all staff must know how to do it properly. Hands are the primary carriers of dirt, viruses, bacteria and other agents. It is observed in surveys that majority of hospital staff do not wash their hands correctly. Majority of infections acquired in the hospital can be prevented by correct hand washing. It is preferable to keep both arms below elbow without clothing

or ornaments. The fingernails should be well-trimmed and clean. Soap and water are ideal if the hands are soiled. In other situations, alcohol-based hand rub may be used. The steps described below should be followed in both cases.

There are five situations where hand washing is required as recommended by the WHO **(Fig. 5.2)**. They are as follows:

1. Before touching a patient
2. Before a clean or aseptic procedure
3. After body fluid exposure risk
4. After touching a patient
5. After touching patient surroundings (bed, bed clothes, tubes, dressings)

Fig. 5.2: Situations requiring hand washing.

Barrier Nursing

Barrier nursing means nursing care used for a patient suffering from a contagious disease to prevent the infection from spreading from

the contagious patient to other patients or staff. This is also called "bedside isolation". The patient is isolated in a room or is provided with barriers on all sides. The medical personnel wear gowns, masks, gloves, goggles and observe all precautions to prevent the spread of infection. All equipments and utensils used by the patient are handled with care and sterilized using sterilizing solutions or steam heat.

Reverse-Barrier Nursing

If a patient is immunosuppressed, the chances of his getting infection from attending medical staff and visitors are very high. Steps to prevent the spread of infection from others to patient are called reverse barrier nursing. It is also called protective isolation for the patient. Patients who have received organ transplant are given reverse-barrier nursing during the post-operative period.

Vaccinations for Staff and Patients

The vaccinations to prevent various diseases should be considered and given to the patient even before the initiation of HD and regularly thereafter. However, if the patient has not received these, it should be started after the treatment of dialysis. The commonly used vaccinations protect against Hepatitis B, influenza and pneumonia. Other immunizations like varicella vaccine, tetanus toxoid and Hepatitis A vaccination may also be given according to the hospital's vaccination protocol. In elderly patients, influenza and pneumococcal vaccine should be administered.

Hepatitis B infection is common, and all patients, staff and trainees working in the dialysis unit should be vaccinated against Hepatitis B. Hepatitis B can spread easily through skin or mucous membrane if there is contact with blood from an infected person. Now, many units have separate dialysis area and machines for Hepatitis B and Hepatitis C. Precautions are very important while handling patients with the above infections and HIV infection.

Recombinant Hepatitis B vaccine 20 µg is to be given subcutaneously at 0, 1 and 6 months for the staff. Since patients with CKD and

undergoing dialysis do not develop the desired level of immunity, a higher dose is necessary. So, it is given as two injections of 20 µg, one in each arm at intervals of 0, 1, 2 and 6 months. The response is checked by testing for anti-HBS antibody titre.

Trivalent inactivated influenza vaccine 0.5 mL by intramuscular injection may be given every year.

Pneumococcal vaccine (23 valent polysaccharide vaccine) may be given once in 5 years.

In view of the pandemic of COVID 19 during 2020, it has become mandatory to immunize patients against COVID 19 by suitable vaccine with a view to reduce morbidity in case the infection relapses.

6 Infrastructure for Hemodialysis Facility

R. Kasi Visweswaran • Supin Vijayan

The requirements and infrastructure for setting up a dialysis unit vary depending on the type of work. If it is attached to a multi-specialty hospital, which handles complicated medical problems, they are likely to have more patients requiring support for acute kidney injury. Procedures like CRRT may be considered in such conditions. Institutions having cases with CKD requiring maintenance Hemodialysis are likely to have stable patients walking in for the procedure. The infrastructure for setting up a home dialysis unit is different. The infrastructure described here is suitable for a unit with about 10–20 dialyzing stations offering mainly maintenance Hemodialysis.

A multi-bed Hemodialysis facility should have the following major arrangements.

1) Area for water treatment and storage in the near vicinity of Hemodialysis area.

   A water treatment system with a standby system should be available. The RO water from a stainless steel (SS) tank with tapering bottom should be conveyed to the waterlines at the required pressure using a booster pump. An on-line ultraviolet filter is also connected to the line from SS tank. The waterlines should be continuous, and there should be no "dead spaces" where water can stagnate. A pressure monitor in the waterline is needed to monitor the water pressure. After supplying all machines, the line should drain excess water back to the tank for re-circulation. The same line can be taken through the washing and reprocessing area or a separate line from the RO water tank may be provided. The reprocessing should also be done using RO water.

2) Dialysis area for accommodating beds/couches, machine, working space for staff and other equipment.

   An area of at least 11 x 10 feet (110 sq. feet) should be provided **for each bed** so that there is space for movement and bringing additional equipment around the bed in case of need. Two rows can be arranged with a wide passage between the rows so that a bed can be wheeled in and out comfortably. Vinyl or Epoxy flooring is preferred since there are no joints, they are skid-proof and they can be easily cleaned. The walls should be water-resistant, smooth and without seams or grooves so that dust does not accumulate and they are easy to clean. It should be possible to dismantle and clean the ceiling also. There should be good natural lighting and ventilation. An air conditioning system should be planned in such a way that the cold blast of air is not directed towards the beds. Appropriate partitions are necessary to ensure patient privacy. Two doors, one for the patient to walk in and a larger door to wheel-in a patient with bed should be provided. The beds should have arrangements for tilting, backrest and height adjustment. There should be provision for storing alcohol-based hand wash dispensers in each bed.

3) A reception area with facilities for recording and checking vital parameters and patient weight just next to the dialysis area will be ideal.

4) Area for record-keeping and a computer station.

5) Waterlines for conveying RO water to machines must be medical-grade PVC, and there should be no metallic connections. (Stainless steel can also be used.) The connections should form a loop. The waterlines should provide outlet ports for each machine, one after another (in series). The unused RO water should be diverted finally to the RO tank. Thus, the loop is completed.

6) Electrical connections for dialysis machine and additional plug connections.

   Powerlines according to the specifications for the machine

should be provided (preferably at the head end of the bed). The lines should be preferably connected to UPS or at least a generator supply line. Frequent power disruptions are to be avoided. In addition, another five plugs should be provided for use of any other equipment that might be needed.

7) Central oxygen supply port should be provided for each bed.

8) Central suction port should be provided for each bed.

9) Drain pipes to drain the dialysis fluid after use.

   The drain pipes for conveying the used dialysis fluid from the machine must be at a height of 18– 24 inches from the ground at the highest point and should have a gentle downward gradient throughout and finally drain outside dialysis room to the disposal area. There should be no stagnation in the drainage line.

10) Pest Control: Rats gain access to the dialysis area at night and nibble tubings in the hydraulic system and damage the machine. Cockroaches creeping into the dialysis area, through drain lines, is also possible. Mosquitos and houseflies should also be prevented from entering the dialysis room. Food materials used by patients should be properly disposed. The staff should be discouraged from using any such items inside the dialysis room. A proper pest control system must be installed and periodically serviced.

11) Central store for storing new dialyzers, tubes, medicines, chemicals, and other equipment. At least one refrigerator should be available for the storage of medicines ("Dry storage").

12) The preparation room should be well ventilated and should have good natural light. An exhaust fan is ideal. Facility for hanging saline bottles and draining used saline and chemicals should be built in at the time of planning. This room should have easy access to the storage area for reused dialyzers and tubings.

13) Washing area with workbench for reuse machine (electrical and water connection as per specifications for the reuse machine).

14) Washing area for manual rinsing for reuse. The manual washing area should have two sinks, one for rinsing the dialyzer and tubings of blood initially. Once the blood is drained and rinsed, it is taken to the next sink where it is connected to running RO water. This sink should have a partition of 6–8 inches below the upper part. This partition should have large openings through which the washed fluid flows freely, but the dialysis set remains on the top shelf. The tap with RO water should have connectors which can be connected to blood tubings and blood port of the artificial kidney. The second set of connectors should be Hansen connectors which can be attached to the dialysis port of the artificial kidney. Hansen connectors are "clip on" connectors which can be attached to the dialysate ports of artificial kidneys. There should be a regular water connection also in the washing and reprocessing area. This water tap should be used for general cleaning where RO water is not necessary.

15) Storage area for storing dialyzers and tubings for reuse ("Wet storage").

    Facilities should be available to have individual compartments and labeled boxes for each patient separately, so that mix-up does not occur. Many institutions have a "pigeon hole" arrangement. Prefabricated shelf for this purpose is also available.

16) One emergency cart with equipments like pulse oximeter with cardiac monitor, infusion pump and endotracheal set should be available for every 6 beds.

17) One defibrillator should be available in the dialysis area.

18) Accurate weighing scales with large platform for weighing even wheelchair-bound patients are necessary. Electronic scales with such arrangements are available. (Bed scales would be ideal for units performing CRRT.)

19) One or more nursing station with all-round clear visibility.

20) Hand-washing area for staff—elbow connectors or automatic water flow arrangement is preferred.

21) Toilets.

22) Duty room for doctors.

23) Audiovisual entertainment facility for patients.

24) Bystander waiting area with telecommunication facility.

It would be ideal to provide additional space for future expansion.

7 Water and Water Treatment for Hemodialysis

R. Kasi Visweswaran • Sreedevi P. A.

Three-fourths of the earth surface is covered by seawater. However, it is not suitable for drinking or regular use. The sources of water for human use are:

a. Rainwater: Water obtained from rain. If collected directly, it will contain only minimal contaminants, like dust, gases and impurities from the atmosphere.

b. Surface water is from the surface of the earth, from rivers, lakes, ponds or reservoirs. Surface water is obtained from rainwater after it falls on the surface of the earth or from the melting of ice in glaciers and mountains. Surface water contains particles, mud and microorganisms.

c. Groundwater: Any surface water can permeate into the soil and remain under the earth's surface. Groundwater comes from shallow wells, springs and deep bore wells. They contain higher concentrations of calcium, magnesium and iron. The microorganisms in groundwater are comparatively lesser than surface water.

Water obtained from any source is purified to remove contaminants and kill bacteria. A normal person needs about 10–15 L of water every week which is used for drinking. Other uses like cooking, washing, bathing and cleaning will require about 50 L per week. The blood or body fluids are protected from the water used for drinking and other purposes by the skin or the mucous membrane of the gastrointestinal tract. Every patient on dialysis comes into contact with at least 400 L of water every week. This water, which comes as dialysis fluid, is separated from the blood only by a thin dialysis membrane. Since substances could cross the membrane in the dialyzer into the patient's blood, water used for preparing dialysis fluid must be free of microorganisms and other contaminants.

There are five major groups of contaminants:

i. Suspended material: Sand, sediments, and suspended particles

ii. Inorganic (non-carbon) impurities: Calcium, magnesium, potassium, sodium, sulphates, nitrates, iron, copper, aluminium, and trace elements

iii. Organic material: Domestic waste, decayed plant/animal waste, pesticides, herbicides, and chloramine

iv. Microbiological: Bacteria, mainly Gram-negative bacteria, endotoxins, viruses, fungi, and algae

v. Dissolved gases: Carbon dioxide and hydrogen sulphide

Even tiny amounts of contaminants can cause discomfort to patients, minor symptoms or even major complications. Therefore, it is necessary to "treat" the incoming water before using it for Hemodialysis. This is important for patient safety.

Every 4-hour session of Hemodialysis will require about 120 L of dialysis fluid and at least 3–5 L for preparation and washing. Therefore, the quality of water used for dialysis is very important. The Association for the Advancement of Medical Instrumentation (AAMI) has prescribed standards for bacteria, endotoxin, metals, salts, trace elements and other substances for the water to be used for dialysis **(Table 7.1).**

Performing dialysis with inadequately treated water may lead to various acute and chronic complications. Complications due to contamination by minerals are shown in **(Table 7.2).** The signs and symptoms due to water contamination are summarized in **(Table 7.3).**

Water Treatment for Dialysis

First, an analysis of the incoming water is performed to plan and finalize the treatment system. The requirements vary with the source of water, the temperature, particulate contamination, whether water is soft or "hard", presence of chlorine/chloramine, minerals, etc. In cold countries, a heat exchange system is used to heat the incoming

Table 7.1: AAMI standards for dialysis water quality

Maximum permitted contaminant levels for water used in conventional Hemodialysis			
Aluminium	0.01	Magnesium	4.0 (0.3 mEq/L)
Antimony	0.006	Mercury	0.0002
Arsenic, lead, silver Each	0.005	Nitrates	2.0
Beryllium	0.0004	Potassium	8.0 (0.2 mEq/L)
Cadmium	0.001	Selenium	0.09
Calcium	2.0 (0.1 mEq/L)	Sodium*	70.0 (3.0 mEq/L)
Chloramines	0.1	Sulfate	100.0
Chlorine (free)	0.5	Thallium	0.002
Chromium	0.014	**Microbial contamination**	**<200 CFU/mL**
Copper, barium, zinc	0.1	**Bacterial endotoxin**	**<2 IU/mL**
Fluoride	0.2		

Table 7.2: Effects and toxicity of mineral contaminants in water

	Contaminant	Limit	Toxicity/effects
1	Aluminium [Al^{3+}]	0.01 mg/dL	Anemia Dementia/encephalopathy Osteomalacia/bone disease
2	Calcium [Ca^{++}] Magnesium [Mg^{++}]	2 mg/dL 4 mg/dL	Hard water syndrome Nausea/omitting/muscle weakness Hypotension/hypertension
3	Chloramine	0.1 mf/dL	Hemolysis, Anemia Methemoglobulinemia
4	Fluoride [F^-]	0.2 mg/dL	Bone weakness (osteomalacia/osteoporosis) May be fatal
5	Copper [Cu^+]	0.1	Nausea Chills/headache Hemolysis Liver damage
6	Nitrates	2.0 mg/dL	Nausea/hypotension Methemoglobulinemia
7	Sodium [Na^+]	70 mg/dL	Vomiting/headache Hypertension/fast heart rate (tachycardia) Pulmonary edema convulsions/coma
8	Zinc [Zn^{++}]	0.1 mg/dL	Anemia
9	Sulphates	100 mg/dL	Nausea/vomiting Metabolic acidosis

Table 7.3: Signs or symptoms due to possible water contamination

Anemia	→	Aluminium, chloramines, copper, zinc
Bone Disease	→	Aluminium, fluoride
Hemolysis	→	Aluminium, copper, nitrates, chloramines
Hypertension	→	Calcium, sodium
Hypotension	→	Bacteria, endotoxins, nitrates
Metabolic Acidosis	→	Low pH, sulphates
Muscle Weakness	→	Calcium, Magnesium
Nausea and Vomiting	→	Bacteria, calcium, copper, endotoxin, low pH, magnesium, nitrates, sulphates, zinc
Neurological deterioration	→	Aluminium
Fever, chills	→	Bacteria, endotoxin, copper, zinc

water which may be very cold. The "heat exchange system" consists of the pipes of cold incoming water and warm outgoing water, side by side, so that the warmth is transferred to the cold water. The temperature of incoming water can be between 25° and 35°C. Heat exchange systems are not needed in tropical countries.

The water supply in municipalities undergoes treatment by—

a. Screening to remove leaves, twigs or larger particles
b. Sedimentation/clarification to remove mud and silt
c. Treatment with alum and lime to flocculate small particles
d. Filtration of smaller particles
e. Disinfection
f. Chlorination

In spite of all these, the municipal water supply reaching the dialysis unit may contain contaminants. Both surface water and underground water also contain various contaminants. Therefore, the incoming water is passed through the water treatment system which consists of a series of filters, each with different functions to achieve the adequate quality of water for dialysis.

Backflow Prevention Device (Non-Return Valve)

There must be a backflow prevention device (non-return valve) in the beginning of the treatment system to prevent water from flowing in the reverse direction.

Multimedia Filter

The first in the line of filters is a sediment filter. A multimedia filter, has different sizes of sand or resin arranged in layers. The top layer has a small pebble-sized material and subsequent deeper layers have more finer material and smaller particles. As water flows from top to bottom, large insoluble contaminants in the water are trapped at the upper layers and finer particles at the lower layers. Insoluble substances up to 10 microns can be removed by this. Accumulation of contaminant particles clogs the filter, and thus, the multimedia filter is cleaned by backwashing and discarding the water containing the filtered ingredients. For backwashing, water is pumped from the bottom to the top, and the trapped particles and impurities are flushed out. The filter can be used repeatedly. It may be necessary to replace the resin after months or a few years depending on the use and quality of incoming water **(Fig. 7.1)**.

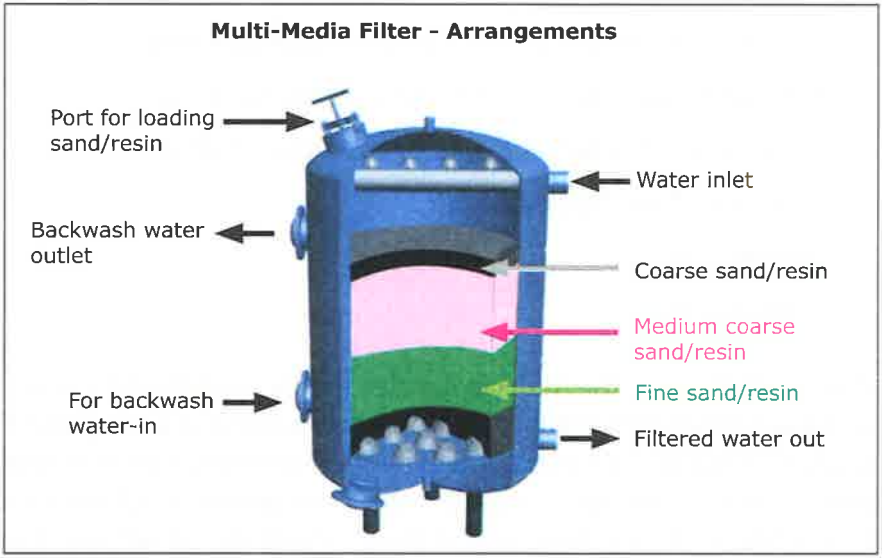


Fig. 7.1: Arrangement in multimedia filter.

Water Softener

The filtered water from the multimedia filter goes to the water softener. Since "hard" water has many minerals, it does not form foam with soap and causes whitish deposits on surfaces called "scaling". The scales will cover the pipelines and tubes, causing inefficient heating or even block the tubes. A water softener is used to remove mainly calcium and magnesium. Other substances like iron and manganese can also be removed. In a water softener, calcium and magnesium are exchanged for sodium by the process of "ion exchange". The water softener is also a cylindrical tank with an inlet for raw water and an outlet for soft water. The tank contains small polystyrene resin beads coated with sodium chloride. The brine (concentrated solution of sodium chloride) tank is also attached to the water softening system. When exposed to hard water, the resin which is coated with sodium chloride attracts positively charged ions like calcium [Ca^{++}] and magnesium [Mg^{++}] and releases sodium [Na^{+}] into the water. When all the sodium has been exchanged, the resin is said to be exhausted. The resin should be recharged by treatment with brine. The softener cannot be used while recharging. When brine is filled into the tank, the calcium and magnesium are released from the resin, sodium gets attached and the resin gets "recharged". The solution in the tank is discarded and the tank is rinsed with water before reuse **(Fig. 7.2)**.

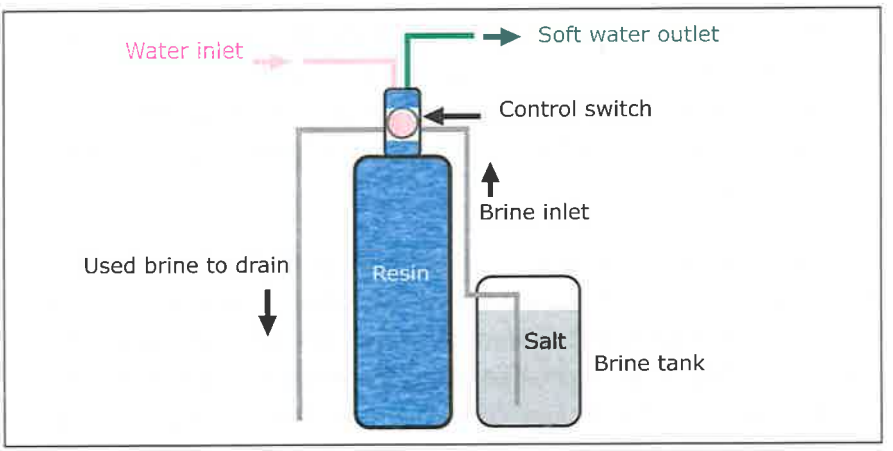


Fig. 7.2: Water softener.

Activated Carbon Tanks

Carbon tanks are also tall cylindrical tanks with connections for inflow of water from softener and outflow to the next step of water treatment. The tank contains activated charcoal in the form of granules. These are capable of adsorbing dissolved organic particles with low molecular weight from water. The main impurities removed are chlorines, pesticide residues, organic substances and industrial waste. Granular activated charcoal is porous, has a large contact area (surface area) and works more efficiently compared to powdered charcoal. Sometimes, two carbon tanks are connected one after the other. Since the duration of contact between the water and granules of charcoal is important for adsorption of substances, two tanks are connected one after the other. The first tank ("the worker") removes most of the impurities and the second tank ("polisher") completes the process. Unlike water softeners, the carbon filters cannot be recharged. When the adsorbing capacity of the filters is completely used up, the charcoal has to be replaced.

Reverse Osmosis

It is necessary to understand the following terms:

i. Feed water: Water that is fed into the RO unit after pre-treatment.

ii. RO-treated water: Water for dialysis after RO treatment.

iii. RO reject water: Water with contaminants rejected as unsuitable by RO system. The reject water contains 95% of ions like sodium (monovalent ions), 99% of ions like calcium (divalent ions) and 99.5% of the viruses and bacteria which are rejected from the feed water.

As discussed in the section on principles of dialysis, osmosis is the movement of solvent from an area of lower solute concentration to an area of higher solute concentration across a semi-permeable membrane **(Fig. 7.3)**. In reverse osmosis, pressure is applied to water on the side of higher solute concentration and the water moves in the opposite direction of osmosis **(Fig. 7.4)**. The water coming from

the carbon filter (feed water) is filtered by the RO membrane, and the RO-treated water comes out of the RO outlet. The contaminants and minerals in the feed water are removed as RO reject water. The RO "reject water" is not suitable for dialysis but can be used for other purposes or sent back to the multimedia filter for re-treatment. The temperature of feed water should be between 72°F and 80°F. Cold or hot water will damage the RO membrane.

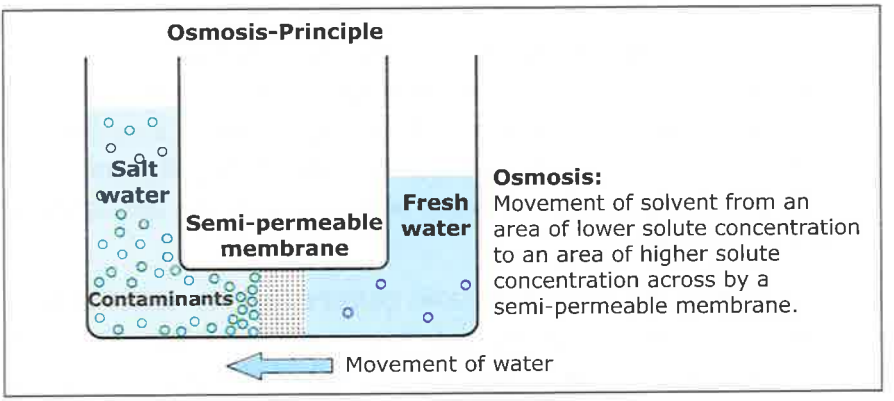


Fig. 7.3: Osmosis.

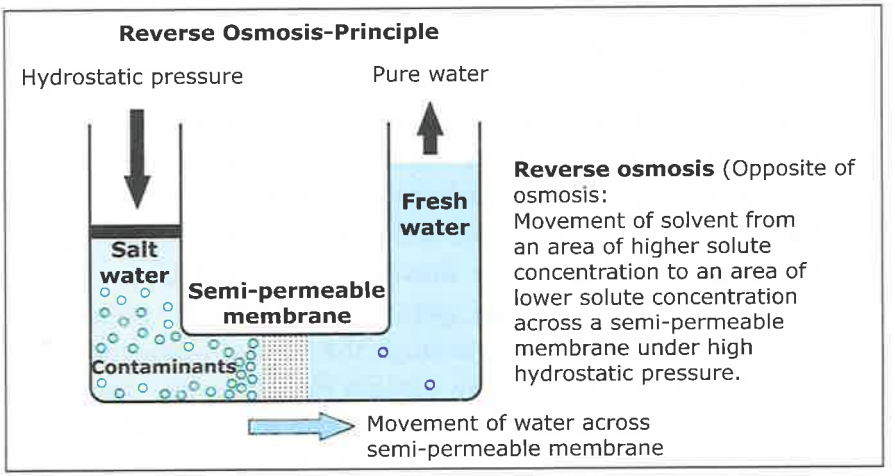


Fig. 7.4: Reverse osmosis.

RO membranes are made up of:

i. Cellulose acetate membrane

ii. Polyamide membrane

iii. Hollow fibre membrane

iv. Spiral wound membrane

v. Thin film composite membrane

The RO system consists of—

a. Pre-filters to filter the water again and remove any particles escaping into the water during pre-treatment.

b. Water pressure pump and motor to increase hydrostatic pressure on one side of the semi-permeable membrane. The pressure meters at incoming and outgoing water lines help to assess the pressure drop and assess the efficiency of membrane. The percentage of reject water also indicates the efficiency of the membrane.

c. RO membrane cartridges are constructed as spiral-wound systems, consisting of multiple layers of membrane, between spacer sheets (which also act as supports) coiled around a central perforated tube. This tube will convey treated RO water and will be connected to the RO water outlet. Layers of a thin semi-permeable membrane with the supporting framework are wound around the central tube in several layers. The spacer sheets are the supporting structure for the RO membrane and are made of a porous material. This is kept in a water-tight canister. The feed water is fed into the canister under pressure with the help of a water pump. The water under pressure moves through the layers of the framework in the cartridge, gets filtered by the RO membrane and pure water comes out through the central water tube. The RO reject water, which may contain metals, salts, chemicals, bacteria, viruses and endotoxins, is drained out as "RO reject" water. Accumulation of contaminants or formation of scales may block the membrane pores and reduce efficiency. This is called "fouling" of the membrane. Membrane efficiency can be assessed by observing the percentage of RO reject water. The membrane should be cleaned regularly. After cleaning, 1% peracetic acid is used to disinfect the membrane.

The RO water is fed into a high-quality stainless steel tank (SS Grade 316), with a round or conical bottom for storage. The conical bottom enables complete drainage of water before cleaning.

Steps in cleaning and disinfecting RO membrane are as follows (follow the instructions from the manufacturer):

i. Shutdown the system and remove the RO membrane canister.

ii. Backwash the membranes at low pressure with RO water.

iii. Use sodium tripolyphosphate and sodium EDTA for removing scales and cleaning the surface of the membrane without damage.

iv. Rinse again with water.

v. Use 2% citric acid for cleaning the system.

vi. Disinfect with peracetic acid 1.0% recirculate and maintain contact for 1 hour for disinfection.

vii. Reinstall the cartridge discard initial RO water flow after cleaning.

De-Ionizer (DI) Bed

De-ionizer (DI) is used to remove all anions (negatively charged ions) and cations (positively charged ions) from the water. It is used only if the water analysis warrants its use. Since the maintenance is cumbersome, it is not used as part of routine water treatment. DI system does not remove non-charged particles. So, bacteria, endotoxins and other non-charged particles are not removed. Moreover, the DI tanks favor bacterial growth inside them unless maintained very carefully. Ideally, there should be four tanks, one with anionic resin, one with cationic resin and two with mixed resins. The anionic resin tank contains electrically charged resin beads capable of exchanging anions for H^+ ions and the cationic resin tank contains resins capable of exchanging cations for OH^- ions. The H^+ and OH^- combine to form water. Mixed bed DI are more efficient as the bed contains both types of resins. Some units use a single mixed bed DI before the carbon filter or after RO before UV irradiation. Because of the disadvantages enumerated below, DI do not form

part of the standard water treatment system, and are not used in most centres.

Disadvantages while using DI are as follows:

a. DI system needs very careful maintenance.

b. Requires frequent change of the resins (when the ions are used up, it will release the materials adsorbed earlier and the pH of dialysis water may change).

c. Bacterial growth occurs in the resins.

d. May even cause death of the patient.

e. Only medical grade resins can be used.

f. DI system may cause formation of nitrosamines (cancer-causing chemical).

Ultraviolet Irradiation

Ultraviolet irradiation destroys microorganisms by affecting their DNA. So, the bacteria are killed or at least growth prevented. The equipment consists of a mercury vapor lamp housed within a quartz sleeve. The water flows over the sleeve and is exposed to UV light as it travels through the cylindrical container. One disadvantage is that even though the microorganisms are killed, the bacterial products of killed bacteria remain in the water. This may cause a pyrogenic reaction (fever). So, if treated water is stored in tanks before being circulated in dialysis machine, UV filters are fitted after the storage tank. The quartz sleeve should be wiped and cleaned and mercury vapor lamp replaced periodically. When connected on line to the waterline supplying the dialysis machines, it continuously provides UV-treated water **(Fig. 7.5).**

The water supply lines within the dialysis unit should not have any dead space (where water can stagnate), and the unused water should be safely returned to the RO water tank for recirculation. It will be better to use the RO water for manual reprocessing or automated reuse machines.

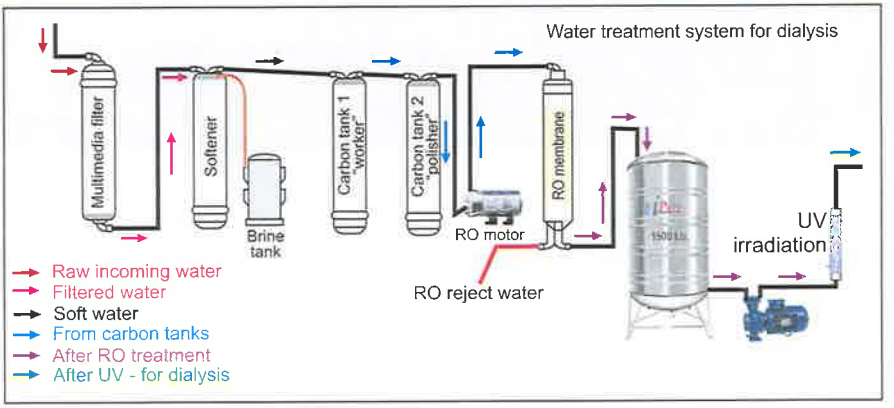


Fig. 7.5: Line diagram of water treatment system for RO water.

Maintenance of the water treatment system is very important and is the duty of the technologist to maintain the system regularly. Most of the filters have pressure monitors at the point of entry and exit of water. Pressure drop in the water leaving the equipment is an indication of decreased efficiency or malfunction. The multimedia filter should be washed almost daily or at least once in 3 days depending on the use and quality of incoming water. The softener should be recharged with brine more frequently in places where incoming water is "hard". There are methods to measure the hardness of water. In the case of membrane filters, any pressure drop >25% will call for replacement of the membrane. The RO membrane efficiency is assessed by the inlet water pressure and rejects water percentage. If the inlet pressure is higher by >25% or rejected water is >75%, it would suggest poor performance. "Fouling" of the membrane is the most important cause for the poor performance of RO system. Culture of water from multiple sites in the water treatment system, including outlets to individual machines, will be necessary to identify the source of infection. Water samples should be drawn for culture and disinfection to be undertaken periodically.

8 Vascular Access for Hemodialysis

R. Kasi Visweswaran • Revathy G.

It is necessary to have good vascular access to draw and divert the blood from the patient to the machine and return the blood back to the body after dialysis. For understanding the formation of vascular access, a clear understanding of the vascular anatomy of the arm, leg and neck is essential.

The arterial supply to the arm is from the aorta through the subclavian artery, which continues as axillary artery (in the axilla) and brachial artery (upper arm). The brachial artery divides into the radial and ulnar arteries below the elbow. The radial artery travels to the wrist laterally (towards the side of the thumb) and ulnar artery medially (towards the side of the little finger). Later they form an arch in the palm (palmar arch) from where branches supply the fingers.

The venous system of the upper limb consists of deep veins and superficial veins. The deep veins accompany the radial and ulnar arteries to form the brachial vein near the elbow and accompany the brachial and axillary arteries to the thorax. There are no superficial veins in the palm. They are formed in the dorsal aspect (back side) of the fingers and hand. There are two major superficial veins (travel through the subcutaneous tissue) in the upper limb, the basilic and cephalic veins. The small veins on the medial side (the side above the little finger) join to form the basilic vein at the wrist. This travels medially through the forearm and upper arm. It joins the brachial vein near the axilla to form the axillary vein. The cephalic vein forms at the lateral side of the wrist (on the side of the thumb) and proceeds up under the skin up to the elbow and thereafter through the lateral part of biceps muscle, and then groove between deltoid and pectoral muscles to drain into axillary vein near the shoulder. The most important interconnection between the two superficial veins is the median cubital vein in the elbow region. There is also a

connection between the deep veins and superficial veins near the elbow. The median cubital vein, cephalic vein and basilic veins at the elbow are the usual sites for venepuncture for drawing blood samples. The cephalic vein at the wrist is the most suitable vein for the creation of AV fistula.

In the neck, the most suitable vein for placing Hemodialysis catheter is the right internal jugular vein. It is close to the common carotid artery. Catheter for dialysis can be placed through the jugular vein into the superior vena cava or right atrium by locating its position by ultrasound. The major vein in the lower limb for placement of dialysis catheter is the femoral vein which is medial to the femoral artery below the inguinal ligament.

AV shunt: Glass tubes were used to cannulate the blood vessels initially. When the need for continuous access to the bloodstream was required, Dr. Belding Scribner (University of Washington) and Wayne Quinton popularized the AV shunts. Since plastic tubes inside the blood vessels cause inflammation and thrombosis, they inserted vessel tips made of Teflon in the blood vessels. The common site of the AV shunt was between the radial artery at the wrist and the cephalic vein in the forearm. The vessel tip is connected to semi-transparent silastic (silicone elastic) tubing. One vessel tip is inserted into the artery and fixed in position and the other tip in the vein. The silastic tube is taken out through the skin by leaving some part in the subcutaneous tissue (subcutaneous tunnel). The end comes out of the body through a skin puncture called exit site. The ends of these two tubes outside the body are connected to each other using a Teflon connector **(Fig. 8.1 A and B)**. This arrangement will permit the blood to flow from the artery to vein through the shunt continuously. During dialysis, the Teflon connector is removed and the silastic tubes are connected to the arterial and venous bloodlines. After treatment, the two tubes are reconnected to each other using the connector. The continuous flow of blood through the shunt tubing is restored. Since the Teflon material does not cause inflammation of the lining of the blood vessels (endothelium) or react with blood, it can be used for a long time. There will be no

need to place tubes for each dialysis session. If carefully used, these AV shunts can be used for many months to years. It is necessary to check for continuous blood flow through the shunt. This can be done by inspection (the colour of blood should be uniformly red and pulsations will be visible). On touching (palpation), there will be slight warmth in the tubing and pulsations may be felt. Auscultation will reveal a bruit due to the rapid blood flow through the shunt. AV shunt is not used now.

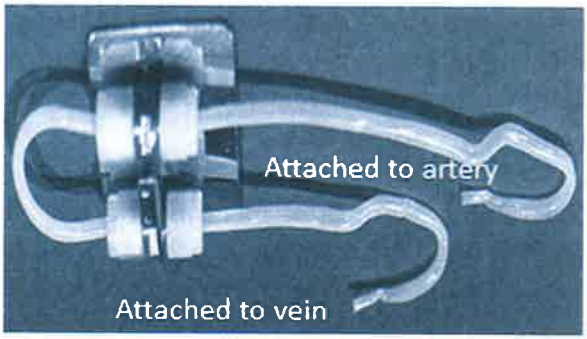


Fig. 8.1A: Highly magnified view of one hollow fibre.

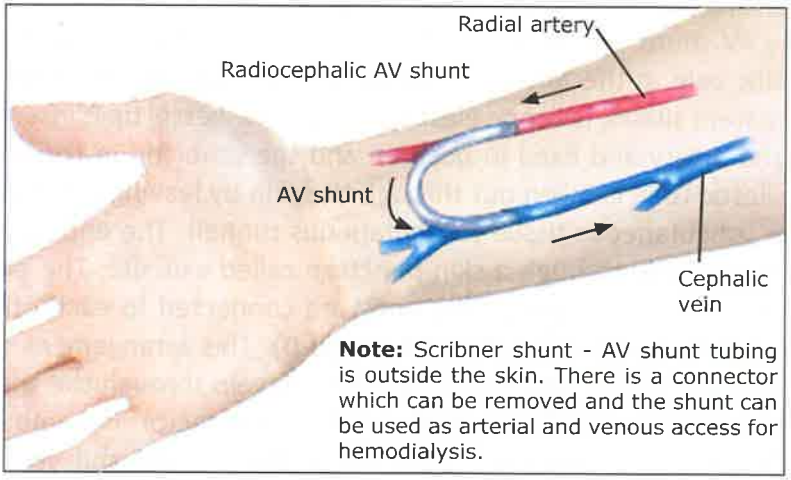


Fig. 8.1B: Scribner shunt (radio-cephalic AV shunt).

Native AV fistula: In order to avoid tubes outside the body, Brescia and Cimeno connected the radial artery with the cephalic vein inside the body surgically (native arteriovenous fistula). The connection

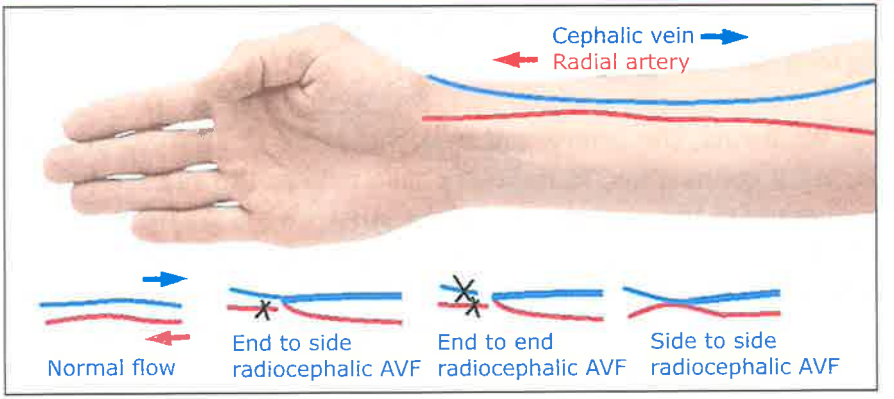


Fig. 8.2: Types of anastomosis of radio-cephalic AV Fistula.

between artery and vein can be end to side, side to side or side to end **(Fig. 8.2)**.

This is the best permanent vascular access for long-term dialysis. High pressure and the volume of blood flow from the artery directly to the vein cause enlargement of the lumen of the vein and thickening of the wall **(Fig. 8.3)**.

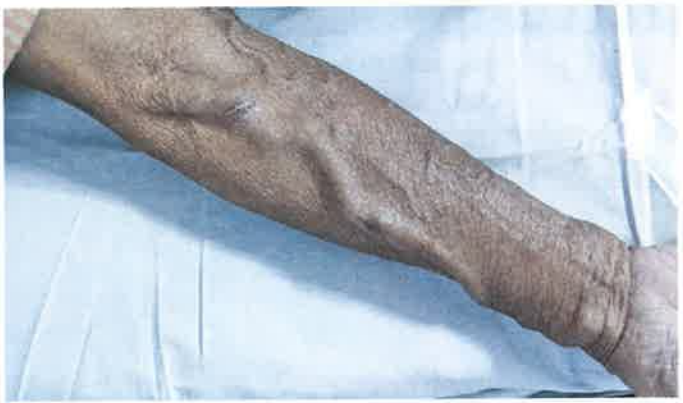


Fig. 8.3: Matured AV fistula.

The vein becomes suitable for cannulation for dialysis in about 2–3 months. The time for maturation will be longer in diabetics. Such "arterialized" vein (matured AV fistula) could be cannulated using a large-bore fistula needle so that adequate blood flow for dialysis is

obtained. A properly working AV fistula is the lifeline for the patient on long-term dialysis.

For AV fistula, the artery and vein should be close to each other for easy connection. In radio-cephalic fistula, the radial artery is connected to the cephalic vein at the wrist. This is the most favored site. In the brachiocephalic AV fistula, the anastomosis of the brachial artery with the cephalic vein is done below the elbow. Brachiobasilic AV fistula is formed by the anastomosis of the brachial artery with the basilic vein. The disadvantage of this approach is that the vein runs on the underside of the arm and is very difficult to cannulate particularly in obese patients.

Disposable fistula needles of suitable sizes are chosen for cannulation of AV fistula **(Figs. 8.4 and 8.5).**

AV fistula needle (red - arterial side, blue - venous side)

The venous is larger (1 SWG) then arterial needle.

Fig. 8.4: AV fistula needles.

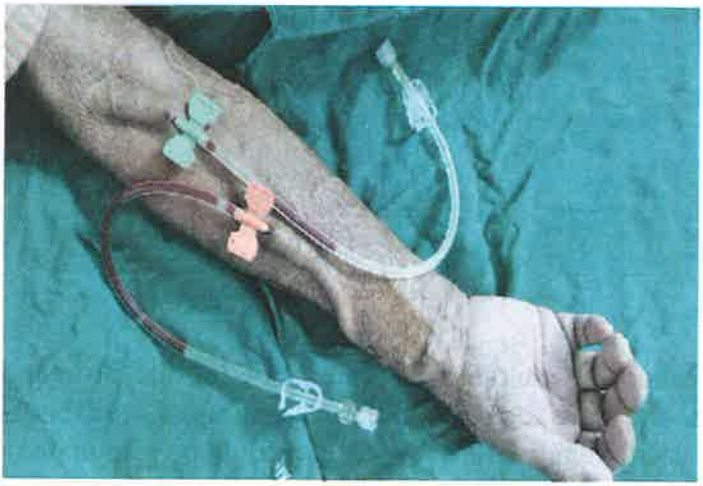


Fig. 8.5: AV fistula with fistula needle inserted.

When AV fistula is not possible or suitable blood vessels are not available, a graft made of Polytetrafluoroethylene (PTFE) can be used to connect the suitable artery and vein. The connection can be a straight graft between the artery in the wrist and the vein at the elbow or a "U"-shaped graft connecting an artery and vein at the elbow **(Fig. 8.6).** Dialysis can be performed by puncturing the graft. The maturation time of PTFE graft is shorter (3–4 weeks). More sites are available for graft placement since the artery and vein need not be close to each other.

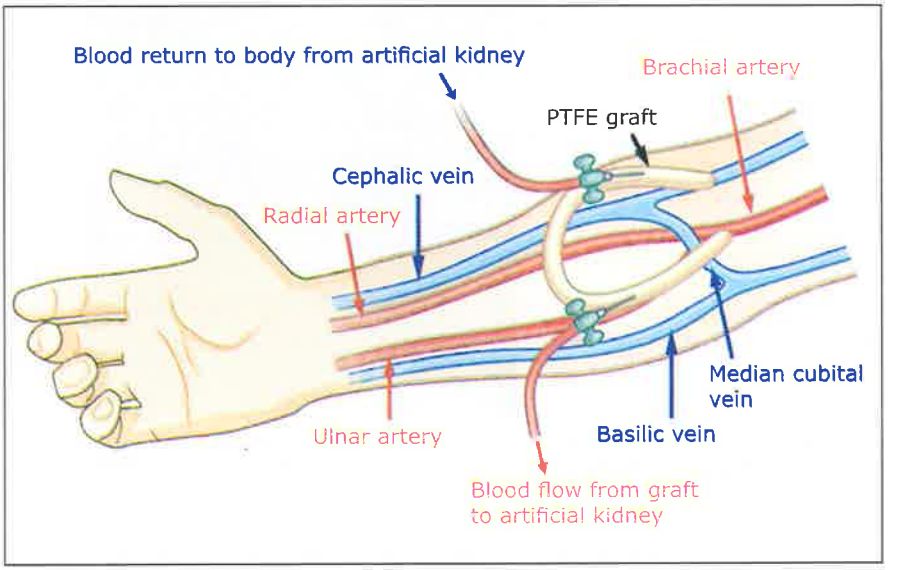


Fig. 8.6: Showing superficial veins in forearm and position of "U"-shaped PTFE graft. The graft is under the skin (subcutaneous tissue).

AV fistula is created at least a few months before the anticipated time of starting dialysis (the "Fistula first" initiative of the International Society of Nephrology).

The vascular access for short-term dialysis is by using double lumen dialysis catheters, which can be easily placed in the femoral, subclavian or jugular vein. They cannot be used for a long term. **Fig. 8.7** shows a double lumen non-cuffed (temporary) Hemodialysis catheter. **Fig. 8.8** shows the X-ray of a patient after placing the right

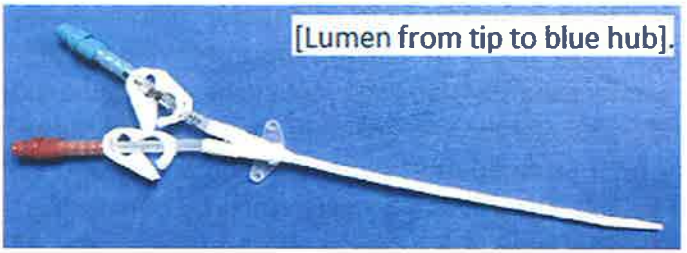


Fig. 8.7: Double lumen (temporary) Hemodialysis catheter.

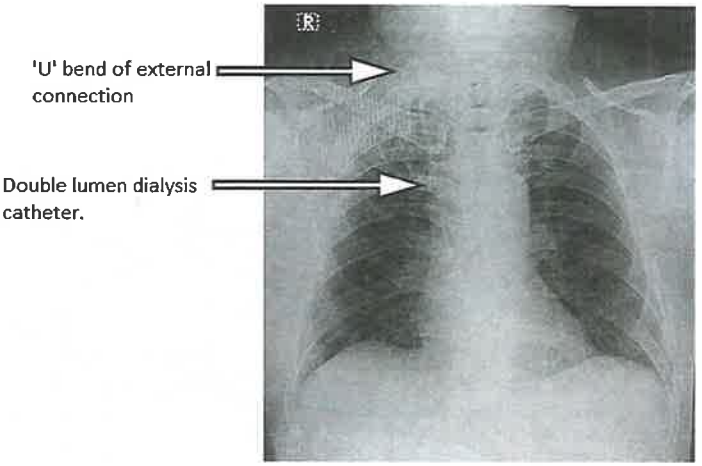


Fig. 8.8: X-ray chest showing temporary (non-cuffed) double lumen hemodialysis catheter introduced through right internal jugular vein.

internal jugular temporary catheter. Since the right internal jugular vein drains directly to the heart, the catheter is straight. The catheter in the left internal jugular vein should have two bends and should be longer.

Special double lumen catheters made of polyurethane or soft silicon material are available. They have a long subcutaneous segment and a cuff near the site of exit of the catheter. This type of catheter is called "permcath" or cuffed central venous catheter and can be used for the long term. The cuff helps to fix the catheter in position and prevents skin or exit site infection from reaching the vascular system through the subcutaneous course of the catheter. If these catheters are handled with care, they can be used for many years **(Fig. 8.9)**.

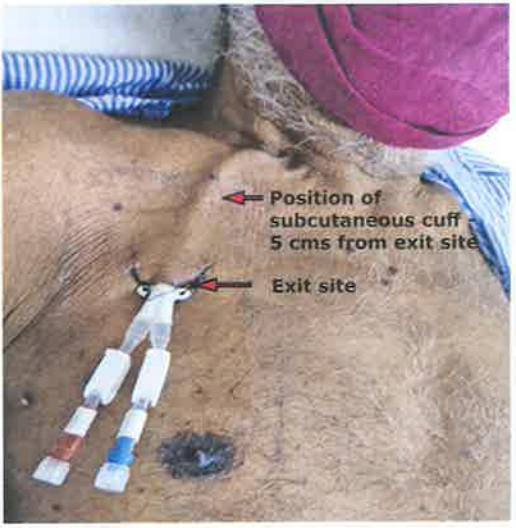


Fig. 8.9: Permcath through right internal jugular vein. Exit site on the anterior chest wall.

The tip of the catheter will be positioned in the right atrium. **Fig. 8.10** shows the X-ray with permcath in the right internal jugular vein with exit site near the right nipple and tip just inside right atrium.

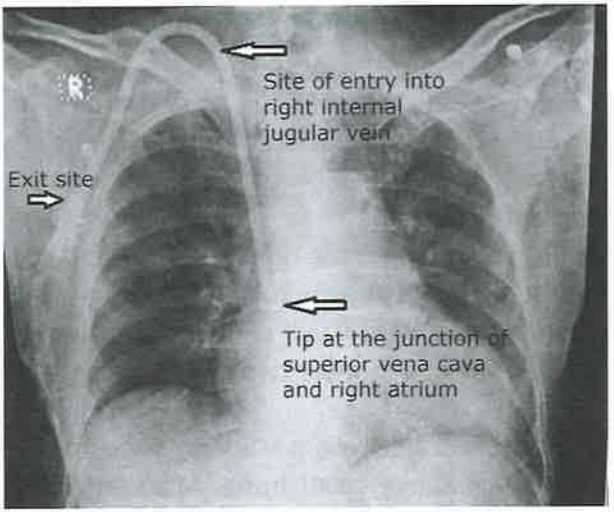


Fig. 8.10: X-ray showing Permcath in right internal jugular vein.

The important veins in the neck are the internal jugular vein and subclavian veins. Long-term cannulation of subclavian veins may lead

to clotting (thrombosis) or narrowing (stenosis) of the vein which result in swelling of the arm on the same side. The subclavian veins can be cannulated below the collar bone **(Fig. 8.11)**, whereas jugular veins are cannulated in the neck (above collar bone). Subclavian cannulation is not commonly used now.

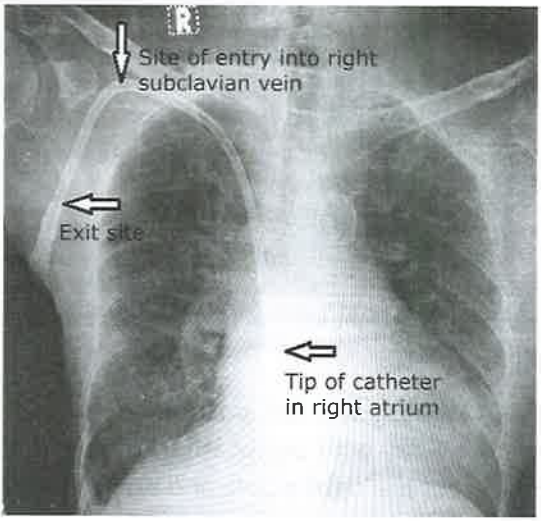


Fig. 8.11: X-ray showing Permcath in right subclavian vein.

The internal jugular vein is close to the carotid artery in the neck. It is a large vein and can be approached from above the clavicle (collar bone). The internal jugular vein on the right side drains to the right atrium through the superior vena cava. The catheter often goes straight (there is no bend) into the right atrium **(Fig. 8.10).** On the left side, the internal jugular vein joins the axillary vein coming from the left arm to form "innominate vein" which joins superior vena cava. Here, the catheter has to negotiate two curves along its course.

Note: The catheter has a curved portion in subcutaneous tissue at the base of the neck above collar bone. After entering the jugular vein, it curves to the right and after reaching superior vena cava, it bends down to reach the right atrium. Compare this to the right sided permanent catheter which runs a straight course in the vein **(Fig. 8.12)**.

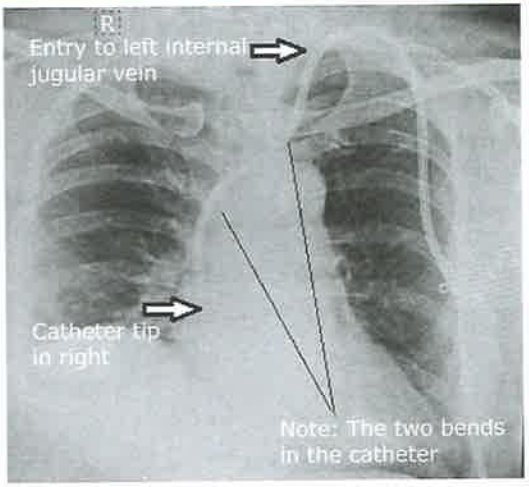


Fig. 8.12: Permcath through left jugular vein.

Very rarely, when all other sites for vascular access are unsuitable, and the patient is not planning to undergo renal transplantation, we may consider femoral vein for permcath insertion. The catheter must be sufficiently long so as to reach the upper part of inferior vena cava. **Fig. 8.13** shows permcath inserted through the right femoral vein with the tip in inferior vena cava and exit site on the anterior abdominal wall in a patient in whom all other vascular accesses failed.

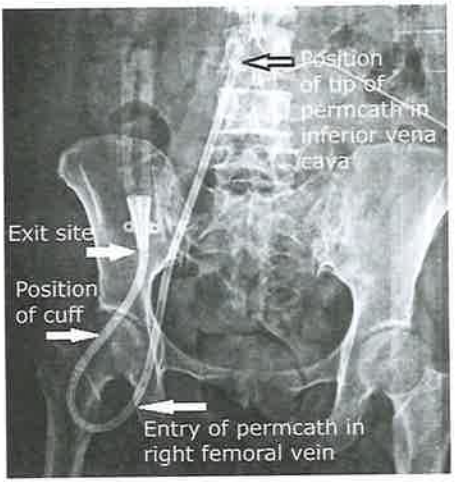


Fig. 8.13: Permcath through the right femoral vein to inferior vena cava and exit site in the anterior abdominal wall (in a patient where other accesses failed).

Vascular access is the lifeline of a patient on maintenance dialysis. If carefully handled, it will last a lifetime. By good care, avoidable complications can be prevented and the patient can be offered good-quality dialysis for many years.

9 Dialysis Membranes and Artificial Kidneys

R. Kasi Visweswaran • Sreedevi P. A.

In Hemodialysis, semi-permeable membranes are used to remove solutes (by diffusion) and fluids (by ultra-filtration). This membrane is made from a material called polymer. Based on the polymer material used, membranes are of four types.

1. Cellulose
2. Substituted cellulose
3. Cellulo-synthetic
4. Synthetic

1. Cellulose membranes

Cellulose is a natural plant fiber derived from processed cotton or wood. In the cellulose polymer, a large number of free hydroxyl (OH^-) groups are present on the surface, and these are responsible for causing adverse symptoms and reactions. Such membranes are not biocompatible. These membranes can be used only once. In the early days of Hemodialysis, cellulosic membranes were commonly used in the preparation of the artificial kidney. Activation of the complement system in the blood gives rise to numerous complications.

Examples of cellulose membranes:

a. Cuprophan

b. Cuprammonium rayon

c. Regenerated cellulose

d. Saponified cellulose ester

2. Substituted cellulose membranes

In substituted cellulose membrane, the OH^- group is often replaced (substituted) with acetate or other functional groups.

Examples of substituted cellulose membranes:

a. Cellulose acetate

b. Cellulose diacetate

c. Cellulose triacetate

3. Cellulo-synthetic membranes

In cellulo-synthetic membrane, a synthetic material is added to liquefied cellulose during manufacture. As a result, the surface of the membrane is altered and biocompatibility increased.

Example of cellulo-synthetic membranes:

a. Cellusyn

b. Hemophan

4. Synthetic membranes

These membranes are synthetic and do not contain any cellulose. Here, the polymer is artificially synthetized from petrochemicals (chemicals derived from petroleum or natural gas) and processed into membranes. The chemical composition is made up of thermoplastic compounds. These are plastic polymers which become soft when heated and hardens when cooled. Major advantages of synthetic membranes are:

a. Improved biocompatibility.

b. Complement activation is minimal.

c. Improved clearance of larger molecular weight substance (high-flux).

d. Low flux and high permeability membranes are available.

e. Some may be reused (if suitable, for the same patient).

Such membranes are used for procedures like hemofiltration, CRRT and membrane plasmapheresis. Examples of synthetic membranes are:

a. Polysulfone

b. Polyamide

c. Polycarbonate

d. Polyacrylonitrile (PAN, AN69)

e. Polymethyl methacrylate (PMMA)

Membranes are manufactured by a process involving—

1. **Liquification:** The polymer compound is made into flat sheets (using chemicals or melting by heat).
2. **Extrusion:** The membrane is made into a fiber and an open core is created (using gas or chemical substances).
3. **Coagulation:** The wall of the hollow fiber is solidified. (The ultra-thin membrane is moulded like the "drinking straw".)
4. **Extraction:** During this stage, pores are created in the membrane. (The size, shape, number, and characteristics of the pores vary depending on the polymer used and manufacturing process.)
5. **Plasticization:** The pore structure of the membrane is fixed by filling the membrane wall with glycerine and then drying. (Glycerin can be seen in the venous drip chamber during the priming of a new dialyzer.)

Artificial Kidney

The earliest practical artificial kidney was conceived by Abel, Rowntree and Turner in 1913. It consisted of numerous colloidin tubes through which the blood was passed. The colloidin tubes were immersed in saline solution in a drum. The blood flowing continuously through the colloidin tubes was exposed to saline solution across the colloidin tubes and some waste products were removed when used in uremic animals. This process was described as "vividiffusion".

Kolff rotating drum dialyzer was developed by Willheim Kolff of Holland in 1943 **(Fig. 9.1).** This was the first successful Hemodialysis in humans. The apparatus consisted of a rotating drum around which a long envelop-shaped cellophane membrane was wrapped in a spiral fashion. The blood was passed through the inside of

the membrane (moulded like a long envelope). The drum was half immersed in a 100 L tank containing dialysis fluid. The rotation of the drum enabled the propulsion of blood through the system and removal of waste products occurred across the membrane.

Fig. 9.1: Rotating drum artificial kidney (Kolff).

Coil dialyzers were designed in 1956 **(Fig. 9.2)**. Here, cellulose membranes fused like a long envelope, with tubings at both ends were coiled around the core in a spiral fashion. The tubings were surrounded by a supporting spiral mesh. The membrane and mesh were encased in a solid plastic case called a canister. During dialysis, blood flow was through the tube and inside of the envelope-shaped membrane. The dialysis fluid circulated outside the membrane and in between the mesh. Thus, the waste products were removed. The movement of water was perpendicular to the direction of the blood flow. Removal of water could be achieved by increasing the pressure in the blood compartment. However, membrane rupture occurred frequently if the pressure in the blood compartment was increased. Since the volume of blood within the blood tubings and twin coil (extracorporeal blood volume) was high, it was necessary to prime the set with blood before connecting the patient. Otherwise, hypotension occurred at the start of the dialysis session.

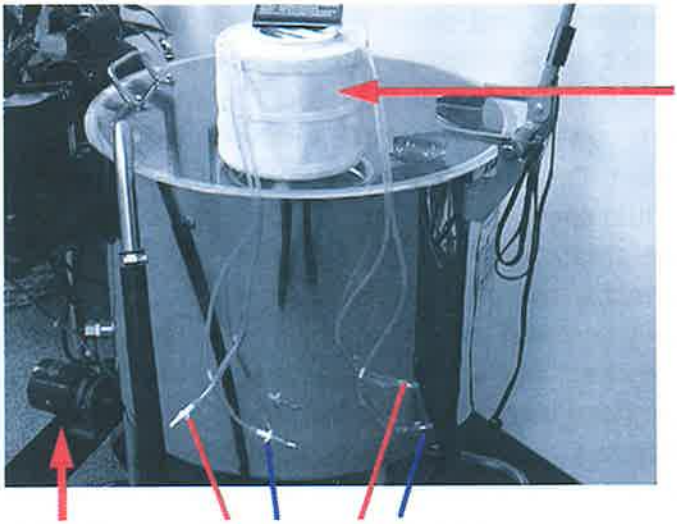


Fig. 9.2: Twin coil dialysis.

The next major development of an artificial kidney was the parallel plate dialyzer developed by Skeggs Leonards in 1948. The bulky equipment had rigid supporting plates with two layers of membrane placed between the adjacent plates. The ends of the plates were sealed. The blood was made to flow between the two sheets of membrane and dialysis fluid circulated on the other side. Thus, each membrane was in contact with blood, on one side, and dialysis fluid, on the other side.

The next improvement in dialyzer was by Friedrich Kiil in Norway in 1960. This was a practical version and was used all over the world during the 1960 and 1970s. The equipment consisted of three heavy polypropylene plates assembled on a trolley with facility for tilting both ways. The inner surface of the plates had minor pyramidal projections which helped to increase the surface area of the membrane placed on it. It is a sandwich-like arrangement which had the following configuration on cross-section from the bottom to the top. It consists of lower plate, small space for dialysate flow, two layers of membrane with blood compartment

between the membranes, and space for dialysate flow between the membrane and the middle plate. The same arrangement was there between the middle and upper plates. The space between the two membranes on either side of the middle plate formed the blood compartment. On either side of the blood compartment was the dialysis fluid compartment. Depending on the size of the plate, the surface area could be changed. The membranes have to be placed correctly, the plates assembled, all the four edges approximated and screwed tightly to make all compartments airtight. This is checked, and all six compartments (two for blood and four dialysate flow) were sterilized and stored for a minimum of 12 hours. Before use, the sterilizing solution (formalin was used earlier) was drained, compartments rinsed with sterile saline and checked for formalin residue before use. After the dialysis session, the screws were loosened, plates dismantled, plates washed and dried before assembling a new set of membranes for dialysis. The used membranes were discarded after use.

Parallel plate dialyzers, which were smaller than the Kiil dialyzer, were used for some time. These dialyzers had parallel plates to support two layers of cuprophane membrane arranged in a folded fashion. There were connectors for blood and dialysate compartments.

Hollow Fibre Artificial Kidney (HFAK)

These types of dialyzers are used commonly now. Each fiber is constructed from a semi-permeable membrane moulded as hollow tubes. Nearly 10,000 to 20,000 such fibers are bundled together and encased in a cylindrical polyurethane housing. The surface area available for dialysis and the efficiency of membrane are modified by changing the number, length of fibers and type of membrane used during manufacture. At both ends, there is a "header" which may be detachable. If the header is detachable, the HFAK can be reused. Blood tubing is connected to the end of the HFAK and the dialysis lines to the ports on either side towards the end.

The basic components of the dialyzer **(Fig. 9.3)** are as follows:

a. Blood compartment (the lumen of the hollow fibers) Highly magnified view of a single fiber is shown in **Fig. 9.4**

b. Dialysate compartment (between the hollow fibers)

c. Semi-permeable membrane (forms the wall of the hollow fibers)

d. Hard plastic housing (membrane support structure)

e. Header with port for bloodlines (one at each end)

f. Dialysate connecting port in the plastic housing (on the side towards each end)

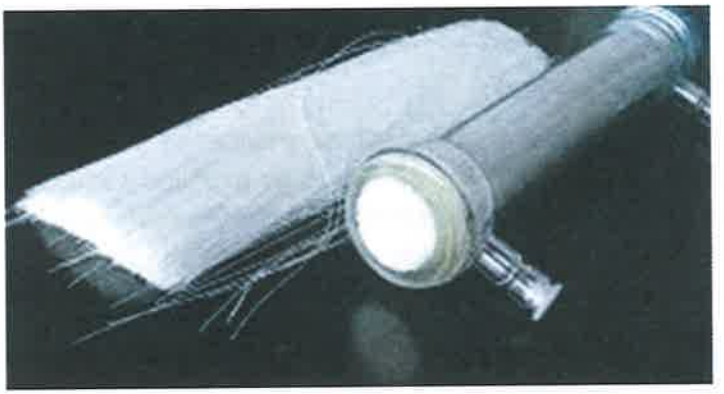


Fig. 9.3: Hollow fiber artificial kidney showing the fibers with header removed to show the arrangement of fibers. In the left side, the fibers have been removed from the housing.

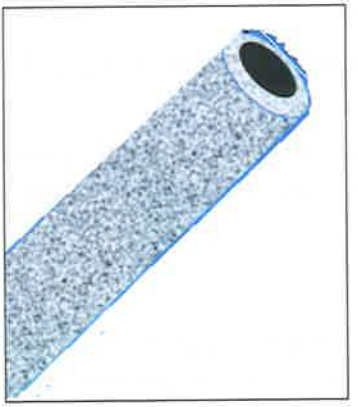


Fig. 9.4: Highly magnified view of one hollow fiber.

Advantages of HFAK:

a. Resistance to blood flow is low. Therefore, a high blood flow rate can be achieved.

b. The volume of blood circulating at a given time is low. So, the volume of blood circulating outside the body at a time (extracorporeal blood volume) can be reduced.

c. The pressure in the dialysate compartment can be adjusted easily because of the hard plastic housing.

d. Ultra-filtration can be easily controlled.

e. If the header is detachable, HFAK can be rinsed, cleaned, re-sterilized and made suitable for reuse for the same patient.

The disadvantages are:

a. Meticulous deaeration is necessary since the fiber bundles may have entrapped air. The air has to be expelled completely from the fibers during priming before starting dialysis. (Air inside the fibers may cause formation of air bubbles and frothing in blood during dialysis. This is harmful and a dangerous complication.)

b. Some fibers may have blood clots even after washing. This reduces the efficiency of dialysis. Fibre bundle volume should be checked before reuse.

c. Blood clots may occur in the inflow and outflow header space due to stagnation.

d. To prevent coagulation, more anticoagulants (heparin) may be needed.

e. Presence of disinfectants and sterilizing solutions in the "potting" material can cause adverse patient reaction. Potting material is used to prevent admixture of blood and dialysis fluid in both ends of the HFAK.

The direction of blood and dialysate flow within the dialyzer also determines the clearance. In co-current flow, the blood and dialysis fluid are moving in the same direction. The dialysis is less efficient

and is used in paediatric dialysis, unstable patients and those in whom rapid changes in blood chemistry is not necessary or may be harmful.

When dialysis is started for the first time in a patient used to high levels of urea for a long time, sudden reduction of urea may result in brain edema and complications. When dialysis is undertaken for a patient with very low serum sodium, rapid correction of sodium will lead to complications. In such situations, very gentle sessions of dialysis are necessary. Using co-current flow, reducing blood flow rate, reducing the dialysate flow rate and using small surface area dialyzers are some of the methods for such situations.

In counter-current flow, the blood and dialysis fluid are made to flow in opposite directions. This helps to maintain adequate concentration gradient along a larger area of the membrane and improving efficiency.

Characteristics of Various Dialyzers

a. Conventional dialyzers:
   i. Made up of cellulose or semi-synthetic membranes
   ii. Surface area varies from 0.5–1.3 m^2
   iii. Low diffusion
   iv. Low ultra-filtration rate (KUF <8 mL /mmHg/hour)
   v. Low molecular cut-off (≈3000 D)
   vi. Minimal adsorption
   vii. High complement activation
b. High-efficiency dialyzers: (Almost same as conventional dialyzers except for more surface area)
   i. Made of cellulose or synthetic
   ii. Surface area varies from 1.4–2.2 m^2
   iii. Higher diffusion (higher surface area)

iv. Moderate ultra-filtration rate (KUF: 5–20 mL/mmHg/hour)

v. Low molecular cut off (≈3000 D)

vi. Minimal adsorption

vii. High complement activation

c. High flux dialyzers (Membrane permeable to high MW substances)

i. Made of synthetic material

ii. Surface area varies from 1.1–2.2 m^2

iii. High diffusion

iv. High ultra-filtration rates (KUF >20 mL/mmHg/hour)

v. High molecular cut off (≈15,000 D)

vi. Moderate to high adsorption

vii. Low complement activation

10 Dialysis Monitors (Machines)

R. Kasi Visweswaran • Supin Vijayan

The dialysis machine (monitor) is designed to—

1. Prepare, check, deliver the dialysis fluid to dialyzer (artificial kidney), receive and check the fluid for blood leak, and control the ultra-filtration (UF). The above three functions are performed by the hydraulic circuit.
2. Pump blood from the patient to the dialyzer and back safely at the desired rate (blood circuit).
3. Monitor various parameters in the hydraulic and blood circuit for patient's safety (safety alarms) **(Fig. 10.1).**

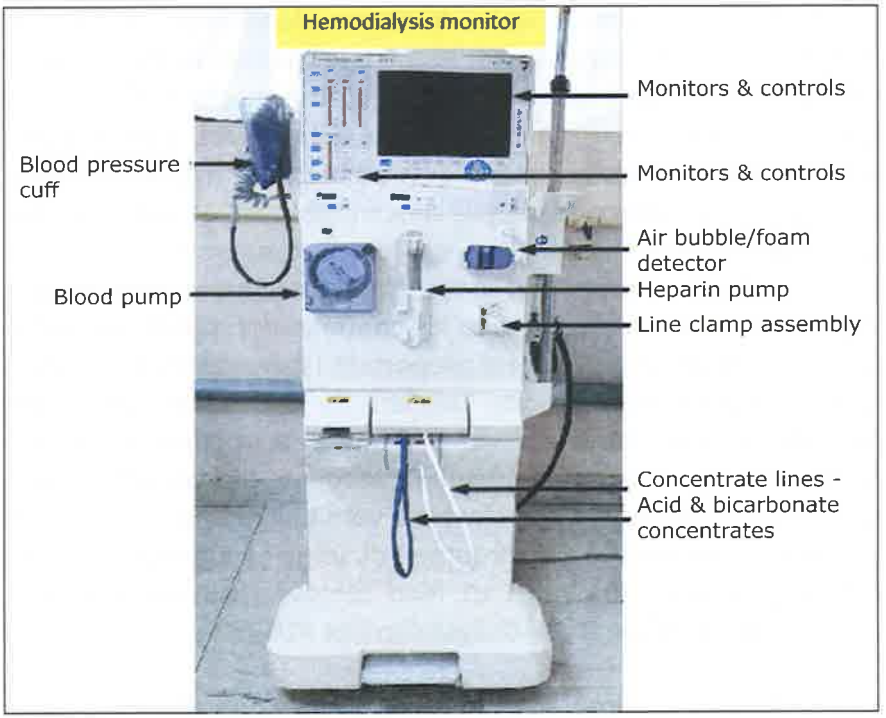


Fig. 10.1: Hemodialysis machine (monitor).

Hydraulic Circuit and Safety Features

The hydraulic function of the dialysis monitor is to prepare the dialysis fluid by mixing the concentrate of dialysis fluid with water, heat to body temperature, check the temperature, final concentration of dialysis fluid, flow rate and pressure before delivering to the dialyzer. The hydraulic circuit has arrangements to reject the fluid if the temperature or concentration is outside prescribed limits. Such rejected fluid bypasses the dialyzer and goes directly to the drain. So, the patient is not harmed. There are alarms to indicate if the flow and pressure of the dialysis fluid is outside the prescribed limits. The machine also monitors the fluid returning from the dialyzer for blood leak. In the event of leakage of blood from the blood compartment in the dialyzer to the dialysis fluid, the blood leak detector gives an alarm and stops the dialysis process. It is also possible to control the rate of removal of fluid from the body during dialysis. There are pumps to exert negative pressure in the dialysis compartment to remove water from the blood circulating in the dialyzer. The balancing chamber in the later models of the machine can control the fluid removal accurately. The machine also has to perform within safety limits and give appropriate alarms when safe limits are exceeded. In earlier machines, the hydraulic system controlling the water and dialysis concentrate worked with the help of the pressure of incoming water. Many pistons work in unison to mix a fixed ratio of water and concentrate. Later, more sophisticated electronic components are used for continuously mixing the water and concentrate in the correct proportion (servo-controlled mixing system). Earlier, only acetate concentrate and water were used (acetate dialysis). Now, instead of acetate, acid concentrate and bicarbonate concentrate are used. Bicarbonate dialysis offers more patient comfort, lesser discomfort and vomiting during HD. Now, it is possible to change the concentration of some electrolytes (sodium profiling), change the rates of fluid removal (UF profiling) and calculating the efficiency of dialysis (on line Kt/V).

The treated water enters the machine at the prescribed pressure. The water moves to a heater chamber where it is heated to about 38°C (1° more than normal body temperature) to account for the loss

of heat as it travels along the machine. Too cold dialysate or too hot dialysate are not tolerated by the patient and will be harmful. The heater is controlled by a thermostat so that the temperature of the water coming out of the heater assembly is constant. Next, the water goes to the deaeration chamber (where air is removed completely) before going to proportionating pump. This pump is programmed to mix water with the dialysis concentrate. Thus, the dialysis fluid is formed from the concentrate. The dialysis concentrate contains various salts (electrolytes), and their concentration is approximately equal to the normal concentration of electrolytes in the blood. The present models of machines with "Three stream proportionating system" have the facility to mix acid concentrate, bicarbonate concentrate and treated water to prepare the dialysis fluid.

Electrolytes dissolved in water conduct electricity and the amount of electricity conducted is measured as conductivity. Conductivity, therefore, gives an idea about the electrolyte concentration in the dialysis fluid. The dialysis fluid moves to the conductivity meter, temperature meter and flow meter. Any dialysis fluid which is outside the safe range for conductivity and temperature is directly diverted to the drain, bypassing the dialyzer. Only the dialysis fluid which has the conductivity and temperature within the accepted range goes into the dialyzer. The conductivity can be controlled within a small range in the machine during the dialysis session.

The fluid coming out of the dialyzer may be blood-stained if there is some damage to the membrane. A blood leak detector **(Fig. 10.2)** is present in the hydraulic circuit as the fluid comes out of the dialyzer. Normally, the dialysis fluid coming from the dialyzer (dialysate) is clear. The blood leak detector is a chamber with a light source at one end and a sensor at the opposite end. When the beam of light is interrupted by even small quantities of blood cells or impurities, the sensor will detect the same and raise an alarm. Simultaneously, the blood pump will be stopped thereby terminating dialysis. The venous line will be clamped thereby preventing the blood from returning to the patient. If a blood leak occurs, there is chance of mixing of blood (sterile) with dialysis fluid (unsterile). The detector can sense even

very small amount of blood in dialysate which cannot be seen by the naked eye. Even if impurities are present, the alarm will work. So, it is necessary to check for false alarms and very minor blood leak, in which case dialysis can be continued. Otherwise, dialysis is discontinued and blood discarded. This decision is taken after assessing the extent of the blood leak.

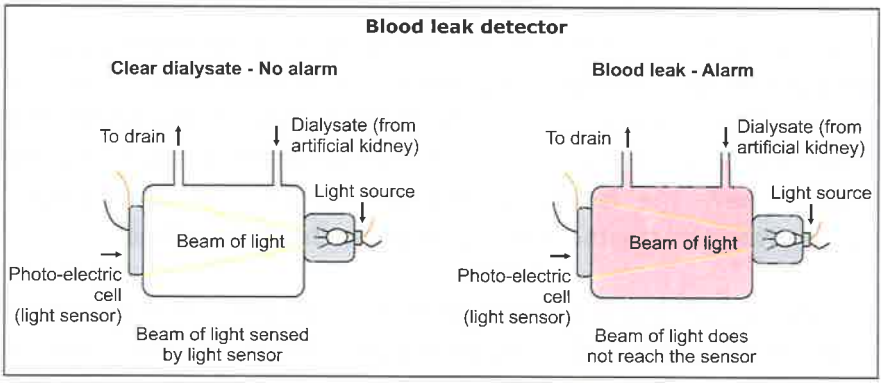


Fig. 10.2: Blood leak detector in the dialysis machine.

Removing excess fluid from the blood is a very important step in dialysis. For this, only fluid and dissolved electrolytes can be removed across the semipermeable membrane. This process is called ultra-filtration (UF). The pressure in the blood compartment is on the positive side and the dialysis fluid compartment should be on the negative side. Therefore, there will be a pressure gradient across the membrane. This pressure gradient is called trans-membrane pressure (TMP). If the TMP is more, more UF occurs and more fluid can be removed. In the dialysis machine, it is possible to increase TMP by increasing the negative pressure in the dialysate compartment. Modern dialysis machines can adjust the negative pressure to achieve the desired weight loss within a specific time. Machines with a facility for volumetric UF can accurately remove larger quantities of fluids if we set the fluid to be removed and the time. The volumetric UF (fluid balancing) system has two chambers. Each chamber has a diaphragm to separate the dialysate going in and coming out of the dialyzer. In volumetric control, the flow to and from the dialyzer is balanced. The volume of dialysate entering and leaving the artificial kidney is equal, because the volume entering

one side of the balance chamber displaces the same amount on the other side. The two sections of both the chambers fill and drain alternately to provide a continuous flow of dialysate entering and leaving the dialyzer **(Fig. 10.3).** Some machines use viscous chamber system in place of balancing chambers.

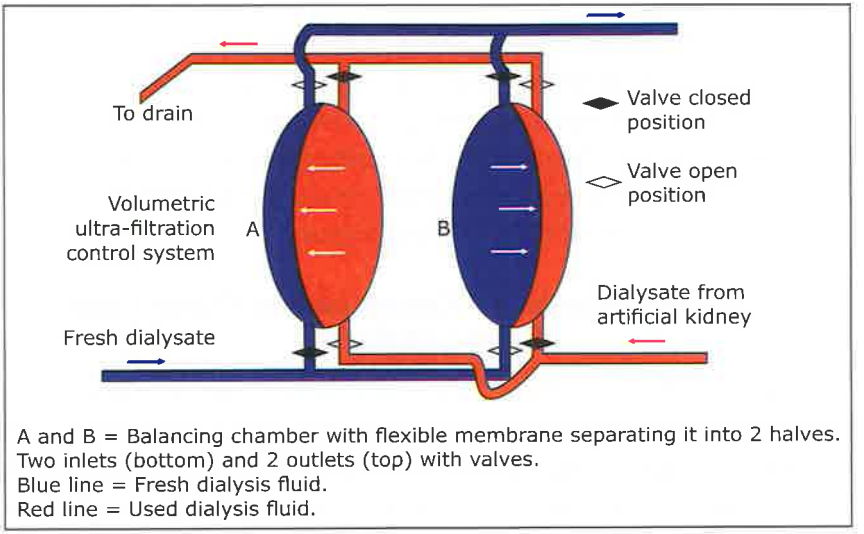


Fig. 10.3: Working of the balancing chamber.

The balancing chambers have a flexible (non-permeable) membrane each which separates each chamber for fresh and used dialysate. The valves regulate the flow of fresh and used dialysate. The Figure shows the cycle where chamber A is filling with used dialysate (shown in light pink), the membrane will bulge and push fresh dialysate to the artificial kidney. Simultaneously, Chamber B will fill up with fresh dialysate (shown in light blue), the membrane will bulge and push the fresh dialysate in A to the artificial kidney and used dialysate in B to the drain. Once this cycle is completed, the valve position and the role of the two balancing chambers reverse. When used dialysate side of chamber A is filling, the fresh dialysate half of the same chamber will be emptying. Simultaneously, the used dialysate half in Chamber B will be emptying and fresh dialysate half-filling.

The final important part of the hydraulic circuit is the UF pump which helps to exert negative pressure in the dialysate compartment and cause more UF. This pump is controlled by the electronic circuit. When we set the amount of fluid to be removed, the pump exerts the necessary negative pressure on the dialysate side and controls fluid removal. If the UF pump is switched off, or UF set at 0, the pump stops and no negative pressure will be there in the dialysis compartment. The used dialysate is sent to the drain.

Trans-membrane pressure (TMP) is the difference between the positive in the blood compartment and negative pressure in dialysate compartment. This is the pressure exerted on the membrane. If the TMP is high, more fluid will be filtered across the dialysis membrane. The amount of fluids removed from the blood (ultrafiltration) depends on TMP and ultrafiltration coefficient (Kuf) of the membrane. In effect, it is the difference between the average positive pressure in blood compartment and average negative pressure in dialysate compartment. Different membranes can withstand different TMPs. If the TMP increases beyond the prescribed limits, the membrane is likely to rupture. The maximum TMP of each membrane is usually displayed in the hollow fiber artificial kidney.

Extracorporeal Circuit (Blood Circuit) and Safety Features

The next important function of the machine is the blood circuit, which draws blood from the body, circulates it through blood tubing to the dialyzer and back to the patient. The extracorporeal circuit includes the pathway for the arterial and venous blood tubing, blood pump, heparin pump, dialyzer clamp, venous line clamp, blood flow monitors, pressure monitors, and air bubble/foam detector. It helps to carry blood from the vascular access to the dialyzer and back to the access. The arterial blood tubing which is connected to the machine has a Luer-lock connector which fits into the vascular access, a blood sampling port, a line for syringe attached to heparin pump, drip chamber, a line for pressure monitoring from the drip chamber, blood pump segment and a connector for attaching to the dialyzer. The blood from the vascular access flows through the tubing where heparin is added by the heparin pump and goes to the drip chamber. Any air bubble is trapped in the drip chamber. The line attached to the pressure monitor in the machine monitors the pressure in the arterial circuit. The position of drip chamber is "pre-pump". Therefore, there is suction exerted by the blood pump and the pressure is negative. Just before the pump segment, there is a saline infusion line. Since it is also located before the pump, it will draw the saline and later air from the saline container. Both clamps (saline set and infusion line of dialysis tubing) must be clamped while not in use. From here, the blood travels to the pump segment.

The blood pump segment is made of softer, easily compressible but is a strong material and has a larger diameter. It is positioned correctly between the housing and the roller. The blood pump has two rollers which occlude the lumen as it rotates. In the blood pump, the rollers squeeze the pump segment and roll in one direction. For proper functioning, the pump rollers should apply enough occlusion to the lumen of the pump segment so that the blood is pushed forward. If the occlusion is more, it may cause the destruction of the red cells (hemolysis) and if it is less, the propulsion of blood will not occur. Usually, the blood flow rate depends on the diameter of the segment and the number of revolutions of the roller per minute. Pump occlusion should be checked and flow rate calibrated periodically. Adjustments will be necessary if the size of the blood tubing or the manufacturer is changed. Most pumps have a hand-cranking lever to rotate the pump manually in case of pump failure. Thus, the blood is continuously propelled forwards. It enters the artificial kidney through the blood port with Luer-lock fitting. All clamps and fittings in the "arterial" line are marked in red **(Fig. 10.4)**.

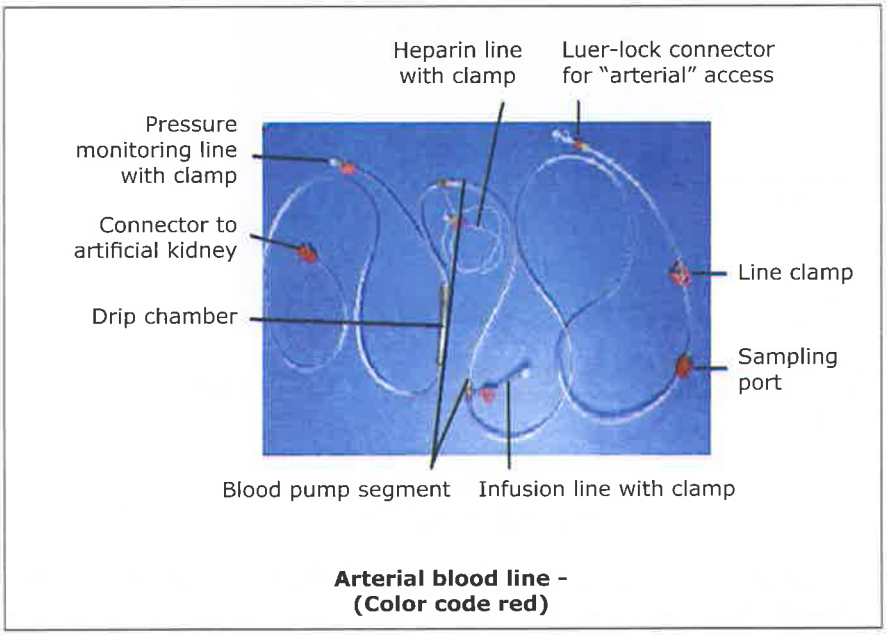


Fig. 10.4: Arterial bloodline for Hemodialysis.

The "venous" line which is marked with blue connectors and clamps transports the blood back to the patient. It starts at the other end of the artificial kidney with a blue-colored Luer-lock fitting. The tube goes into another drip chamber which also has a line attached to a pressure monitor (venous pressure monitor). In some sets, a small mesh-like net is provided inside the venous drip chamber which is meant to prevent blood clots from entering the bloodstream. Such blood tubing sets cannot be reused. This drip chamber is placed within a foam and level detector in the machine. There is a blood sensor in the clamp assembly. If there is no blood passing through, the line clamp downstream is activated. Only during the rinsing and sterilizing cycle, clear fluid will be allowed to pass through this part of the tubing system. The blood pump also automatically stops when the line is clamped. There is also an audio alarm. The venous bloodline passes through the above-mentioned clamp before returning to the venous return side of the vascular access. There is also a blood sampling port on the venous line **(Fig. 10.5).**

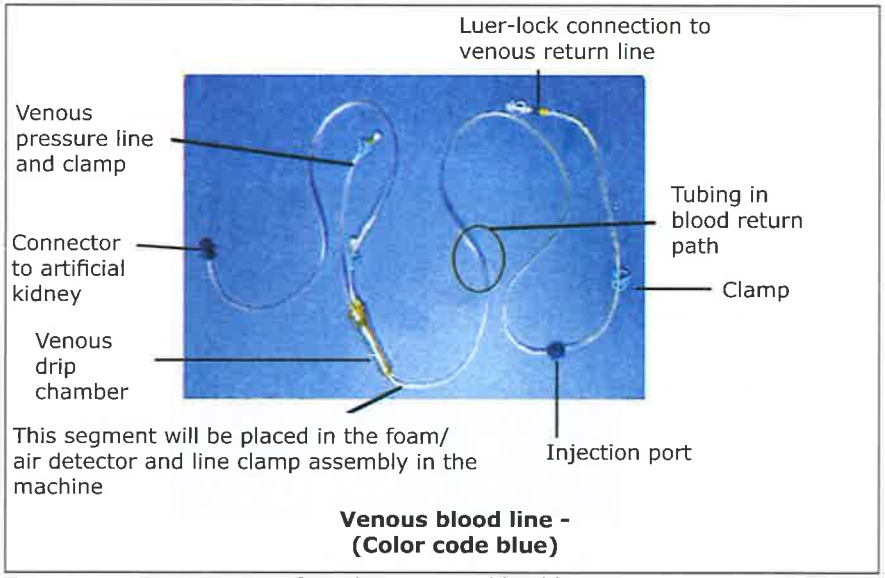


Fig. 10.5: Venous blood line.

Transducer protectors are small disposable filters that act as a barrier between the blood in the tubing and the transducer (pressure monitoring device) in the machine. Any blood or moisture entering

the transducer will cause the malfunction of pressure monitors **(Fig. 10.6).**

Fig. 10.6: Transducer protector.

Alarms in extracorporeal circuit are the pressure monitor and alarm in the arterial drip chamber. The pressure monitoring tube is connected to a monitor. As the drip chamber is pre-pump and the pump draws and propels the blood forwards, the pressure is negative. The alarm limits can be set between -300 and +300 mmHg). If there is obstruction to the free flow of blood while the pump is working, the pressure will change and give alarm. If the pressure monitor is pre-pump, when there is obstruction before the pump it will cause "suction" and the pressure will go to a high minus level. If the obstruction is after the pump, the pressure will be high on the positive side. When the alarm sounds, the blood pump will stop and the venous clamp in the venous line will clamp to prevent the return of blood. The blood coming from the dialyzer goes to the venous drip chamber which is also connected to a pressure monitor. The pressure of blood in the venous bulb is usually positive. The safety limit can be set manually and is usually between −50 and +500 mmHg. Similar to the arterial drip chamber, the alarm will sound if the pressure in the venous bulb exceeds the prescribed range. In some machines, the venous drip chamber is placed in a level detector and foam detector unit which will detect the presence

of foam or level of blood in the chamber. If there is air, foam, or if the level of blood goes down in the drip chamber, an alarm will sound and clamp the outlet tube. This will prevent the entry of foam or air into the body. In other machines, the tube from the venous bulb back to the patient is threaded into an arrangement which has foam/bubble detector and line clamp assembly.

Other options available in the monitor are as follows:

I. Level adjustment in the arterial and venous drip chamber.

II. Adjustable bicarbonate: Concentration of bicarbonate can be varied in a small range.

III. Sodium profiling: The concentration of sodium can be changed to different levels at different times during dialysis.

IV. UF profiling: Programmable UF. The rate of UF can be programmed as desired (e.g., it will be possible to set UF at 1.5 L in the first hour followed by 750 mL/hour for the next 3 hours, and so on).

V. Dialysate flow rate adjustment.

VI. Dialysate urea sensor.

VII. Blood temperature control module.

VIII. Blood volume monitors.

IX. Single blood pathway ("single-needle") devices.

11 Dialysis Fluid/Dialysate Solution

R. Kasi Visweswaran • Mohammed Althaf

For preparing the dialysis fluid in Hemodialysis (HD), a "concentrate" is used. It is a mixture of treated water and chemicals mixed in the proper proportion and stored in a concentrated form. This is called the dialysis concentrate and is used for preparing the dialysis fluid (dialysate). The machine prepares the dialysate by mixing the correct volume of concentrate and treated water to make the dialysate. The prepared dialysate circulates in the dialysate side of the artificial kidney and the blood circulates through the blood compartment. Here, interaction takes place across a semipermeable membrane. The accumulated waste products are moved from the blood to the dialysate side and are then removed. The normal concentration of electrolytes and acid-base in the blood are restored by movement of electrolytes depending on concentration difference, and the blood chemistry is normalized. The fresh dialysate contains electrolytes such as sodium [Na], potassium [K^+], calcium [Ca^{++}], magnesium [Mg^{++}], chloride [Cl^-], and bicarbonate [HCO_3^-]. It also contains non-electrolyte substances like glucose. The permeability and concentration gradient determine the rate of diffusion across the membrane.

The osmolality of dialysis fluid must be close to that of normal blood. Osmotically active substances exert osmotic force and will cause the movement of water from an area of lower solute concentration to higher solute concentration. So, if the dialysis fluid has higher osmolality, it will draw fluid from blood to dialysis fluid. This is more relevant in peritoneal dialysis than HD.

There are two types of concentrates used in Hemodialysis (HD).

Acetate concentrate was used in the earlier models of dialysis machines to prepare dialysis fluid. Acetate dialysis is not good for patients undergoing long-term dialysis and cannot be used with

high flux membranes. In addition to sodium, potassium, calcium, magnesium, chloride and glucose, it also contains acetate. After about 3–4 hours after entering the bloodstream, acetate is converted to bicarbonate by the liver and finally utilised by the body. Patients with liver impairment cannot metabolize acetate into bicarbonate. The presence of acetate in blood gives rise to uncomfortable symptoms for the patient. The acetate concentrate can be stored for a long time without precipitate formation and bacterial growth. Machines offering acetate dialysis have a mixing system to add 1 volume of acetate concentrate to 34 volumes of water to prepare the dialysate. The final concentration of elements in dialysate used for acetate dialysis is:

Sodium	:	135–145 mEq/L
Potassium	:	0–4 mEq/L (can be varied as needed)
Calcium	:	2.5–3.5 mEq/L
Magnesium	:	0.5–1.0 mEq/L
Chloride	:	100–119 mEq/L
Acetate	:	35–38 mEq/L
Glucose	:	0–200 mg% (can be varied)

On the other hand, bicarbonate dialysis has many advantages. Many centres use bicarbonate dialysis because of higher patient acceptance and lesser complications. The correction of acidosis is almost immediate, because bicarbonate is directly supplied to the blood. While using bicarbonate dialysis, patients are more stable, have fewer symptoms and tolerate dialysis on the long term. However, the disadvantages are that the bicarbonate concentrate has to be freshly prepared before each dialysis session. It cannot be stored. The shelf life is very short and bacterial growth occurs easily in the bicarbonate concentrate. The machines for bicarbonate dialysis have two mixing systems, one for "acid" concentrate and another for bicarbonate concentrate. In the machine, mixing occurs in the following proportion – acid concentrate:treated water:bicarbonate concentrate = 1:34:1.83. The final composition of electrolytes in dialysis fluid for bicarbonate dialysis is similar to the acetate dialysis,

except that the acetate is replaced with bicarbonate. The ingredients of the acid concentrate (A) and bicarbonate solution (B) used for bicarbonate dialysis are shown in **Table 11.1**.

Table 11.1: Ingredients and their concentration in dialysis fluids

PART A [Acid concentrate]	Concentration in dialysis fluid [mEq/L]
Sodium	82
Potassium	2–4
Calcium	2.5–3.5
Magnesium	1.0
Chloride	90
Dextrose	5.04 mmol/L
Acetate	4

PART B [Bicarbonate]	Concentration in dialysis fluid [mEq/L]
Sodium	59
-	-
-	-
-	-
Chloride	20
-	-
Bicarbonate	34

Contents in Dialysate and Functions

The concentrate is prepared with medial grade chemicals in the correct proportion. Each ingredient has a specific function, and the final concentration in the dialysis fluid is almost similar to that found in normal plasma. If dialysis is performed against an abnormal concentration of chemicals in the dialysis fluid, it may result in harm to the patient.

Sodium [Na^+] – Normal Blood Level 135–145 mEq/L

Na^+ is the major electrolyte in the plasma and extracellular compartment in the body. It controls the osmotic pressure mainly and causes the shifting of fluids within the body. Both low and high levels of sodium are harmful to the body. The sodium level should not be corrected suddenly. The dialysis fluid has a sodium concentration of around 140 mEq/L. The concentration of sodium in the dialysate prepared by the machine is indicated by "conductivity". When sodium is dissolved in water, it permits electricity to pass through (conductive). The amount of electricity depends on the concentration of sodium. This is measured as "conductivity" by the machine. The machine is programmed to discard the dialysis fluid if the conductivity is beyond the permitted range. Recent models of machines can adjust the Na^+ concentration during dialysis sessions according to the set pattern (sodium profiling).

Potassium [K^{++}]

Ninety-eight percent of K^+ in the body is intracellular (inside the cell). The blood contains only 3– 4.5 mmol/L of K^+. The blood level of K^+ has to be maintained within the normal range, because high or low levels can affect the heart and cause arrhythmias. Severe muscle weakness may also occur. Since most patients on dialysis have relatively higher levels of K^+ before dialysis, the dialysis fluid K^+ is maintained at 2 mmol/L so that by the end of dialysis, the blood level comes down to about 3 mmol/L. In patients who have a low pre-dialysis K^+ level, the concentration potassium in the dialysis fluid can be increased by adding potassium chloride to the dialysis concentrate so that the dialysate K^+ level is around 4 mmol/L. When 30 gms of potassium chloride salt is added to 20 L of conventional acid concentrate, it increases the final dialysate potassium content from 2 to 4 mmol/L. Normal potassium concentration in the final dialysate is required when dialyzing patients with pre-existing hypokalaemia. Some patients who are on a cardiac drug (digoxin) have to be dialyzed with normal potassium dialysate instead of conventional potassium concentration of around 2 mmol/L, to prevent cardiac arrhythmias (heart beat irregularity).

Calcium [Ca^{++}]

Calcium is important for muscle contraction, nerve conduction, enzyme action, strengthening of bones and blood clotting. The total calcium in the blood is about 9–11 mg% while the ionized calcium is 2.5–3.5 mmol/L. The dialysate calcium should be within this range. Increased serum calcium is called hypercalcemia. Sometimes, dialysis with low calcium dialysate has to be performed for severe hypercalcemia. Hypocalcemia may cause muscle spasms called tetany and correction is done by administering intravenous calcium carefully.

Magnesium [Mg^{++}]

Mg is also an intracellular ion like K^+. It is necessary for metabolism and is involved in many enzyme systems. The normal blood level ranges from 0.85 to 1.1 mmol/L. Hypomagnesemia may be associated with weakness, and severe hypermagnesemia may result in the stoppage

of breathing (respiratory arrest).

Bicarbonate [HCO_3^-]

Bicarbonate helps to regulate the acid-base balance. The acids produced in the body as a result of diet and metabolism are neutralized by bicarbonate. Normally, this function is performed by the kidneys. In dialysis patients, since the kidneys are not functioning properly, acid ions accumulate and cause a condition called "acidemia". Too much bicarbonate causes a condition called "alkalemia". Therefore, the bicarbonate concentration level in blood should be kept in the normal range of 24–26 mmol/L. As mentioned earlier, bicarbonate dialysis provides bicarbonate directly through the dialysis fluid. In acetate dialysis, the absorbed acetate should be converted in the liver to bicarbonate.

Small quantities of sodium acetate and citric acid are added to dialysis concentrate as "buffers" to prevent gross changes in the pH and maintain it between 7.1 and 7.3.

12 Blood Clotting and Anticoagulation for Dialysis

R. Kasi Visweswaran

It is necessary to understand the normal mechanisms of blood clotting, also called blood coagulation. When blood circulates in the vascular system, it does not clot normally. When blood comes out of the vascular system or when the vascular lining of the blood vessel is damaged, clotting occurs. Clotting of blood helps to prevent excessive bleeding from injuries and wounds. There is a delicate balance of factors which favor clotting (pro-coagulant factors) and factors which prevent clotting (anticoagulant factors) in blood. When anticoagulants are more, bleeding occurs and when pro-coagulants are more, clotting may occur.

Normal Blood Coagulation

Blood coagulation is a mechanism that results in the formation of a stable fibrin clot. This process involves the interaction of clotting factors in plasma, platelets and tissue materials (tissue thromboplastin). The coagulation process consists of two pathways, the extrinsic and the intrinsic system. In the extrinsic system, tissue thromboplastin converts prothrombin to thrombin which in turn, converts fibrinogen to fibrin. Later, the fibrin is converted into insoluble fibrin which binds with other blood components and forms a blood clot. The intrinsic system involves a series of coagulation factors which are proteins in the blood. Activation of factor XII leads to a chain reaction which ultimately converts fibrinogen to insoluble fibrin which is the essence of the blood clot.

The process of blood coagulation can be stopped at various points. Since coagulation of blood should be prevented in the extracorporeal circuit (artificial kidney and blood tubing) for successful dialysis, it is often necessary to use some form of anticoagulation.

Anticoagulation During Dialysis

Anticoagulation is essential to prevent blood clotting in the extracorporeal circuit, but it should not affect membrane efficiency. Factors favoring clotting of the extracorporeal circuit are:

1. Low blood flow

2. High hematocrit
3. High ultrafiltration rate
4. Dialysis access recirculation
5. Blood and blood product transfusion during dialysis
6. Administration of intravenous alimentation during dialysis (not used now)
7. Stagnation and frothing in drip chambers

Signs of clotting in the extracorporeal circuit include the extremely dark colour of blood, black streaks in the dialyzer, high venous pressure or membrane rupture. The clotting in the extracorporeal circuits leads to blood loss and reduced solute clearance and reduced ultrafiltration due to reduction in dialyzer surface area. Hence, it is important to prevent clotting and assess the adequacy of anticoagulation. Unfractionated heparin (conventional heparin) is used routinely for regular Hemodialysis. Citrate anticoagulation, use of low molecular weight (fractionated) heparin, fondaparinux and prostacyclin are also available now but are more expensive.

Heparin

Heparin is a complex carbohydrate (mucopolysaccharide), strongly acidic, anionic and has very high sulfuric acid content. The molecular weight ranges from 6,000 to 25,000 D. It acts as an anticoagulant by retarding the generation of thromboplastin, conversion of prothrombin to thrombin and blocks the action of thrombin on fibrinogen. Heparin is used during the priming of the blood tubings and artificial kidney before dialysis. All side tubings in the bloodlines must be rinsed with heparinized saline. The patient is given a loading dose of heparin and continuous infusion of heparin administered through heparin pump inbuilt in the dialysis machine. It is possible to model a heparin dose for individual patients. The techniques of heparin administration may also be by bolus-loading dose followed by intermittent loading dose or continuous infusion.

Heparin is available as 5 mL vials containing 5000 iu/mL (25000 iu per vial) and is commonly used in dialysis rooms. The bolus-loading dose is 35–55 units/Kg followed by 10–20 iu/Kg boluses every hour. Half-life of heparin is about 1 hour (range 50–120 minutes). The heparin administration is discontinued 30 minutes or just before closing dialysis if the patient is on a

venous catheter and 60 minutes if dialysis is through AV fistula. Usually, the heparin effect will continue for about 6–8 hours after stopping. Injections other than intravenous and surgical procedures are avoided for at least 6 hours after a dialysis session.

Usually, for a 60 kg individual, 2 ml (10,000 iu) of heparin is diluted with normal saline to 20 ml, 5 ml of the diluted heparin is used for rinsing and recirculation and 2 ml is given as loading dose into the arterial line before connecting bloodlines to the patient. Thereafter, 1.5–2 mL per hour is given through the heparin pump. By monitoring APTT, the optimum dose for each patient can be found out.

For testing adequacy of anticoagulation during dialysis, sample should be taken from the arterial line, proximal to the heparin infusion site. The whole blood clotting time (WBCT) described by Lee-White is performed by adding 0.4 ml blood to a glass tube and inverting the tube every 30 seconds until the blood clots. Normal clotting time is 3–6 minutes. It will be ideal to maintain the clotting time between 15 and 20 minutes during dialysis. This test is rarely done nowadays.

Activated whole blood coagulation time is performed similar to WBCT by adding an activator to the blood sample to speedup clotting in the tube. Normal activated WBCT is between 90 and 150 seconds and during dialysis, it should be maintained in the range of 200–240 seconds.

More accurate measurement of effect of heparin is by activated partial thromboplastin time (aPTT). The normal values for aPTT varies between laboratories. A target value of about 2–2.5 times the control suggests adequate heparinization.

If bleeding occurs due to heparin use, it should be assumed that the cause is excess heparin. Nose bleeds, bleeding in the sclera of the eye (white part of eyeball), prolonged bleeding from the site of vein puncture, hematoma (bleeding into tissue) or ecchymosis (bleeding under the skin) are the common manifestations. Excess of heparin can be neutralized immediately by using infusion of protamine sulphate. Protamine sulphate should be available in the emergency trolley in the dialysis room at all times. Clinically, 100 units of heparin is neutralized by 1 mg protamine sulphate. [One ampoule (10 mL) of protamine containing 10 mg neutralizes 1000 iu of heparin.]

There are many types of heparinization.

I. **Systemic heparinization:** An initial bolus dose of 2000 iu is given. After waiting for 3 minutes, for the distribution within the bloodstream and the effect to commence, dialysis is initiated. The dose of heparin is controlled by monitoring aPTT every hour. The aPTT should be maintained about twice the control value during dialysis and 1.5 times towards the end of dialysis. As mentioned earlier, heparin can be administered as continuous infusion 750–1000 iu per hour or intermittent hourly bolus (1000 iu). Since the action lasts for nearly 1 hour, the infusion may be discontinued 30–60 minutes before the closing time of the dialysis session.

II. **Tight/controlled/low-dose heparinization:** It is used in patients at risk of bleeding. In tight heparinization, the aPTT is maintained at around 1.5 times the baseline throughout dialysis. The initial bolus dose of 750–1000 units followed by infusion of 600–750 units per hour. The aPTT is monitored more closely.

III. **Regional heparinization:** In regional heparinization, only the extracorporeal system gets the anticoagulation (heparin) and the anticoagulant is neutralized before the blood is returned to the body. It is not widely used because it is difficult to balance the doses of heparin and protamine. Prolonged use may cause bleeding complications due to heparin rebound or complications due to protamine.

Regional citrate anticoagulation also employs identical principles with citrate as anticoagulant and calcium as the neutralizing agent. Ionic calcium is essential for the clotting of blood. When trisodium citrate is administered through the arterial limb, it reduces ionic calcium. The dialysis fluid is also prepared calcium-free. Part of the administered citrate is dialyzed and the remaining is converted into bicarbonate by the body. Use of citrate may lead to the development of alkalosis. As the blood is returning to the body, calcium is administered. The monitoring is done by frequent serum calcium estimation. Regional citrate anticoagulation is used mainly in continuous renal replacement therapies (CRRT).

Low Molecular Weight Heparin (LMWH)

As the name suggests, the molecular weight of LMWH is between 4000–6000 D. The duration of action is longer and side effects like bleeding are lesser. A single dose of LMWH at the start of dialysis is often enough, unless the dialysis treatment is extended beyond 4 hours. It has less effect

on platelet function compared to conventional (unfractionated) heparin. However, anaphylactic reaction, bleeding complications in patients receiving aspirin or clopidogrel and the high cost are factors which prevent their routine use in Hemodialysis. Moreover, unlike conventional heparin, its effect cannot be neutralized. Dalteparin, nadroparin or enoxaparin are some examples of LMWH.

Bicarbonate Dialysis Solution with Low Citrate (Citrasate)

Here, citric acid is added to the dialysate solution instead of acetic acid to achieve a concentration of about 2.4 mEq/L in dialysate. The citrate freely diffuses to the blood compartment and acts as an anticoagulant by binding with calcium. It is converted into carbon dioxide and water in the body. Use of citrasate also improves the reusability of artificial kidney.

Heparin-Free Dialysis

Heparin-free dialysis may be necessary in patients under the following circumstances:

a. Patients having active bleeding/increased risk of bleeding/ coagulopathy

b. Immediate postoperative/patients going in for surgery soon after dialysis

c. Pericarditis

d. Thrombocytopenia

e. Recent cardiac/vascular/ophthalmic or neuro surgery

f. Intracranial/active gastrointestinal haemorrhage

The important steps for successful heparin-free dialysis starts from the stage of rinsing the system. 3000 iu heparin is used for rinsing the artificial kidney and blood tubing sets. This priming fluid is drained and the system filled with sterile saline or patient's blood. Dialysis is continued with a high blood flow rate of 300–400 mL/min. Such high blood flow rates may increase clearance and may predispose to the development of dialysis disequilibrium. Therefore, smaller surface area kidneys, co-current flow and slower dialysate flow rate can be tried. The inflow bloodline is clamped and saline flushes (about 100–200 mL) every 30 minutes. Periodic rinsing also enables visualization of the tubing and hollow fibre artificial kidney for evidence of clotting. The excess volume administered is removed by

adjusting the rate of ultrafiltration. Heparin-coated dialysis membranes allow heparin-free or low-dose heparin dialysis more effectively.

Side effects of heparin include bleeding (often due to excess heparin), increase in blood lipids, worsening of hyperkalemia and heparin-induced thrombocytopenia (low platelets), also known as HIT. A new drug called Argatroban which inhibits thrombin is used in patients with HIT. Thrombin is important in blood clotting, because it participates in the final step in blood clotting [thrombin + fibrinogen = fibrin (clot)].

13 Starting and Closing of Hemodialysis

R. Kasi Visweswaran • Reshma T.

Before starting dialysis, a series of pre-dialysis safety checks are necessary.

Pre-Dialysis Safety Checks

1. Ensure that the water treatment plant is functioning and adequate water is available in storage tank (if used) for the entire session.
2. Ensure that the chemicals used to disinfect dialysis machine is washed off completely during rinsing.
3. Ensure that the correct concentrate is kept ready in the concentrate container.
4. Ensure that adequate amount of dialysis concentrate is present for the entire dialysis session.
5. Switch on the dialysis machines, go to rinse mode and complete the cycle.
6. Ensure proper functioning of dialysis machine by checking conductivity, pH, temperature and alarms.
7. Ensure that correct dialyzer and blood testing sets of the patient are connected correctly. This must be cross-checked by a second staff.
8. If reuse is practiced, ensure proper rinsing and absence of sterilant in the extracorporeal circuit. If formaldehyde is used, the concentration should be less than 5 ppm (parts per million) or if Renalin (mixture of hydrogen peroxide, peroxyacetic acid and acetic acid) is used, its concentration should be less than 3 ppm.

Patient Assessment

It is recommended to follow the below said steps relating to the

patient before they are taken to the dialysis station.

1. Understand the disease condition and indication for dialysis.
2. Record weight of patient. Assess inter-dialysis weight gain and assess deviation from dry weight of patient.
3. Measure and record blood pressure in lying and standing position.
4. Check vital signs, look for leg edema and overall status of patient.
5. Assess patient for any new symptoms.
6. Examine the AV fistula/graft/catheter: Check for signs of infection to see if it is functioning properly (redness, tenderness, warmth or discharge suggests infection. Feeling the vibration of blood flow through the access or "thrill" and draining vein suggests proper functioning of AVF).
7. Pulse augmentation: This test is done to confirm good inflow into the AV fistula and rule out collaterals. If the distended fistula is occluded with the thumb, away from anastomosis, the portion between the fistula and occlusion should become more pulsatile. At the same time, the bruit in the fistula beyond the thumb should disappear. They will reappear when the pressure is released. If the bruit beyond the thumb persists, while occluding the fistula, it means there are collaterals.
8. Hand-raising test: When the fistula arm is raised up straight, the fistula should "collapse" meaning thereby that the prominence will disappear and pulse becomes weak. If there is obstruction to the fistula near the shoulder or chest, the vein will not collapse when the hand is raised up.
9. Check for edema of the limb with AVF.
10. Ascertain the dialysis prescription from treating clinician.
11. Reassure anxious patients.
12. Ensure that the consent is taken (as per the hospital protocol).

Priming the Extracorporeal Circuit

The label in tubing sets and HFAK should be checked for patient's name and hospital registration number to confirm that it matches with the patient for whom dialysis session is being prepared. The dialyzer and blood tubing set should be primed before use. Initial step is to rinse with sterile normal saline. Extracorporeal circuit consisting of blood tubing sets and dialyzer are checked for leaks during rinsing.

All new sets should be labeled with (permanent marker) the name and patient identification/registration number before use. For new tubings and dialyzers, 1 L normal saline is used for priming. After rinsing with 500 mL plain saline, 1000 iu regular heparin is added to the remaining saline to prime the tubings and blood compartment of the HFAK. The dialysate compartment may be rinsed with dialysis fluid for 5 minutes and the heparin saline can be re-circulated in the extracorporeal circuit before connecting to the patient.

In the case of reuse, it is necessary to recheck and re-confirm the label with the name of the patient and hospital registration number. This step must be undertaken by two persons and recorded. Two liters of sterile normal saline are needed to prime blood tubing set and the dialyzers for reuse. This is done to eliminate all the air and residual sterilant from the reused extracorporeal circuit.

The below said steps are followed for initiating Hemodialysis for all patients. The security of the staff must be ensured. Universal precautions should be followed (Refer Chapter 5).

Hemodialysis Prescription

The indications and requirements for each patient are different. The set of instructions to be followed for each patient is called the dialysis prescription. The prescription will be different for a patient with AKI and maintenance Hemodialysis. For a patient on long-term dialysis, the dialysis prescription does not vary significantly. A typical dialysis prescription for maintenance Hemodialysis will include:

I. Dialysis modality (e.g. acetate/bicarbonate/HD/SLEDD/CRRT)
II. Frequency (e.g. daily/two/three times a week)
III. Duration (number of hours)
IV. Dialysis dose (Target URR/Kt/V)
V. Dialysate temperature
VI. Dialysate sodium (if variable sodium, sodium level at all phases)
VII. Potassium (potassium free/2 mmols/L/4 mmols/L)
VIII. Target weight loss
IX. Heparin (normal/tight heparinization/heparin-free)
X. Blood flow rate (Qb)
XI. Dialysate flow rate (Qd)
XII. Dialyzer (low flux/high flux/single use/reuse)
XIII. Medications during-/post-HD (50% glucose/normal saline/packed red cells/plasma/IV iron/erythropoietin/antibiotic/other drugs)

Usually, most of the parameters are fixed for each patient who is stable on maintenance dialysis. It will be necessary to modify only fluid removal depending on inter-dialytic weight gain and blood pressure. In AKI, the prescription regarding mode of dialysis, duration, artificial kidney, blood flow rate, dialysate flow, heparin, medications, etc. will have to be changed for each dialysis session.

Cannulation of AV Fistula and AV Graft

Patient is received and pre-dialysis patient checks done before receiving the patient in the dialysis station.

1. Select needle site: Avoid surgical scars, aneurysms, hematoma and infected areas. The arterial puncture should be at least 3 cm away from the arterial anastomosis site. The venous needle should be at least 5–7 cms away from the arterial site. This will prevent recirculation. If "button hole" technique is followed, the same needle point can be used for repeated dialysis. Otherwise,

the site of puncture is "rotated" in a "step ladder" pattern.

2. Select appropriate needle size. The needle number (Gauge or SWG) indicates the lumen. Larger lumen gives higher blood flow rate. The lumen of the needle increases as the SWG number decreases. (14 G needle will have more lumen compared to 18 G needle). Usually, the larger bore needle is used for returning the blood ("venous" side) and next smaller size for drawing blood from "arterial" side. SWG 15 or 16 for venous and 16 or 17 needle for arterial are usually used. Blood flow rate of over 300 mL/min can be achieved with these needles.

3. Direction of cannulation: The direction of arterial needle is towards the anastomotic site and is opposite to the direction of blood flow. The venous needle is directed in the direction of blood flow in the AVF. In the case of AV graft, the position of needle insertion should be varied. If the graft is placed in a "U"-shaped fashion in the forearm, both the needles should be directed towards the elbow.

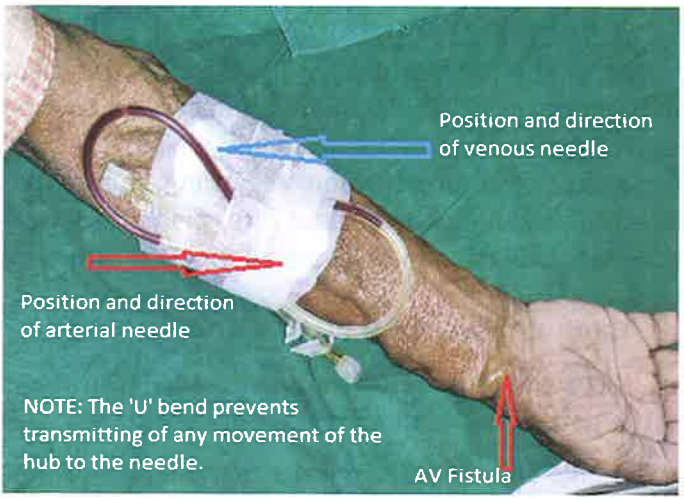


Fig. 13.1: Photo of arterial and venous cannulation sites and direction of needle.

4. Clean the selected sites with povidone iodine for a full 10 minutes. Disinfection is carried out by using circular motion outward, starting in the center.

5. If anaesthesia is necessary, the patient may be directed to apply & retain prilocaine ointment over the puncture site for about 1 hour before dialysis.
6. The venous needle is inserted first at the selected site. The direction is usually "towards the heart". The needle is inserted bevel up at a 45° angle and smooth steady blood flow should be confirmed by aspirating and pushing back the blood. Avoid rotation of the needle after insertion. The needle is taped securely. The extension tube is bent as "U" and taped securely. Fixing after making U bend will prevent movement of the needle even when the connection end of the fistula needle is handled.
7. Arterial needle is inserted at least 3 cm away from the site of AVF anastomosis. The procedure is the same as venous needle but direction is towards the AVF **(Fig. 13.1).**

In buttonhole technique, the same site is used for arterial and venous punctures. In step ladder puncture technique, the site is changed in a "step ladder" pattern. Different points of arterial and venous puncture every time. Each unit will have a different protocol for each patient.

Double Lumen Venous Catheters

Double lumen venous catheters are used as temporary access for Hemodialysis. These catheters are prone to infection because the catheters enter the vein directly, and there is no subcutaneous tunnel. Thus, they should be handled very carefully. In the case of permanent catheter ("permcath"), there is a long subcutaneous tunnel, and a cuff will prevent the infection from the skin reaching the catheter tip. The material used for the catheter is softer and will remain in the vascular compartment for a long time without damage.

1. During catheter connection and disconnection procedure, both dialysis staff, helper and patient should wear surgical masks.
2. The dialysis staff performing the procedure should use sterile

gloves (and gown/face shield, as per institutional policy).

3. Always inspect the exit site (the place where the catheter enters the skin) for any evidence of infection.
4. The exit site should be cleaned with betadine, dried and dressing given with Mupirocin, Betadine cream/ointment (if necessary).
5. First clean the exit site with disinfectant using aseptic technique. The cleaning is from inside to outside so that the bacteria in the skin are not pushed into the body. After cleaning the exit site with disinfectant, discard the gauze piece. Using a new gauze piece, clean both the limbs of the catheter with disinfectant and allow 10 minutes for disinfectant to work.
6. The catheter should not be pulled, disturbed or moved unnecessarily during any procedure.
7. Aspirate residual heparin or clot from each catheter lumen and discard. Check easy blood flow from both catheter lumen.
8. The lumen and catheter hub (connector end) should never remain exposed to air. A cap or syringe should always be attached to the hubs.
9. If the caps are reused, they should be kept in disinfectant or soaked in povidone iodine for the entire length of dialysis.
10. Dialysis catheters should be handled preferably by dialysis personnel only. It should not be used for routine injections in the wards. Triple lumen catheters have a separate site for administering injections which may be used carefully.
11. The patient should be counselled to maintain the exit site dressings clean and dry.

Initial Heparin Administration

Priming the dialyzer and tubings during rinsing with heparinized saline has been explained earlier in this chapter. For anticoagulation during dialysis, a bolus dose of 1000–2000 iu conventional heparin is administered into the arterial line leading to the dialysis just before starting the blood flow through the blood tubing.

Initiation of Dialysis

1. Blood pump speed is initially set at 50 mL/min, then gradually increased to 100 mL/min and the blood flow through the tubing and artificial kidney is observed until the blood column reaches the venous line. The priming fluid (heparinized saline) is discarded.
2. In some instances like low blood pressure or severe anaemia where the patient may not withstand removal of 100–125 ml of blood, the tubing and artificial kidney are primed with saline, plasma or blood before starting dialysis. In this case, both arterial and venous lines are connected simultaneously and blood flow rate increased gradually to desired level, usually 300 mL/min.
3. Proper level should be maintained in both arterial and venous drip chambers and the pressure monitoring lines from the drip chamber must be connected to the respective monitors. There should be transducer protectors in each connection.
4. Monitor for changes in the pressures as the blood flow rate is increased. In arterial drip chamber, the pressure is negative, and if it becomes more negative, it suggests inadequate flow from the arterial line. The pressure on the venous side is on the positive side. If it increases, it suggests obstruction to the return of blood in the venous segment or vein.
5. Ensure that the alarm limits are set correctly.
6. After starting dialysis, heparin pump is switched on to deliver the desired rate of heparin continuously (Refer chapter 12).
7. Ensure proper fluid removal parameters are set (negative pressure).
8. Ensure that proper dialysate temperature and dialysate flow rate are set.

Before starting, the blood should flow into the kidney from bottom up. Once the kidney is filled completely with blood, it is inverted so that the blood flow is top down and the dialysate flows bottom-up.

This is called counter-current flow and is a much efficient dialysis method. If the blood flow and dialysate flow in the artificial kidney are in the same direction, it is called co-current flow. The efficiency of dialysis will be lesser than counter-current flow.

Once the blood column reaches the venous segment, the pump is stopped, the venous end is connected to the venous access, clamps in blood line opened and blood pump restarted. If the flow and pressures are set, the pump speed is increased to the prescribed level.

Documentation/Charting of Treatment

Dialysis is an artificial procedure. Numerous changes may occur in the body during dialysis. Therefore, all steps, events, drugs used during dialysis should be charted and documented. The dialysis prescription includes the instructions from the treating physician regarding weight loss, ideal body weight, blood flow rate, dialysate flow rate and other parameters.

Termination of Treatment

1. Heparin infusion is discontinued half or one hour before the end of dialysis. The timing of discontinuation differs between different vascular accesses.
2. If, for any reason dialysis is slowed or discontinued during the prescribed time, dialysis should be continued longer than the prescribed time to compensate for the time lost.
3. After completing the dialysis time, the blood flow rate is reduced to 100 mL/min. The blood pump is stopped for a few seconds during which—
    a. The arterial end of fistula needle or catheter is clamped.
    b. Blood tubing separated at the arterial end.
    c. Pump is restarted at 100 mL/min flow rate.
    d. Some units connect normal saline to arterial line, whereas some permit air to enter the tubing and artificial kidney.

e. The blood is returned to the patient and the line is clamped and blood pump stopped to prevent air or saline used for return from entering the patient.

f. In the case of reuse, the artificial kidney and tubings are taken to the wash area for immediate rinsing and reprocessing.

Removing the AV Fistula Needles

The following precautions are taken during removal of fistula needle from the vein.

1. Check the patient's blood pressure,
2. Administer drugs, if any,
3. Remove one needle at a time,
4. Un-tape the needle and withdraw the needle at same angle as it was inserted,
5. Do not apply any pressure until the needle is completely withdrawn from the skin,
6. Apply moderate, direct pressure over the site, where the needle entered the blood vessel (not the insertion site in the skin) for 5 to 10 minutes,
7. Palpate the access above and below the site, for a thrill/bruit,
8. Clean and dress the site when bleeding has stopped completely,
9. Apply light tourniquet or dressing. This should not restrict flow through the access. Recheck for "thrill"/bruit,
10. Patient is advised to loosen the dressing or tourniquet straps after 4–6 hours and remove the tourniquet if there is no oozing from the puncture site.

14 Complications During Hemodialysis

R. Kasi Visweswaran • Priya J.

With the use of modern machines, Hemodialysis (HD) has become a safe and well-tolerated procedure. Dialysis involves diverting blood from the body, purifying it by passing through artificial kidney and returning it to the body. Complication that occurs during this process is called intradialytic complication. Complications that occur after many years are called long-term complications. During Hemodialysis, blood is exposed to foreign substances like blood tubing, dialysis membrane, substances used for sterilization and some impurities in the water which may be present even after water treatment.

The complications that occur during dialysis are:

A. Anaphylaxis or anaphylaxis-like reaction (anaphylactoid reaction)

This is a sudden, allergic type of reaction. The symptoms appear within 5 minutes of starting treatment. Symptoms may vary and include:

i. Burning sensation and feeling of heat all over the body

ii. Numbness in the fingers, toes, lips and tongue

iii. Watering from eyes and nose

iv. Nausea/vomiting

v. Abdominal pain and diarrhoea

vi. Dyspnoea, chest pain and choking sensation (in severe cases). Choking is caused by sudden swelling of the vocal cords causing obstruction to breathing

vii. Sudden collapse

Immediate administration of drugs like adrenaline, cortico-steroids and antihistamines will be necessary depending on the severity.

B. First-use syndrome

This is a type of anaphylaxis occurring in some patients who are exposed to a new artificial kidney. It is due to the presence of traces of ethylene oxide which may be present in spite of rinsing. In the case of reused dialyzers, a similar reaction may follow due to traces of substances used for sterilization [formaldehyde, Renalin (combination of peracetic acid and hydrogen peroxide) or glutaraldehyde].

Interaction between the dialysis membrane and some drugs used by the patient (e.g., angiotensin converting enzyme inhibitors) and iron may cause a similar reaction. Such reactions are due to release of substances like bradykinin and histamine in the body.

Reactions which occur within 10–30 minutes after starting dialysis may be due to cellulose membrane. Usually they subside. In such patients, artificial kidney made from non-cellulose membrane may be used (Refer Chapter 9).

C. Fever and shivering

Fever and shivering may occur at any time during dialysis and is due to contamination by live or dead bacteria (bacterial toxin). If many patients develop fever with shivering during the same dialysis session, contamination of water coming from water treatment system or plumbing lines should be suspected and steps taken to correct them. This can be prevented by observing infection control protocols correctly. Dressing infected open wounds should not be performed inside the dialysis area. Another cause of shivering during dialysis is use of cold dialysis fluid. This does not occur if the machine is set correctly at the optimum temperature and the alarm is working.

D. Hypotension during dialysis

This is a relatively common event during dialysis; the causes are many. It is necessary to correct the blood pressure immediately and take steps to prevent its recurrence.

The common causes are:

I. Excessive fluid removal: The fluid removal is planned as per the dialysis prescription. If the rate of removal is more, the blood volume will decrease and the blood pressure will fall. As fluid is removed from the blood during dialysis, fluid it will move from the extracellular compartment to the intravascular compartment.

II. This may not occur in patients with low levels of serum albumin, gross ascites or those patients with bleeding and hypotension.

III. It may also occur if the heart is weak due to ischemic heart disease, irregular heartbeat (arrhythmia) or blood or fluid accumulation outside the heart (pericardial tamponade).

IV. Other causes include anemia, sepsis, use of antihypertensive drugs before dialysis.

V. If a patient eats a heavy meal during dialysis, the blood flow is partly diverted to the digestive system and the blood pressure may come down.

VI. Low level of sodium, acetate dialysis, high dialysate temperatures and complement activation are some dialysis-related factors causing hypertension.

The symptoms are usually dizziness, coma, yawning, nausea, vomiting, muscle cramps, fast pulse rate (tachycardia), and low blood pressure. The patient should be placed in the head low position at 15° tilt. This is called Trendelenburg position. This position enables faster return of blood from the legs to the heart and brain.

Hypotension is often due to excessive fluid removal therefore the ultrafiltration is stopped and patient is given 50–100 ml of normal saline rapidly through the blood tubing set. Sometimes, more saline may be needed to improve the blood pressure. Oxygen inhalation will help. If BP does not improve, call for medical help. If patient develops intradialytic hypotension

frequently, precautions are:

i. Restrict inter-dialytic weight gain to less than three kilograms,

ii. Restrict salt and fluid,

iii. Skip using BP medicines which fall due before the time of dialysis,

iv. Avoid heavy food intake during dialysis or just before it.

The technician must take care to observe the following steps:

i. Use bicarbonate dialysis,

ii. Use machines with ultrafiltration control,

iii. Adjust dialysate sodium level by sodium profiling,

iv. Adjust dialysis fluid temperature at 35° to 36° Celsius,

v. Correct anemia,

vi. Inform clinician (cardiac check-up may be necessary).

E. Hypertension during dialysis

The common causes of development of hypertension during dialysis are:

i. Volume overload (Body weight is more than the "dry weight").

ii. Use of erythropoietin (EPO): A hormone which is given for improving the haemoglobin.

iii. High sodium in dialysate.

iv. Removal by dialysis of BP medicines: Drugs like ACE inhibitors and beta blockers are removed by dialysis.

If the blood pressure is over 180 systolic, the patients should be asked to take their regular antihypertensive medication (BP medicine). Use of drugs like Clonidine or nifedipine can quickly bring the BP to acceptable levels. Each dialysis unit will have a protocol which should be followed. The cause of intradialytic hypertension should be identified and corrected. In patients who develop intradialytic hypertension frequently, "dry weight"

should be calculated accurately and achieved. This will be more useful than increasing the dose of BP medicines.

F. Headache, mental confusion or fits

These symptoms may be related to hypertension, bleeding into the brain or sudden changes in the biochemical environment.

G. Heart and related complications

Most patients who are on maintenance Hemodialysis have associated heart disease. Irregular heartbeat (cardiac arrhythmia), myocardial infarction (heart attack), heart failure, pericardial tamponade (compression of the heart within the pericardium) and sudden cardiac death occur more commonly during dialysis compared to those not needing dialysis. When arrhythmia develops, the concentration of potassium in dialysate should be checked since both high and low potassium can precipitate arrhythmias.

H. Muscle cramps

This is also a common complication and may occur due to—

i. Hypotension

ii. Hypovolemia

iii. Low sodium in dialysate

iv. High rate UF

v. Low calcium in dialysate

vi. Carnitine deficiency

This can be managed by restricting fluid removal to <1 L/hour (0.3 mL/Kg body weight/hour). If more fluid removal is needed, the time of dialysis may be extended or "Isolated UF" tried for a limited period during the session. Administration of 50% dextrose (25–50 mL or 20–30 mL) 3% sodium chloride or raising the sodium in dialysate to 145 mmol/L. L-carnitine infusions help in those with carnitine deficiency. Stretching to the involved muscles and regular stretching of muscles during dialysis will be useful. Intradialytic exercise is useful not only in

preventing cramps but also improving clearance of substances. Counselling to restrict weight gain between dialysis sessions (interdialytic weight gain) is the most important strategy to prevent cramps.

I. Nausea/vomiting

This was one of the commonest symptoms during Hemodialysis when acetate dialysis was used in the past. Nausea, yawning, and tiredness are the earliest symptoms of impending hypotension. The treatment is symptomatic. Nausea and vomiting are early manifestations of "dialysis disequilibrium syndrome".

J. Dialysis disequilibrium syndrome

Urea contributes to osmolality of blood. In a patient having high urea levels for a long time, the blood and cells in the body will have nearly the same amount of urea and therefore, same level of osmolality. When starting dialysis in such a patient, if urea is removed rapidly from the blood stream, the blood osmolality will drop suddenly. There is a difference in the osmolality between the blood and cells. Then, fluid will enter the cells and cause brain edema. This can occur in patients who have high levels of urea in blood (>250 mg/dL), and should not be brought down rapidly. Mild symptoms include headache, nausea, vomiting, hypotension, breathlessness, blurring of vision. In severe cases, mental confusion, drowsiness, coma or convulsions may occur. Seizures may also occur due to stroke (blocking of blood supply or bleeding in brain).

It is important to prevent this complication by reducing the dialysis dose while starting dialysis in a patient who has very high urea levels. This is achieved by—

i. Reducing blood flow rate

ii. Reducing dialysate flow rate

iii. Permitting "co-current" flow (blood flow and dialysate flow in the same direction)

iv. Reducing the time (usually 1.5–2.5 hours for the initial three sessions)

v. Using a smaller surface area in the artificial kidney

vi. Reducing the urea by only, 30% (URR <30) for the first few dialysis sessions

Mild and early symptoms can be managed with 50% glucose infusion which will temporarily increase the osmolality. If the patient responds, dialysis can be continued by readjusting the blood and dialysis flow rate for the stipulated time, otherwise discontinued. Such dialysis sessions are continued for three to four times before a full 4-hour session with countercurrent blood flow at 300 mL/min and dialysate flow of 500–600 mL/min is started.

K. Technological complications

Technological complications are preventable; the technician should be watchful throughout.

i. Air embolism: Normally, the dialysis circuit is an airtight circuit. If any connection is loose or drip bottles are connected to the system, the blood pump will suck the air from the bottle when it is empty. Although the machine has alarm and line clamp for detecting air inside the tubing, entry of air should be prevented at all times for patient safety. If air enters the body through the venous return, it will travel to the heart, form froth and prevent circulation of blood in the lung and the patient may even die.

   The precautions to prevent air embolism are:

   a. Tape needles securely,

   b. Remove all air and bubbles during initial priming,

   c. Check all connections and tighten them,

   d. Adjust levels in the drip chamber,

   e. Saline and blood bags should be removed when empty.

ii. Hemolysis: Hemolysis means rupture (bursting) of the

red blood cells (RBCs). The blood cells can burst due to mechanical or chemical forces. The common causes are:

a. If the rollers in the blood pump are too tight (more occlusion in pump segment and crushing of RBCs).

b. Kinks in the tubings.

c. High dialysis fluid temperature.

d. Contamination of water with chlorines and chloramines. This complication may occur if the carbon filter is not functioning properly.

e. Presence of formaldehyde in the blood circuit.

iii. Clotting of dialyzer/blood tubing: This can occur if the blood flow rate is slow, heparin-free dialysis is tried with no adequate saline flushes, insufficient anticoagulation and air in blood lines. If anticoagulants (Heparin) is used, the blood sample should be tested by doing APTT (activated partial thromboplastin time) test as prescribed by the unit.

iv. Exsanguination: If any connection is loose or dislodged when blood pump is working, large volumes of blood will be lost rapidly. The connection between the access and blood tubings should be exposed and not covered under the bed-sheet or blanket. Careful supervision is necessary throughout dialysis, and this complication should never occur. The patient will die within a few minutes if not corrected.

L. Long-term complications:

Since Hemodialysis is an artificial process, patients who are on regular dialysis for many years may develop complications over time. Some are preventable—

i. Cardiac disease: many types of cardiac involvement can occur in patients on long-term dialysis. Cardiac enlargement due to hypertension, heart failure or cardiomyopathy (weakness of heart muscle) can occur. These patients have higher chances of getting heart attack or even sudden death.

If dialysis is not adequate, they may develop thickening, stiffness or fluid accumulation within the covering of heart (Pericardium). Poor blood supply to the heart due to blockage of coronary arteries may also occur.

ii. Long-standing high blood pressure (if not well controlled) will also harm the heart and cause enlargement and failure.

iii. Nutrition is very important in patients with long-term HD. If nutritional intake is insufficient, they develop malnutrition and vitamin deficiencies. Vitamins B and C are removed from the blood during dialysis and should be replaced, otherwise deficiencies may occur.

iv. Since damaged kidneys do not produce the blood-forming hormone called erythropoietin, many patients develop anemia. Erythropoietin is an expensive injection which patients may not take regularly because of price factor. The intake of other substances for blood formation like iron and vitamins may be poor.

v. Bone disease may occur due to deficiency of active Vitamin D. Since kidneys convert inactive Vitamin D to active Vitamin D, these patients need supplementation with active Vitamin D.

vi. Vitamin deficiency and diseases like diabetes contribute to numbness and weakness of legs due to neuropathy. Muscles may also become weak and wasted (thin).

vii. Psychological strain may occur due to many factors: financial, social and family stress. Some patients may have suicidal tendency also.

viii. Infections like tuberculosis, Hepatitis B, Hepatitis C develop in many patients. HIV, Hepatitis B and C may spread between patients within the dialysis unit, and such patients should be isolated to a different dialysis area with dedicated machines to prevent spread to others. Necessary precautions should be strictly followed. Many units do not permit reuse in such patients because it is a risk for the staff. Units have different

protocols for Hepatitis B, C and HIV patients who are on dialysis.

ix. Over the years, vascular access may get damaged due to repeated use. The access problems are:

   a. Access stenosis (narrowing of artery or vein. Narrowing of vein near the fistula causes poor flow in the fistula. Narrowing in the upper arm near the junction of vein to the axillary vein causes edema of the limb).

   b. Thrombosis (blood clotting).

   c. Failure (insufficient blood flow).

   d. Aneurism (bulging).

   e. "Steal" syndrome and limb ischemia (excessive blood flow through the fistula resulting in poor blood circulation to limb on the side of fistula).

   f. Infection.

x. Other long-term complications are:

   a. Amyloidosis (accumulation of beta 2 microglobulin and deposition of amyloid in tissues).

   b. Acquired cysts in the kidneys.

   c. Higher chances of tumors.

15 Patient Monitoring, Investigations and Assessing Dialysis Adequacy in Hemodialysis

R. Kasi Visweswaran • Sreedevi P. A.

Initial assessment, constant monitoring of the patient and preventive maintenance of both water treatment and dialysis equipment is an important role to be performed by the dialysis personnel.

General assessment of the patient:

a. Collecting data from interviews:
   i. Interviews and ascertaining development of new symptoms
   ii. Activities/whether pursuing profession
   iii. Leisure activities
   iv. Social activities, etc.

b. Physical examination:
   i. Weight: Pre-dialysis weight, post-dialysis weight, intra-dialysis weight loss (weight lost during dialysis procedure), inter-dialysis weight gain (difference between the post-dialysis weight of the one dialysis and the pre-dialysis weight of next dialysis) and deviation from "Dry" weight are important. The clinician prescribes the "Dry" weight and dialysis personnel should try and achieve dry weight and maintain the same. The co-operation from the patient is also important for maintaining dry weight. Dry weight is the ideal post dialysis weight after removal of all or most of excess body fluids. Usually, the maximum inter-dialysis weight gain should be restricted to a maximum of 3 kg. Any excessive weight gain >3 kg suggests non-compliance with fluid restriction. Usually, patients tolerate UF of 500–750 mL/hour without developing unpleasant symptoms. So, ideally, the weight loss (ultrafiltration) targeted during a 4-hour session of dialysis should be restricted to about 3 kg. If weight loss

of >3 kg is attempted in 4 hours, chances of hypotension, muscle cramps, vomiting, other unpleasant symptoms or precipitation of cardiac events is high.

ii. Blood pressure (BP): Good control of BP helps to provide smooth dialysis and prevents unpleasant symptoms. Usually, patients are advised to avoid taking the pre-dialysis dose of antihypertensive drug if they tend to develop hypotension during dialysis. In most patients, the BP is volume mediated—(i.e., if the blood volume is high, the BP is high, and as the blood volume comes down, by ultrafiltration, the BP also comes down). If the pre-dialysis BP is high and intradialytic hypertension (BP increasing significantly during dialysis) also develops, such patients may continue the pre-dialysis dose of antihypertensive drug and additional dose during dialysis as per the treating clinician's advice. Maintaining dry body weight is very important in such patients. Small fluctuations in BP occur during Hemodialysis, and BP should be monitored closely.

iii. Respiratory rate and dyspnoea (breathlessness): Patients on dialysis may develop breathlessness due to excessive fluid intake, associated cardiac failure or other causes. Dyspnoea is often due to pulmonary edema (fluid accumulation in the lung). Here also, improvement in fluid overload, edema, maintaining dry weight are important. If cardiac disease is the cause, appropriate treatment is given. Development of acute pulmonary edema is a medical emergency. If any patient on maintenance HD develops pulmonary edema, immediate dialysis will relieve the condition within a short time. Fluid removal by ultrafiltration will clear the accumulated fluid from the lungs.

iv. Body temperature: If the body temperature is higher, it may suggest an infection. A careful search for the infective focus is essential. If fever/shivering develops during dialysis, the vascular access must be inspected. Skin infection, exit site infection in dialysis catheters or infection in the catheter lumen/tip should be monitored. Such infection results in

entry of bacteria into the blood stream. Fever or "hot feeling" during dialysis can also be caused by higher dialysate temperature or as part of pyrogen reaction. Presence of bacterial toxins in the water may cause fever/chills during dialysis. If many patients in the same shift have the same symptoms, the water supply line should be checked and corrective action taken. If patients being dialyzed in the same machine develop similar symptoms, the machine should be thoroughly checked, disinfected, made pyrogen-free before use.

v. Irregular pulse suggests cardiac problem. Fast pulse rate (tachycardia) can be due to fever, hypotension or cardiac problem.

vi. Engorged neck veins suggest fluid overload or cardiac failure. Rarely, patients with pericardial effusion (common in renal failure on dialysis) may have engorged neck veins.

vii. Skin infection: Thick reddish skin anywhere in the body is suggestive of skin infection (cellulitis). The area around the vascular access should be inspected carefully.

viii. Maintenance of records is very important in all dialysis units. Most dialysis units have a proforma which has to be completed for each patient for each session of dialysis. In the proforma, the vitals of the patient and dialysis parameters are recorded, completed and signed by the technician/staff in-charge of the patient.

c. Investigations:

Each center will have its own protocol of investigations to be performed in patients on maintenance Hemodialysis. In addition to the investigations performed on each patient at the time of starting dialysis, a set of investigations are done periodically. The periodicity may vary between centers. Routine instigations to assess the patient and adequacy are done monthly or at least every 2 months. Complete general investigations including infection screening are done at least every 6 months. If circumstances warrant, investigations are performed more

frequently as per need and instructions from the treating clinician. It will be possible to assess adequacy by simple tests, and importantly they should be performed periodically.

The common investigations to be repeated periodically (monthly or every two months) are:

Hemoglobin/hematocrit/random blood sugar/pre-dialysis urea or BUN/pre-dialysis creatinine/sodium/potassium/post-dialysis urea or BUN. Other investigations as ordered by the treating clinician may also be done. BUN levels are about half of urea levels.

More complete investigations like infection screening, assessment of iron status, calcium, phosphorus and parathyroid hormone level, etc., are done every 6 months in addition to the routine tests.

The tests recommended every 6 months are:

Complete hemogram/iron studies (serum iron, serum ferritin, total iron-binding capacity, percentage saturation)/Liver function tests (serum bilirubin, ALT, AST, serum protein, albumin, globulins), calcium, phosphorus, magnesium, alkaline phosphatase, PTH (parathyroid hormone), and infection screening (Hepatitis B, Hepatitis C, HIV I and II). Tests for Vit B_{12} and Vit D levels may also be considered.

Assessing Dialysis Adequacy for Hemodialysis

Optimal dialysis should provide a degree of health so that they can perform all activities as a person without renal disease and dialysis and live a normal life. The most important factor is early starting of treatment, good quality dialysis and patient compliance. If the patient gets a higher "dose of dialysis", the outcome is better. A minimum of 12 hours of dialysis is required (3 sessions of 4 hours each). Other options like daily dialysis, nocturnal dialysis, etc. are discussed separately (Refer Chapter 19) .

Urea reduction ratio (URR): This measures the percentage of reduction of urea during one dialysis session. It can be calculated from pre- and post-dialysis urea values using a simple formula.

$$\textbf{Urea reduction ratio [URR]} = \frac{[\text{Pre HD urea} - \text{Post HD urea}]}{\text{Pre HD urea}} \times 100$$

Example: If pre-HD urea is 120 and post HD urea is 40,

$$\text{URR} = \frac{[120 - 40]}{120} \times 100 = \frac{80}{120} \times 100 = 66.6\%$$

Kt/V urea is a test to measure the effectiveness of dialysis treatment (dialysis dose delivered). It measures urea clearance and time of dialysis to the volume of distribution of urea. A delivered Kt/V value of 1.2 is the minimum for thrice weekly dialysis schedule.

Urea is a small molecular weight substance (molecular weight 60) and is an end product of protein metabolism. It is excreted from the body in urine. The level of urea in blood also correlates with nutrition, protein catabolism and is easily measured in most laboratories. In the Kt/V formula, K = dialyzer clearance of urea in mL/min, t = dialysis time in minutes and V is volume of distribution of urea in the body. (Remember, urea is distributed in all body fluids.)

Single pool Kt/V [spKt/V] means, the post-dialysis sample is taken soon after closing dialysis session.

Equilibrated Kt/V [eKt/V] means the post-dialysis blood sample is taken 30 minutes after hemodialysis is complete. During this time, the urea will redistribute itself from tissues to blood and the Kt/V will be lesser than spKt/V. Although eKt/V is more reliable, it can be done only if the patient waits for additional time after dialysis is closed.

Factors affecting dialysis adequacy are summarized:

a. Poor blood flow through vascular access.

b. Access recirculation (reverse connection in double lumen catheters). NOTE: In cuffed central venous palindrome dialysis catheters reverse connection may not result in recirculation. In

the case of AV fistula or graft, if the arterial and venous needles are too close, recirculation may occur. If there is obstruction to free flow in the AV fistula also, recirculation may occur.

c. Inadequate dialyzer reprocessing (in case of reuse).

d. Low fiber bundle volume (in case of reuse).

e. Small surface area dialyzer used.

f. Error in blood flow rate (to check blood pump occlusion).

g. Error in dialysate flow setting (to adjust machine settings).

h. Interruptions during dialysis (blood leak, hypotension, etc.).

i. Reduced treatment time: Any time lost during dialysis must be compensated by adding additional time after 4 hours. (Like adding "injury time" after every each session in a football match.)

j. Blood sampling and laboratory errors.

k. Dilution of blood sample with saline.

l. Wrong timing of blood sampling:

   i. Taking pre-HD sample after starting.

   ii. Taking post-HD sample before closing.

   iii. Delay in drawing post-dialysis blood sample (calculation of spKt/V will be wrong if there is delay).

16 Reprocessing of Dialyzer and Tubing for Reuse

R. Kasi Visweswaran • Reshma T.

Reprocessing dialyzer for reuse has been practiced even in "developed" countries. Since the cost of treatment is lesser to reprocess dialyzer and tubes, it is commonly practiced in many centers. Reprocessing is avoided in patients who have Hepatitis B, Hepatitis C, or HIV, since the risk of transmission is high. If the dialyzer and tubings are reused, special precautions are necessary. They should be—

i. Reused for the same patient strictly.
ii. Should be properly labeled.
iii. Kept in separate labeled, dedicated boxes.
iv. Under no circumstance, the kit should be used for another patient.
v. The number of re-use should be included in the label.
vi. Fibre bundle volume should be recorded after use.
vii. The reprocessing area should be well-ventilated, should have sufficient natural lighting and have smooth surfaces for easy cleaning.
viii. An exhaust fan should be provided.

Reprocessing can be done manually or using automated reprocessing machines. The procedure involves cleaning, testing, filling the dialyzer with high-level disinfectant or sterilant, inspecting, labeling, storing, rinsing and rechecking the label before reuse.

Automated Reuse System

Automated machines are available for reprocessing artificial kidneys for reuse. These machines use microprocessor, electronic components and hydraulic system to perform most of the steps mentioned above. The failure rate is low and more reuses can be

achieved. Human errors are avoided. Elaborate washing area is not necessary. The machine, the electrical connections, water supply and drain can be arranged in a work station. Blood tubings should not be reprocessed in the automated system.

Immediately after dialysis, the artificial kidney (HFAK) is detached and re-attached to the four labeled connections in the machine. Two connections are meant for the blood side and the other two connections for the dialysate side. The machine does the rinsing, "reverse ultrafiltration", cleaning, testing for leak and calculates total cell volume before refilling with sterilant. Once the cycle is over, appropriate caps are applied, and the artificial kidney is stored for reuse when the patient comes for the next dialysis. Most reuse machines can reprocess 2 HFAKs simultaneously.

Manual Reprocessing

For manual reprocessing, a clean washing and reprocessing area with two sinks, plain water and RO water connections and drainage system is required. The staff should wear protective gloves, fluid-resistant gowns, cap, mask and face shield/goggles. The six most important steps in reprocessing are:

i. Patient identification and labeling: The artificial kidney and blood tubing should be labeled with the name of the patient, registration number, date of previous use, number of reuse and fibre bundle volume.

ii. Rinsing during blood return and in the machine: The artificial kidney is filled with heparinized saline during blood return, taking care to avoid returning of the heparinized saline back to the patient. Rinsing should start immediately after the patient is disconnected from the dialyzer. The blood compartment is rinsed with the remaining saline using the blood pump. The dialysate flow is maintained in the reverse direction for a few minutes before detaching the set from the machine.

iii. Disconnect HFAK and blood tubing.

iv. Tubing cleaning: Connect both tubings to one another and

connect one end to tap water. Let water flow at a pressure of about 20PSI until all traces of blood are drained off. Gentle agitation or dislodging any blood by tapping outside the tube may be done. This must be done in the first sink. This may take 10 minutes. Tubing can be cleaned using liquid bleach 0.5% for 15 minutes. Then, it is rinsed again with water. Re-sterilizing can be done after attaching to the cleaned HFAK (see below).

v. Rinsing of HFAK: Rinse blood side and dialysate side with RO water to remove excess blood. Open the header and remove any blood or blood clot from there. Secure the header and see that the "O ring" is properly placed. Now, fill the dialysate side with 3.5% hydrogen peroxide solution and cap both dialysate caps. Hydrogen peroxide will be seen to bubble out from the blood side. Wait for a few minutes.

vi. Reverse ultrafiltration: Remove one of the caps in the dialysate side and use RO water under pressure on the dialysate side. The water will cross the membrane in reverse direction (dialysate side to blood side) and clean up the fibers. This procedure is done till the fluid is clear.

vii. Testing and visual inspection. The total cell volume is calculated with water in both compartments. The quantity of water held in blood compartment is let out and measured. This is compared with the TCV of the HFAK of the same brand and same surface area. If suitable, it is disinfected and stored. If TCV is less, the HFAK is replaced as per the institutional protocol. It should be discarded if CV is less than 60%.

viii. Visual inspection: Finally, the set is inspected visually. There should be only minimal signs of clotting in fibers. The headers should be clear.

ix. Disinfecting/sterilizing/storage: Both compartments are filled with 1.5% Renalin ensuring that there are no air bubbles. The four openings in the HFAK are capped and taken to the storage box earmarked for the patient. (Some units re-attach the cleaned tubings and re-sterilize the set together.)

x. Formalin is not used now. Formalin sterilization takes 24 hours

while Renalin sterilization takes at least 12 hours.

xi. Rinsing and removal of sterilant before reuse: The set must be emptied of the sterilant, and all side tubings must be cleared of the sterilant. Flushing is done first with 500 mL sterile normal saline followed by 500 mL heparinized saline (1000 iu heparin in 500 mL saline). The final effluent is checked for residual sterilant, and if there is no trace of sterilant, it can be used for the same patient.

Unless the procedure is done carefully, damage to the fibres may lead to blood leak during subsequent use. Bacterial contamination during washing or even the contaminated sterilant may result in infection. The patient may develop reaction if the sterilant has not been removed completely. There is a possibility of mix-up and reuse to a different patient, which should be avoided strictly by ensuring careful labeling and rechecking.

However, there are some advantages of reuse. Some proteins adhere to the membrane and improve the biocompatibility. The chances of ethylene oxide reaction (first-use syndrome) can be avoided. By carefully reusing, the total cost of dialysis can be reduced.

17 Infections in Dialysis Patients

Umesh B. Khanna • Hemant Chougule

Patients undergoing dialysis are highly prone to most infections because of varied factors. Usually, it is due to the poorly functioning immune system (immunosuppressed condition) uremia, poor nutrition, uncontrolled diabetes and vitamin deficiency. In addition, patients with catheters develop infections more frequently. Infection can spread from contamination of dialysis water, dialysis machine or cross-contamination with other patients within dialysis area.

Infection in dialysis patients is the leading cause of morbidity and mortality. Infection in venous catheter is a leading cause of catheter loss and difficulty in continuing dialysis. Thus, it is responsible for increased morbidity and mortality. Infection can spread from the skin, through the catheter track outside the catheter or through its lumen.

Exit Site and Tunnel Infection

Spread of skin bacteria onto the outer catheter surface to the body may lead to exit site infection which is associated with redness, pain and pus discharge at the exit site of catheter from skin. Exit site infection can be managed by cleaning, dressing with local antibiotic and good hygiene. While dressing the exit site, the cleaning should be from "inside out" direction so that any secretions between the catheter and skin is cleared outside. At the same time, there should be no tug or pull on the catheter **(Fig. 17.1).**

Fig. 17.1: The strokes direction of cleaning the exit site.

Tunnel infection means infection along the course of the catheter through subcutaneous tissues. These patients may develop fever, chillness and increase of the blood count. Tunnel infection may lead to transfer of infection from skin to blood stream. Therefore, if a patient has tunnel infection and when it is not controlled, it will be advisable to remove the catheter and use a new catheter in a different location.

Double Lumen Dialysis Venous Catheter Infection

Infection can directly enter the blood stream through the hemodialysis catheter. Organisms may form colonies at the catheter tip and spread to blood stream. This results in catheter-related blood-stream infections (CRBI or CRBSI). Patient may develop complications like spread of infection, septicemia, abscesses or even death following CRBI. Such infections may or may not be associated with systemic symptoms like fever or chillness. Milder cases present with fever, chillness after start of hemodialysis. Severe cases present with "shock" (cold hands and legs, low BP, high pulse rate) along with fever and chills. Patient may become very unwell. Complications like infection in heart valves (endocarditis), lung, brain, skin, bone or joint may occur. Blood sample should be sent for culture through dialysis port. Sometimes, two sets of cultures are done, one from the catheter and the other from blood drawn from another vein. Paracetamol, either oral or injection, may be given for temporary relief of fever. Appropriate intravenous antibiotics should be given for 2–4 weeks. If infection persists, the catheter should be replaced.

Measures to prevent CRBSI starts from the time of insertion of catheter. Thorough aseptic precautions should be taken during catheter insertion. After insertion, the catheter should be covered with sterile dry dressing. Catheter dressing should be maintained dry at all times, including bathing time. Both dialysis staff and patients should wear surgical mask and observe universal precautions during starting, closing or when catheter is manipulated. Dialysis staff should wash hand with soap and water or alcohol-based chlorhexidine solution (0.5%) before touching the catheter. Catheter lumen should never remain open to air, and the lumen must be kept sterile.

The threads in the catheter hub for fixing the cap should be cleaned well with chlorhexidine-based solution. The cap for closing the hub should be maintained in a sterile condition or a new cap should be used every time. Betadine ointment or mupirocin cream is applied to the exit site and sterile dressing done.

Infection from RO Plant and HD Machine

Infection can occur due to growth of bacteria in water treatment system, storage tank, pipe or HD machine. If such infection is present, many of patients in dialysis unit will have fever, chillness and/or low BP simultaneously. In such cases, the dialysis is discontinued while symptomatic treatment will be continued and RO water culture is collected. Immediate disinfection of the water treatment system is performed before taking up patients for dialysis. Organisms grow easily in the bicarbonate concentrate and so it should be prepared freshly before each dialysis and unfinished bicarbonate concentrate discarded at the end of the day. Every dialysis machine should be subjected to surface cleaning with disinfectant and heat disinfection (of hydraulic system) followed by rinse after each dialysis.

Infection in Dialysis Patients Unrelated to Access Site

In addition to dialysis-related infections, these patients have higher chances of developing infections like other persons. Out of these, Hepatitis B and Hepatitis C infections are common and may spread to other patients within the same dialysis unit. Special care is needed to prevent the spread of such infections.

Viral Infections

Hepatitis B Infection

Prevention of hepatitis B infection is very important, and all patients are tested for Hepatitis B surface antigen (HbsAg) and given hepatitis B vaccination if they are HbsAg negative. Anti-HBsAB titre is checked to confirm that the patient has satisfactory levels of antibody response. (See chapter 5 on Infection control and vaccinations in dialysis room).

Dialysis patients are susceptible to hepatitis B infection due to cross infection from other patients in dialysis unit or blood transfusion. Most

of the patients do not have symptoms or any discomfort. However, while testing the blood periodically, Patients have increase in blood level of enzymes suggesting liver injury like SGOT/SGPT. The test for Hepatitis B surface antigen (HbsAg) will be positive. Further tests like HBV DNA (hepatitis B virus DNA) titre are done before deciding treatment. The drugs used are lamivudine, adefovir or entecavir. A course of Entecavir is the best treatment available.

Hepatitis C virus (HCV) Infection

Hepatitis C infection is higher in dialysis patients as compared to the general population. Most patients do not have any symptoms. Patients have increased SGOT/SGPT, cirrhosis of liver with ascites or even liver cancer. Diagnosis is confirmed by checking for anti-HCV antibody. The severity can be assessed by checking HCV RNA level in blood. It can be treated by specific antiviral drugs like daclatasvir, asunaprevir or sofosbuvir for 12 weeks. The chance of spread among other patients in the dialysis area is common, and many units isolate these patients to prevent the spread. Staff must take extra precautions while handling such cases.

HIV Infection

The number of patients with HIV positive cases requiring dialysis is increasing. Patient may be asymptomatic or may present with features of AIDS. Diagnosis is done by HIV ELISA test.

Treatment begins with combination of anti-retroviral therapy. Strict precautions should be taken by staff and other patients against infection. The institution protocol should be followed regarding isolation of HIV positive patient.

Urinary Tract Infection (UTI)

Urinary tract infection is common amongst patients on hemodialysis, especially in those with polycystic kidney disease and neurogenic bladder. Patient may have lower abdomen pain, pus cells in urine, and the urine may show organisms when cultured. Treatment is carried out with appropriate antibiotics.

Pneumonia

It is the important cause of death in dialysis patients. Patient develops fever, cough, breathing difficulty. The diagnosis is suspected by clinical examination, confirmed with the help of X-Ray and sputum examination. Treatment is by appropriate medications depending on whether the infection is bacterial or viral.

Abdominal Infections

Abdominal infection include diverticulitis (infection of diverticula which are small projections from the intestine), loose motion, acalculous cholecystitis (infection of gall bladder). Patient complains of abdominal pain. Diagnosis is done by sonography and CT scan and necessary treatment started.

Tuberculosis (TB)

TB is ten times more common in dialysis patients compared to other patients. Extrapulmonary TB (infection outside the chest) is more common than pulmonary TB (lung TB) in dialysis patients. Diagnosis can be made by appropriate tests like blood tests, chest X-ray, sonography, Ct scan chest, Lymph node biopsy, other tests to identify the DNA of M. tuberculosis and culture of the tissue. Treatment for tuberculosis with at least 4 drugs for the first 2 months followed by 3 drugs for 4–9 months more will be required for complete treatment. These patients should be followed-up for recurrence.

Other infections, such as listeriosis, salmonella septicemia, mucormycosis (fungal infection), are also common in patients with long-term hemodialysis.

18 Procedures in Nephrology

R. Kasi Visweswaran • Revathy G.

Generally, dialysis technician and nurses assist the doctor in performing procedures related to patients with kidney disease. The doctors themselves prefer to perform these procedures in or near dialysis unit and the technicians or nurses have the responsibility to arrange and assist the procedure. Therefore, an awareness and the steps followed in performing these procedures will be useful. In this chapter, the important steps in Seldinger method of cannulating large veins for dialysis, insertion of temporary dialysis catheter, permcath and renal biopsy are discussed.

Seldinger Method of Cannulation of Major Deep Veins (Jugular/Femoral/Subclavian)

As discussed earlier, placing a double lumen dialysis catheter in a major vein is necessary for starting dialysis if the patient needs urgent dialysis. Although subclavian vein was used earlier, it was associated with complications, and the jugular vein is preferred now. Femoral vein is also avoided as far as possible. The principle of Seldinger method is the same irrespective of the vein chosen.

The right jugular vein is preferred since the vein drains directly into the superior vena cava and right atrium. The steps for right jugular vein cannulation using Seldinger method for placing double lumen dialysis catheter are explained.

Items Required

1. Sterile tray containing small bowls 2, cotton balls 4, gauze pads 4, hole towel, sponge holding forceps, needle holder
2. 5 mL syringe with needle (for drawing local anesthesia)
3. Additional sterile needle 24 F and 2.5 cms (for injecting local anesthesia)

4. Sterile pack of new catheter kit with catheter, guide wire, dilators, caps, introducer needle and dressings. (Confirm that the size and length of catheter are suitable for the patient before opening the pack.)
5. Betadine/chlorhexidine (in one bowl)
6. Local anaesthetic (Xylocaine)
7. Dressings, sticking plaster, etc.

Patient Positioning

For femoral cannulation, patient should be lying supine with a small sand bag in the lower part of spine. This helps to keep the hip slightly extended and the vein can be more easily accessed.

For cannulating the internal jugular vein, the patient should be lying with a small sandbag in the upper part of chest so that the neck is extended. The neck should be turned to the opposite side of the puncture site. During the procedure, the foot end of the bed is elevated to about 15° (Trendelenburg position). This position makes the vein more distended and prevents air from entering the circulation (air embolism). After the catheter is placed and secured, the patient is given head up position using the back rest at 30°–45° angle.

Marking and locating the internal jugular vein: the sternomastoid muscle extends from the mastoid process behind the ear to the sternum and collar bone on each side. In the lower part of neck, it divides into two parts to get attached to the sternum and middle part of collar bone. When ultrasonography was not available, the marking is made in the front of neck where the two parts of sternomastoid muscle separates. This point corresponds to the apex of the triangle formed by the two parts of the sternomastoid muscle and collar bone (at the base). The internal jugular vein is close to the carotid artery. The pulsation of carotid artery is identified and the skin just lateral to the pulsation is anesthetized. After proper skin preparation, local anesthesia is administered. A 3.5 cm, 18–20 gauge needle is used as guiding needle to locate the vein and

is directed from this point at 45° angle and in the direction of the nipple. Gentle suction is given and backflow of blood occurs when the needle enters the vein. The color of venous blood is dark and slightly bluish but arterial blood is bright red. The larger needle is introduced in the same direction close to the guiding needle for the same length. Now, the ultrasound examination is done to see the vein and the puncture is done under guidance by ultrasonography. If pressure is applied, the vein may collapse and the needle may enter the common carotid artery nearby. Once the needle tip is in the vein, the syringe is disconnected to see "venous blood" trickling from the needle hub. If the carotid artery is punctured by mistake, bright red blood will jet out from the needle. The "J" end of the appropriate-sized guide wire is introduced into the vein for a depth of about 20 cms. If X-ray or fluoroscopy is available, the position of guide wire can be checked.

The needle alone is gently withdrawn and removed, leaving the guide wire inside. A small incision is made (about 3–4 mm) at the site of entry of guide wire in the skin. This will permit the dilator to pierce the skin without damage to the tip of the dilator. The dilator is advanced over the guide wire into the vein. First, the smaller of the two dilators is gently threaded over the guide wire into the vein and withdrawn. Next, the bigger of the two dilators is advanced into the vein and withdrawn. This will create a smooth pathway for placing and positioning the catheter without damage. No pressure should be exerted on any of the equipment used at any step, as it will damage the vein, the guide wire, dilator or catheter. Once the catheter is placed in position, the guide wire is withdrawn completely. The guide wire should not be pulled hard since it may break. The catheter lumens are flushed with normal saline after checking that the flow is adequate. The lumens are filled with heparinized saline, and X-ray is taken to confirm the position. The catheter is fixed by suturing with the skin and sterile dressing applied. The catheter can be used after confirming the position by X-ray.

In the case of subclavian vein, a small pillow or sandbag is kept between the shoulder blades, and the patient is kept in

Trendelenburg position. The needle puncture (after anesthetizing the area) is below the collar bone. The point is approximately the junction between the middle and outer one-third of the collar bone. The needle is directed below, then behind and parallel to the bed. Thus, the needle will travel behind the collar bone and manubrium sterni (upper part of sternum). The direction of the needle is towards the opposite sternoclavicular joint. As the needle tip enters the vein, blood will enter the syringe. After confirming that the blood is from the vein (by color and pressure), a guide wire is placed and the remaining steps are similar to jugular vein cannulation.

In the case of femoral cannulation, the femoral artery is palpated in the upper thigh, about 1 inch below the middle of the inguinal ligament. The vein is immediately medial to the artery and can be cannulated easily. Once the position of needle tip is confirmed by observing the backflow of venous blood, the remaining steps as explained in previous paragraph are followed.

For renal biopsy, usually the left side is chosen. The patient is in the prone position with a pillow under the abdomen. The position of the lower pole of left kidney is identified by ultrasound examination and X-ray. After preparing the skin, anesthesia is given from the selected point to deeper parts up to the kidney surface. A long thin needle (usually an 18 G lumbar puncture needle) is used to assess the depth of the kidney from the surface. The patient should be trained to hold the breath when the needle enters the kidney. If the needle tip is in the kidney, it will move up and down when the patient is breathing. The needle should not be touched while the patient is breathing. This step will help to find out how deep the kidney is from the skin. A small incision is made in the skin so that the tip of the biopsy gun passes through the skin easily. When the patient is holding the breath in inspiration, the gun is advanced up to the desired length, fired and withdrawn before the patient takes the next breath. Pressure is applied over the site for a few minutes and ultrasonography is performed again to look for any bleeding. After applying a compression bandage, the patient is observed for 4–6 hours. Samples of urine are collected over next few hours to look

for hematuria. Pulse rate and blood pressure are also monitored.

Permcath Placement

Permcath placement is usually done through right internal jugular vein in a minor operating theatre where there are more facilities such as "C Arm" or fluoroscopy. The patient is in Trendelenburg position. For permcath placement, the site of exit is marked on the skin by considering the length of the catheter so that the tip of the catheter will be in the right atrium of the heart. The jugular vein is the commonest site for permcath placement. The steps for right jugular catheter placement are followed as explained above, and the guide wire is placed in position. Now, local anesthesia is given from the planned exit site to about 1.5 cm outside the position of guide wire. An incision is made in the neck where the guide wire comes out of the skin towards the shoulder for about 1–1.5 cm. A small pocket is created under the skin in the neck to accommodate the smooth curved portion of the catheter. A puncture is made (0.5 cm) at the exit site. The permcath, which is rinsed and filled with sterile saline, is connected to the introducer, and the tip of the introducer is advanced from the exit site towards the neck through the subcutaneous tissue so that it comes out through the outer part of the 1.5 cm incision in the neck. The introducer with the attached catheter is pulled through. The cuff of the permcath which is usually 5 cm from the hub should be in the subcutaneous tissue and there should be no kinks. The metallic introducer is removed.

The dilators are introduced over the guide wire one by one. Usually, for permcath, there are three dilators and a "peel-away" sheath. The peel-away sheath is attached to the largest dilator and introduced over the guide wire. The dilator is removed leaving the peel-away sheath inside. There is usually a valve to prevent backflow of blood. If it is not there, syringe is attached to the end to prevent backflow of blood. The tip of the permcath is introduced through the peel-away sheath through the superior vena cava into the right atrium. The sheath can be split into two parts, peeled off and removed gently. The flow through both lumens is checked and the lumens are filled with appropriate volume of Heparin and saline. The small incision

in the neck is sutured. The catheters are NOT puncture-proof and extreme care is taken to avoid needle puncture of the catheter. The wings of the catheter hub are fixed with sutures, and chlorhexidine dressings applied. Betadine is avoided when using permcath.

19 Dialysis Under Special Situations

Umesh B. Khanna • Ankit Mody • Kamal Shah • Chintan Shah

Sometimes, it may be necessary to undertake dialysis procedures under special situations. In patients who are unstable clinically, have hypotension or weak cardiovascular function, may not be able to withstand the strain of conventional full dialysis with blood flow rate of 300 mL/min, using a high flux dialyzer and trying to remove larger volumes of fluid. In such cases, CRRT may be more useful. Considering the additional cost and equipment, the procedure may not be available in all dialysis units. In such cases, the conventional dialysis can be modified and offered as sustained low efficiency dialysis (SLEDD) or **sustained** low efficiency dialysis with filtration (SLEDD-F). With the advancement in the dialysis machine and availability of accessories for children, paediatric Hemodialysis is also possible. Children on Hemodialysis have to be handled differently. Rarely, dialysis and other procedures are undertaken for conditions other than renal diseases. Such conditions are also discussed in this chapter.

Sustained Low Efficiency Dialysis (SLED)

Critically ill patients may not be able to tolerate conventional intermittent Hemodialysis (IHD) or peritoneal dialysis. Patients with acute kidney injury or multi-organ failure or patients who are already on chronic dialysis admitted to ICU in critical condition may not withstand Hemodialysis. They may have hypotension (blood pressure <90 mmHg), fluid overload with pulmonary edema (fluid accumulation in lungs), metabolic acidosis (with low blood pH and bicarbonate levels) and hyperkalemia (potassium level in blood >6 mEq/L). In such cases, hybrid forms of dialysis like sustained low efficiency daily dialysis (SLEDD) or continuous renal replacement therapy (CRRT) may be necessary.

Principles of SLEDD

SLEDD is based on the same principles as conventional Hemodialysis like diffusion of solutes and ultrafiltration of fluid across a semipermeable membrane. This allows the removal of accumulated waste products, correction of electrolyte imbalance and removal of excess fluid from the body. The blood flow rate and dialysate flow rate are reduced so that the weak cardiovascular system is not put to additional strain. However, this is not advised in neurological cases and after brain surgery.

Advantages of SLEDD

1. Easy to perform.
2. Regular dialysis machine and dialyzer can be used. No additional/special equipment necessary. Thus, it can be performed in any regular dialysis unit.
3. Better tolerated than HD in unstable patients with low blood pressure or weak heart (hemodynamic ally unstable).
4. Usually lasts for 6–8 hours only at a time. (In CRRT, the procedure goes on continuously for 48–72 hours.)
5. Corrects electrolyte imbalance rapidly and solute removal is smooth and steady.
6. Heparin can be used as anticoagulant. Heparin-free dialysis can be done in patients with bleeding diathesis or postsurgical patients.
7. Composition of dialysate can be modified as per requirement.
8. Cost of treatment is much less compared to CRRT.

Sustained Low Efficiency Dialysis with Filtration (SLEDD-F)

In this procedure, in addition to the parameters for SLEDD, the amount of fluid removal can also be prescribed. A typical dialysis prescription for SLEDD-F treatment will be as follows:

- Duration: 8 hours (6–8 hours)
- Blood flow: 150 mL/min (100–200 mL/min)

- Dialysate flow: 300 (200–300 mL/min) NOTE: In many dialysis machines, the dialysate rate cannot be reduced below 300
- Ultrafiltration: Depending on patient's condition (variable is max 250 mL/hour)
- Total UF: 1200 mL
- Dialysate temperature: 35–36° Celsius
- Dialysate Sodium: 130–140 mEq/L
- Dialysate Potassium: 0–4 mEq/L (variable depending on K^+ level)
- Anticoagulation: Conventional heparin/LMW heparin/heparin-free.

Short Daily Dialysis

Two factors are very important in Hemodialysis, namely, duration of dialysis and the number of dialysis sessions per week (frequency). The total number of hours of dialysis that a patient gets per week is obtained by multiplying these two. For example, if someone is getting 4 hours three times a week, the total numbers of hours per week is 12 hours. The problems associated with conventional thrice weekly dialysis are:

1. Because of the gap of nearly 2 days, too much fluid accumulation may occur between two sessions. This may cause strain on the heart.
2. Too much fluid accumulation may result in pulmonary edema which will need "emergency dialysis".
3. Too much fluid cannot be removed in the 4-hour session. (Maximum fluid removal per hour for patient comfort = 1 L.)
4. Too rapid fluid removal may cause hypotension and post-dialysis fatigue.

Short Daily Dialysis is practiced in some centres. This means, that the patient gets 2 or 3 hours of dialysis six times a week (12–18 hours per week). The total number of hours remains little more than three times a week schedule. The gap between sessions is only one day, and the fluid is never allowed to build up too much. The excess fluid in the body is never too high and can be easily removed

during dialysis, and the patient has lesser chances of hypotension and discomfort. The strain on the heart is also reduced by this. If the weight gain cannot be restricted by the patient, 3 hour dialysis may be considered for smooth and steady fluid removal.

This modality of short daily dialysis has many advantages compared to the regular thrice weekly dialysis. The gap between two sessions is less and the weight gain between dialysis is lesser. More solute clearance and fluid removal are possible. Therefore, the patient may have more liberal diet and fluid intake.

Nocturnal Long HD

The total dialysis time per week (by increasing duration and frequency) can be improved by nearly three to four times by nocturnal long HD. In this modality, the patient gets dialysis 5–6 nights a week for 7–8 hours each night. The total number of hours by this therapy is between 35–48 hours per week. With this modality, the patient does not build up too much water in their body because the gap between the sessions is less than 24 hours. Also, since the duration of the session is about 7–8 hours, the UF rate is also low which results in very gentle dialysis without any strain on the heart.

Patients on home Hemodialysis opt for this since they can remain and sleep at home during the procedure. Most patients can have a completely normal diet and fluid intake. The long-term outcome of patients on daily nocturnal Hemodialysis is very good and patients lead a nearly normal life. They have good quality of life, live longer, have no anaemia, have no high blood pressure, good phosphate control and have good cardiovascular function. Although performed preferably at home, nocturnal HD can also be performed in dialysis centres by clubbing the patients in long night shifts. Such patients have the major advantage of full employment during day time and night dialysis while sleeping.

However, some disadvantages of long nocturnal Hemodialysis are non-availability of help in case of emergencies if performed at home. Frequent alarms may require constant supervision and vigilance by a

trained person. Dialysate concentrations of calcium and phosphates have to be monitored. Procedures like Heparin-free dialysis which needs close monitoring may not be possible.

Home Hemodialysis

Home Hemodialysis is done using a regular Hemodialysis machine installed in the home of the patient along with a small capacity water treatment system including RO plant. Once the plumbing lines and electrical connections are ready, the machine is installed. The water quality and cultures are checked. If the reports are satisfactory, dialysis can be initiated. Most patients in India have a technician who comes home as per the plan and performs the procedure. In many countries, patients or family members get trained and perform dialysis themselves. Most patients undergo two or three sessions per week at any time suitable for them. The service provider supplies the consumables required for dialysis and arrangements are made for disposal of biomedical waste. Usually, the biomedical waste is carried in sealed bags to the respective dialysis centres for proper disposal. In some countries, easy-to-use machines which are designed for home use are available (NxStage System One **Fig. 19.1**). This machine is portable, about the size of a desktop printer.

Fig. 19.1: Portable dialysis unit (NxStage System One) with the box for transport.

Fig. 19.2: NxStage is a simple, flexible and portable system.

Advantages of Home Hemodialysis for the Patient

i. Not necessary to go to the centre or hospital.

ii. Dialysis in the comfort of their home.

iii. Convenient timings.

iv. Individual attention.

v. Dedicated machine (since other patients are not dialyzed in the same machine, no chances of cross infection).

vi. Family can be around during dialysis.

vii. Improved quality of life and better survival compared with in-center dialysis.

Only a small group of affluent patients will be able to manage home Hemodialysis. The ideal patient for home Hemodialysis should have:

I. Financial stability.

II. Facilities for setting up dialysis at home (suitable space, water supply, steady power supply).

III. Motivation, family support and technical support as needed.

IV. Knowledge and willingness for regular monitoring of clinical and technical parameters.

However, there are some disadvantages and advantages for home Hemodialysis:

I. More expensive compared to dialysis in a centre.

II. Lack of hospital/ICU back-up in case of emergency.

III. Periodic supervision by nephrologist may be difficult.

IV. No chances of interaction and friendship with other patients.

V. Hospital atmosphere at home.

VI. Short daily dialysis is possible.

VII. Long nocturnal dialysis is also possible.

REcirculation of DialYsate (REDY) System

REcirculation of DialYsate, or "REDY" system or Sorbent system, is a system tried first in the 1990s but was discarded later. It is a useful system for home dialysis since it requires only 6 Liters of potable tap water. Extensive water treatment is not necessary. A sorbent column is used to regenerate the dialysate. The sorbent column is capable of adsorption, catalytic conversion and ion exchange. The first layer containing activated charcoal (adsorption) binds to heavy metals, oxidants, chloramines, creatinine, uric acid, middle molecules and other organic materials. The next layer is the urease (catalytic conversion) layer. Urease is an enzyme which converts urea into ammonia and carbon dioxide. In the third layer contains zirconium phosphate and also contains sodium (Na^+) and H^+. They adsorb potassium (K^+), Calcium (Ca^{++}), Magnesium (Mg^{++}), and ammonium (NH_4^{++}) in exchange for (Na^+ and H^+) (ion exchange). Any ammonium produced in the urease layer is removed. The fourth layer is a combination of zirconium oxide and zirconium carbonate. This layer helps to adsorb and exchange phosphates (PO_4^{3-}), fluoride and heavy metals for Na^+, H^+ HCO_3^- and acetate. The cartridge acts as a bacterial filter and adsorbs endotoxins and cytokines. Therefore, all the impurities in the used dialysate are removed and the regenerated dialysate can be used for continuing dialysis. The bacterial count of <1 CFU/mL and endotoxin level of <0.3 EU/mL are obtained by REDY system.

The advantages are that the sorbent system can be transported, used in future models of portable kidney, works on small volume of tap water, has no chance of infection or machine damage due to calcification. It can be used for home dialysis, dialysis while traveling or in places with severe water scarcity since it needs only 6 L of drinking water. The disadvantages are the cost and lack of experience in its usage. When advancement like "suit case kidney" is developed, such a system may become useful.

20 Pediatric Hemodialysis

Umesh B. Khanna • Chintan Shah

Kidney failure in children can be caused by conditions such as birth defects, infections, kidney injuries, and hereditary diseases that may be passed from parents to children. End-stage renal disease (ESRD) in a child requires dialysis or kidney transplant to survive. Dialysis in children is a challenge. It will be an overwhelming experience and associated with anxiety for the children and the family. Advances in technical aspects in Hemodialysis and the availability of pediatric size dialyzers and equipment have made it possible to offer Hemodialysis in children with ESRD. Pediatric Hemodialysis must be done in a well-equipped center with a team consisting of a pediatric nephrologist, experienced dialysis nurse, technician, social worker, administrator and dietician.

The same dialysis machine meant for adult can be used for children. The machine should have provision of low blood flow and volumetric ultrafiltration. The ideal vascular access for chronic Hemodialysis will be good arteriovenous [AV] fistulas if possible. This may be possible in children over 9 years. Dialysis through AV fistula allows high and consistent flow rates and low risks of infection and thrombosis.

If AV fistula is not possible, cuffed venous catheter (CVC/permcath) will be the second choice. Percutaneous temporary dual lumen catheters [8–13 French (Fr)] are stiff, and there is no subcutaneous tunnel. So, they can be used only for short-term dialysis. The CVC dual lumen catheters are softer, more pliable and have a cuff in the subcutaneous path of the catheter. They are used for long-term dialysis. These catheters have the following advantages compared to temporary dual lumen catheters:

a. Allow high blood flow rate
b. Low risk of recirculation

c. Lower risk of blood stream infections
d. Longer life
e. Not stiff

For children older than 10 years and/or weighing ≥20 kg, arteriovenous fistulas, or arteriovenous grafts, are preferred if long-term dialysis is anticipated. If the child comes as emergency case needing urgent Hemodialysis, then temporary catheter is used. For children with chronic kidney disease (CKD), early planning will help to obtain an ideal vascular access for long-term dialysis. The right internal jugular is preferred since its direct angle to the heart achieves high blood flow rates. The catheter should not be placed on the same side as a maturing AV access. It is possible to offer Hemodialysis to smaller children in specialized pediatric nephrology units. The special requirements and precautions are:

- Catheter: The size is chosen depending on body weight of the child **(Table 20.1)**. The size of catheter is calibrated in French gauge or French scale system (Fr OR F). One F size catheter is very small with diameter of 1/3 or 0.33 mm. Thus, a 9 Fr and 12 F catheter will have a diameter of 3 and 4 mm, respectively. Thus, if the Fr is smaller, the lumen is also smaller. (See the difference in numbering of I.V. cannulas in the BOX below the table.)

Table 20.1: Sizes of the catheter according to the body weight of the child

Weight of child	Catheter size – French (Fr)	Length to add
3–15 kg	7/8 Fr	Various lengths are available
16–30 Kg	9/10 Fr	-do-
>30kg	11/12 Fr	-do-

NOTE:

The intravenous cannula is labeled and color coded according to Gauge (G). The bigger cannulas have smaller numbers. For example, 16G I.V. cannula has a diameter of 1.72 mm and permits flow rate of 200 mL/minute, whereas 22 G I.V. cannula has only 0.91 mm diameter and permits a flow of only 32 mL/min.

If size is marked as French (Fr) scale, bigger the number, bigger the size.

- Dialyzers: Size of the dialyzer is decided according to the body surface area of the child. The ratio of dialyzer to body surface area should be 07:1.0. Dialyzers suitable for children are F4 (surface area 0.8 m^2), F5 (surface area 1.0 m^2), and if weight is more than 30 kg F6 (surface area 1.3 m^2) dialyzer can be used.
- Dialysis tubing: The lumens of blood tubing are smaller and the capacity will be low. Children should be dialyzed using pediatric tubing only, because they may not tolerate higher extracorporeal volumes of adult tubing sets. Blood tubing sets for pediatric dialysis are available in two sizes. The priming volume is lesser than the standard adult tubings. For neonatal blood tubings, the priming volume is 25 mL, and for pediatric blood tubing sets, it is 75 mL.
- Priming volume: In children, if the extracorporeal circuit volume exceeds 10% of total blood volume, the circuit should be primed with normal saline, blood or 5% albumin. The circuit volume includes the dialyzer priming volume and the volume of blood lines.
- Blood flow rate: The blood flow rate should be lower than 4–5 mL/kg/min during the first dialysis session and gradually increased to 8–10 mL/kg/min.
- Dialysate flow rates: The dialysate flow rates are maintained between 300–500 mL/min in children weighing <20 Kg and 500–800 mL/min in >20 Kg. Most centres maintain the dialysate flow rate around 500–600 mL/min.
- Ultrafiltration: The amount of ultrafiltration required is estimated based on the dry weight, the interdialytic weight gain, edema and the vital signs. The initial ultrafiltration rate may be set at 8 mL/kg/hr and increased as tolerated to maximum of 12 mL/kg/hr. Ultrafiltration should not exceed 5% of the body weight.
- Length and frequency of dialysis: The first dialysis session is very short, in order to prevent occurrence of dialysis disequilibrium syndrome. The aim is to achieve only 30% reduction in urea during the first dialysis, which is usually 30–45 min. During the next two dialysis sessions, 50% urea reduction may be targeted by

increasing the time to 1.5 to 2 hrs. Thereafter, the target should be ≥70% reduction in urea during the 3–4 hour sessions. For children, chronic maintenance HD is done three times a week.

- Anticoagulation: Unfractionated heparin is used. A loading dose of 20 U/Kg bolus is administered into the heparin line in arterial end of the tubing before the blood enters the dialyzer. This is followed by continuous heparin infusion at 10 U/Kg/hr. The infusion is continued till the end of the session if catheter is used as access. In the case of AV fistulas, the heparin infusion is stopped 30–60 minutes before end of the session. This will minimize chances of bleeding from the needle puncture site when the needle is taken out. If the Hemodialysis catheter is inserted just before or on the same day of dialysis, heparin-free dialysis should be done.

Complications

- **Hypotension**: There are various causes for hypotension during dialysis like sepsis, anaemia, overestimation of dry weight, high ultrafiltration rate. It can be prevented by maintaining haemoglobin between 11–12 g/dL and avoiding pre-HD antihypertensive drugs. Hypotension is treated by reducing UF to minimum, raising the legs passively above heart level and administering 50–100 mL 0.9% normal saline. Once the child is stable, UF can be restarted.
- **Dialysis disequilibrium syndrome:** This is caused by rapid reduction of urea which leads to cerebral edema. This complication can be prevented by keeping the first dialysis short and gradually increasing the dose on daily basis. The aim should be to reduce urea level by less than 20%, 30%, and 40% for the first three dialysis sessions. Use of Mannitol, 25% Dextrose or 3% saline may help to reduce cerebral edema.
- **Muscle cramps:** Risk factors for development of muscle cramps are high UF, hypotension, hypovolemia, and low dialysate sodium.
- **Nutrition:** Serum albumin can be used as a marker for the nutritional status. Children with ESRD, and those on dialysis who

have lower levels of albumin, have higher morbidity/mortality. Fluid and sodium restriction are advised according to the blood pressure and urine output.

- **Cardiac condition like left ventricular hypertrophy:** Cardiac function improves in well-dialyzed children who have no fluid overload and well-controlled blood pressure for at least 6 months.
- **Vaccination:** Vaccines are important in children on dialysis and those who are being prepared for renal transplantation. The recommended vaccines include flu (or influenza), hepatitis B, pneumococcal, TDAP (tetanus/diphtheria/pertussis), measles, mumps, and rubella (MMR), varicella (chickenpox), meningococcal and human papilloma virus (HPV).
- **Recombinant human erythropoietin (epoetin):** Treatment of patients with anaemia on Hemodialysis is using subcutaneous erythropoietin (EPO) after correcting iron deficiency and control of infection. Treatment with erythropoietin may be ineffective in patients who have insufficient blood forming factors like iron, vitamin B12 and Folic acid. Rarely, antibodies to EPO may cause lack of response to erythropoietin injections.

21 Continuous Renal Replacement Therapy

Umesh B. Khanna • Ankit Mody

Continuous renal replacement therapy (CRRT) is performed for continuous removal of solute and/or fluid and is usually done only in critically ill patient. This procedure allows for slow and smooth removal of fluid so that the unstable cardiovascular system is not subjected to additional strain. Ultrafiltration can also be done in a slow and steady manner. Thus, the hemodynamic tolerance is better even in patients with shock and severe fluid overload. This process can be applied to both adults and children. The procedure is continued for 48–72 hours and the parameters in CRRT can be modified during treatment. For example, if necessary, the CRRT can be modified during the procedure depending on the response of the patient.

The main goals of using CRRT are:

i. Slow and steady removal of waste products
ii. Restoration (correction) of acid-base balance
iii. Correction of electrolyte abnormalities
iv. Stabilization of hemodynamic (pulse, blood pressure, cardiac output)
v. Maintaining fluid balance
vi. Providing nutritional support
vii. Removal and/or modulation mediators of sepsis from blood

The accepted indications for CRRT are patients with acute kidney injury (AKI) combined with:

I. Hemodynamic instability—low blood pressure/rapid pulse rate/unstable heart pumping or rhythm and other cardiovascular disorders.

II. Severe fluid overload with fluid accumulation in lungs (pulmonary edema) and other parts of the body not responding to medicines (diuretics).

III. Hyper catabolic states (excessive muscle & tissue breakdown)/ trauma (extensive injuries)—more creatinine from the damaged muscles will have to be excreted.

IV. Rhabdomyolysis (damage to muscles).

V. Need for giving larger volumes of liquids as part of treatment (nutrition, use of blood, or blood products).

CRRT may be useful in patients even without kidney failure. They are:

I. Treatment of sepsis (to remove mediators of sepsis)

II. Lactic acidosis (to clear the accumulated lactic acid from the body)

III. Acute respiratory distress syndrome (to support the lung and remove excess fluid)

IV. Multiple organ dysfunction syndrome (MODS)

V. Chronic congestive heart failure (CHF) and decompensated CHF (to remove fluid and reduce strain on the heart)

VI. For cardiac surgery and coronary artery bypass graft (CABG)

VII. During extracorporeal membrane oxygenation (ECMO) treatment

The advantages of CRRT are:

I. CRRT is a slow gentle and continuous form of dialysis compared to conventional hemodialysis which is performed in 4 hours.

II. CRRT provides improved hemodynamic stability and can be performed in patients who have hemodynamic instability.

III. CRRT provides continuous fluid and electrolyte management (avoids rapid fluid and electrolyte shifts which cause strain on the heart).

IV. Since high flux membranes are used, cytokines and mediators of sepsis are removed.

V. Suitable for the needs of critically ill patients.

However, there are some limitations for regular use of CRRT in many centres. The procedure takes a long time (48–72 hours or more). Therefore, the duration of anticoagulation is also prolonged. One of the central veins has to be cannulated for the procedure, and the patient has to remain in bed for prolonged periods. Most important limitation of CRRT is the cost. There is need for special machine; the disposable sets are very expensive. No reuse is possible. Many litres of sterile fluid will be necessary as replacement fluid. Special trained staff should be available to perform and closely supervise and monitor the patient.

The principles are nearly the same as conventional hemodialysis. They are:

I. Diffusion (movement of solutes through a semi-permeable membrane from an area of higher solute concentration to an area of lower solute concentration until equilibrium has been established).

II. Convection/solvent drag/advection is the one-way movement of solutes through a semi-permeable membrane along with the flow of water.

III. Ultrafiltration (movement of fluid through a semi-permeable membrane along with a pressure gradient).

IV. Adsorption (adherence of solutes and biological matter to the surface of a membrane).

CRRT includes several treatment modalities that use a veno-venous access. The choice will depend on the needs of the patient and on the preference of the physician.

Slow Continuous Ultrafiltration (SCUF): Removal of ultrafiltrate at low rates without administration of a substitution solution. The purpose is to prevent or treat volume overload. There will be no removal of waste products or correction of pH. Thus, the procedure helps to remove only the fluids.

Continuous Veno-Venous Hemofiltration (CVVH): Continuous removal of waste products, both small and large molecules, takes place by convection. A substitution solution is administered to replace the fluid removed. The electrolyte status is monitored to decide the replacement fluid to be given.

Continuous Veno-Venous Hemodialysis (CVVHD): Here, there is continuous removal of waste products, mainly small molecules by diffusion using a dialysis solution.

Continuous Veno-Venous Hemodiafiltration (CVVHDF): This helps to remove continuously small and large molecular weight waste products and fluids by diffusion and convection utilizing both dialysate and substitution solution.

Components of A CRRT Program

In addition to trained staff and infrastructure, the other requirements for a CRRT programme are:

I. Vascular access → (Conventional double or triple lumen HD catheter is inserted in internal jugular vein.)

II. Anticoagulation → (low dose heparin/citrate anticoagulation) Heparin is the most frequently used anticoagulant. It is commonly used during the priming of the hemofilter and is infused into the CRRT circuit after the blood pump and before the filter. The typical heparin schedules in CRRT are:

   a. Typical low-dose pre-filter heparin (Approximately 5–10 units/kg/hr delivered into the CRRT circuit.)

   b. Typical medium-dose pre-filter heparin (Approximately 8–10 units/kg/hr delivered into the CRRT circuit.)

   c. Therapeutic systemic heparin by infusion pump (Dose based on aPTT for those who need systemic heparinization.)

   d. Regional heparin (Rarely used. Aim is to anticoagulate the circuit only without anticoagulating the patient. Heparin is

infused pre-filter and protamine infused post-filter to reverse effects of heparin.)

e. Low-molecular weight heparin: [Less chances for heparin-induced thrombocytopenia (low platelet count). Disadvantages are it is very expensive, difficult to monitor and not possible to reverse the action by antidote.]

f. No anticoagulation: In patients with active bleeding, low platelet count, liver failure or prolonged aPTT.

The CRRT System

For delivering CRRT, an integrated system consisting of:

- Machine (CRRT machine **(Fig. 21.1)** has more features compared to the regular dialysis machine.)
- Hemofilter (Similar to artificial kidney for hemodialysis, but the membranes are synthetic and capable of filtering large volumes.)
- Line sets (These are different from conventional dialysis blood lines.)
- Solutions (Large quantities of sterile replacement fluids with different compositions will be required.)
- Accessories: Numerous accessories will be required for CRRT session.

Drainage bags/Three-way or four-way adaptor (manifold)/ Stop cocks/Syringes/Anticoagulant/Priming solution/Dual-lumen catheters

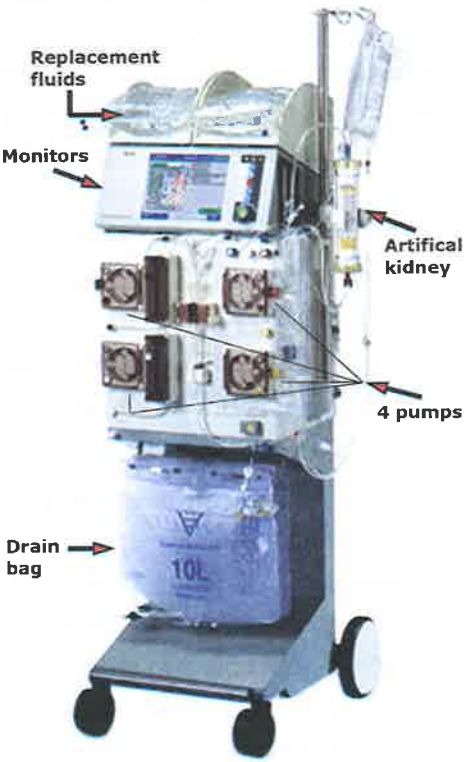


Fig. 21.1: CRRT machine.

Fluid Management

The goals of CRRT are to achieve two important functions:

- Solute removal
- Fluid removal

Substitution and dialysate solutions are used to facilitate the removal of solutes from the patient's blood using convection and/or diffusion. The fluid and solutes removed by convection is replaced as replacement fluid and dialysis fluid helps removal of solutes by diffusion. The CRRT machine balances the fluid removed and the fluid administered so that the circulating volumes in the patient are maintained. Substitution solutions can be infused before the filter (pre-dilution) and after the filter (post-dilution). The total intake of the patient, both non-CRRT and CRRT-related intake and fluid removal from the patient and CRRT fluid removed, should be balanced. Fluids removed from the patient (patient fluid removal) and other fluids (substitution solutions and dialysate solutions) are collected, as filtrate, in the drainage bag. The inflow of substitution fluid is regulated by the output volume.

Substitution Solution

- Primary function: Removal of solutes via convection (small, medium, large).
- Does not affect the patient's intravascular volume.
- Must contain physiological concentration of electrolytes.
- Fluid should be sterile.
- It can be infused into the patient's blood pre-dilution, post-dilution or both.
- Formulation, volume, and infusion method (pre- or post-dilution) are prescribed by a physician.
- Substitution solution allows convective clearance.
- The volume of substitution solutions infused is automatically removed by the machine.
- Sometimes referred to as "replacement fluid".

Dialysate Solution

Primary function:

- Removal of solutes via diffusion (small)
- Does not affect the patient's intravascular volume
- Must be physiological and should be sterile
- Commercially available
- Prescribed by a physician
- Dialysate solution allows diffusive clearance
- Infused into the external dialysate port of the hemofilter counter-current to the blood flow
- The volume of dialysate solutions infused is automatically removed by the machine
- Buffers include lactate and bicarbonate
- Formulation is usually calcium-free when used with citrate anticoagulation

Patient Fluid Removal

- Fluid removed directly from the patient's intravascular compartment.
- Hourly rate of removal is prescribed by the physician.
- Non-CRRT intakes and outputs must be calculated and considered.
- Fluid removal occurs by ultrafiltration. Fluids removed contain components of plasma water.

Filtrate

- Filtrate is a combination of the substitution fluid, dialysate fluid and fluid removed from the patient.
- Components of filtrate include water, electrolytes, waste products, immune mediators, drugs, vitamins and amino acids.
- Filtrate is removed from the filtrate port of the hemofilter into a drainage bag.

- Filtrate is a biological waste substance; hospital protocols should be followed.

Complications

1. Central venous line related: Hematoma/hemothorax/pneumothorax
2. Circuit-related complications:
   - Air embolism
   - Clotting of circuits
   - Bleeding from systemic anticoagulation
   - DIC
   - Anemia
   - Thrombocytopenia
   - Hypothermia
   - Hypotension
   - Electrolyte derangements
     - Hypokalaemia, hypomagnesemia, hypophosphatemia
   - Dialysis disequilibrium syndrome (DDS)
     - Much less common with CRRT than intermittent hemodialysis
3. Anticoagulation complications:
   - Heparin
     - Hemorrhage, heparin-induced thrombocytopenia (HIT)
   - Citrate
     - Metabolic alkalosis and hypocalcemia

22 Hemodiafiltration

Umesh B. Khanna • Rajesh Kumar

Conventional Hemodialysis is the most widely used renal replacement therapy for end-stage renal disease in the world. In Hemodialysis, waste products and water are removed by diffusion across a semi-permeable membrane. It effectively removes small solutes (urea & creatinine), for balances fluids & electrolyte levels and maintains acid-base balance. However, it is not effective for removal of larger solutes, such as β2-microglobulin. Middle molecules toxins accumulate in the body over time and are known to cause long-term complications like β2 amyloidosis. Even when using high-flux membranes, diffusion coefficients for solutes decrease with the increasing molecular size of solute. To improve the removal of these middle molecules, convective transport across high flux membranes has been tried. Hemofiltration was the first convective therapy implemented (1970). Later, Hemodiafiltration was developed in 1980. In Hemodiafiltration, conventional Hemodialysis (small molecular clearance) and Hemofiltration (middle molecular clearance) are combined **(Fig. 22.1).**

Definitions

Hemodialysis is a type of renal replacement therapy where patient›s blood is passed through blood tubing via a machine to the dialyzer, and waste products and water are removed by diffusion and convection. Solutes/wastes diffuse along its concentration gradient from blood compartment to dialysate compartment.

Hemofiltration is a type of renal replacement therapy where patient›s blood is passed through blood tubing to a Hemofilter

where waste products and water are removed by ultra-filtration through convection. For hemofiltration, dialysate is not used. Instead, a positive pressure in the blood compartment drives water and solute across the membrane. Solutes, both small and large, get dragged through the membrane at a similar rate along with flow of water. Larger solutes are also moved with the fluid removed from blood. The Hemofilters are manufactured from polymeric thermoplastics and have high KUF and high flux properties, e.g., polysulfone, polyacrylonitrile (PAN), AN-69, polyamide and polymethyl methacrylate.

Slow Continuous Ultrafiltration (SCUF)

A smaller Hemofilter with a lower hydraulic permeability (KUF 4.0) and small surface area of 0.3 m^2 is satisfactory for slow continuous ultrafiltration (SCUF). This procedure can be employed for fluid removal only, and there is no dialysis going on. This is useful for cardiac failure resistant to diuretic therapy or in life-threatening situations with fluid overload.

Hemodiafiltration is combination of Hemofiltration with Hemodialysis. The membrane used is a high flux membrane. Dialysate fluid runs through the dialysate compartment of the dialyzer similar to conventional Hemodialysis. When blood is pumped through the blood compartment, there is a high rate of water movement, and solutes are dragged from blood to dialysate along with water movement. Since the dialysis fluid also is circulating in dialysate compartment, diffusion takes place simultaneously. Majority of ultra-filtrate is replaced by the substitution fluid which is infused directly into the blood line. The rate of fluid administered and the fluid removed can be monitored and adjusted. The replacement fluid is the prepared sterile fluid from pharmacy.

Online HDF: In online HDF, sterile, nonpyrogenic replacement fluids are prepared by the dialysis machine from the used dialysate

fluid using two endotoxin filters. The fluid can now be infused into the patient's blood directly. Thus, there is no need to infuse fresh sterile replacement fluid from external sources.

In India, Hemodialysis is the most popular modality of treatment. Hemofiltration can be performed with a blood pump and some monitors in the dialysis machine, but the dialysis circuit of regular dialysis is not required. However, it is not used in many centers. Hemodiafiltration is very expensive and requires more sophisticated machines compared to the regular dialysis machine. In view of the patient comfort, many centers are performing Hemodiafiltration regularly. Brief summary and advantages and disadvantages of the therapies are shown in **Table 22.1**.

Table 22.1: Comparison of the three different modalities of treatment

Type of Modalities->	Hemodialysis	Hemofiltration	Hemodiafiltration
India	Most Common	Rare	Upcoming
Dialyzer	Low or High Flux	High Flux	High Flux
Kuf	10–20 mL/hr per mm Hg per m^2	>20 mL/h per mm Hg per m^2	>20 mL/h per mm Hg per m^2
Diffusion	+++	–	++
Convection	+	+++	+++
Dialysate	++	– –	++++
Replacement Fluids	–	+++	++++
Uremic Toxin Removal	Low Molecular Weight	Middle Molecules	Middle Molecules
Clotting	+	++	+++
Endotoxin Filter	+	++	++
Cost	+	++	++++

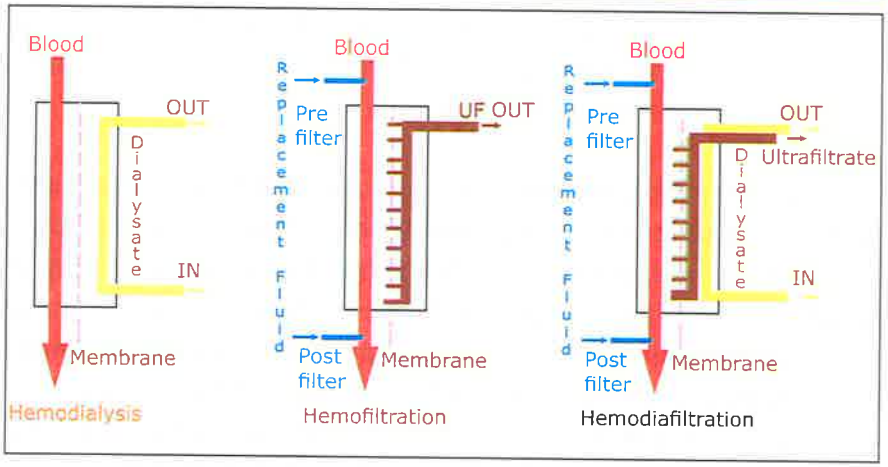


Fig. 22.1: Salient features of Hemodialysis, Hemofiltration and Hemodiafiltration.

Red → Blood pathway/Yellow → Dialysis fluid pathway/Dark brown → Ultrafiltrate only/Light brown → Ultrafiltrate mixed with dialysis fluid/Blue → Replacement fluid/Light pink → Semipermeable membrane.

Note:

In Hemodialysis, Only blood and dialysis fluid across semipermeable membrane removed is replaced with substitution fluid.

In Hemodiafiltration, dialysis, ultrafiltration and substitution of fluid removed is taking place simultaneously.

Technical Requirements for HDF (Table 22.2)

HDF Machines

Development of online preparation of replacement fluid has helped to make HDF a practical and routine therapy. Online preparation of replacement fluid is made possible by adding three additional components to conventional HD machines:

1. Pump for delivering substitution fluid,
2. Series of ultra-filters for producing sterile replacement fluid from dialysate, and

3. Volumetric control system to regulate the ultra-filtration volume and net fluid removal as desired.

Similar to conventional dialysis machines, HDF machines also prepare dialysate from RO water and concentrates. The used dialysate goes through a series of sterilizing ultra-filters which are incorporated in the dialysate pathway. This helps to produce sterile, nonpyrogenic replacement fluid from the used dialysate. This newly prepared fluid is ready to be used as replacement fluid and can be administered as infusion to blood circuit. The ultrafilters and machine are disinfected together after each dialysis session. The ultrafilters should be replaced periodically according to the manufacturer's instructions so that their efficacy to sterilize and remove endotoxin from dialysate is preserved. The integrity of the ultrafilter is tested by pressure-holding test or bubble test before each treatment. This test is performed automatically as the machine is prepared for HDF.

In addition, HDF machines include an infusion pump that can infuse replacement fluid into the blood at different points in the

Table 22.2: Technical requirements for Hemodiafiltration (HDF)

Hemodialyzer	High flux, 1.6–2.2 m^2
Ultrafiltration coefficient (KuF)	>20 mL/h per mm Hg per m^2
Sieving coefficient	0.6 for B_2-Microglobulin; 0.001 for Albumin
Vascular access	AV Fistula, AV Graft & Tunneled dialysis catheter
Anticoagulation	Unfractionated heparin, Low molecular weight heparin
Blood flow rate	350–450 mL/min
Dialysate flow rate (Total) Dialysate flow rate through Dialyzer	600–1000 mL/min 500–600 mL/min
Post-dilution Pre-dilution Mid-dilution or mixed dilution	23 L per treatment or 26 L/1.73 m^2 46 L per treatment or 52 L/1.73 m^2 35 L per treatment or 40 L/1.73 m^2

extracorporeal circuit. If the replacement fluid is administered (to the arterial blood line) before the blood enters the artificial kidney, it is called pre-dilution.

If replacement fluid is administered after the artificial kidney into the venous blood line before returning blood to the patient, it is called post-dilution. Mid-dilution allows substitution fluid to be introduced directly into the dialyzer at the midpoint of the blood pathway. The last method is to administer both pre- and post-dilution simultaneously. This is called mixed dilution. In the case of mixed dilution, the ratio of pre-dilution to post-dilution volumes is adjusted automatically by the machine to maintain transmembrane pressure in the range of 150–300 mm Hg. Post-dilution is the most common and cost-effective method as it provides the highest solute clearance.

Preparation of Dialysis Fluid

Dialysate used for online HDF must have stringent quality standards, because dialysate itself is used to prepare the large amount of replacement fluid needed. If there is no online HDF, large volumes of sterile fluid should be administered for HDF. Water treatment and dialysate preparation must be acceptable to meet the strict quality requirements of the online HDF system. The treatment time and schedule for HDF is not different from conventional Hemodialysis. HDF is not done to shorten the duration of dialysis, but to enhance middle molecules removal. The composition of the dialysate is same for both HDF and HD but dialyzer, blood and dialysate flow rates, administration of anticoagulant, convection and replacement fluid volumes will be different.

Hemodialyzers

Dialyzer with high membrane permeability (KUF of >20), which combine both diffusion and convection, is used for HDF. Hemodialyzer with reduced fibre wall thickness, slightly larger fibre internal diameter (less resistance to blood flow) and increased fibre length add to the efficiency.

Blood and Dialysate Flow Rate

The effective blood flow rate and treatment time are important. The correct volumes of fluid should be removed and the rate of ultrafiltration rate should be limited to 25–30% of the blood flow rate. If higher volumes are filtered, chances of Hemoconcentration and dialyzer clotting are high.

In online HDF, the dialysate flow into two streams—one flows through the dialysate compartment and allows solute removal by diffusion, whereas in the other stream, dialysate (substitution fluid) is infused in the patient's blood (in the dialyzer).

Convection Volume

The convection volume should be 20% of the total blood volume per session of HDF and is the sum of the substitution fluid volume and the net ultrafiltration volume required to correct the patient's interdialytic weight gain.

[Net Ultrafiltration = Convection volume – Substitution volume]

Benefits of Hemodiafiltration

1. HDF increases the clearance of B_2-microglobulin by 30–40% compared with HD and prevents development of B_2-microglobulin amyloidosis, and thus reducing the incidence of carpal tunnel syndrome.
2. Increased phosphate removal with post-dilution HDF (15–20% greater than high-flux HD)
3. HDF provides higher clearances of—
   - Complement factor D (proinflammatory mediator)
   - Leptin (responsible for loss of appetite)
   - Fibroblast growth factor 23 (role in metabolic bone disorders and vascular calcification)
4. Reduced dose requirements for erythropoietin
5. Reduction in episodes of intradialytic hypotension
6. Increased protein intake and preservation of muscle mass

Conclusion

Online HDF is no longer considered as an experimental treatment but is now considered to be an effective renal replacement therapy. The quality of life of patients on dialysis can be improved. Online HDF is now commonly used in Europe and Japan. Online HDF is a safe and practical method to remove middle molecular weight uremic toxins and reduce intradialytic hypotension. It also reduces dialysis-related long-term complications such as amyloidosis and accelerated atherosclerosis.

23 Diet in Hemodialysis Patients

Umesh B. Khanna • Rachna Jasnani

Patients with CKD and those on dialysis are often unable to take normal and nutritious diet because of various reasons. Therefore, nutritional deficiencies and other abnormalities in metabolism are common. If the protein intake is poor, the patient's own muscles are utilised for protein catabolism and a condition called "negative nitrogen balance" occurs. This leads to muscle wasting (thinning) and weakness. If the nutrition is well maintained, the quality of life is also better.

Role of Nutrition Therapy

Nutrition therapy plays an integral role in patients receiving maintenance hemodialysis (MHD). Before prescribing the nutrition therapy, it is important to understand the purpose of good nutritional support.

Nutrition therapy for patients receiving MHD should aim to:

i. Prevent the accumulation of electrolytes and minimize fluid imbalance

ii. Achieve and maintain neutral or positive nitrogen balance

iii. Minimize the effect of metabolic disorders associated with CKD

iv. Achieve and maintain good nutritional status for a better quality life

Malnutrition

Malnutrition is common in hemodialysis and peritoneal dialysis patients and is associated with an increased chance of disability and death (morbidity and mortality). Prevention or early treatment of malnutrition is important to give better quality and longer life for patients on dialysis. The causes that lead to malnutrition are:

i. Anorexia (dislike for food due to altered taste sensation, mental depression and associated illnesses)

ii. Catabolism (protein breakdown) due to illness

iii. Loss of amino acids, vitamins and other nutrients during dialysis

iv. Complement activation due to exposure to various dialyzer membranes

v. Endocrine disorders due to uremia

vi. Blood loss

In order to achieve a good nutritional status, hemodialysis patients are required to follow:

- High protein diet
- Adequate calories (to provide energy)
- Low salt diet
- Low fluid diet
- Low potassium diet
- Low phosphorus diet

The importance of each of the above aspects of diet in dialysis patients is explained below:

1. High protein diet

- Adequate protein intake is required to ensure that the patient maintains positive or neutral nitrogen balance. According to the latest guidelines, patients on hemodialysis should use diet containing 1.0–1.2 grams proteins/Kg body weight per day. 50–70% of this protein should be high biological value protein (HBV). Animal protein and other HBV proteins are used more efficiently and provide the required essential amino acids to our body.
- Sources of HBV protein are milk and milk products like paneer, curd, cheese, animal proteins like eggs, fish, chicken, mutton and other types of meat. However, lean meat should be preferred over red meat.

- The amount of protein required in the diet is based on body weight, nutritional status, dialysis modality and adequacy. Protein energy status can be monitored by evaluating subjective global assessment, measurements like mid-arm muscle circumference, skin-told thickness or by blood tests for serum albumin, serum creatinine and serum cholesterol. For example, if the blood urea level is disproportionately low, it suggests poor protein intake.
- Periodic checking of serum albumin is most widely used in MHD patients.

2. Calories

- Carbohydrates are the main sources of energy. They are converted to glucose which is the main source of energy. Every adult on dialysis should receive approximately 35 Kilocalories per Kg body weight. This is necessary for the normal metabolism and body functions. Thus, a 60 kg person will need 60 × 35 = 2100 calories daily. The energy is obtained from carbohydrates, proteins and fats. A dietician would prescribe a diet consisting of about 200–250 gm carbohydrate diet (800–1000 calories), 60 gm proteins (250–300 calories) and the rest as fat (600–900 calories). In addition, necessary vitamins and minerals may be included in diet.

3. Low salt diet

- Normal kidney is capable of retaining salt in the body if salt intake is low and excreting excess salt in urine if the salt intake is high. As the kidney function [glomerular filtration rate (GFR)] decreases, this ability is lost. Thus, if the salt intake is high, it cannot be excreted leading to sodium retention. In addition, the GFR usually decreases further in the first year of HD and the urine output decreases or becomes nearly absent. At this stage, it is important to prevent the accumulation of both salt and fluids. Use of excessive fluid and salt between treatments can result in sodium and fluid overload leading to edema, hypertension, breathing

difficulty and cardiac problems, such as congestive cardiac failure (CCF).

- It is possible to find out if the fluid and salt intake are appropriate by monitoring blood pressure, interdialytic weight gains, signs of edema and thirst. In patients who have some urine output, the fluid intake can be regulated in such a way that the weight gain between two sessions of dialysis (interdialytic weight gain) is 2 Kg and the blood pressure is controlled. Interdialytic weight gain is the difference between the pre-dialysis weight and the immediate post-dialysis weight. The patient should be instructed to restrict the interdialytic weight gain to about 2 Kg only.
- Sodium intake should be advised for individual patient depending on the blood pressure and hydration status so that fluid overload, pulmonary edema and CCF are prevented.
- Patients on hemodialysis should prefer a low salt diet, i.e., 2–3 grams per litre of fluid allowance. In order to maintain a low salt diet, they need to:
  i. Avoid adding salt to food items.
  ii. Add permitted salt only where needed to make food palatable.
  iii. Avoid jams/jellies/sauces/pickles/papads/breads/biscuits like salted biscuits/chips/khari/butter, etc.
  iv. Prefer normal iodized salt and avoid/rock salt/pink salt or other substitutes.
  v. To add taste to food, lime juice, tamarind or vinegar powder can be added.
  vi. For additional flavor, fresh or dried basil leaves or oregano or mixed herbs can be added.

4. Low fluid diet

- Fluid allowance is based primarily on urinary output and dialysis modality. Other considerations include the presence of edema, congestive heart failure, degree of

sodium restriction, and diuretic therapy. Fluid intake should be modified to maintain interdialytic weight gain less than 3–4% (not exceeding 5%) of dry weight.

- The amount of fluid allowance should be urinary output volume + 500 mL. This extra 500 mL is to compensate for the loss of fluid that is not measurable like through skin (sweating) and breath. Thus, for a patient with zero urine output, the daily input of fluids should be limited to 500 mL. Practical tips for fluid restriction:
  i. Patients should prefer healthy fluids like milk/tea/milk/dals as they supply protein.
  ii. Other fluids like soups/beverages like tea/coffee/fruit juices/coconut water/aerated drinks should be avoided as they do not provide any proteins but they contribute to high amount of potassium.
  iii. Patients should always prefer to use measured bottles and maintain the liquids consumed within prescribed limit.
  iv. Patients may be advised to gargle and spit the water since it helps to moisten and relieve the dry sensation in mouth.
  v. It is advisable to drink warm to hot water in smaller cups, as this helps to prevent excessive water intake. Use of chilled water increases craving and thirst.
  vi. Patients should avoid exercising, i.e., walking/yoga in hot conditions, they should prefer indoors to stay comfortable and avoid drinking excess water.

5. Low potassium diet

Both high and low potassium levels in blood are harmful. High potassium (hyperkalemia) is more common in patients on regular dialysis.

- As the GFR declines, kidneys lose their ability to excrete potassium in urine. Potassium clearance (removal) during dialysis depends on the dialyzer clearance and the dialysate

potassium concentration.

- Potassium intake must be controlled to prevent both hyperkalemia and hypokalemia. The dietary potassium recommendation is usually based on serum potassium levels, remaining (residual) kidney function, drugs used by the patient, and dialysis modality.
- Vomiting, diarrhoea, and the use of diuretics which cause potassium excretion can result in lowered serum potassium levels.
- Patients in whom urine output is low or absent (oliguric or anuric) are at increased risk for hyperkalemia.
- It is possible to "leach" potassium from vegetable if the vegetables are kept in hot/warm water after slicing and discarding the water after 20 minutes. The potassium will leach into the water. Such vegetables can be used for cooking.
- Other causes of hyperkalemia include gastrointestinal bleeding, acidosis, catabolism, hypoaldosteronism, and hyperglycemia. Dietary instructions to reduce potassium intake are very important and are summarized below:
  i. Patients should avoid most fruits, fruit juices, and coconut in all forms.
  ii. They should avoid aerated, alcoholic, flavored drinks, and beverages.
  iii. They should avoid all salt substitutes.
  iv. They should avoid tobacco chewing, paan, cigarette smoking.
  v. They should avoid packaged food items. (High potassium and sodium, instant soup mixes, gravy mixes, jams, jellies, fried chips, and sauces.)
  vi. Patients should avoid vegetables rich in potassium.
  vii. They may use low potassium vegetables like green peas, lettuce, beetroot, methi leaves, pink radish.

viii. Patients should avoid fruits with high potassium.

ix. They can use small quantities of low potassium fruits like apple, pear, papaya and pineapple.

6. Low phosphorus diet

Both high and low phosphorus levels in blood are harmful. High phosphorus (hyperphosphatemia) is more common in patients with CKD and those on regular dialysis.

- Phosphorus is a mineral present in the body along with calcium. Weak kidneys cannot flush out phosphorus from the body hence, its level starts rising in blood.
- High phosphorus levels can lead to weak and fragile bones and secondary hyperparathyroidism leading to metastatic calcification.
- For controlling hyperphosphatemia, dietary restriction of phosphorus is the first step. Diet low in phosphate is advised. Egg white is a high biological value protein and it is not very high in phosphorus. Meat products and milk are high in phosphates. The dietary phosphorus intake can be reduced by:

  i. Avoiding processed food items (colas, cold drinks)

  ii. Limiting breads and other bakery products

  iii. Preferring vegetarian food and egg white

  iv. Preparing food after prolonged boiling

  v. Taking phosphate binders regularly as recommended

Phosphate binders are medicines which bind to phosphates in the diet in the alimentary canal so that it is not absorbed into the blood. Medicines like calcium acetate, calcium chloride, sevelamer and lanthanum are the commonly used phosphate binders. In addition to dietary restriction, phosphate binders are used to control serum phosphorus levels in the majority of patients.

24 Plasmapheresis

Umesh B. Khanna • Amit Jain

Plasmapheresis or therapeutic plasma exchange is the process in which large quantities of plasma (containing unwanted substances) are removed from the blood and replaced with fresh frozen plasma (FFP), 5% albumin or saline. The term is derived from the Greek word "apheresis" which means "remove forcibly". Therapeutic plasma exchange (TPE) and plasma exchange (PLEX) are the other names used for the procedure. Plasma is the water component of blood. It contains various molecules like proteins (enzymes, antibodies, compliment), electrolytes, and toxins. Based on molecular weight [MW], they can be divided as:

a. Small molecules: MW up to 500 Dalton (e.g., sodium, potassium, calcium, urea, creatinine, many drugs)

b. Middle molecule: MW 500 to 60,000 Dalton (e.g., beta 2 microglobulin)

c. Large molecule: MW >60,000 Dalton (e.g., albumin, immunoglobulins, antibodies, complement proteins, clotting factors)

The method of separation and removal of substances can be by:

a. **Centrifugal separation** method (spinning the blood in high speed)—by this process, the blood cells and plasma are separated due to the centrifugal force. Centrifugal separation method is used in blood banks for separation of blood components. Two methods of centrifugal separation for plasmapheresis are

   (i) Intermittent flow method, in which small volume of blood is drawn, plasma and blood cells separated, new plasma added and re-infused to the patient. The separated plasma is discarded. This cycle is repeated. This method is not in use now.

(ii) Continuous flow method: In this method, the plasma is separated continuously by the machine and replacement added and blood is returned to the patient continuously. Therefore, the blood volume does not change significantly.

b. **Membrane separation:** The method is similar to hemofiltration. The blood is passed through special membrane with larger pores. The plasmapheresis membrane will not permit blood cells to pass through. Therefore, plasma is separated and discarded. New plasma replacement is given equal to the volume removed. **Fig. 24.1** shows the blood and plasma pathways in conventional membrane plasmapheresis. (Refer practical points below.)

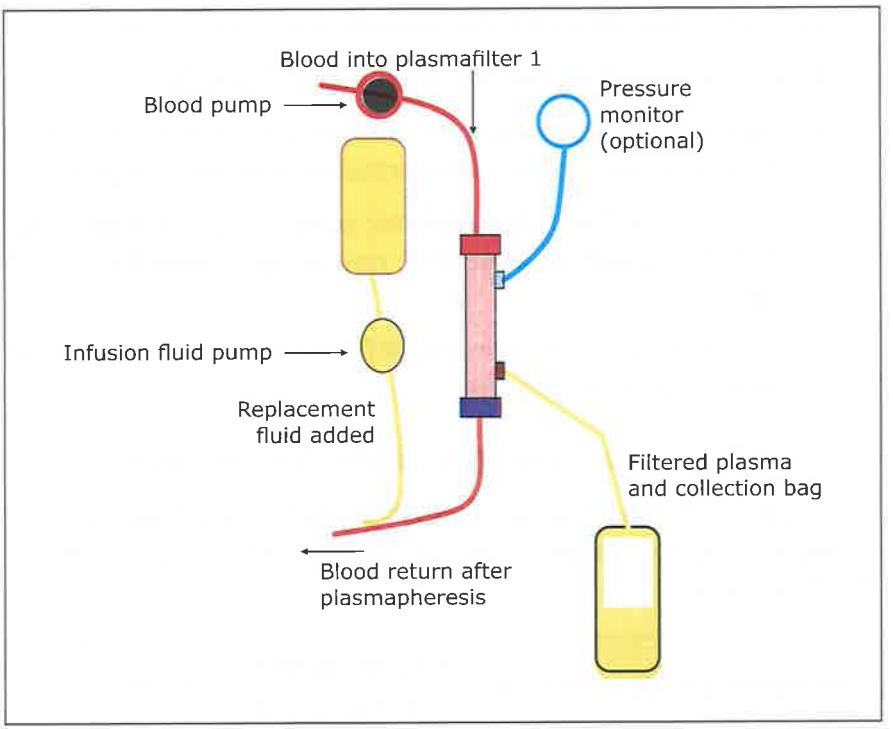


Fig. 24.1: Conventional membrane plasmapheresis.

Uses of Plasmapheresis

a) Removal of disease-causing antibody from blood: Examples—

i. Guillain-Barré syndrome (disease of the nervous system, causing paralysis of limbs),

ii. Myasthenia Gravis (weakness of muscles)

iii. Anti-Glomerular basement Membrane Disease (kidney failure due to antibodies against glomerular basement membrane)

iv. Viral encephalitis (some severe viral infections of CNS)

v. Poisoning with drugs which are protein bound

vi. Treatment of antibody mediated rejection of kidney transplant

vii. Desensitization for ABO incompatible renal transplant (To reduce chances of rejection when doing kidney transplant without blood group matching.)

viii. To remove inflammatory mediators and toxic factors.

b) Replacement of deficient factors in blood: Examples—

i. Hemolytic uremic syndrome (sudden development of kidney failure, anaemia due to abnormal complement system)

ii. Thrombotic thrombocytopenic purpura (sudden development of anaemia, bleeding, neurological symptoms, and renal failure)

iii. Sickle cell crisis (abnormality of RBCs which may form clumps and block blood vessels).

Efficiency of Immunoglobulin (Ig) Removal

The removal of immunoglobulin by plasmapheresis can be assessed by large molecule clearance. The calculation is similar to calculation of urea clearance.

$$\text{Macromolecule reduction ratio} = \frac{\text{Pre-post (plasma Ig)}}{\text{Pre-plasma Ig}} \text{ X } 100$$

Practical points:

i. Each session of plasmapheresis lasts for 2 hours.

ii. It will be beneficial to do the procedure at intervals of 24–36 hours so that there is time for redistribution of antibodies into blood.

iii. Plasma *volume is* calculated using Kaplan formula based on height, weight, and hematocrit (see BOX).

> Kaplan formula:
> For Estimated plasma volume
> = [0.065 × Weight (kg)] × [1 – Hematocrit]

iv. Average PV in a normal 70 kg adult is 3.5 L (50–55 mL/kg).

v. Rule of thumb is to calculate plasma volume →

Plasma volume = Ideal body weight × 40 mL.

vi. Five sessions of plasmapheresis will remove 1 plasma volume.

vii. 1 plasma volume causes macromolecule reduction of about 60%.

viii. 2 plasma volume = 86%

ix. 3 plasma volume = 95%

x. 4 plasma volume = 97%

xi. 5 plasma volume = 99%

xii. Clinical improvement is commonly seen after the third cycle.

xiii. 5 plasma volumes should be exchanged for complete replacement of plasma.

xiv. **Replacement solution** (should maintain normal osmotic pressure):

a. Fresh frozen plasma

Physiological, maintains oncotic pressure

Provides proteins

Provides clotting factors

Risk of allergic reactions high

Risk of cross infection through plasma.

b. Albumin—provides only proteins

c. 0.9% saline—provides only replacement of water and sodium.

d. Ringer lactate—replaces sodium, potassium and water.

xv. AV access is often double lumen dialysis catheter or AVF if available.

xvi. Blood flow rate is maintained between 10–150 mL/min only.

xvii. Heparin dose 50 units/Kg loading and 1000 iu/hour. To stop infusion ½ hour before closure, maintain activated clotting time (ACT) between 180–220 secs. Doses can vary depending on clinical circumstances.

Complications

Steps should be taken to avoid or handle complications that may occur due to the procedure.

i. Hypotension—risk is high due to protein loss.

ii. Anaphylaxis—due to use of FFP, exposure to extracorporeal circuit (plasma filter, tubing).

iii. Bleeding—due to loss of clotting factors/heparinization.

iv. Infection—due to loss of protective antibody along with target antibody.

v. Citrate anticoagulation if used can cause numbness, paresthesia, tremors, hypotension, cardiac arrhythmias.

vi. Hypothermia—if cold replacement solution is used.

Recent Advances

The recent advances are:

I. Double Filtration Plasmapheresis: A procedure where the patient's own plasma is passed through a purification system online. After removing the pathogenic molecule, the same plasma is re-infused to the patient as the replacement volume. Thus, there is no need for large quantities of replacement solutions **(Fig. 24.2).**

II. Selective apheresis: Low density lipoprotein (LDL) apheresis can

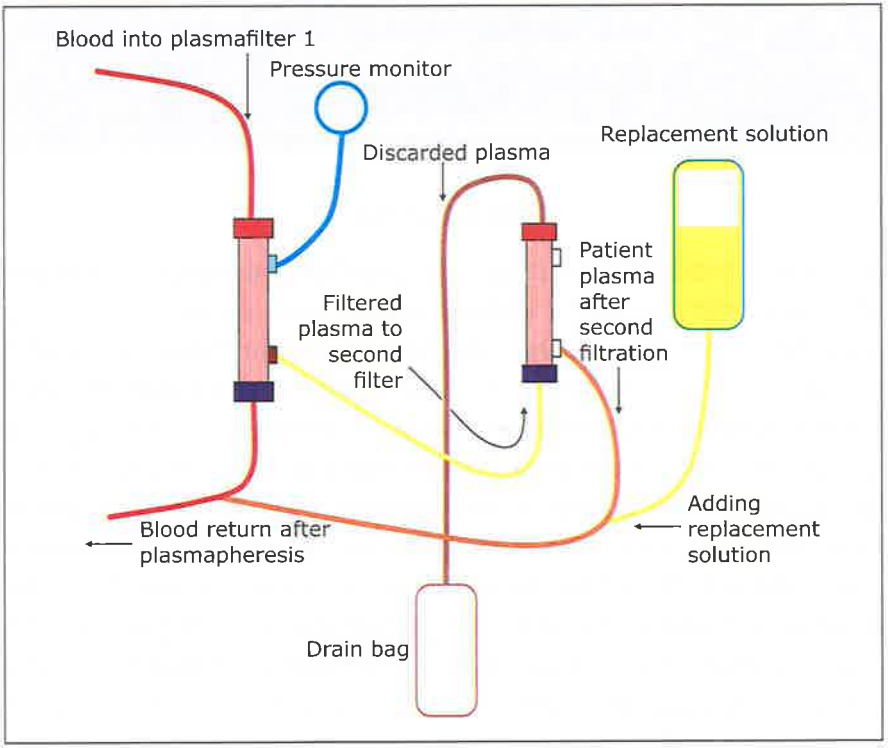


Fig. 24.2: Double filtration plasmapheresis.

be done in patients with very high blood levels of LDL.

III. Immunoadsorption columns: Filters which selectively remove only antibody due to the adsorption. They prevent loss of other important proteins, and hence avoid complications like bleeding and hypotension.

25 Drugs, Dialysis, and Extracorporeal Therapies in Poisoning

Umesh B. Khanna • Ankit Mody

Introduction

All natural products and drugs are chemical substances. They are absorbed, distributed to various tissues and excreted from the body. Kidneys and Liver are important organs for metabolizing and excreting many drugs/toxins (harmful substances). So, patients with kidney diseases may not be capable of excreting them. This may lead to accumulation of the drug in the body and result in side effects. Since patients on dialysis have advanced renal failure, the doses of many drugs have to be modified. Some drugs which have lower molecular weight and not bound to proteins are removed from the body during dialysis. In such cases, additional dose of drugs will be required after dialysis. Drug overdose can also be treated by dialysis if the drug is dialyzable. Some protein-bound drugs and those which have higher molecular weight can be removed from the body by hemoperfusion or CRRT. Peritoneal dialysis also helps in removing some drugs from the body.

Drugs may affect the kidney if the dose is exceeded or even following a single dose. The following are the commonly used drugs which affect the kidney. They are:

a. Aminoglycoside antibiotics (Gentamicin, Amikacin, Tobramycin, etc.)

b. Non-steroidal anti-inflammatory drugs, or NSAIDs (Ibuprofen, Diclofenac, Celecoxib, etc.)

c. Angiotensin converting enzyme inhibitors (Captopril, Enalapril, Telmisartan, etc.)

d. Radiocontrast agents (Those used for contrast radiography/CT scan)

Many other drugs also cause kidney damage due to allergic reaction. Combination of such drugs is very harmful. In order to prevent damage to kidney, it is advisable to calculate the kidney function roughly using the blood reports. The dosage for each level of kidney function is often given in the pamphlet distributed with the medicine. This will help us choose the correct dose. Sometimes, patients come with drug overdose/drug poisoning. In such cases, measures like gastric lavage (stomach wash to remove any drug in stomach), activated charcoal (to prevent absorption of the drug), specific antidotes (if any) and respiratory support (if needed) are tried. If these have failed or are not feasible or the patient's condition worsens, dialysis or other treatment modalities may be considered. Hemodialysis, continuous renal replacement therapy (CRRT) and hemoperfusion are important in the management of certain drug overdoses. Such extracorporeal procedures should be considered in addition to other measures and supportive care. Extracorporeal techniques include dialysis and hemoperfusion; dialysis therapies include intermittent hemodialysis, CRRT, and peritoneal dialysis. Peritoneal dialysis does not help in treatment of drug overdosage/ poisoning in adults.

Indications

a. Progressive deterioration of the patient's condition in spite of intensive supportive treatment.
b. Decreased level of consciousness with suppression of brain functions.
c. Risk of complications of prolonged coma (aspiration pneumonia).
d. Large amount of toxin ingested.
e. If faster removal of drug/toxin is possible (compared to normal clearance by the body).
f. If the body cannot clear the drug/toxin because of acute kidney injury

Key Principles

a. Molecular size, charge and protein binding of the drug will determine the choice of extracorporeal therapies.

b. If the drug/toxin is water-soluble, it can be easily removed.

c. Lipid-soluble molecules are more difficult to remove.

d. Protein-bound drugs are also not easily removable.

e. High-efficiency dialyzer will be more useful for some drugs (more surface area/greater diffusion/greater convective solute clearance).

Modalities of Extracorporeal Removal of Toxin (Table 25.1)

a. Hemodialysis is the modality of choice for low molecular weight, water-soluble molecules, especially those that have small volumes of distribution and are not protein-bound or lipid-bound. It is ideal for molecules that diffuse easily across dialysis membranes.

b. CRRT can be used in patients who have ingested substances that are highly lipid-bound and in hemodynamically unstable patients.

c. Hemoperfusion uses a cartridge which contains "albumin-coated activated charcoal" or resin. The charcoal is capable of adsorbing drugs and toxins from the blood. The toxins are removed from the blood by binding to activated charcoal or resin as the blood passes through the cartridge. The procedure is run on a dialysis machine using regular dialysis pumps and monitors in the blood circuit. Dialysate is not necessary. It is useful with highly protein-bound and lipid-bound molecules. Disadvantages include saturation of the cartridge and the need to change it every 2–3 hours. Rarely charcoal particles may enter the body through the blood return causing "charcoal embolism". It is a rare complication. Sometimes, platelets are also adsorbed by the charcoal column resulting in thrombocytopenia.

d. Peritoneal dialysis is not very effective in removing toxins. It is useful in small children in whom hemodialysis may be difficult.

Table 25.1: Drugs, toxins amenable to extracorporeal removal by extracorporeal modality*

Hemodialysis	CRRT	Hemoperfusion	Plasmapheresis
Aminoglycosides	Aminoglycosides		
Lithium	Lithium[a]	Carbamezapine	Immunoglobulins
Ethylene glycol	Theophylline[a]	Theophylline	Antibodies
Methanol	Valproic acid[a]	Paraquat	Protein-bound toxins
Salicylates	Valproic acid[a]	Diazepam	
Valproic acid			
Metformin			
Theophylline			
Long acting barbiturates (phenobarbitone)			

*Peritoneal dialysis is not useful.

[a] Hemodialysis is the preferred method when blood pressure permits.

CRRT = Continuous renal replacement therapy.

Technical Aspects

The technical aspects of toxin removal by extracorporeal means are largely related to access and equipment. In hemodialysis, CRRT, and hemoperfusion, access is through a 10–11.5 French dual-lumen dialysis catheter in a central vein because smaller catheters are unable to support the necessary blood flow of 200–450 mL/min. Except where contra-indicated, heparin should be used to anticoagulate the system to improve dialyzer clearance and prevent blood loss and the loss of time in replacing the dialysis circuit if it clots. Heparin should not be used in dialyzing patients with methanol toxicity. High-flux, high-efficiency dialysis membranes should be used to maximize pore size and surface area for toxin removal by both diffusion and convection. The comparison of the three modalities for treatment of acute poisoning are summarized in **Table 25.2.**

Table 25.2: Comparison of hemodialysis, hemoperfusion, and CRRT in acute intoxication

Parameter	Hemodialysis	Hemoperfusion	CRRT
Renal replacement therapy	Yes	No	Yes
Restores electrolyte balance	Yes	No	Yes
Corrects volume status	Yes	No	Yes
Risk of thrombocytopenia	Unusual	Yes	Yes
Removes very large molecules	No	Yes	No
Removes protein-bound drugs	No	Yes	Limited
Removes water-soluble drugs	Yes	No	Yes
Removes lipid-bound drugs	No	Yes	Theoretical
Higher blood flow rate improves drug removal	Yes	Yes	Yes
Cartridge saturation	No	Yes	No
Can be used in patient with low blood pressure	No	No	Yes

Some Examples

Example 1: If aminoglycoside antibiotic Gentamicin or Amikacin is required for a patient, the first dose can be given as per normal person. Thereafter, the dose is calculated and the modified smaller dose given at the prescribed interval or the interval between doses increased. However, gentamicin is a dialyzable drug, and so a booster dose will be required after dialysis.

Example 2: If a patient has come following overdose of the drug phenobarbitone, after the preliminary treatment, if the patient

is still unconscious, regular dialysis can be done. Since the drug is dialyzable, the patient will improve after a few hours. Prolonged dialysis may be necessary. If the patient has consumed many different drugs, it will be better to subject the patient to hemoperfusion.

Example 3: Paraquat is a herbicide which is used in agriculture and farming. Since it is easily available, it may be used as poison for suicidal purposes. Early treatment with clearing of consumed substance from the stomach and general measures are tried. Repeated sessions of hemoperfusion, CRRT or hemodialysis may be necessary. Lung involvement is common and oxygen given only if oxygen levels are low.

Complications

Complications from toxin removal by hemodialysis include hypokalaemia and alkalosis due to diffusion of potassium into the dialysate and diffusion of bicarbonate from the dialysate, particularly given the need for high efficiency dialysis membranes. The complications of CRRT include hypocalcemia, particularly when using citrate anticoagulation. Hemoperfusion has been associated with lymphopenia and thrombocytopenia.

Conclusion

Use of Extracorporeal therapies in poisoning can be lifesaving in a selected group of patients. However, these patients should be judiciously selected according to the principles outlined above otherwise the use of extracorporeal therapies can be counterproductive and harmful to the patient.

26 Wearable Artificial Kidney

Umesh B. Khanna • Ankit Mody

Introduction

About 200,000 new patients develop end-stage kidney failure every year in India. Many of these patients are young, in the prime of their lives—bread-winners of families or homemakers. Their only survival options are either dialysis or kidney transplantation. In centers, hemodialysis (HD) is preferred by nearly 95% of patients and 5% opt for peritoneal dialysis (PD). Home hemodialysis will become an option in the future. Dialysis is associated with not only complications of treatment but also cause heavy financial strain on the patient and family. Access to kidney transplant is also limited due to difficulty in procuring organs for transplantation.

Worldwide, efforts are undertaken to find an alternative form of treatment to renal failure patients. New modalities currently in testing include wearable (WAK), automated wearable artificial kidney (AWAK) and implantable artificial kidneys (IAKs). Both AWAK and WAK are currently undergoing trials in humans. They aim to change dialysis from intermittent treatments to continuous one using compact portable machines that can be worn throughout the day. The patients can move about and continue to be active in their day-to-day life, and even travel. The size of the machinery, the weight, power requirements and amount of dialysate required are the important barriers to development of portable compact dialysis devices.

Wearable Artificial Kidney

Wearable artificial kidney (WAK) is based on the principle of hemodialysis. It can achieve average creatinine clearance of about 20 mL/min. It is undergoing clinical trials which have been approved by the US FDA.

It is a portable renal replacement device, which provides dialysis continuously. A double lumen catheter is used as vascular access. AV fistula cannulation is not preferred, because the risk of needle dislodgement and bleeding are more.

The WAK can be worn like a belt or a vest. It uses multiple AA batteries providing 9V for power supply. The total amount of water is less than half a litre. Pulsatile and alternating blood and dialysate flow is used. So, low blood flow rates are possible (~100 cc/minute), with adequate clearance. The dialysate is regenerated and UF is collected in a waste bag.

The third-generation wearable artificial kidney (WAK 3.0) is expected to undergo a new round of human trials soon. These will extend the connected time to the wearable kidney from 24hours (in the previous study) to a full week.

Implantable Artificial Kidney (Fig 26.1)

Implantable Artificial Kidney (IAK) is being developed by the Vanderbilt University Medical Center and University of California, San Francisco, USA. It is undergoing animal trials. It combines silicon nanotechnology and tissue engineering in a device that can mimic a native kidney. It can be surgically implanted in the human body with the arterial blood flow acting as the pump, avoiding need for an external power source.

The IAK mimics the normal kidney in terms of glomerular filtration and tubular function. The high efficiency filter (HemoCartridge) mimics a glomerulus by filtering the blood. The filtrate goes through a bioreactor of cultured renal tubular cells (BioCartridge) which function like the renal tubules. Thus, it mimics the functioning of the human nephron. Ultrafiltrate is generated in the HemoCartridge which then passes through the BioCartridge, where it is processed. Salt, water and glucose are returned to the blood. In the end, a small volume of fluid (similar to urine), which is concentrated in toxins meant for excretion, is collected and can be drained.

The IAK has several advantages. It provides a slow continuous filtration and attempts to substitute natural renal physiology. The tubule cells and the patient's immune system are separated by a silicon scaffold barrier. So there will be no contact with the immune system and no need for immunosuppression. Approximately 2–4 liters per day of waste liquid (similar to urine) is produced. Therefore, the patient's oral fluid intake can be adjusted accordingly to maintain adequate volume. The cells used in the development of BioCartridge are derived from cadaveric kidneys deemed unsuitable for transplant, thereby minimizing organ wastage.

However, there are a few limitations for the use of IAK. The creatinine clearance expected with IAK would be approximately 30 cc/minute (approximately one-third of normal kidney function). Cultured cells may undergo gradual loss of function thereby reducing efficiency of dialysis in due course. Being a foreign body, the chances of thrombosis are high. In spite of some success in animal models, the IAK has to be developed further to start human trials.

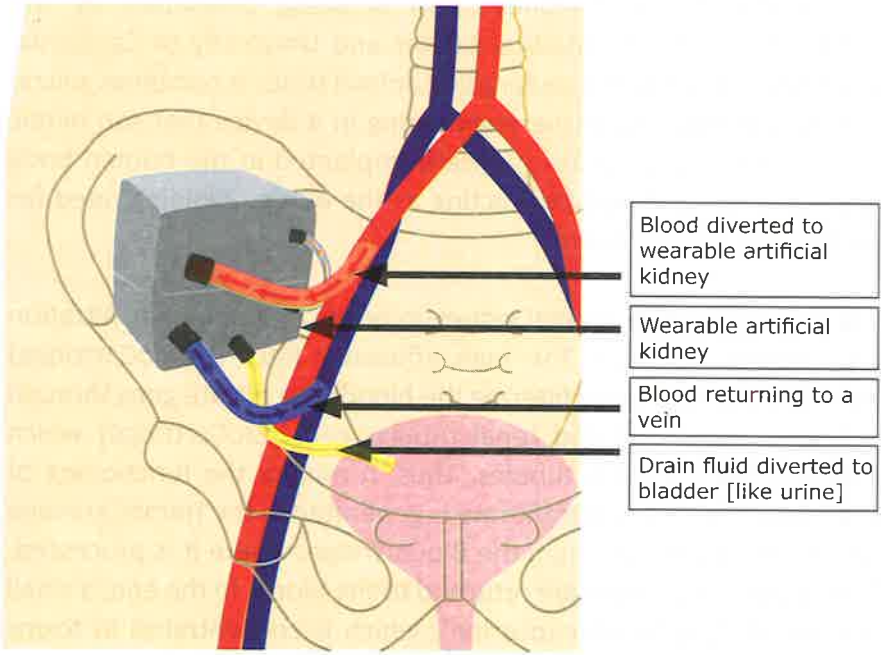


Fig. 26.1: Schematic of an Implantable Artificial Kidney.

Automated Wearable Artificial Kidney (AWAK) (AWAK Technologies Pte, LTD)

This system is undergoing human trials and is based on the principle of peritoneal dialysis. This can achieve average creatinine clearance of just >30 mL/min. The chapter on Peritoneal dialysis elaborates on this.

The WAK and AWAK have already been subjected to human trials, while the IAK is yet to complete animal trials. The wearable kidney devices must prove to be safe, effective and have better clinical outcomes. It can improve the quality of life of patients and can prove to be a suitable replacement alternative for a failing kidney.

27 Other Related Procedures and their use in Non-Renal Indications

R. Kasi Visweswaran • Sreedevi P. A.

Other modalities of treatment and hemodialysis can be used for indications other than removal of uremic toxins and correcting electrolyte imbalance. Newer modalities of treatment have been developed. Plasmapheresis is discussed separately in another chapter. Other procedures like hemoperfusion, immunoadsorption, molecular adsorbent recirculation system (MARS) and indications for dialysis/CRRT in non-renal conditions are discussed in this chapter.

Hemoperfusion

Hemoperfusion is an extracorporeal blood purification system. In this, the blood is passed through a cartridge which contains adsorbent particles. It is used to remove substances with molecular weight of 100–40,000 D. Thus, some toxins, poisons, cytokines from the blood, which cannot be removed effectively by hemodialysis, can be removed. The two main types of adsorbents are charcoal and resins. Activated charcoal granules are coated with albumin, enclosed in a cartridge and sterilized. Charcoal has greater capacity to adsorb water-soluble molecules. The resins (polystyrene or hydrocarbon polymers) have greater affinity for fat-soluble molecules. Priming the system is done with 500 mL of 5% Dextrose first followed by 500 mL of Normal saline + 2500 IU heparin before use. As the blood circulates between the granular carbon particles, adsorption occurs. Filters in the cartridge prevent entry of carbon particles with the returning blood.

The vascular access is usually a double lumen dialysis catheter. Heparin is administered to maintain the activated clotting time (ACT) at double the baseline. ACT should be monitored and heparin dose adjusted carefully. The system is primed twice before connecting the patient. Hemoperfusion can be continued for 3–4 hours. The cartridge must be changed after 4 hours if longer treatment is necessary. Many

protein-bound drugs and those with higher molecular weight can be removed by hemoperfusion (e.g., Theophylline, Short acting barbiturates, Digoxin, Phenytoin, etc.)

The complications include thrombocytopenia, leukopenia, hypoglycaemia and bleeding. The bleeding is due to higher requirement of heparin, thrombocytopenia and adsorption of clotting factors.

Immunoadsorption

Immunoadsorption is also an extracorporeal technique. It is used for the removal of antibodies and molecules from the blood and was developed in the 1990s. Different adsorbents are used for the removal of all subclasses of immunoglobulins, such as IgG. Special absorbents for selective removal of disease-specific molecules, such as lipoprotein(a) and CRP, are also available. Highly efficient removal of the molecule selectively has made immunoadsorption very useful in management of autoimmune diseases. The side effects are also minimal. It is now used for removal of cytokines in the management of sepsis.

This is a closed system and a central venous catheter is used to draw blood from the patient and return. Blood first passes to plasma filter where plasma and cells are separated. Plasma then passes on to immunoadsorption column before returning to patient. In the dual column system, as the plasma is passing through one column, the second column gets regenerated and vice versa. Adsorption-Desorption-Automated system (ADAsorb, Medicap Clinic GmbH) is the most common dual column system in use today. The regenerated plasma is added to the separated cells before returning to the body.

All columns have a matrix containing the specific molecule which will bind the required immunoglobulin as the plasma flows through.

For example, protein A is found in the cell wall of *Staphylococcus aureus* and will bind particularly immunoglobulin G [IgG] with high affinity. It has very little binding of other immunoglobulins. Different

material are available for binding different substances like CRP, immunoglobulins, lipoproteins, ABO blood group antibodies, etc. CytoSorb is a single-use column designed for the removal of excessive cytokines.

Molecular Adsorbent Recirculating System (MARS)

This is also known as liver dialysis or albumin dialysis. MARS helps to remove toxins which accumulate in fulminant (very severe, life-threatening) liver failure and Hepato renal syndrome (a condition where liver disease also causes worsening of kidney function). Substances like bilirubin, ammonia, lactate, free fatty acids, and aromatic amino acids accumulate in the body. MARS helps to remove albumin-bound substances as well as water-soluble substances. The main use of MARS is in management of fulminant hepatic failure till recovery of liver function occurs or till liver transplantation can be done **(Fig. 27.1)**.

The MARS system consists of three compartments:

a. Blood circuit
b. Albumin circuit
c. High flux HD circuit

The blood passes through high flux polysulfone membrane in the HD circuit. The albumin-bound toxins are adsorbed on the membrane. 20% albumin is circulated in the dialysate compartment. The albumin-bound toxins are taken up by the albumin in dialysate compartment. The albumin dialysate goes through the albumin regeneration circuit which consists of a conventional low flux bicarbonate dialysis to remove water-soluble toxins (like hemodialysis). Then, the albumin-containing toxin is regenerated by passing it through activated charcoal column followed by a column containing anion exchange resin. The regenerated albumin is circulated again through the artificial kidney. Although MARS is effective in removing toxic substances normally excreted by the liver, it cannot be done repeatedly and for prolonged periods. Moreover, it is very expensive and not available in most centers. It is used to tide over the Fulminant hepatic failure

till recovery of liver function occurs or until liver transplantation takes place.

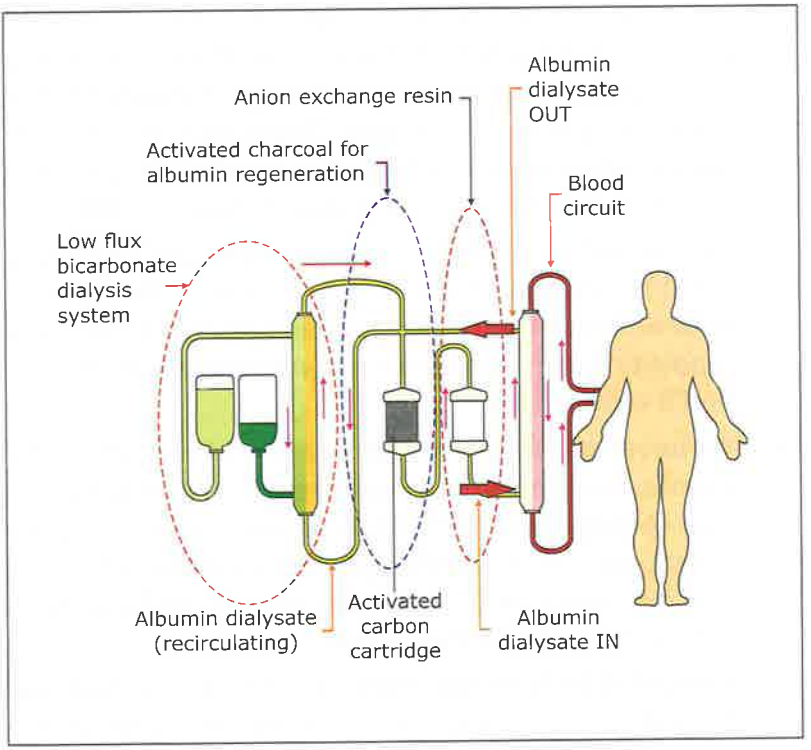


Fig. 27.1: Molecular adsorbent recirculating system (MARS).

Nonrenal Indications of Dialysis & Related Procedures

Various forms of dialysis like conventional HD, SLED, CRRT and Peritoneal Dialysis (PD) are frequently used to treat patients with acute kidney injury (AKI) and end-stage renal failure (CKD V_D). However, some of these modalities can be used to treat patients with non-renal diseases as well. Use of CRRT in critically ill patients with cardiovascular instability, severe fluid overload, cerebral edema, hypercatabolic patients is very well-established.

1. NON-RENAL INDICATIONS OF HD

Conventional HD as well as SLEDs are used frequently in the management of many non-renal conditions. The success of such therapies depends on the cause and the type of dialysis.

a. **Poisoning:** Overdose of various drugs and toxins can be more efficiently treated by dialysis. Water-soluble substances and low molecular weight substances are effectively removed by dialysis. Therefore, HD removes non-lipophilic and non-protein-bound substances are more efficient as compared to lipophilic and protein-bound drugs. Lithium, Methanol, Ethylene glycol, Salicylates, Theophylline, long-acting barbiturates (phenobarbitone) and Valproate are some of the drugs which can be removed effectively by HD.

b. **Sepsis:** HD and SLED can be used in patients with renal failure and sepsis as it may help in the removal of inflammatory mediators. Immunoadsorption is a newer modality being used. Since it is very expensive, most units find it unaffordable.

c. **Removal of radiocontrast agents:** Most radiocontrast agents have small molecular weight, and they can easily pass-through dialysis membrane. Since some radiocontrast agents cause acute kidney injury, HD is considered soon after contrast exposure. The chances of contrast-induced acute kidney injury can be minimized.

d. **Control of body temperature:** Using a warm or cold dialysis fluid, the temperature of blood in the extracorporeal circuit can be modified. This method is used rarely to control hypothermia (low body temperature) or hyperthermia (high body temperature) when other measures fail.

e. **Hypercalcemia:** Very high levels of calcium (>12 mg %) in blood may be associated with complications in the nervous system. Patients of hypercalcemia who are not effectively controlled by medical treatment can be subjected to HD which will rapidly lower serum calcium levels.

2. **NON-RENAL INDICATIONS OF CRRT**

a. **Sepsis and septic shock:** Sepsis and other inflammatory disorders are the most common non-renal indications for CRRT. Hemofiltration mode of CRRT removes inflammatory mediators like cytokines from the circulation.

b. **Acute respiratory distress syndrome (ARDS):** CRRT helps to

eliminate inflammatory mediators as well as fluid from the blood. The reduction of extra fluid in the lungs is helpful in patients with ARDS.

c. **Cardiopulmonary bypass (CPB):** Hemofiltration can be performed during major heart surgeries using CPB. Inflammatory mediators are also removed and fluid status maintained. This helps in good oxygenation and successful outcome.

d. **Congestive heart failure (CHF):** Heart failure with lot of fluid accumulation in the body causes difficulty in breathing and edema. If treatment with diuretics is not successful, ultrafiltration can be done by hemofiltration or ultrafiltration using the dialysis machine.

e. **Inborn errors of metabolism:** Inborn errors of metabolism include a group of diseases with abnormal metabolism and accumulation of toxic metabolites in the body. CRRT can rapidly remove these toxic metabolites and help in recovery.

f. **Lactic acidosis**: CRRT can help by removal of lactic acid in patients with accumulation of lactic acid in the body.

g. **Crush injury and tumor lysis syndrome**: In any crush injury, the muscles are damaged and myoglobin escapes into the blood. This is excreted by the kidneys, and kidneys in turn are damaged if too much of myoglobin is present in the blood. When treatment for cancer is started, many cells die and the uric acid level in the blood goes up. This can also damage the kidney. CRRT helps by removing myoglobin and uric acid from the blood. So the complications due to myoglobin and high uric acid levels can be prevented.

28 Preventive Maintenance of Hemodialysis Machine, Water Treatment System, and Bicarbonate Mixer

R. Kasi Visweswaran

Proper maintenance of all equipment will help to maintain their usefulness, life and efficiency. Most of these machines have sophisticated electronic components and most are under periodic maintenance contract and service, if any major issue crop up. The day-to-day maintenance is in the hands of the dialysis technician. In this chapter, a brief summary of periodic maintenance of the common equipment used for dialysis are highlighted.

Hemodialysis Monitors

Since the Hemodialysis machines have high chances of contamination after each treatment, it is necessary to clean and disinfect the machine after each treatment. If it is not done, the chances of cross-infection between patients will be high. Infections like Hepatitis B, Hepatitis C and some bacterial infections spread very easily between patients in the dialysis room. Extreme care, in addition to "universal precautions" is necessary to prevent this.

The Hemodialysis machine must undergo a complete disinfection after dialysis. Both heat and chemical sterilant are used after each treatment. The surface of the machine should be wiped with moist dilute (0.5%) sodium hypochlorite solution. Thereafter, the machine is put in rinse mode and cycle completed before using for the next patient. At the end of treatment every day, Formalin treatment and heat disinfection is given.

The conductivity of the ultrafiltration pump are calibrated frequently and electrolyte content of final dialysate is checked at least every month or earlier if any patient develops an unexpected event during dialysis. Blood pump occlusion has to be checked and recalibrated if different brand of blood tubing is used. If the blood flow in the arterial bulb appears jerky or unsteady, one of the causes may be

poor pump occlusion. Checking dialysate flow rate is usually done during periodic maintenance by the service engineer.

Periodic Maintenance of Water Treatment System

The maintenance of water treatment system is based on procedures such as:

a. Backwash
b. Rinsing
c. Regeneration (of resins)
d. Replacement of chemical/resin/carbon
e. Chemical washing
f. Manual cleaning (water tank)

The sediment filter's water flows from top to bottom. The sediments form a layer at the top. They can be removed by back wash. When water under pressure is directed from the bottom upwards, the accumulated dirt is removed from the system and the filtering particles (sand) is also cleaned. Backwashing is done depending on the suspended impurities in the incoming water. If the suspended impurities are high, it will be better to have two sediment filters. They have to be backwashed at least every 3 days or more frequently depending on the incoming water quality.

Water softeners contain resins containing sodium chloride. They remove calcium and magnesium from water by exchanging sodium for calcium and magnesium. After some time, the resin will lose all the sodium and will not be able to provide sodium for exchange. The resin should be recharged by adding concentrated sodium chloride (brine solution) to rinse the resin so that the calcium and magnesium are replaced by sodium. The rinsing fluid is discarded and the water softener can be used now. Hardness can be tested by using water hardness test strips or using soap to check if good lathering occurs. The brine recharge should be done based on hardness test. It may be necessary almost every day if the incoming water is "hard". Otherwise, recharging can be done every 3 days.

In the case of charcoal filters, there is no means of removing the contaminants (chlorine, chloramine, etc.), which are adsorbed by the granular-activated charcoal. When the efficiency decreases, the charcoal should be replaced. It is better to have two carbon tanks, one for preliminary purification and next one for "polishing" for completing the purification. If the chlorine content of water leaving the carbon filter is high, the carbon has to be replaced.

The RO system has pressure monitors in the incoming and outgoing lines. If the pressure drop is high, the membrane "fouling" is suspected and the membrane is cleaned. Similarly, if the percentage of reject water is high, a fault in water pressure pump or membrane fouling is suspected and corrective action taken.

Tank washing is another important step undertaken in the periodic maintenance of the water treatment system. The inside of the tank is cleaned with liquid bleach as follows: 5 L liquid bleach is added to the tank filled with water and mixed. It is allowed to remain for 1 hour and drained. The inside is rinsed well with water jet, the water is drained until last drop, tank dried and refilled with fresh RO water. The RO system is usually cleaned by the service engineer. The flow meter in the RO can be cleaned by removing the cap on the top to clean the inside.

The UV filter can be dismantled. The surface of the UV light source and inner surface of the container is wiped with soft cloth to remove any slime or dirt. The set can easily be reassembled.

The plumbing lines can also be cleaned by circulating liquid bleach and rinsing with water. After using of any chemical substance, the system should be rinsed and checked for any residual chemicals before the next use.

29 Introduction to Peritoneal Dialysis and Dialysis Solutions

Girish Narayen

Introduction

Peritoneal dialysis is a relatively simpler way of performing dialysis. There is no need for machines or sophisticated equipment, and it can be performed in places with limited facilities, and even in small hospitals. For this type of dialysis, patient's own peritoneal membrane which acts as semipermeable membrane is used. The peritoneal membrane is utilized as the "dialyzer" across which fluid and solutes can move **(Fig. 29.1)**. Sterile dialysate fluid is installed into the peritoneal cavity through a catheter placed inside the cavity. Periodically, the fluid is drained and cavity is filled up with a fresh fluid. There are different types of peritoneal dialysis **(Table 29.1)** which can be chosen depending upon the condition, the need of the individual patient and the facilities available.

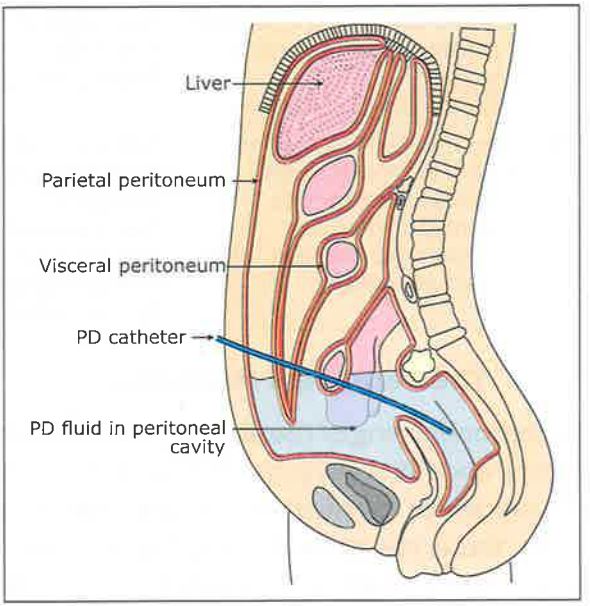


Fig. 29.1: The peritoneum, peritoneal cavity and catheter in the cavity.

Table 29.1: Different types of manual and automated peritoneal dialysis

Procedures	Actual procedure and timing	Catheter & exchanges
Acute intermittent PD	Manual exchanges One exchange every hour (10′ inflow, 30′ dwell and 20′ outflow)	Rigid catheter 40 L exchanges over 36–48 hours
CAPD	Manual exchanges 3–4 exchanges Long night dwell	CAPD catheter 2 L exchanges for adult Daytime dwell 4 hours
Daytime PD (DPD)	Manual exchanges 3–4 exchanges No night dwell	CAPD catheter 2 L exchanges for adult Daytime dwell 4 hours
Nocturnal intermittent PD (NIPD)	Automated (PD cycler) Daytime = "DRY" (No PD) Cycler used for multiple night time exchanges	CAPD catheter Exchange volume as tolerated Short dwell period
Continuous cyclical PD (CCPD)	Automated (PD cycler) Long day dwell Short multiple night-time exchanges	CAPD catheter Exchange volume as tolerated Short dwell period
Intermittent cyclical PD	Automated (PD cycler) Rapid multiple exchanges Intermittent (4 days a week) No dialysis in between	CAPD catheter Exchange volume as tolerated Short dwell period
Tidal PD (TPD)	Automated (PD cycler) No daytime dialysis Multiple exchanges at night. Fluid not completely drained after each exchange.	CAPD catheter Exchange volume as tolerated Part removal of fluid and refilling the amount drained automatically by the cycler.

The Peritoneal Membrane

Peritoneum is the inner lining of the abdomen wall and it also covers most of the intra-abdominal organs. The peritoneal membrane is a thin membrane which consists of a single layer of mesothelial cells. Deeper to these mesothelial cells, there is the interstitium which contains blood vessels and lymphatics. The peritoneum is only few millimeters thick. These characteristics help in utilizing it as semipermeable membrane through which dialysis can take

place. Fluids and solutes move across the membrane depending on osmotic pressure across it. The peritoneal space is a "potential" space between parietal peritoneum (which covers abdominal wall) and visceral peritoneum (which covers all the internal abdominal organs) **(Fig 29.1).** In males, the peritoneal cavity is a closed space but in females it communicates with exterior via pelvic organs, fallopian tubes and uterine cavity. The peritoneum secretes approximately 50 ml of clear serous fluid daily.

Principles of Dialysis

Diffusion

The movement of a solute from an area of higher solute concentration to lower solute concentration is termed as diffusion. It is dependent on the gradient in concentration **(Refer Fig 4.1 of Chapter 4).** Diffusion is bidirectional (occurs in both directions). Uremic solutes like urea, phosphorus and creatinine are higher in blood. Peritoneal dialysis fluid does not contain these substances. Thus, they move across peritoneal membrane from blood to dialysis fluid. At the same time, substance like dextrose and lactate (alkali) move from dialysis fluid into blood in peritoneal capillaries. Smaller solutes diffuse at a faster rate, especially at the beginning, but as the concentration gradient decreases, the diffusion also decreases.

Osmosis

It is the movement of solvent particles from a dilute solution (lower solute concentration) to concentrated solution (higher solute concentration) across a semipermeable membrane **(Refer Fig. 4.22 of Chapter 4).** The movement of solvent particles dilutes the concentrated solution till the concentration is equal on both sides of the membrane. Classical example of osmosis is the movement of water in plant root hairs which facilitates the nutrition of plants and trees. The difference between diffusion and osmosis is explained in **Table 29.2**. Diffusion can occur in any mixture whether there is a semipermeable membrane or not. For example, if sugar syrup is added to a cup of water, the sugar molecules diffuse throughout the container even without mixing by diffusion. Diffusion can also occur

across a semipermeable membrane. At the same time, osmosis occurs only across a semipermeable membrane.

Table 29.2: Difference between osmosis and diffusion

Osmosis	Diffusion
Movement of solvent molecules	Movement of solute molecules
Movement occurs across a semipermeable membrane.	Diffusion occurs in any liquid medium or across semipermeable membrane.
Solvent molecules move from lower solute concentration to higher solute concentration across the semipermeable membrane.	Solute molecules move from higher solute concentration to lower solute concentration.
Example: Absorption of water from soil by the root hairs of plants. Water removal in peritoneal dialysis is based on this principle.	Example: Adding sugar syrup to water Removal of small molecules in Hemodialysis is based on diffusion and advection.

Convection/Ultra-Filtration

During dialysis, solutes are transported along with water, and this process is known as "solvent drag" or convective solute transport. With the osmotic force created by high glucose content or other osmotic agents in PD fluid, large molecules like albumin also cross the peritoneal membrane. This occurs by convection utilizing large pores in the peritoneal membrane. Fluid can be absorbed from the peritoneal cavity through the lymphatic system. The net fluid moment or ultra-filtration (UF) is the sum of fluid transferred into peritoneal cavity and uptake of the fluid out of peritoneum through lymphatics. There are three size pores in the capillary wall—

a) Small pores for the transport of small molecular weight solutes.

b) Large pores for the transport of large molecular weight solutes.

c) Ultra-small pores or *aquapores* which are permeable only through water. These are the major water channels. Ultra-filtration occurs through tiny pores and through these water channels.

Peritoneal Dialysis Fluid

The main purpose of dialysis is to remove waste products (solutes) and water from the body. It also helps to correct electrolyte and acid-base abnormalities. The normal serum osmolarity is 280–290 milliOsmoles/kg [mOsm/Kg]. Peritoneal dialysis should be able to remove solute (clearance) in a steady and predictable manner. The difference in concentration of the solute across the membrane will help solute clearance. The PD solution should also have an osmotic agent which will help to remove water from the body. At the same time, the osmotic agent should not be absorbed into the system. The most commonly used osmotic agent in dialysis fluid is dextrose. Too much of glucose absorption will result in very high blood sugar levels. The PD fluid solution should be free of microorganisms, pyrogen and should not cause any toxicity. The concentration of various solutes and electrolytes in various PD solutions is shown in **Table 29.3**.

Table 29.3: Composition of various glucose containing PD fluids

Content in PD fluid	Concentration	Normal blood concentration	Function
Sodium [Na]	132–134 mEq/L	135–145 mEq/L	Sodium moves from PD fluid to plasma if plasma level is low and from blood to plasma if plasma level is high.
Potassium [K]	0–2 mEq/L	3–4.5 mEq/L	Patients often have hyperkalemia [High K^+]. So, potassium moves out from blood to PD fluid.
Chloride [Cl]	96–102 mEq/L	96–102 mEq/L	Chloride moves from PD fluid to plasma if plasma level is low and from blood to plasma if plasma level is high.
Lactate	35–40 mEq/L	Bicarbonate 24–26 mmol/L	Lactate is absorbed and is converted to bicarbonate in the body by the liver. (Bicarbonate cannot be mixed with other chemicals and stored.)
Calcium [Ca]	3.5–4.5 mEq/L	8.5–10.5 mg/dL [4.3–5.2 mEq/L]	Corrects serum calcium level.

(Continued...)

Table 29.3: Composition of various glucose containing PD fluids (Continued)

Content in PD fluid	Concentration	Normal blood concentration	Function
Magnesium	0.25–0.5 mEq/L	1.5–2.0 mEq/L	Corrects serum Magnesium level.
Glucose	1.5 gm /L 2.5 gm/L 4.5 gm/L	90–140 mg%	Glucose is the main osmotic agent. It helps to remove fluids from the body because of higher osmotic pressure compared to blood plasma. As the concentration of glucose increases, it helps to remove more fluid from the body by osmosis.
Osmolality [mOsm/Kg]	1.5 % = 345 2.5 % = 395 4.5 % = 485	280–290	If osmolality is higher, more fluid can be removed by ultra-filtration. However, more glucose re-absorption takes place from the PD fluid to the body. The blood sugar may increase to very high levels and should be monitored and corrected with insulin.

Alternate Dialysis Fluids

There are several new solutions available now. They help to reduce or avoid some of the problems of standard dextrose containing dialysate. It is aimed at improving the biocompatibility and also prolong life of the peritoneal membrane.

1. **Icodextrine:** This has a similar structure of glycogen and is produced by hydrolysis of starch. Each molecule of icodextrine contains between 20 and >500 glucose molecules linked together. This is isosmotic with human serum with osmolality of 282 mOsm/kg. This allows long dwell and ultra-filtration to continue over a longer period. There is very little back diffusion from peritoneal cavity into circulation. As ultra-filtration with icodextrin is slow and occurs evenly, it is preferred for overnight dwell in CAPD. Use of icodextrin provides same ultrafiltrate as of 4.25% Dextrose and three to four times more than 1.5% Dextrose. There are lesser chances of developing hyperglycemia and lipid abnormalities. As it contains lactate and the pH of dialysate is acidic (pH5.0), it can cause some discomfort to patients. When it gets metabolized to maltose, elevated plasma maltose levels may occur. Icodextrin may also cause sterile peritonitis.

2. **Amino acid dialysate:** This dialysate has 1.5% amino acid in the solution and is used predominantly to improve nutrition. The patient should also have adequate calories in diet otherwise aminoacids will not be taken up by the tissues. As dextrose exposure is minimized, patients have lesser chances of hyperglycemia and hyperlipidaemia. Icodextrin is very expensive and used only for specific indications.

Newer Dialysate Bags

Newer technology has allowed manufacture of double or triple chambered bags (**Fig. 29.2 A and B**). Some of them are used in a limited fashion because their long-term beneficial effects are not clearly proved. Glucose-based peritoneal dialysis solution with a physiologic bicarbonate/lactate buffer are presented in a dual-chamber container which separates the glucose-containing solution from the alkaline bicarbonate/lactate or buffer solution, allowing bicarbonate to be separated from calcium and magnesium in order to prevent precipitation of calcium carbonate during sterilization and storage. As dextrose is in a separate chamber, it minimizes formation of glucose degradation products (GDP) during sterilization and storage. It is reported to be safe and effective in patients on CAPD and APD, and its use is associated with reduced infusion pain.

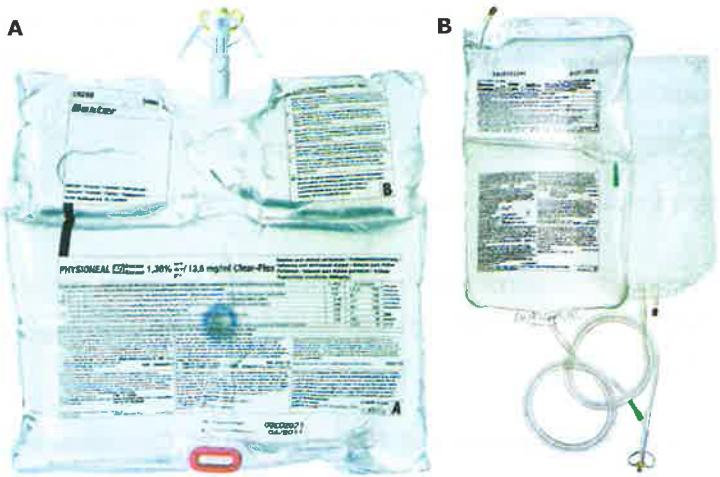


Fig. 29.2 A and B: Double and triple bag systems for CAPD.

30 Intermittent Peritoneal Dialysis: Procedures

Girish Narayen

Intermittent, acute peritoneal dialysis (PD) can be performed even in smaller institutions where there is no facility for hemodialysis. It is a useful and life-saving procedure. When patients come with sudden deterioration of kidney function (AKI), PD can be started early. Even for patients with dialysis requiring stage 5 of chronic kidney disease (CKD stage V), long-term dialysis in the form of CAPD can be offered. Now, machines are also available for performing the PD exchanges (automatic PD cyclers). The most recent development is the automated wearable artificial kidney (AWAK) system which is a PD-based artificial kidney. Peritoneal dialysis is avoided in the following conditions:

i. When there is abnormality with blood clotting

ii. Large hernia

iii. Peritoneal adhesions (Peritoneal cavity is not free and peritoneal membrane is sticking to each other in many places within the abdomen.)

iv. Infections like tuberculosis of peritoneum

v. Recent operations in the abdomen

In some types of peritoneal infection, PD is done to wash the peritoneum with sterile peritoneal fluid and give antibiotics into the peritoneum.

Acute Intermittent PD with Rigid Catheters

Here, PD can be started by carefully introducing a stiff catheter on a stylet into the peritoneal cavity through a small incision below the umbilicus in the midline. Once the tip is in the peritoneal cavity, and positioned near the rectum or bladder, PD can be started.

Materials required for acute PD

1) Peritoneal catheter (rigid) kit consisting of (a) Stiff catheter with stylet, (b) Connector set, (c) Disposable scalpel blade with handle **(Fig. 30.1)**
2) PD fluid administration Y-set
3) Drain bag (ordinary Urobag can be used)
4) Local antiseptic lotion, Betadine/isopropyl alcohol/Chlorhexidine.
5) Local anaesthetic agent, Lignocaine 1%, dressings, cotton swabs, gauze
6) Suturing needle and silk thread
7) Adhesive tape/sterile drape to cover abdomen

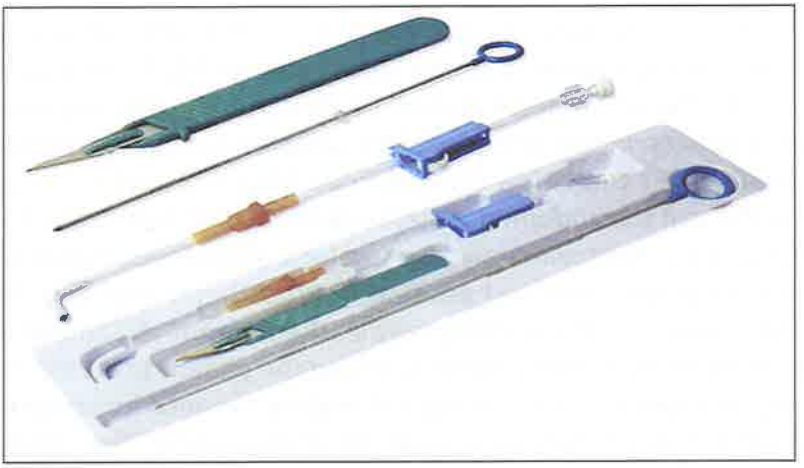


Fig. 30.1: Disposable stiff PD catheter set with stylet.

The procedure for acute PD can be divided into the following four sequential steps:

Step 1- Preparation of the abdomen

Step 2- Priming of the abdomen with fluid

Step 3- PD catheter insertion

Step 4- Conducting PD fluid exchanges

Step 1: Preparation of the Abdomen

The rectum and urinary bladder are to be emptied before the procedure for which rectal enema and evacuation of urinary bladder may be needed. The abdominal hair is to be clipped or shaved in case of adult males. If possible, the patient should be given a bath or sponge bath with betadine/soap. The operator should use sterile gloves, gown, cap and mask. The patient should wear a mask over their mouth and nose. The skin over the front of whole abdomen should be cleaned initially with chlorhexidine/isopropyl alcohol and later povidone iodine lotion to ensure sterility. The area below the umbilicus is draped with sterile towels. The procedure should be done preferably in a special room and entry should be restricted to only necessary personnel wearing mask and cap. Street clothes and footwear should not be used.

Step 2: Priming of the Peritoneal Cavity with Fluid

It is necessary to confirm that there is no distention of intestine and the urinary bladder is empty before start of PD. Priming needle should be placed in the peritoneal cavity correctly. This is the most important step in the procedure. PD catheter is usually inserted in the midline 2–3 cms below the umbilicus. After thorough cleaning of the surface of the abdomen, a sterile central hole towel is placed on the abdomen. Approximately 10 mL of local anaesthetic (lignocaine) is instilled at the proposed position of PD catheter insertion. Prior to introduction of the priming needle, the anterior abdominal wall is to be made taut. This is done by asking the patient to lift the head against resistance or by straining and making the anterior abdominal wall tight. This will help ease insertion of the needle. The needle is to be introduced vertically into the abdominal wall by piercing the skin, linea alba and finally the parietal peritoneum. After this, about 300–500 mL (40–50 mL/kg in children) of the PD fluid is used to fill the abdomen. Now, needles which are less likely to injure intra-abdominal organs during puncture of abdominal wall are available.

Step 3: PD Catheter Insertion

Once the abdomen is filled up with about 300 to 500 mL of PD fluid, the priming needle is withdrawn. A small nick is made at the

same site with a surgical blade. The stylet with rigid PD catheter attached is introduced into the abdomen perpendicularly. At this stage, the patient is asked to lift the head or strain so as to make the anterior abdominal wall taut. If a child is crying, the abdomen becomes taut by itself and the puncture with stylet and catheter can be done easily. As the catheter is advanced, there is initial resistance followed by a feeling of "giving in". Once the stylet enters the abdominal cavity, the stiff catheter alone is advanced so that the tip is pointing downwards and in the pelvic cavity. Care should be taken not to puncture the intestine or urinary bladder. Once the catheter is in position, the stylet is removed, extra length of the catheter outside the body cut off (leaving s short stump) the connection set attached and administration set is connected to the connection set. The connection set which has been connected to the PD fluid should be flushed so that there is no air or air bubbles in the system. Now, the PD fluid can be infused into the peritoneal cavity. If the position of catheter tip is good, good inflow of PD fluid can be observed in the air chamber of the administration set.

Step 4: PD Exchanges

The "Y type PD set" with a three-way connector is used to regulate the direction of PD fluid. One or two litre bag of peritoneal dialysis solution is used. The three limbs of the "Y" connector are connected to the sterile PD bag, catheter and the drain bag.

Each fluid cycle has three components—

a) PD fluid inflow (usually 10 minutes)
b) Dwell time (30 minutes): The fluid remains in the peritoneal cavity.
c) Drainage time (usually 20 minutes)

Initially 10–20 mL/Kg of fluid is instilled to fill the abdomen, which is later increased to 30–40 mL/Kg. Fluid is kept in dwelling for 30–40 minutes, before it is drained. The drainage occurs by "siphon action". The time varies depending on the catheter position. Drain time is usually between 15 and 20 minutes. If it takes more than

40 minutes, it means the catheter is not well positioned or there is obstruction to the system. There must be no air at all in the system, because sometimes "air-lock" can prevent the siphon action and drainage will not occur even though the abdomen is full. At the end of drain, the fluid in and out are recorded and a fresh dialysis fluid is filled up. The clamps must be handled carefully, otherwise, the PD fluid may run directly from the container to drain bag. The process of filling up, dwell and drain takes approximately one hour, and this is considered one cycle. Maintaining sterile connections, exchanges are done at hourly intervals. In presence of hyper catabolic state or hyperkalemia, the dwell time is shortened to 10 minutes for faster correction. Hourly inflow, hourly outflow, total inflow and total outflow are tabulated. If extra ultrafiltration is necessary, PD fluid with either 2.5% or 4% dextrose is used. If hypertonic fluid is not available then 50–100 mL of high concentration dextrose (25% or 50%) is added into each PD fluid bag before instilling the fluid into the abdomen. Two to three such high concentration exchanges are performed to achieve extra ultrafiltration. Accurate charting of the PD fluid administered and drainage should be maintained. The net balance for every exchange and cumulative total for the whole session should be maintained. Positive net balance means, administered fluid is not drained completely and negative net balance means, the fluid drained is more that the fluid administered during the session. Blood glucose should be monitored every 4 hours in diabetics and insulin is to be administered as per the blood sugar levels. 40 Liter PD fluid exchange is considered as one PD session. A minimum of 24 hours and a maximum of 72 hours of PD is usually done. At the end, the rigid PD catheter is removed and a skin suture is applied. Depending upon the patient's need, few such sessions of PD procedure can be repeated. During this period, the patient's Acute Kidney Injury (AKI) may recover with no need for further dialysis. In some patients with AKI, where they require a greater number of dialysis sessions, instead of repeated puncture with a stiff catheter, a soft silicon PD catheter with a single cuff can be placed. The cuff will be under the skin. The catheter can be used for intermittent dialysis for few weeks, till the patient recovers from acute kidney injury.

If the tip of catheter has entered the intestine, there will be passage of PD fluid through rectum when more fluid is filled in. If the catheter is in the bladder, as the PD fluid flows, the patient will have pain in lower abdomen and will pass the fluid out through urethra.

Automated Peritoneal Dialysis (APD)

For better metabolic and fluid control, some patients are shifted to dialysis with automated machine. Instead of performing manual peritoneal dialysis exchanges several times throughout the day, patients can be given automated peritoneal dialysis while they sleep at night. In automated peritoneal dialysis (APD), the Tenckhoff catheter has to be placed (Refer CAPD chapter) and the patient can now be connected to the machine. Patient and attendant are required to wear a mask over their nose and mouth during the set-up, connection and disconnection of the catheter to the APD machine. Hand hygiene and sterile precautions are followed strictly. These simple steps help in prevent infections.

The following equipment and disposables are necessary for performing APD:

i) APD machine

ii) Large bags of PD fluid (6 or 10 Liters)

iii) Drain line and bag

iv) Casette and tubings

v) Documentation

i. APD machine: The APD machine automatically fills up the peritoneal cavity with the prescribed volume of pre-warmed PD fluid, from the bags. The volume of PD fluid, the temperature, dwell time for each cycle can be preset in the machine according to the prescription. The fluid is allowed to remain for a certain time (dwell time), after which it is drained from the peritoneum to the drain bag. Once the draining is completed, new dialysis solution is released from a dialysis solution bag to the peritoneal cavity again. This process goes on until the cycles of APD

treatment is completed. As machine, special bags and tubings are required, this form of PD is very expensive compared to standard manual PD. APD machine can be used for performing acute PD in ICUs or for CAPD at night in the home of patients.

ii. Large bags of PD fluid: Each PD fluid bag is filled with about 6 or 10 liters of sterile PD fluid. Two or three bags are generally used through the night. The PD fluid bags are connected to a cassette in front of the cycler machine. The exit from the cassette is connected to the person's peritoneal catheter. The machine controls the flow of fluid through the cassette. First, the specified amount of dialysis fluid is instilled into the peritoneal cavity. The PD solution is allowed to remain (dwell) inside the peritoneal cavity for the desired time following which it is drained into the drainage bag. Then the cycle repeats. There are alarms if the fluid inflow or outflow are not proper.

iii. Drain line and drain bag: The drain line and the attached bag form a single unit. The capacity of the clear bag is more than 20 L. It is attached at a lower level compared to the patient. Since the drain line and bag are clear, it will be possible to see the fluid that has been drained. The used PD fluid should be very clear. If it is slightly turbid or cloudy, it may be an early sign of infection. If cloudiness is observed, the patient should call their PD nurse/coordinator for further evaluation and advise. Standard protocols are followed for "cloudy effluent".

iv. Cassette and tubing: The various tubes used to perform APD are gathered and arranged into one area of the cycle called the cassette or organizer. The cassette is mounted onto the machine so that mistakes in connection are avoided and everything is organized. There are tubes that connect the cassette to each dialysis solution bag. Depending on the patient's prescription, there can be one to four bags for each treatment. The PD catheter and drain bag are also attached to the respective slots in the cassette. Thus, the patient needs to connect the bags, line to PD catheter and drain line in respective places before switching on the machine.

v. Documenting APD treatment: Documentation of treatment is important. Patients are trained to keep the dialysis chart record. This allows the treating doctor and nurse to monitor the performance and progress. This helps in adjusting the treatment recommendations. There are different persons to do this depending on the dialysis system that the patient choses. Dialysis nurse/technicians and coordinators help the patient with his training, needs and requirements.

31 Continuous Ambulatory Peritoneal Dialysis

Girish Narayen

In contrast to intermittent acute PD, patients with chronic kidney diseases who require long-term dialysis can be dialyzed by placing a soft PD catheter with two Dacron cuffs (Tenckhoff catheter **Fig. 31.1).** This modality of dialysis is known as Chronic (ambulatory) Peritoneal Dialysis (CAPD). In this procedure, the peritoneal cavity is filled up with fluid which is allowed to remain inside for 5–6 hrs during which period the patient is ambulant and not confined to bed. At the end of 6 hours, the fluid is drained and filled up with a fresh dialysate, using a specialized bag connection.

Tenckhoff catheter has made long-term CAPD practical. Depending on the need, different types of catheters are available. The catheter can be placed surgically in the abdomen by many methods. Of the two cuffs, one is positioned before the entry of catheter into peritoneal cavity (pre-peritoneal space) and another cuff under the skin. This allows the catheter to remain in peritoneal cavity for a long-term and prevents risks of infections. The intra-abdominal portion of the catheter has side perforations that facilitate fluid movement.

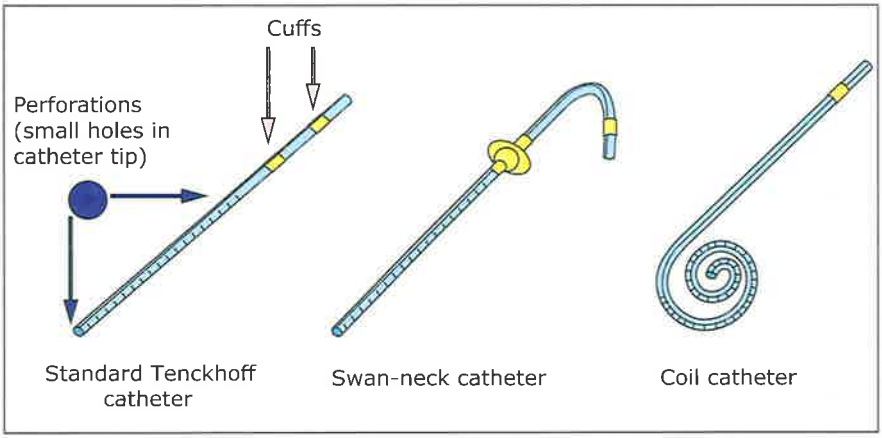


Fig. 31.1: Some types of Tenchkoff catheters.

Contraindication for CAPD

1) Uncooperative patients who are not motivated.
2) Those who are unable to manage peritoneal exchanges with sterile technique and maintain hygiene/asepsis.
3) Incapacitated patients with no family/social support. (One or two trained person should be available for exchanges three to four times a day.)
4) Those without financial stability or support.
5) Patients who had abdominal surgeries earlier. (They are likely to have multiple peritoneal adhesions. So the peritoneal area available for dialysis will be less and fluid drainage from the abdomen may be slow.)
6) Large abdominal hernia or diaphragmatic leak.
7) Obese patients with BMI of >35 kg/M^2.
8) Very small patients who cannot tolerate installation of required volumes of fluid in the peritoneum. (Usually, the fluid volume per exchange is 50 mL/Kg body weight.)
9) Patients with chronic respiratory diseases may not tolerate large volumes of abdominal fluid.
10) Patients with large polycystic kidneys may not tolerate fluid in peritoneal cavity.
11) Patients with ischemic bowel diseases, diverticulitis can develop infection across the bowel wall.
12) Patients who have severe malnutrition and hypoalbuminemia. (Risk due to excessive protein loss in PD drainage fluid. The diet should be very high in protein. Delayed healing and fluid leakage are other problems in malnourished patients.)

Careful selection of patients for CAPD is necessary. CAPD should be attempted only in motivated and stable patients who have the resources and support to continue treatment. The patient and attendants should be counselled and trained well.

Pre-Operative Preparation

The Tenckhoff catheter should be placed under aseptic conditions preferably in an operation theatre. The patient should be given a scrub bath 3 days before procedure, if possible. Abdominal preparation includes close trimming of hair or shaving to be done as for a major abdominal surgery. A laxative is given previous night for bowel preparation. Preoperative antibiotic is usually given as prophylaxis. Use of prophylactic antibiotic reduces the risk of exit site infections.

Placement of CAPD Catheter

The catheter can be placed surgically by—

a) Open method which can be performed under light general or local anesthesia.

b) Percutaneous Seldinger insertion technique is a blind procedure but often successful. This needs only local anesthesia.

c) By laparoscopic method, the catheter can be positioned exactly. For this, general anesthesia is required.

In open method after local injection of lignocaine, a small incision is made below the umbilicus and the abdomen is opened. After opening the peritoneum, the catheter is placed in abdomen under direct vision and is usually placed in either of iliac fossa or deep into pelvis behind the bladder. The catheter may be kept in position using a suture. The deep cuff is placed in paramedian position behind the rectus muscle. Catheter is taken out through a tunnel in the subcutaneous tissue. The catheter comes out of the skin laterally approximately 3 centimeters from the superficial cuff. If the catheter is placed under direct vision, the chances of good drainage are excellent and there may be lesser chances of infection and peri catheter leak.

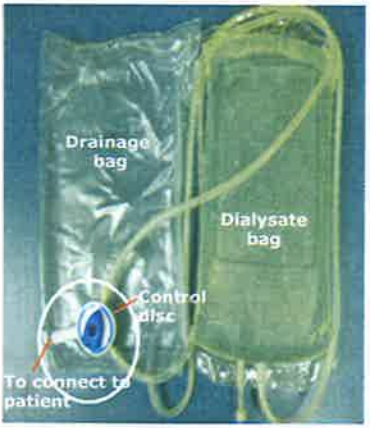
In Seldinger technique, the abdominal wall is punctured by a 16–18 G needle with plastic sheath (intra cath). Once the abdomen is punctured, 500–1000 mL of normal saline is instilled into the

peritoneum and a guide wire is passed. After dilating the track with an appropriate dilator, a peel away sheath over a dilator is placed over the guide wire. After removing the guide wire and dilator, the catheter can be placed into the peritoneum and sheath is peeled off. It is to ensure that the deeper Dacron cuff is embedded deep in the skin. The subcutaneous tunnel is prepared and the exit site is planned 3 cms from the cuff.

Once the catheter placement is done, it is flushed with PD fluid to verify free flow of fluid, proper drainage and remove the fluid instilled. Other attachments called "Titanium adapter" and "transfer set" are connected to the catheter to enable continuation of dialysis using the CAPD bags. The wound is closed and proper dressing is done. Normally after 1 or 2 days, the catheter is flushed to see its functioning. A waiting time (break in period) of two weeks is allowed for the tract to heal and the cuff to be embedded in tissue. This prevents pericatheter leak which can happen if the dialysis is started early. However, in emergency situation, the patient can be started on dialysis with patient in recumbent position and using small volume exchange either manually or by cycler. The patient is also to be trained about the technique of dialysis exchanges and need for strict asepsis. Dedicated team of staff is desirable who can monitor, counsel the patient about various steps to be taken while carrying out the dialysis exchange.

PD Bags, Connections and Exchange

Initially different types of bags and connecting sets were available. To begin with, only one bag with fluid and set was available. After filling of peritoneal cavity, the empty bag was folded and kept and can also be used for drainage. At the end of cycle after draining the fluid, the set and bag were discarded. With the availability of double bags system and separate bag for drain, the risk of peritonitis has been greatly reduced **Fig. 31.2**. In the present system, there is only a single connection between catheter and administration set. To reduce the risk of infection before filling the abdomen, the initial fluid of about 100 ml is used to flush the catheter and connection following which the abdomen is filled (flush before fill) **Fig. 31.3.**



Consists of a full bag (2 L) dialysis fluid with "Y" tube connections to the patient and empty drain bag.

The disc system has a knob which can be turned to regulate the fluid flow.

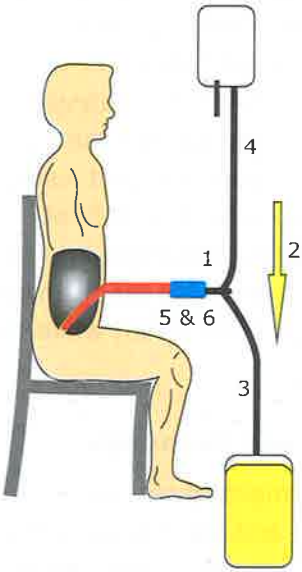
a. From bag to drain (for flush before fill)

b. From bag to patient

c. Patient to drain

d. All closed

Fig. 31.2: CAPD double bag with disc system.



Step 1: Connect "Y" set to catheter;

Step 2: Open drain bag clamp and flush with 100 mL of fresh PD fluid from dialysate bag;

Step 3: Close dialysate bag clamp and let the fluid from abdomen drain fully;

Step 4: Close drain bag clamp and open dialysate bag to fill the abdomen with dialysate;

Step 5: Keep PD catheter cap ready and close catheter immediately on removal on "Y" set;

Step 6: Disconnect the "Y" set with attached (full) drain bag and (empty) dialysate bag.

Fig. 31.3: CAPD exchange. Steps for flush before filling.

After the tract heals, patient is allowed to commence his exchanges as planned.

Complications

Complications in patients with long-term peritoneal dialysis can broadly be surgical, medical or metabolic.

1. **Surgical complications** usually occur after catheter insertion.
    a. Improper position of catheter results in poor in-flow or incomplete drain. It may be due to the catheter not positioned in the dependent part, deep into pelvis or migration of catheter towards the upper part of abdomen.
    b. Constipation and loaded colon are important causes for poor drainage. If suspected, laxative or enema may help.
    c. Intra-abdominal adhesion due to previous surgeries could be the reason for inadequate inflow and outflow. If the adhesions are too many, the patient may be unsuitable for continuation of peritoneal dialysis.
    d. Sometimes there could be covering of part of the catheter with holes by omentum (omental wrap) which is responsible for malfunctioning.
    e. Fibrin clot can form at any time and may block the tube. Addition of heparin to the dialysate prevents fibrin clot formation. If a blood clot blocks the catheter tip, heparin or urokinase infusion in the catheter may help to dissolve the clot.
    f. Bleeding and hemoperitoneum: This could occur immediately after catheter insertion due to initial trauma while puncturing the abdomen. Minor bleedings may subside on its own many times. Rarely, injury to blood vessels inside may cause prolonged bleeding.
    g. Catheter leak can occur due to damaged catheter or if the site of entry of catheter into peritoneum is not securely sutured.
    h. Catheter expulsion or extrusion of cuff may occur if subcutaneous cuff is not correctly positioned.
    i. Hernias: Raised abdominal pressure over a long period, due to PD fluid makes these patients prone to develop hernias. They could develop umbilical, anterior abdominal wall (due to weakening in rectus muscles), inguinal, vaginal and diaphragmatic hernias.

2. Medical complications

Infections: Infection is a common cause for failure of peritoneal dialysis. Bacterial infection with various organisms is common. Sometimes, susceptible patients may develop infection with opportunistic organisms like tuberculosis or fungi. Proper care of the exit site by regular cleaning with antimicrobial solution and application of antimicrobial cream helps to reduce the chances of infection. Similarly, proper aseptic techniques while changing the bags, connecting and disconnecting the set goes a long way in preventing infections.

Exit site infection: The infection of exit site can occur at any time and is suspected if any area of redness at the site or exudate and crusting occurs in dressing. Sometimes frank pus can be seen and rarely abscess. When infection spreads deeper into the subcutaneous tissue, it results in tunnel infection. The above infections are outside the catheter.

Peritonitis: Infection in the peritoneum can be suspected by noting the cloudiness of the effluent. The easiest method is to keep the effluent bag over a newspaper. If the effluent is very clear, it will be possible to see the print clearly. In presence of infection, the cloudy effluent makes it difficult to see the print clearly. Sometimes the patient complains of pain while the fluid is filled and even during drain period. If infection is suspected, the effluent fluid is collected in a sterile container and sent to laboratory for pathology and biochemistry and microbiology lab for analysis. If the suspicion is strong, antibiotic is started immediately, even before cultures report is ready. There are guidelines about which antibiotic should be started first, before getting the culture report. Later when the culture report is available, appropriate change is made. Peritonitis is a major complication and, if not treated, can lead to lot of discomfort, failure of CAPD or even death of the patient. When infection occurs, efficacy of the peritoneal membranes decreases, adhesions may occur and the catheter may have to be removed in some cases. Therefore, every effort should be made to observe strict aseptic technique while performing exchanges.

Infection of the peritoneal membrane is termed as peritonitis. Infection can occur by—

a) Spread through the catheter

b) Spread through blood stream

c) Spread from the intestine (transperitoneal through the bowel)

Of this the most common and important is through the catheter which can be prevented by taking proper care of the catheter and taking proper precautions.

The following terms are used to define peritonitis—

1) Recurrent Peritonitis: Within four weeks of completion of treatment but with a different organism.

2) Relapsing peritonitis: Occurrence of peritonitis with the same organism, within four weeks of completion of treatment for the previous episode.

3) Refractory peritonitis: If the effluent does not clear (peritonitis has not improved) within five days of appropriate treatment.

4) Repeal peritonitis: When peritonitis occurs with the same organism, four weeks after completion of treatment.

Other medical problems: The other problems that can be seen are:

i. Anemia

ii. Hypoalbuminemia

iii. Malnutrition

iv. Muscle wasting

v. Metabolic bone disease (low turnover bone disease)

vi. Neurological complications (peripheral neuropathy)

vii. Metabolic encephalopathy

viii. Electrolyte abnormalities

ix. Cardiovascular complications

x. Cerebrovascular accidents

3. Metabolic:

a. Diabetic nephropathy is the most common cause of ESRD in majority of adults on CAPD. Moreover, non-diabetic patients of Chronic Kidney Diseases also have impaired glucose tolerance, since PD fluid contains large concentration of glucose. So, these patients are at the risk of developing severe hyperglycemia. They should be carefully monitored for proper glucose control and treated with addition of insulin in the PD bags for better control of sugars. However, by puncturing and adding insulin, there is increased risk of contamination and infection.

b. Dyslipidemia: Long-standing hyperglycemia results in abnormalities in lipid metabolism with elevated triglycerides and other lipids. They also have risk of accelerated atherosclerosis and cardiovascular complications. Therefore, good management of hyperglycemia is important for preventing complications.

32 Monitoring CAPD and Recent Advances

Girish Narayen

A CAPD coordinator and a close-knit team are necessary for successful running of a CAPD program. Patient selection is equally important. The clinician prescribes the dialysis schedule and is modified from time to time based on the progress and test results. The number and glucose concentration of CAPD fluid are changed as per need.

There is great variation in the permeability of peritoneal membrane between patients. These characteristics may change in the same patient over time. In some individuals, the solute clearance is better than ultrafiltration, whereas in some others the ultrafiltration capacity is good but solute clearance is slow. Peritoneal Equilibration Test (PET) is done to assess peritoneal membrane permeability. It is a semi-quantitative test based on which the dialysis prescription can be modified depending upon the need of individual patient.

Peritoneal Equilibration Test

PET is performed after the patient is stabilized on dialysis for few weeks. The steps are as follows:

a) The overnight fluid after 8–12 hrs dwell fluid is drained with the patient in erect position. Two litre CAPD bag containing 2.5% Dextrose is filled into the peritoneal cavity, while the patient is in supine position. The patient is asked to roll over from side to side four to five times while the fluid is being infused, approximately once after every 400 ml of fluid is filled. (Dialysate sample is D and plasma sample is P. The numbers 0, 2, 4 indicate the time of sample collection in relation to the test.)

b) Time is noted after all the dialysate has been run in as "D0". Immediately 200 mL of fluid is drained back into dialysate bag, 10 mL sample is taken and the remaining 190 mL reinfused. Simultaneously, a blood sample is drawn for glucose and creatinine estimation.

c) The patient is asked to walk around and be ambulant (not idle) during the period. After 2 hours of dwell "D2", the process of dialysate sampling is repeated and blood sample P2 is taken for creatinine.

d) At the end of 4 hrs, the dialysate is drained completely with the patient in upright position. The drain volume is measured and 10 ml of fluid is collected for tests. (D4 glucose and D4 Creatinine). Serum sample is also taken for Creatinine (P4 Creatinine).

From the samples DO, D2 D4 glucose and creatinine and P0, P2 and P4 creatinine, calculations are made. The ratio of glucose in dialysate D2/D0 and D4/D0 and D2/P2 and D4/P4 (ratio of creatinine at 2 hrs and 4 hours) are calculated and plotted in a standard graph. Using D/P ratio of creatinine, and D/0 glucose patients are classified into one of the four transport categories, namely (i) High (H), (ii) High average (HA), (iii) Low average (LA), and (iv) Low transporters (L).

High transporter means solute clearance (waste removal) is fast. Glucose absorption may also be fast but water removal is slow. Fast transporters quickly lose their osmotic gradient and have poor ultrafiltration and develop fluid overload. The levels of urea and creatinine will be low. These patients will need short and quicker exchanges (less dwell time).

Low means solute clearance is slow but water removal is good. These patients may not develop fluid overload but may have higher levels of creatinine. The other two categories are in between the two.

Adequacy of Peritoneal Dialysis

It is important to assess the adequacy of dialysis since the permeability of solutes and ultrafiltration in the peritoneum is not uniform in all patients. There are various parameters which have to be assessed to see if the dialysis is effective and patient is getting full benefit of the procedure. PD adequacy is assessed by:

a) Clinical response

b) Solute clearance for small and large solutes

c) Electrolytes
d) Acid-base balance
e) Fluid balance
f) Nutrition

Clinical Response

With proper dialysis, uremic symptoms subside and patients have sense of well-being. Their appetite improves, nausea subsides and fluid overload gets controlled. With improved nutrition and proper diet, their muscle mass, serum proteins and albumin levels increase. Hemoglobin starts improving with iron and erythropoietin use. The metabolic complications also show improvement. Since they feel fit, they are able to return to normal activity.

Solute Clearance

The maintenance of electrolyte and acid-base balance can be assessed by performing PET test, urea, creatinine, electrolytes and bicarbonate tests periodically.

Fluid Balance

Maintenance of electrolytes and fluid balance is essential for long-term benefits. Those who are high transporters (as per PET) have inadequate fluid removal. They have increased risk of fluid overload, hypertension and related complications. The daily fluid intake has to be restricted usually depending on patient's urine output. In those whose urine is less than 200–300 mL, there is a need to restrict fluid and salt intake Patient counselling and compliance is very important. Use of diuretics like furosemide may be of little help in whom the residual renal function (urine output) is low. Ultrafiltration can be enhanced by increasing dialysate glucose concentration with 2.5% Dextrose or even 4.5% Dextrose that would help in achieving the required ultrafiltration. Initially, there is better removal of fluid and control of hypertension. If high concentration of glucose in PD fluid is used over long-term, the ultrafiltration capacity of peritoneum is altered. Therefore, fluid retention, uncontrolled hypertension and need for higher dose of anti-hypertensive will be necessary. If anyone has increased absorption of fluid in the late phase of dwell,

automated peritoneal dialysis (APD) at night with frequent short dwells may be tried. Icodextrin (Polyglucose dialysis fluid) is a very expensive PD fluid which can be used in such situations for day time long dwell.

Nutrition

In the initial years after starting Peritoneal Dialysis, CAPD patients may gain weight and increase in muscle mass. This is usually due to glucose absorption from fluid in peritoneum (400–500 calories per day). There will be need for higher dose of insulin and anti-diabetic drugs. Close monitoring of blood sugar is essential. Persistent hyperglycemia results in complications like hypertriglyceridemia and cardiac problems. There is significant loss of albumin in the dialysis fluid. About 10–15 gms of protein may be lost in the PD fluid. Unless this is compensated by high protein diet, patients become malnourished, develop hypo albuminemia and muscle wasting.

Automated Wearable Artificial Kidney (AWAK)

The AWAK system is a PD-based artificial kidney. It is being developed. It is an automatic system delivering short frequent dialysate exchanges. In contrast to traditional CAPD where 2–2.5 litres of fluid is instilled and exchanged every 4–8 hours, three to four times a day, AWAK system performs 500 mL exchanges eight times an hour automatically. This system is composed of a tubing (PD catheter), a purse-like storage chamber which has a storage module, a sorbent cartridge which regenerates PD fluid, and an enrichment compartment which replenishes electrolytes. The ultrafiltrate (UF) is drained into an UF bag which can be discarded when the cartridge is replaced, which is required every 7 hours. The advantages of AWAK are that it uses a bloodless system. So, there is no chance of accidental blood loss. Since smaller dialysate dwell volumes are used, there is minimum discomfort and complications compared to traditional PD. However, long-term trials are necessary to identify risks of peritonitis, membrane failure and encapsulating peritoneal sclerosis.

33 Kidney Transplantation

Umesh B. Khanna • Shruti Tapiawala

Introduction

End Stage Kidney Disease (ESKD) is also called CKD sage 5 and at this stage, the kidney function is almost completely lost. Kidneys cannot perform its functions sufficiently to sustain life of the patient. Life-long dialysis or kidney transplantation which are important forms of Renal replacement therapy becomes mandatory for survival. Kidney transplantation is the best form of renal replacement therapy as the patient enjoys better quality and the longevity of life after successful kidney transplantation. Moreover, transplantation is more cost-effective, affords normal lifestyle and improved survival. The wrong perception that kidney transplantation procedure is extremely difficult and risky prevents patients and their families to accept this form of treatment.

For kidney transplantation, there should be a donor from whom one kidney can be transplanted to the patient who is called the recipient. Kidney donors can be either—

i. Living related donor—usually a close blood relative: As per the laws in India—parents, grandparents, siblings, children, and spouse qualify as "near relative".

ii. Living unrelated donor who is ready to donate. Distant relatives may be included in this category. The law forbids "selling of kidneys" for a consideration. There are Authorization committees which scrutinize and give permission in such cases.

iii. Deceased (Cadaver) Donor—is a person who is declared as "brain dead" and is medically fit to donate organs. Strict rules apply here also for certifying a patient as brain dead. The following organs Kidneys, heart, Liver, lungs, intestine, and even hands can be transplanted if consent is obtained from the next of kin. After following the legal formalities and procedures, the organ can be

removed and used for transplantation. Eye transplantation is also very common and the eye can be removed within 2 hours after death. In the case of other organs, the organs must be removed soon shortly after brain death is certified.

In the case of living donors, consent and donation should be totally voluntary. Then, the donor is subjected to a series of tests to confirm that he has no significant illness, has 2 well-functioning kidneys and removal of one kidney will not affect the health of the donor. Once the donor's normal health is confirmed, tests to confirm that there is blood group matching. Now, costly medicines and procedures are available which permit transplantation between donor and recipient even though the blood groups are not matching.

All patients with ESKD should be assessed for suitability of kidney transplantation and counselled regarding the advantages and disadvantages. The recipient should be prepared for transplantation and the dialysis staff may be involved in various steps. Some of the precautions in the case of recipients are:

i. The recipient should undergo complete physical examination and undergo psychiatric evaluation to confirm that he has understood the nature of illness, details of treatment and need for lifelong medicines and follow up.

ii. Tests to assess cardiac function: ECG, Echocardiogram and angiogram followed by angioplasty or bypass operation as needed.

iii. Pulmonary function tests.

iv. Gastrointestinal evaluation to confirm that he has no ulcer which may worsen with surgery and lifelong drug treatment.

v. Patients having a cancer and active Infection cannot be considered for kidney transplantation.

vi. The recipient should be dialyzed adequately.

vii. Blood transfusions are preferably avoided. Blood transfusions may stimulate formation of antibodies which may damage

the transplanted kidney. In rare cases where transfusions are needed, WBC free washed red cells may be given. WBC filter can be used in the infusion line which will filter WBCs and prevent their entry to blood stream during transfusion. Depending on the instructions from treating doctor, immunosuppressive drugs are also given for a few days to prevent formation of antibodies.

viii. Steps to maintain the hemoglobin level >10 gm% at least should be targeted. Appropriate doses of Iron, Vitamins and Erythropoietin should be administered.

ix. Reuse of dialyzer is preferably avoided.

x. HLA typing of donor and recipient helps to identify the matching and mismatching. Cross match test between the donor and recipient is done to rule out whether the recipient already has antibodies against the donor. In such cases, the recipient has to undergo further tests and procedures.

xi. The recipient should be vaccinated against Hepatitis B, pneumococcus and other illness depending on the protocol of individual hospitals.

xii. Tests for various types of antibodies, cross match between donor and recipient are rechecked one day before transplantation to confirm that they are normal.

xiii. The recipient is usually started on immunosuppressive drugs a few days before the date for transplantation.

xiv. Some patients need very expensive antibodies to prevent rejection of transplanted kidneys and these are administered carefully by staff trained in dialysis or transplantation.

xv. The donor and recipient are prepared for surgery as per the institution protocol.

The surgery involves—

i. Donor nephrectomy: This can be performed by
   a. Conventional open method
   b. Laparoscopic method

ii. The whole kidney together with the surrounding fat, renal artery, renal vein and a length of ureter are carefully removed.

iii. Immediately after removal, the kidney is perfused using a special ice-cold solution containing drugs prevent clotting and spasm of blood vessels using a canula in the renal artery. The blood inside

the kidney is drained off and the core of the kidney is cooled. The surface of kidney is also cooled using flakes of ice prepared from saline.

iv. Once the kidney is cooled, it becomes pale and firm.

v. The iliac fossa of the recipient is exposed to prepare a "bed" for the transplanted kidney.

vi. The artery (internal iliac or common iliac artery), external iliac vein, and dome of the urinary bladder are exposed and prepared for anastomosis.

vii. The anastomosis (joining together) is between—

   a. The renal artery of the donor kidney with internal/common iliac artery of recipient

   b. Renal vein of donor kidney with external iliac vein of recipient

   c. Ureter of donor kidney to the bladder of recipient

viii. When blood flow is restored, the pale kidney becomes pink and starts producing urine.

ix. The surgeon then completes the remaining steps in the operation.

Post operative care, monitoring urine output, administration of adequate fluids and monitoring of vitals are important during post operative period. Immunosuppressive drugs are continued with a view to prevent rejection of the graft.

Advances like Laparoscopic donor nephrectomy and Robot assisted kidney transplantation are available in advanced centers. These help to reduce chances of infection, reduce pain and duration of hospital stay. The donor has to take rest for a few weeks and avoid lifting heavy objects. Otherwise, he can lead a normal life. Annual check-up is advised.

The recipient will be fit for discharge by 10–15 days. Frequent follow up with blood tests are required for the first month followed by less frequent follow up for 3 months. They can resume normal work by 3–6 months. Life long medicines are necessary and discontinuation of medicines may lead to grave consequences. As mentioned earlier, the quality of life after successful transplantation is better than maintenance hemodialysis.

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