HEMODIALYSIS IN CANINE UREMIA

P.G. BABY, M.V.Sc.,
(ID. No. 213)

Thesis submitted in partial fulfilment of the
requirements for the degree of
DOCTOR OF PHILOSOPHY
in
CLINICAL MEDICINE AND THARAPEUTICS
to the
Tamil Nadu Veterinary and Animal Sciences University
Madras - 600 007

DEPARTMENT OF CLINICAL MEDICINE AND THERAPEUTICS
MADRAS VETERINARY COLLEGE
TAMIL NADU VETERINARY AND ANIMAL SCIENCES UNIVERSITY
MADRAS - 600 007

1994

CERTIFICATE

This is to certify that the thesis entitled, **"HEMODIALYSIS IN CANINE UREMIA"**, submitted in part fulfilment of the requirements for the degree of **DOCTOR OF PHILOSOPHY (VETERINARY)** in **CLINICAL MEDICINE AND THERAPEUTICS** to the Tamil Nadu Veterinary and Animal Sciences University, Madras is a bonafide research work carried out by **P.G.BABY**, under my supervision and guidance and that no part of this thesis has been submitted for the award of any other degree, diploma, fellowship or other similar titles or prizes and that the work has not been published in part or full in any scientific or popular journal or magazine.

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Dr.R.VENKATARAMAN
Chairman

Approved

Chairman: **Dr.R.VENKATARAMAN** 16/5/94

Members:

1. **Dr.P.DHANAPALAN**
2. **Dr.M.THANIKACHALAM** 16.5.94
3. **Dr.S.PRATHABAN**

Date : 16/5/94

External Examiner

DR. P.C. CHOUDHURI.

CURRICULUM VITAE

Name of the Candidate	:	**P.G.BABY**
Date of Birth	:	27.05.1952
Place of Birth	:	Mannuthy - **Kerala**
Major Field of Specialization	:	Clinical Medicine and Therapeutics
Educational Status	:	Completed B.V.Sc. and A.H. in 1976 **at** Kerala Agricultural University
		Completed M.V.Sc. in 1989 at **Kerala** Agricultural University
		Joined Ph.D. programme in 1991
Professional Experience	:	Junior Assistant Professor Kerala Agricultural University from 03.12.1977
		Assistant Professor Kerala Agricultural University from 20.06.1986 to till date
Marital Status	:	Married
Permanent Address	:	Payyappilly House Mannuthy 680 651 Trichur, Kerala.
Publications Made	:	Research articles
		Popular articles
Membership of Professional Society	:	Member of Indian Society for Veterinary Medicine.
		Member of Indian Veterinary Association.

ACKNOWLEDGEMENTS

The author expresses his sincere gratitude to **Dr.R.Venkataraman**, M.V.Sc., Ph.D., Director of Clinics, Tamil Nadu Veterinary and Animal Sciences, University and Chairman Advisory Committee for his valuable guidance, advice and constant encouragement given to him through out the course of this study.

The author humbly places on record his thanks to **Dr.V.Gnanaprakasam**, M.V.Sc., Ph.D., Vice-Chancelor, Tamil Nadu Veterinary & Animal Sciences, University for all the help and guidance extended to him as former advisory committee member during the initial period of the study.

The author is extremely thankful to the members of his advisory committee, **Dr.P.Dhanapalan**, M.V.Sc., Ph.D., Professor and Head, Department of Clinical Medicine and Therapeutics, **Dr.M.Thanikachalam**, M.V.Sc., Ph.D., Associate Professor, Department of Pathology and **Dr.S.Prathaban**, M.V.Sc., Ph.D., Associate Professor, Department of Clinical Medicine and Therapeutics, Madras Veterinary College for their valuable suggestions and assistance at every stage of the study.

With deep gratitude the author expresses his sincere thanks to **Dr.T.S.S.Rajan**, M.V.Sc., Ph.D., Professor and Head, Department of Clinical Medicine and Therapeutics, Veterinary College and Research Institute, Namakkal for the valuable guidance, advice and suggestions given to him as former Chairman, Advisory Committee during the initial period of the study.

The author is indebted to **Dr.S.R.Srinivasan**, M.V.Sc., Ph.D., Technical Officer to the Director of Clinics, Tamil Nadu Veterinary & Animal Sciences and to all the staff members of Department of Clinical Medicines and Therapeutics who have been helping hands to him during the entire period of study and stay at Madras.

The author wishes to offer his thanks to **Mr.T.Radhakrishnan, M.Sc.**(Statistics) for his help in statistical analysis.

The author would be failing in his duty if he forgets to mention **Dr.K.S.Prabhakar**, M.D., D.N.B., Nephrologist and **Mr.K.Balaji**, Dialysis Technician, Southern Railway Head Quarters Hospital, Madras, who helped him in understanding the complicated hemodialysis procedures.

The author wishes to offer his thanks to **Dr.A.D.Joy**, **Dr.P.C.Alex**, **Dr.M.R.Saseendranath**, **Dr.P.C.Saseendran**, **Dr.D.V.Keskar** and **Dr.Srinibas Das** and other friends for their valuable help and assistance rendered during the study period.

The author humbly places on record his indebtedness to the **Indian Council of Agricultural Research** for awarding Senior Fellowship and **Kerala Agricultural University** for having deputed him for Ph.D. programme.

With deep sense of gratitude and affection, he thanks his parents, wife and daughters who withstood the manifold stresses consequent of his undertaking this study, for their help, encouragement and co-operation during the entire study period.

ABSTRACT

Name & Degree : **P.G.BABY, M.V.Sc.**

Chairman : **Dr.R.VENKATARAMAN, Ph.D.**
Director of Clinics
Tamil Nadu Veterinary & Animal **Sciences**
University, Madras.

The study on "Hemodialysis in canine uremia" was undertaken in 30 experimental and 12 clinical cases of uremia to ascertain the feasibility and the usefulness of hemodialysis in canine. Uremia was induced experimentally by oral administration of ethylene glycol or intravenous administration of mercuric chloride in fifteen animals each. The following characters were studied before and after dialysis: Pathological constituents of urine, hemogram and leucogram, and serum urea, creatinine, total protein, sodium, potassium and chloride.

Proteinuria and cylindruria were the significant abnormalities both in experimentally induced and clinical cases of uremia. There was significant elevation of serum urea, creatinine and potassium in all the uremic animals. Crystalluria and increased packed cell volume were also evident in experimentally induced uremia. There was hypoproteinemia in all clinical cases of uremia.

In experimentally induced uremia after hemodialysis or peritoneal dialysis there was significant reduction in the packed cell volume. The elevated serum urea, creatinine and potassium values were brought down to normalcy after dialysis and all the animals were recovered from the uremic crisis. Hypoproteinemia was developed in animals which were treated by peritoneal dialysis. Hemodialysis was found to be superior than peritoneal dialysis with respect to the rate of extraction of uremic toxins and lesser time required for the course of treatment.

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CHAPTER I

INTRODUCTION

It is well known that renal disease is one of the most common disorders of dogs. Since one of the primary functions of the kidney is the removal of waste products of metabolism, any severe disturbance in the function of this organ will result in an abnormal accumulation of these toxic products. The milder forms of renal disease may go unnoticed, since the kidneys have great compensatory powers. However, when the limit of compensation is exceeded, and the kidneys are no longer able to excrete sufficient waste products of metabolism to assure a proper chemical balance in the body, uremia results. Uremia may develop slowly as the result of gradual deterioration of renal function or it may occur suddenly as a result of stress, toxaemia or infection. Whatever the cause, and no matter whether it is acute or chronic when uremia does occur it is necessary to provide some extra-renal means of eleminating some of the waste products in order to prolong the life of the patient (Jackson, 1964).

Dialysis is the recommended treatment for patients with acute reversible renal failure during the period of compromised renal function (Thornhill, 1984). This procedure avoids the progressive uremic state and allows the kidneys to regenerate and regain their functions (Shahar and Holmberg, 1985).

In animals with acute or chronic renal failure, peritoneal dialysis allows removal of waste products from the plasma to the dialysate and transfer of

olutes from the dialysate to the patient through a concentration gradient. 'eritoneal dialysis can be used to sustain life in the azotemic patients until enal function returns to normal or substantially improved till the renal ondition can be evaluated by renal biopsy for prognosis and further treatment ttempted.

Hemodialysis was found to be both effective and efficient means to ontrol many of the metabolic disturbances of acute uremia. Biochemical and netabolic upsets can be normalized in hours, in contrast to peritoneal dialysis n which 24-48 hours of continuous exchange is necessary to effect comparable legree of improvement. The purpose of such therapy is to maintain the normalcy of body fluids and support the patient's life while the failing kidney epairs and assume functional capabilities (Cowgill and Bovee, 1975).

Although haemodialysis is used frequently in human medicine, it has played an insignificant role in the management of renal failure in veterinary patients. It is limited by economic factors, technical complexity of the equipment needed and complications of the procedure. Compared to the human literature, references on the performance of hemodialysis in the veterinary field are few. Owing to the paucity of information available on the dialysis of dogs, knowledge and skill regarding vascular access, anti-coagulation and actual dialysis procedures, have been adopted from human medicine.

With these background information in mind, this study on Hemodialysis in canine uremia was undertaken with the following objectives:

a) To study the incidence of uremic syndrome among the dogs brought to the Madras Veterinary College Hospital.

b) To study the biochemical profile, hematology and changes in urine during uremic syndrome.

c) To study the feasibility and efficacy of hemodialysis in canine uremia.

d) To compare the efficacy of hemodialysis and peritoneal dialysis in canine uremia.

Review of Literature

CHAPTER II

REVIEW OF LITERATURE

2.1 CANINE UREMIA

Uremia may be defined in accord with its etymology and original meaning as the symptom complex resulting from renal insufficiency and accompanying retention of urinary constituents in the organism. It may be a late development of a wide variety of renal diseases (Schreiner and Meher, 1961).

It is a constellation of biochemical changes caused by a critical loss of functioning nephrons. Uremia may develop in both acute or chronic renal failure. In acute renal failure as compared to chronic renal failure, uremic changes are some what different and attenuated due to its short time course (Bovee, 1976; Chew and DiBartola, 1986).

'Uremia' is a term coined in 1840 by Piorry and L' Heriter to describe kidney failure. It meant retention of urine in the blood which was thought to be difficult. In current usage uremia indicate a complex of symptoms and findings resulting from disordered biochemical processes of the entire body when kidney function fails; it is a syndrome rather than a disease (Gutch and Stoner, 1983).

Uremia is defined as abnormal quantities of urine constituents in blood caused by primary generalized renal disease and as the polysystemic toxic

syndrome that occurs as a result of abnormal renal function. This polysystemic toxic syndrome is the result of three underlying phenomena. The first and most obvious signs caused by generalized renal lesion directly referable to the kidneys are renal pain, alteration in renal size, hematuria etc. The second phenomenon represents, polysystemic signs associated with autointoxication caused by a reduction of renal function below that required to clear plasma of metabolic waste products, an impaired ability of tubules to conserve vital metabolites in glomerular filtrate and reduced synthesis and reduced degradation and/or elimination of hormones. The third phenomenon consists of the body's compensatory responses to the metabolic deficits and excesses caused by these abnormalities in an attempt to maintain homeostasis. The common denominator underlying the polysystemic clinical and laboratory manifestations of uremia is the summation of the results of deficits and excesses in fluid, electrolyte, acid-base, endocrine, nutrient and caloric balances and metabolic waste products. Each individual component encompassed in these categories may be insufficient to cause a severe disturbance, but collectively they are capable of inducing profound alteration in homeostasis and even death (Osborne *et al.*, 1983).

2.1.1 Incidence of renal insufficiency and uremia

Chronic renal failure would appear to be the renal disorder most commonly encountered in the dog and chronic interstitial nephritis is believed to be responsible for most cases of chronic renal failure (Bloom, 1954).

Kirk *et al.* (1968) stated that renal disorders are the most common diseases of the dog and majority of old dogs have suffered some degree of kidney damage.

Renal disease is one of the most common disorders of dogs. And in any renal malfunction, uremia is a common consequences (Tabotabo *et al.*, 1970; Murray *et al.*, 1971).

Bush (1972) reported that from the stand point of veterinary clinician, three main syndromes of canine renal disease could be recognized; the nephrotic syndrome, acute renal failure and chronic renal failure.

Renal failure is a recognized cause of morbidity and mortality in geriatric dogs. It is not limited to any age, sex or breed of dog but is more prevelant in aged animals. In 170 dogs with renal failure presented to the Veterinary Medical Teaching Hospital of the University of California for a five year period, the mean age was 6.95 years (Cowgill and Splanger, 1981).

Low (1981) reported that the incidence of renal problem was 1.8 per cent of hospital admissions in dogs.

Incidence of confirmed cases of renal disease was about 1.1 per cent of clinic admissions in dogs (Doxey, 1983).

2.1.2 Etiology of Uremia

The uremic syndrome is almost always due to bilateral renal disease or to unilateral renal disease or rendered ineffectual by external obstruction,

congenital hypogenesis or previous destruction by a pathological process (Schreiner and Maher, 1961).

Pre-renal uremia is caused by abnormalities due to cardiac diseases, shock, dehydration and hypoadrenalcorticism, which reduce renal function by decreasing renal perfusion with blood. Primary uremia maybe caused by large number of diseases like renal ischemia, toxic agents, obstruction congenital anomalies and neoplasm which destroy at least three fourth of the parenchyma of both kidneys. Post renal uremia is caused by diseases which prevent excretion of urine from the body such as obstruction of urethra, bladder or both ureters and rupture of the excretory pathways (Osborne *et al.*, 1972).

Diseases that obstruct urine outflow from both kidneys may rapidly induce metabolic disturbances characterized by azotemia, hyperosmolality, hyperkalemia, hyperphosphatemia, hypermagnesemia, severe acidosis, dehydration and retention of metabolic waste products (Chisholm and Osborne, 1976).

Osborne *et al.* (1977) stated that abnormal elevation in the serum concentration of urea nitrogen and creatinine may occur in association with an elevated urine specific gravity in some patients with primary renal failure caused by generalized glomerular disease.

Uremia is characterized by multiple physiologic and metabolic alterations that result from renal insufficiency. Renal insufficiencies may be caused by any disorder that damages the functional capacity of approximately

70 to 75 per cent or more of the nephrons. Primary renal azotemia in dogs and cats may be caused by a variety of different agents that damage nephron rapidly (acute) or slowly (chronic). It may be 1) reversible, 2) irreversible or non-progressive or 3) irreversible progressive and oliguric and/or polyuric.To recapitualate renal disease may precede renal failure and likewise renal failure may precede uremia (Osborne and Polzin, 1983).

2.1.3 Clinical signs

Jackson (1964) opined that the signs of uremia, if any were ambiguous. The only obvious signs were anorexia and vomiting, which if present were usually considered by the owner to be an indication of stomach upset and due to that there was often delay in bringing the dog for treatment.

Tabotabo *et al.* (1970) reported that anorexia, retching, vomiting, arching of the back and straining were the common signs of uremia in dogs.

Bush (1972) stated that the signs of uremia were stomatitis, anorexia, vomiting and diarrhoea. In terminal stages because of increased capillary fragility, haematemesis and malaena were observed. Further he stated that ulceration of the mouth, bleeding from the gum and general signs of depression and apathy were also observed which might progress to coma.

A history of sudden illness and anorexia with little if any elevation of body temperature should lead one to suspect acute renal failure. The oliguric or anuric phase is usually of two to ten days duration, but may be as brief as one day or as long as three weeks. In the oliguric phase, associated with the

development of uremia, there are signs of mental depression and anorexia often accompanied by vomiting and reduction in fluid intake (English, 1974).

Macdougall *et al.* (1977) recorded diarrhoea, anorexia, halitosis, intermittent vomiting and weight loss for a period of two months as clinical signs of uremia in six and a half year old collie dog.

According to Watson (1977) the predominant clinical signs in compensated renal failure were polyurea and polydipsia. When those signs were overlooked by the owner, that lead to uremia.

Kelly (1979) reported that the clinical signs of uremia were depression, muscular weakness, deep laboured respiration, oliguira or anuria, loss of body condition, dehydration, gradually increasing anorexia, vomiting, hyperemic mucous membrane, ulceration in the buccal mucosa, coma and death.

In acute renal disease the onset of signs will be abrupt and these signs will include anorexia, depression, vomiting and thirst. The rectal temperature was often normal, but an arched back, stiff gait, pain in the lumbar region and full pulse may be encountered. In chronic cases signs were progressively increasing thirst, polyurea and loss of weight. In more advanced cases anorexia, vomiting, halitosis and dyspepsia will be observed. Uremia with necrosis of tongue was a late sign (Doxey, 1983).

Weakness, lethargy and vomiting of 48 hours duration were reported in ethylene glycol poisoning acute renal failure in a dog (Dibartola *et al.*, 1985).

Fleming *et al.* (1989) described the signs of uremia as sudden onset of vomiting, diarrhoea, constipation, depression and oliguria or anuria.

Acute lethargy, anorexia, vomiting, diarrhoea and melena were common clinical signs in animals with acute renal failure. Gastrointestinal abnormalities such as diffuse errosive gastritis and uremic colitis were also reported. Gastrointestinal haemorrhage remains a major cause of morbidity and mortality in patients with acute renal failure (Labato, 1992).

2.1.4 Patho-physiology of Uremia

Uremia may be defined as the constellation of clinical signs and biochemical abnormalities associated with a critical loss of functioning of nephrons (Bovee, 1976). It may be considered a pervasive intoxication caused by the combined effects of many metabolites retained as a result of loss of renal excretory function (Bergstorom and Frust, 1978). The syndrome of uremia, however also includes many metabolic and endocrine disturbances that arise from loss of renal homeostatic, synthetic and catabolic functions as well as abnormalities that are consequences of renal compensatory mechanisms and therapeutic intervention (Chew and DiBartola, 1989).

An early concept was that the signs and effects of renal failure could be explained by retention during failure of a compound normally excreted by the kidneys. The success of hemodialysis and peritoneal dialysis in alleviating most signs of renal failure supported this concept. Among the presumed culprits that have been incriminated over the years are urea, ammonia, creatinine, uric acid, hippuric acid, leucine, tyrosine sulfates, phosphates, chlorides, potassium,

acidosis, organic acids, indicans, guanidine and its derivatives, such as methyl guanidine and guanidosuccinic acid, phenols, aromatic oxyacids, urinary alkaloids and hyperosmolality (Schreiner and Maher, 1961).

Stein *et al.* (1969) have shown that urea retention increases quanido acetic acid concentration in the blood and this substance may be an important uremic toxin.

Urea and creatinine are markers of decreased glomerular filtration rate and are unlikely to be important uremic toxins. Urea is the most abundant nitrogenous product which accumulates in body fluids during renal failure. High concentration of urea, however can lead to fatigue, nausea, weakness, anorexia, vomiting and bleeding tendency (Johnson, 1972).

Furst *et al.* (1973) stated that middle molecules were responsible for many uremic abnormalities. These are molecules with molecular weight of 350-2000 which were incriminated as causes of uremic neuropathy if not removed by dialysis. These middle molecules appear to be a mixture of different peptides, but their specific identity has not been established.

Most uremic animals and human suffer from low grade malnutrition as they progress into renal failure and the primary factor is failure to eat properly during a prolonged debilitating illness, but specific intestinal absorption defects also probably play an important role (Bovee, 1976).

Anaemia is a common finding in renal failure. It is due to the inadequate production of hormone erythropoietin by the diseased kidneys. The

bleeding tendency of uremia resulting from platelet dysfunction, also leads to blood loss and may result in anaemia (Bovee, 1976; Fisher, 1980).

Lucke (1978) reported that vomiting is a common clinical sign of uremia in dogs. It was thought to be due to stimulation of the chemoreceptor trigger zone in the medulla by an unidentified uremic toxin. Methylguanidine, a bacterial degradation product of creatinine and urea had been considered as possible toxins in the pathogenesis of vomiting in uremia.

Uremic encephalopathy, an uncommon complication in dogs has been reported in three dogs. These dogs displayed facial twitching, head babbing, abnormal behaviour, tremors and seizures (Wolf, 1980).

Wooly (1987) reported that uremia was characterized by abnormal hemostasis and patient with acute and chronic renal failure were predisposed to haemorrhage. In dogs and cats gastrointestinal bleeding was most common. The major hemostatic abnormality in uremia is a qualitative defect in platelet function.

2.1.5 Pathological constituents of urine

Jackson (1964) opined that urinalysis was helpful in the diagnosis of kidney disease and should of course, be done when uremia was suspected. The most common abnormalities of uremic dogs were albuminuria and low specific gravity which were characteristic of interstitial nephritis. Pus and blood cells or cast might be found in infection or other inflammatory conditions. However abnormalities in the urine merely served to indicate the presence of kidney

damage, but did not offer any quantitative measure of the extent of damage nor did they necessarily suggest uremia. Conversely acute uremia occured with normal urinary findings.

A significant number of casts indicates renal disease. Hyaline casts are commonly seen in association with proteinuria and are not reliable index of the severity of the disease state (Osborne *et al.*, 1972).

Oxalic acid crystals in the urine may indicate ethylene glycol toxicity as etiology of renal failure (English, 1974).

DiBartola *et al.* (1980) suggested that the consistent presence of protein indicate glomerular damage or inflammation in the lower parts of the urinary tract.

Many of the changes seen in urine are related to non-renal urinary tract diseases or pre-renal conditions (Doxey, 1983).

Renal proteinuria may occur in nephritis, in which it is a direct result of the increased permeability of the glomerular filtrate. Acute generalized nephritis results in a marked proteinuria and the presence of casts in voided urine. A wide variety of conditions may culminate in proteinuria. In general proteinuria points to a urogenital tract abnormality and may be a sensitive index of the presence of such abnormalities. The presence of casts in the urine usually indicate a pathologic change in the kidney. If casts are present in large numbers, it is always an indication of renal disease. Crystals in the sediment of animal urine seldom have any clinical significance. Calcium oxalate and

hippuric acid may be present but are less common. Large number of calcium oxalate and hippuric acid may be present but are less common. Large number of calcium oxalate in the urine of animals with renal failure may suggest ethylene glycol toxicity (Coles, 1986).

2.1.6 Hematology

In naturally occurring cases of uremic interstitial nephritis McIntyre (1954) noted the presence of anaemia in 57 per cent was chronic renal failure and in 20 per cent of animals suffering from the most severe form of the primary renal failure.

The occurrence of anemia in chronic renal disease is well recognized and experimentally by means of nephrectomy a relationship between renal failure, anaemia and uremia has been defined (Naets, 1963).

Bentinck-Smith (1969) presented the normal hematological values in dogs as follows. Hemoglobin (Hb) 12-18 (15) g per cent; packed cell volume (PVC) 37-55 (45) per cent; erythrocytes (RBC) 5.5-8.5 (6.8) million/cumm; total leucocyte count (WBC) 6000-17000/ cumm; segmented neutrophils 3000-11500 (7000)/cumm; eosinophils 100-1250(550)/cumm monocytes 150-1350(750)/cumm and lymphocytes 1000-4800 (2800)/cumm.

Generalized renal diseases are usually associated with physiological leukocytosis and lymphopenia (Osborne *et al.*, 1972).

A nonregenerative normocytic normochromic anaemia often observed in association with chronic renal failure (Osborne *et al.*, 1972; Schalm *et al.*, 1975; Finco,1980).

A complete blood count can help to determine the presence of chronic renal failure and inflamatory renal desease. Anaemia is commonly associated with chronic renal failure (Cowgill, 1983).

Dibartola *et al.* (1985) recorded leucocytosis (23000/μl) with neutrophilia (20060/μl) and a left shift (2100 band cells/μl) in acute renal failure due to ethylene glycol ingestion.

Hematology may show a strees picture with mature neutrophilia in post renal azotemia due to uroperitoneum. Packed cell volume and plasma proteins may be elevated due to intravascular dehydration in uremia (Chew and DiBartola, 1986).

Among many other host defense mechanisms granulocyte chemotaxis has been shown to be impaired in the uremic state. It has been reported that the generation of chemotactic factors is deficient in uremic serum. Defective chemotaxis perse may be the cause for increased susceptibility to infection (Modai *et al.*, 1988).

Rachel (1988) recorded the following haematological values in apprently healthy mongrel dogs: hemoglobin 10.45 $\pm$ 0.33 g per cent, erythrocytes 5.20 $\pm$ 0.29 million/μl and packed cell volume 34.47 per cent.

McCaw *et al.* (1989) opined that renal failure accompanied by a neutrophilia with left shift was suggestive of pyelonephritis.

Robinson *et al.* (1989) reported the hematological values in chronic renal desease in Bull terriers as follows: PCV 35V/L-, Hb 130g/L, WBC-17208/μl, Band neutrophills -70/μl, segmented neutrophills-13772/μl, Lymphocytes 1430/μl, Monocytes-1154/μl and eosinophils-720/μl.

2.1.7 Blood Biochemistry

2.1.7.1 Blood urea nitrogen and creatinine

An increase in blood urea and symptoms mimicking chronic nephritis were found by Prevot and Dumas in 1821 in nephrectomized animals and in 1853 Jaccoud proposed creatinine as the toxin of uremia (Schreiner and Maher, 1961).

Jackson (1964) opined that blood urea and blood urea nitrogen (BUN) were the best indices of the amount of toxic products retained in the body as a result of malfunctioning of kidneys. Normal values in the dogs were 40 mg/dl or less of blood urea and 20 mg/dl or less of BUN. In different types of uremias the abnormal level of BUN were at the range of 80 to 380 mg/dl. Plasma creatinine values were helpful in the prognosis of uremia. Normal creatinine values for the dog was 1 to 2 mg/dl; 2 to 5 mg/dl-guarded; 5 to 7 mg/dl - poor prognosis and above 7 mg/dl-unfavourable prognosis.

Plasma creatinine values in the normal dog fall within the range of 1.0-2.0 mg/dl. Creatinine levels of 4 to 5 mg/dl were considered indicative of

serious renal damage and levels above 7.5 mg/dl were critical (Richards and Hoe, 1967).

Tabotabo *et al.* (1970), recorded BUN values ranging from 47 to 70 mg/dl with a mean of 61.5 mg/dl in urethral obstruction of dogs.

BUN values exceeding 45 mg/dl indicate diminishing glomerular filtration rate (Osborne *et al.* 1972).

English (1974) opined that in acute renal failure a daily increase in BUN of less than 10 mg/dl of plasma would indicate mild catabolism and likelihood of recovery even with conservative treatment. A daily increase of BUN of 10 to 30 mg/dl would indicate moderate and over 50 mg/dl severe catabolism, necessitating active treatment including dialysis.

Finco and Duncan (1976) reported the elevated mean BUN values of 89 $\pm$ 11.8 mg/dl, 140 $\pm$ 11.6 mg/dl and 194 $\pm$ 15.3 mg/dl and mean serum creatinine values of 2.4 $\pm$ 0.4 mg/dl, 4.9 $\pm$ 0.3 mg/dl and 9.1 $\pm$ 1.2 mg/dl in pre-renal, renal and post-renal uremia, respectively in dogs.

Macdougall *et al.* (1977) reported increased level of blood urea and serum creatinine as 76 μmol/L and 964 μmol/L, respectively in a chronic case of renal failure with vomiting, diarrhoea and weight loss over a period of two months.

Urea is a small molecule (molecular weight-60 dalton) that diffuses readily through out all body fluid compartments. Because its concentration is

equal in intracellular and extracellular fluid, its concentration is similar in whole blood, plasma and serum (Dunegan *et al.*, 1978).

If the kidney is diseased or malfunctioning or if the glomerular filtration rate is reduced because of extra renal factors such as dehydration and shock, then the rate of urea excretion will fall and the circulating urea will rise. An increased rate of protein catabolism also increases urea level. The measurement of circulating urea and creatinine level is a simple means of measuring approximately the glomerular filtration rate. The normal level of blood urea in dog is 3 to 7.5 mmol/L. A 50 per cent reduction in GFR will raise the dogs circulating urea level to about 10 mmol/L, while a 75 per cent reduction will raise the level to around 20 mmol/L (English *et al.*, 1980).

According to Doxey (1983) elevated blood urea levels above 10 mmol/L should be regarded as indicative of some impairment of renal function. Levels above 20 mmol/L was considered serious and above 50 mmol/L as extremely serious. He has also stated that high blood urea level did not always indicate renal damage as in the case of dehydrated animals, where blood urea level above 30 mmol/L can occur when the kidneys are histologically normal.

Finco (1980) stated that creatinine is a larger molecule than urea (Molecular weight-113 dalton) and itistherefore diffused through out fluid compartments more slowly than urea. Creatinine was formed during muscle metabolism and were not reutilized as urea. So the blood creatinine level could be used as a measure of GFR. Normal serum level depended on the level of muscular activity, but was usually in the range of 70 to 160 μmol/L. Levels above 180 μmol/L indicated that GFR was reduced.

The kidneys are a major route of excretion of creatinine from the body. As with BUN any abnormality that decreases GFR will cause an increase in the serum concentration of creatinine. Concentration of serum creatinine is affected by fewer variables than BUN. When the concentration of creatinine exceeds 1.2 to 2.0 mg/dl of plasma or serum, GFR is reduced. As with BUN the reduction in GFR may be caused by pre-renal, renal and post-renal uremia (Osborne and Polzin, 1983).

Dibartola *et al.* (1985) reported the elevation of BUN to 120 mg/dl and serum creatinine to 12 mg/dl in acute renal failure due to ethylene glycol.

Robinson *et al.* (1989) recorded elevated blood urea levels of 14 to 160 mmol/L with an average of 67 mmol/L and creatinine levels of 260 to 1,178 μmol/L with an average of 699 μmol/L in chronic renal disease of Bull terriers.

Srinivasan (1990) reported elevated values of blood urea in chronic renal insufficiency, acute renal insufficiency, nephrotic syndrome and experimentally induced renal insufficiency as 78.18 $\pm$ 7.06 mg/dl, 102.34 $\pm$ 17.46 mg/dl, 98.67 $\pm$ 40.70 mg/dl and 57.14 $\pm$ 6.4 mg/dl, respectively. The corresponding serum creatinine values were 4.56 $\pm$ 0.73 mg/dl, 4.63 $\pm$ 1.29 mg/dl, 3.20 $\pm$ 1.91 mg/dl and 3.42 $\pm$ 0.6 mg/dl, respectively.

According to Clement (1991) the blood urea values in pre-renal, primary renal and experimentally induced uremia were 131.17 $\pm$ 16.60 mg/dl, 134.4 $\pm$ 20.18 mg/dl and 103 $\pm$ 7.1 mg/dl, respectively. The serum creatinine

values were 2.95 ± 1.41 mg/dl, 4.36 ± 1.78 mg/dl and 4.6 ± 1.85 mg/dl, respectively.

2.1.7.2 Total Protein

Wiseman *et al.* (1980) stated that serum protein levels were reduced in a wide variety of diseases including the various types of glomerulonephritis, amyloidosis and nephrosis. They explained that total serum protein levels were reduced due to urinary protein loss.

A low serum protein level in the absence of excessive protein loss in the urine is not indicative of renal diseases and it may result from a vide variety of other diseases (Hall, 1983).

Srinivasan, (1990) reported low levels of total serum protein in chronic renal insufficiency, acute renal insufficiency, nephrotic syndrome and experimentally induced renal insufficiency to be 5.24 ± 0.22 g/dl, 5.11 ± 0.27 g/dl, 4.62 ± 0.32 g/dl and 5.58 ± 0.30 g/dl, respectively.

Clement (1991) recorded low total protein values in pre-renal uremia and primary renal uremia.

2.1.7.3 Sodium, Potassium and chloride.

Hyperkalemia is a common finding with anuric renal failure and has great clinical significance because of the role of this ion in neuromuscular transmission. Intracellular to extracellular shifts in potassium that occur in

association with metabolic acidosis may also contribute to the hyperkalemia (Hoff *et al.*, 1941).

Plasma concentrations of the electrolytes sodium, potassium, chloride, bicarbonate and magnesium are likely to alter at some stage in the course of acute renal failure. The normal plasma sodium concentration is about 43 $\pm$ 5 mEq/L although considerable variation has been reported in the normal dog (Hoe and O'shea, 1965).

The plasma concentration of potassium must elevate to some extent from the normal value of 4.3 $\pm$ 0.8 mEq/L in acute renal failure (Pits, 1968).

English (1974) stated that hyponatremia tended to develop most rapidly in the oliguric phase and it was usually accompanied by a hyperkalemia. A fall in the sodium concentration to 130 mEq/L or lower might result from sodium shifting intracellularly and water shifting extracellularly and if vomiting and diarrhoea occured the extra renal loss of sodium resulted.

In cats with urinary obstruction metabolic acidosis, mild hypernatremia, hyperkalemia, hypermagnesemia, hypercalcemia, hyperphosphatemia and hypoproteinemia were usually accompanied the azotemia. In dogs with bladder ruputre hyperkalemia, marked hyponatremia, hypochloremia, and compensated metabolic acidosis were reported (Burrows and Bovee, 1974; 1978; Finco and Cornelius, 1977).

During the progression of chronic renal failure, a defect in renal tubular reabsorption of sodium occurs and progresses in parallel with decrease in GFR.

This defect in sodium reabsorption was manifested clinically by polyuria, hypotonic urine and compensatory polydipsia. The loss of urinary sodium was always associated with urinary water loss which lead to dehydration and aggravation of azotemia by further reducing GFR. In addition loss of sodium was accompanied by a urinary loss of bicarbonate which may lead to metabolic acidosis in the late stage of renal failure (Bovee, 1976).

The most common cause of hyponatremia is chronic interstitial nephritis. The renal tubular damage results in loss of sodium resorption and thus loss of fluid. In addition there may be reduction in excretion of potassium and hydrogen ions. In pre-renal and post-renal uremia hyperkalemia is quite frequently seen. Once the plasma potassium values rise above 6.5 mEq/L cardiac arrhythmias will appear (Rose *et al.*, 1977). DiBartola *et al.* (1985) recorded hyperkalemia (5.6 to 8.9 mEq/L), hyponatremia (126 to 139 mEq/L) and hypochloremia (90 to 102 mEq/L) in acute renal failure due to ethylene glycol ingestion.

Robinson *et al.* (1989) reported the mean values of sodium and potassium to be 147 mEq/L and 4.8 mEq/L, respectively in chronic renal disease in Bull terriers.

2.2 EXPERIMENTAL INDUCTION OF UREMIA

A vast number of substances have been indicated as causing renal diseases. The overwhelming majority of these produce primarily a tubular or interstitial lesion (Schriner and Maher, 1965).

Kersting and Nielson (1966) induced experimental ethylene glycol poisoning in the dog by oral administration of ethylene glycol at the dose rate of 6.6 ml/kg body weight.

Ethylene glycol toxicosis involves alcohol dehydrogenase dependent oxidation of ethylene glycol to metabolites which results in acidosis and cytotoxicosis. Oxalic acid is the primary toxic intermediate producing tubular epithelial cell necrosis and intratubular obstruction secondary to calcium oxalate crystal deposition (Bovee, 1966; Cowgill, 1984).

The chemical poisons like mercuric chloride produces toxic tubular necrosis. The irritant toxic substance acts directly and without any previous hypersensitization to produce fatty changes and necrosis of delicate epithelial cells lining the tubules (Smith *et al.*, 1972).

Thrall *et al.* (1984) reported the clinico pathological findings in dogs and cats with ethylene glycol intoxication. Common clinical signs were ataxia, depression, vomiting and hypothermia. Characteristic alterations in the hemogram and serum chemical profile included neutrophils, lymphopenia, azotemia, hyperphosphatemia and decreased whole blood bicarbonate. Urinalysis findings included isosthenuria, proteinuria, hematuria, calcium oxalate and hippurate crystalluria and the presence of renal epithilial cells, white blood cells and granular and cellular casts in the urine sediment.

Srinivasan (1990) induced renal failure by administration of mercuric chloride intravenously at the dose rate of 2 mg/kg body weight as a two per cent solution.

2.3 HISTORY OF DIALYSIS

The first dialysis experiments on living animals were performed by Abel Rountree and Turner in 1913. Nephrectomized dogs were treated by dialysis as early as 1938 by Thalheimer (Wing and Magowan, 1975). Dialysis as a treatment of uremia is at least as old as ancient Romans, who discovered that steaming hot bath could remove uremic substances from the body (Schlesinger, 1980). The instillation of fluid into the peritoneal cavity for the purpose of dialysing was first performed on animals by Wegner in 1877 (Flamenbaum and Hanburger, 1982).

The term dialysis was coined by Thomas Graham, a scot chemist during his studies on semipermeable membrane. When using albumin coated parchment, he determined that only crystalloid material diffused through the parchment membrane into the surrounding water. Reporting this findings in 1854 he had the vision to add that they might have an application to medicine. Now over 130 years later dialysis has become a widely established technique for the management of patients with renal failure (Davison, 1988). Over the years four methods of extrarenal removal of waste products have been tried, mostly in the field of human medicine. 1. Exchange tranfusions-total exsanguination and replacement of blood. 2. Gastro-duodenal suction and the production of diarrhoea. 3. Hemodialysis, sometimes called VIVO-dialysis - the use of the artificial kidnev. 4.Peritoneal dialysis (Jackson, 1964).

2.4 PRINCIPLES OF DIALYSIS

Diffusion is the movement of molecules and ions by their random thermal movements. When two parts of a system possess different concentration of solutes, a concentration gradient exists (Fig.1). Diffusion will result in net transfer of solute from the compartment of higher concentration of solute to the compartment of lower concentration (Butler, 1968).

Dialysis was defined as the transfer of substances across a semipermeable membrane by diffusion (Ash, 1980).

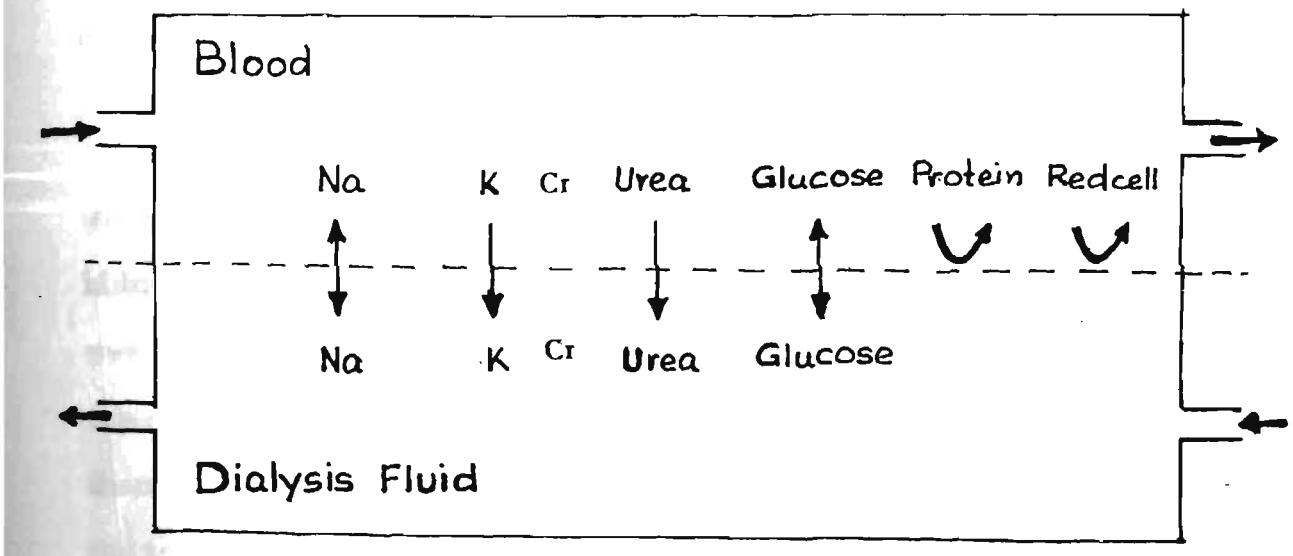
In clinical medicine dialysis can be defined as the clearance of solutes from the plasma into a dialysate solution across a semipermeable membrane (Gordon, 1983).

2.5 INDICATIONS FOR DIALYSIS

Bliss *et al.* (1931) were able to keep bilaterally nephrectomized dogs alive for 13 to 16 days with the use of peritoneal dialysis as compared to 3 days for the untreated controls.

Wear *et al.* (1938) reported that in normal dogs more urea could be removed from the blood by dialysis than was excreted by the kidneys in the same period. Seligman *et al.* (1946) prolonged the life of nephrectomized dogs upto 13 days with dialysis. They concluded that peritoneal dialysis was 40 to 75 percent as effective as normal kidney function in clearing urea from the blood.

Fig. 1 PRINCIPLES OF DIALYSIS



(Gordon, 1983.)

Grollman *et al.* (1951) were able to keep nephrectomized dogs alive for 70 days by employing peritoneal dialysis.

Kirk (1957) reported that dogs have been kept alive as long as 111 days by intermittant peritoneal lavage, which served as a substitute for the excretory, but not the metabolic functions of the kidneys. In acute uremia lavages were useful following severe crush injuries, nephrotoxic poisonings, tubular necrosis, sulfonamide crystalluria, acute nephritis, leptospirosis and intoxication with bromides, salicylates and barbiturates.

Peritoneal dialysis was indicated in all cases of uremia in dogs except that in which there was already overwhelming and irreversible damage of the kidney. It was most useful in acute uremias precipitated by stress. Dialysis was useful in uremia due to urethral obstruction of long standing. In such cases dialysis could be used to reduce the uremia rapidly prior to surgery, thereby decreasing operation risk. Dialysis has been shown to be of value in the treatment of uremia due to renal insufficiency caused by infection such as leptospirosis. It was a temporary means of eleminating the waste products of metabolism until such time as the renal function was restored (Jackson, 1964).

Osborne *et al.* (1972) stated that peritoneal dialysis is indicated in acute renal failure, chronic renal failure, over hydration and intoxication of drugs like barbiturates, digoxin, arsenic, sulphonamides etc.

Hemodialysis was found to be effective and efficient means to control many of the metabolic disturbances of acute uremia. The ideal candidate for hemodialysis in Veterinary Medicine is the acute renal failure patient that

cannot be managed by conservative measures alone. Biochemical and metabolic upsets could be normalized in hours, in contrast to peritoneal dialysis in which 24 to 48 hours continuous exchange was necessary to effect a comparable degree of improvement. Nephrectomized acutely uremic dogs were kept in satisfactory health for 26 days with alternate days of hemodialysis (Cowgill and Bovee, 1975; Cowgill, 1980.

Macdougall *et al.* (1977) have successfully carried out hemodialysis in an acutely uremic dog and according to them hemodialysis as an emergency procedure might have application in cases of acute renal failure and acute poisoning.

In dog and cat, peritoneal dialysis was indicated for life support when renal function was insufficient to excrete non-protein nitrogenous wastes and conservative management has failed to control the signs and symptoms of uremia (Thornhill, 1981).

According to Schmitt and Bach (1982) dialysis could be of potential value in a great variety of circumstances viz.

a) acute renal failure
b) end stage renal failure
c) moderate renal failure (Plasma creatinine of 4 to 8 mg/dl)
d) fluid over-load
e) metabolic acidosis or alkalosis
f) hyper or hypocalcemia
g) hyperkalemia

h) drug intoxication and

i) poisoning with methanol, ethylene glycol, carbon-tetrachloride, etc.

A bilaterally nephrectomized dog was successfully supported with peritoneal dialysis for 54 days using a radially new design access catheter and a human dialysis schedule designated as continuous ambulatory peritoneal dialysis (Thornhill *et al.*, 1984).

Shahar and Holmberg (1985) recommended the dialysis for patients with acute reversible renal failure, during the period of compromised renal function. This procedure avoids the progressive uremic state and allows the kidneys to regenerate and regain their function.

DiBartola *et al.* (1985) reported that dogs with established acute renal failure due to ethylene glycol ingestion could be maintained by hemodialysis for long periods.

In animals with acute or chronic renal failure peritoneal dialysis allows removal of waste products. Peritoneal dialysis can be used to sustain life in the azotemic patients until renal function returns to normal or substantially improves, until results of renal biopsy can be evaluated for prognosis and further treatment. It can also be used to remove toxins such as ethylene glycol and its metabolites (Crisp *et al.*, 1989).

Hemodialysis was an effective form of therapy for small animals with renal failure which did not respond to fluid therapy and medication (Takeda, 1992; Tani, 1993).

2.6 HEMODIALYSIS

In hemodialysis processed cellulose capillaries serve as semipermeable membrane for hollow fiber kidneys. Around the capillaries, rapid counter current flow of dialysate interfaces with blood establishing diffusion gradients for removal of uremic wastes. Hemodialysis is an effective therapeutic modality for oliguric acute renal failure in the dog (Thornhill, 1981).

Hemodialysis is the process of diffusion of substances across a semipermeable membrane, to or from blood. Hemodialysis substitute for some of the excretory functions of the diseased kidney without providing any of the hormonal function of that organ. It is a standard technique for the management of acute renal failure and end-stage renal disease in human (Dhein, 1981).

In hemodialysis an extracorporeal system is utilised to provide semipermeable membrane through which dialysis can occur. It incorporates five separate components viz. 1) the patient 2) dialysis delivery system 3) the dialyzer 4) blood access and canula and 5) dialysate solution (Parker, 1981).

2.6.1 Dialysis delivery system

The function of the dialysis delivery system is to prepare and deliver the dialysate fluid to the dialyzer at the proper composition, pressure and

temperature. The proportionating system automatically prepares the dialysate from the premixed aqueous concentrate by continuous dilution of the concentrate in the ratio of 1 to 35 with tap water (Parker, 1981).

Dhein (1981) has described three different types of delivery systems viz. recirculating, single pass and recirculating-single pass delivery systems. In recirculating system, the dialysate that contacts the dialysis membrane does not contain any waste products, but the waste product concentration gradually increases as the fluid recirculating through the system. In single pass system, fresh dialysate is always presented to the extracorporeal kidney for the largest concentration gradient between the blood and dialysate. In the third type recirculating single pass, a small volume of dialysate may be regenerated by running through a sorbent cartridge. The dialysis delivery system unit is also provided with a blood pump (a roller pump), a heparin pump, ultrafiltration facility and monitoring devices to prevent technical errors.

The dialysis delivery system is a sophisticated monitoring device to ensure that water and the dialysate concentrate are mixed in appropriate proportion. This solution is then deaerated, warmed to 38°C and passed through the dialyzer at a flow rate of 500 ml/min. In addition the dialysis machine will ensure that the blood flow is maintained at a constant rate. Machine is fitted with fail safe devices where by the dialysis procedure is stopped should any of the monitored parameters fall outside the normal limits. All machines are fitted with audible and visual alarms so that any fault can be readily detected and corrected. In this way dialysis can be undertaken safely even in the sleeping patients (Davison, 1988).

2.6.2 Dialyzer (artificial kidney)

The first clinically successful artificial kidney was developed by Wilhelm J.Kolff, a Dutch physician. His rotating drum device, a prototype for the present day artificial kidney was developed in the early 1940 (Schlesinger, 1980).

Three major types of artificial kidneys are available, viz. plate coil and hollow fiber dialyzers. Plate dialyzer consists of parallel cellophane sheets with membrane support between them to restrict the amount of blood filling the packages. Plate dialyzer have low internal dialysate volume and require relatively low dialysate flow rates. In coil dialyzer blood enters a long spiral cellophane tube which is wrapped around a porous screen over a plastic core. Blood enters the spiral from inside of the coil and exits from the outside. Hollow fiber dialyzers are comprised of 10000 to 20000, 200 μ hollow fibers enclosed in a cylinder case (Ash 1980; Parker 1981).

Most membranes of artificial kidneys were constructed from cellulose which is the matrix of plant walls. The cellulose was regenerated from solution into sheets or tube of 11 to 17 μ thick (Ash, 1981).

The average pore size of cellulose membrane is 50 A. Small molecules less than 300 dalton pass through the pores. The total membrane surface area of dialyzers are varied from 0.5 to 2.5 M^2 (Henderson, 1979).

Ash (1981) reported that large proteins and blood cells were rejected while small molecules such as urea (60 dalton) and creatinine (113 dalton) cross easily through the membrane pores.

Thornhill (1981) stated that the hollow fiber artificial kidney has a long membrane surface area with many pores, but a small mean-pore radius specially designed for clearance of small molecules such as urea, creatinine, sodium, potassium and phosphorus. On the other hand the peritoneal membrane has fewer pores but a large mean pore radius, which allows the clearance of larger molecular weight substances like proteins.

Pediatric dialyzers with a fill volume of 10 to 50 ml and pediatric blood lines with fill volume of 30 ml are available for the dialysis of small animal patients (Dhien, 1981). DiBartola *et al.* (1985) used 0.6 M^2 hollow-fiber artificial kidney and a single pass hemodialysis delivery system with counter current flow of blood and dialysate for the hemodialysis of a dog with acute renal failure. The blood flow as adjusted to 100 to 200 ml/min and dialysate flow to 500 ml/min.

Takeda (1992) successfully performed hemodialysis in dogs with 0.05 to 1.5 M^2 membrane size hollow-fiber dialyzers and in cats with 0.1 to 0.15 M^2 membrane size dialyzers. Blood flow rates were 17 to 100 ml/min in dogs and 10 or 15 ml/min in cats.

2.6.3 Blood Access

In the dog the creation of unilateral external shunts from femoral artery to femoral vein or from common carotid artery to external jugular vein was the approach most commonly used for hemodialysis (Parker *et al.*, 1972; Parker, 1981).

Gourly *et al.* (1973) prepared arterio-venous shunts for hemodialysis between the right carotid artery and the left external jugular vein. Beveled non-stick plastic canulas were inserted into the blood vessels using as large a canula as could be inserted. The canulas were connected to plastic tubing which was passed subcutaneously to the dorsal cervical region just behind the ears of the dog and the tubes were connected over the dorsum of the neck with a non-stick plastic shunt connector. Blood flow was started at a slow rate (approximately 45 ml/min) and kept at this rate for three minutes. Flow rate was increased to 80 ml/min for another three minutes and subsequently was kept at 100 ml/min (approximately 5 per cent of the cardic output of the patient).

Cowgill and Bovee (1975) created blood access using standard Teflon silatic arterio venous shunts. Arterio-venous shunt was surgically introduced into the femoral artery and vein under local analgesia or general anaesthesia. Femoral arterial blood flows through the artificial kidney and dialysed blood returned to the femoral vein through the venous blood line.

Macdougall *et al.* (1977) used a modified 8.3 cm 16 gauge Angiocath for blood access in dog. It was inserted under local anaesthesia into the jugular vein and

was secured with a matress suture. After heparinization of blood circuit the primed 'Y' piece was connected to the catheter and fitted into the clamping device. The blood lines were connected and with the clamps alternating on a four second cycle, flow in the blood circuit was gradually raised to 60 ml/min.

Ash (1980) has stated that because most dialyzers require rapid blood flow rates (100 to 300 ml/min) and large fill volume (90 to 300 ml), canulation of large blood vessel was necessary to perform hemodialysis.

In human medicine the need for the immediate access to the blood circulation was being met for the most part by percutaneous catheterization of the femoral artery and vein. More recently this procedure has been modified to veno-veno hemodialysis, single percutaneous femoral vein puncture using the single needle hemodialysis technique (Schmitt and Bach, 1982). DiBartola *et al.* (1985) conducted hemodialysis in dogs by creating jugular carotid arteriovenous shunt made of silastic tubing with a teflon connector. Artificial kidney used was 0.6 M^2 hollow fiber and blood flow was 100-200 ml/min.

Stertmann *et al.* (1990) created a shunt between the carotid artery and jugular vein using polytetrafluroethylene prosthesis in 12 sheep. Connection to the extracorporeal circulation was achieved via catheters and maintained using a pump with an output of upto 300 ml/min. This enabled extracorporeal circulation for several hours without clinical impairment to the animals. The arterio venous shunt remained functional upto 253 days.

Takedo (1992) performed hemodialysis in four dogs with experimentally induced acute renal failure. Blood was drawn from the saphenous vein and

returned to the cephalic vein. The flow rates were 35 or 50 ml/min and dialyzers were 0.1 to 0.5 M^2 membrane size. In clinical cases, blood was drawn from jugular vein and returned to cephalic vein. Blood flow rates ranged from 17 to 100 ml/min in dogs and 10 or 15 ml/min in cats. He also created three types of internal arteriovenous shunts in experimental dogs as follows : 1) the carotid artery - jugular vein 2) the median artery - the cephalic vein and 3) the femoral artery - the femoral vein.

Tani (1993) reported that in order to obtain a higher flow rate, a 18 gauge winged indwelling needle or 19 gauge needle with side holes was inserted into the cervical vein. By the use of 19 gauge indwelling needle a much higher flow rate of about 4 ml/kg/min was obtained. A flow rate of 3 ml/kg/min was obtained from cephalic vein with 19 gauge indwelling needle. A satisfactory flow rate was obained by blood access of the vein type and there was no necessity for blood access by surgical operation.

2.6.4 Dialysate

Gourley *et al.* (1973) recommended a dialysate solution for dogs having an osmolality of 325 mosm/L with an ionic composition of 145 mEq/L of sodium, 1 mEq/L of potassium, 1.5 mEq/L of magnesium, 2.5 mEq/L of calcium, 48 mg/100 ml acetate and 270 mg/100 ml of glucose. With this dialysate there was virtually no change in the plasma osmolality across the dialyzer and there was no hemolysis during hemodialysis.

Dextrose may or may not be added to dialysate. Dextrose contributes to the osmolality of the solution to achieve a dialysate osmolality equal to that of

plasma and prevent hypoglycemia during dialysis. The chloride level in the dialysate was adjusted to complete the anionic composition of the dialysate. When the sodium concentration was too low excessive sodium loss would result in hypotension (Wing and Magowan, 1975).

Handerson (1976) opined that renal failure patients frequently have increases in total body sodium, hence sodium levels in dialysate fluid would be slightly lower than the serum levels to remove some sodium during dialysis. Hyperkalemia in acute renal failure patients could be corrected by dialysis against potassium free dialysate. Correction of the pH, which accompanies dialysis would reduce plasma potassium, even with little or no loss across the membrane due to potassium movement into the cells.

Either bicarbonate or acetate should be present in dialysis fluid to correct the acidosis in renal failure. Bicarbonate precipitates the calcium and magnesium in a concentrated state if the pH of the solution is alkaline, so it is not ideal for correcting the acidosis. Acetate is metabolised to bicarbonate in the liver and therefore would substitute for bicarbonate in dialysate (Gotch, 1976).

Calcium and magnesium are 56 and 72 per cent protein bound, respectively. The plasma bound portion was not diffusible and did not contribute to the concentration gradient. This must be taken into consideration in preparation of dialysis fluid to prevent hypercalcemia and hypermagnesemia. A small uptake of calcium was desired (Henderson, 1979).

Stone (1980) reported that higher concentration of sodium in the dialysate was associated with increased vascular stability and volume and reduced concentration leads to symptomatic hypotension, so that there has been a trend toward physiological sodium concentration in the dialysate.

Dialysate did not contain urea, creatinine or inorganic phosphorus. There was a concentration gradient for these substances from blood to dialysate. Diffusion occurred down this concentration gradient during dialysis, resulted in a net removal of these substances from the blood. Diffusible substances that were normally low in the blood could be increased by having a higher concentration of these substances in the dialysate, creating a concentration gradient from the dialysate to the blood. There was no net change in concentration of substances present in the blood in normal concentration, if the dialysate contain the same concentration of these substances (Dhein, 1981).

A suitable dialysate solution would include no urea, no creatinine, a low concentration of potassium (2 or 3 m mol/L), and pH of about 7.4 usually maintained by acetate, rather than bicarbonate. Acetate was more suitable and could not precipitate calcium and magnesium. A low phosphate concentration, a sodium concentration of 140 m mol/L and a normoglycemic glucose concentration were ideal for dialysate (Gordon, 1983).

2.6.5 Procedure

Gourley *et al.* (1973) studied the responses of nephrectomized dogs during hemodialysis. Dialysis was done using a dialyzer and a proportining

type dialysate delivery system. Before dialysis the dog was weighed and its movement was restricted to standing by placing it in a sling mounted in a narrow stall. Initial heparinization of the dog was accomplished by intravenously injecting sodium heparin at the dose level of 0.25 mg/kg body weight. Heparinization was continuously maintained by injection of heparinized saline solution (0.1 mg of heparin per 1 ml of saline) into the arterial blood line with an infusion pump at the rate of approximately 0.19 ml/minute. The dialyzer was sterlized by formalin and flushed with a prime solution of 5 per cent dextrose and connected to the arterial and venous sides of the arterio-venous shunt of the dog. Blood flow was started at a slow rate (approximately 45 ml/minute) and kept at this rate for 3 minutes. The flow rate was then increased to 80 ml/min for another 3 minutes and subsequently was kept at 100 ml/minute (approximately 5 per cent of the cardiac output). The temperature of the dialysate entering the dialyzer was automatically controlled to 40°C. This temperature could be adjusted to maintain the body temperature of the dog. A pressure gradient of approximately -100 mm of Hg was maintained across the membrane between the blood and the dialysate. This controlled the movement of water and prevented over-hydration of the dog. A single treatment lasted for 3 to 4 hours, depending on the initial blood solute levels of the dog. At the end of the dialysis the arterial line was disconnected and the dialyzer was flushed with 500 ml of 5 per cent dextose solution, returning the blood from the extracorporeal system to the dog. Subsequently the arteriovenous shunt of the dog was re-established, the dog was weighed and returned to its cage.

Macdougall *et al.* (1977) performed the dialysis with a single catheter technique and using pediatric blood lines. The dialyzer and the blood lines were sterilized with 1.5 per cent formalin. A 1 in 35 dilution of concentrated dialysate was prepared and the fluid circuit primed. The flow of the dialysate was adjusted to 500 ml/min. The 140 ml blood circuit was primed with 0.9 per cent saline. After heparinization (1510 IU) of the blood circuit the blood lines were connected to the catheter and then connected to the clamping device. Blood flow was adjusted to 60 ml/min. Further heparin (1510 IU) was administered at 30 minutes intervals. After three hours of dialysis the arterial line was disconnected and the blood in the extracorporeal circuit returned to the dog alongwith enough saline to keep the patient in overall fluid balance. Finally the catheter was removed, pressure applied to control haemorrhage and the retaining suture tightened.

According to Dhein (1981) the exact format for hemodialysis varies with the equipment available and experience of the operator. The blood lines and kidney were primed with sterile solution (such as Ringer's). The patient was restrained in a standing sling or was recumbent on a table if extremely depressed. The arterio-venous sides were attached to the appropriate blood lines. The blood pump was started slowly. Three thousand units of heparin was injected into the blood line for systemic anticoagulation. Ultrafiltration could be accomplished by applying positive pressure to the blood or negative pressure to the dialysate. Blood flow was maintained at approximately 5 per cent of cardiac output (about 200 ml/minute in a 35 kg dog) and the dialysate flow rate was 500 ml/minute. Each dialysis episode lasted four hours. The frequency and length of each dialysis session was determined on an individual patient

basis. Water balance, sodium balance and level of azotemia as well as patient's clinical condition all play a role in determining the dialysis schedule.

Parker (1981) suggested that for systemic anti-coagulation heparin is infused at a slow constant rate (1500 IU/min) after the dog has been given an intravenous priming dose of 200 U/kg. Clinical experience has shown that when properly cleaned and sterilized, the units would be reused several times, which materially reduces the cost per dialysis.

DeBartola *et al.* (1985) reported the successful hemodialysis of a dog with acute renal failure. Blood access was maintained by a jugular carotid arteriovenous shunt and 0.6 M^2 hollow fiber artificial kidney was used for dialysis. Blood flow was adjusted to 100 to 200 ml/min and dialysate flow 500 ml/min. The dog was given 2000 U of heparin intravenously. Dialysis was performed for 5 hours and after dialysis the effects of the heparin was reversed with 50 mg of protamine sulfate and an aspirin suppository (650 mg). The dog remained oliguric and dialysis was performed 4 hours daily on days 2 to 4.

Tani (1993) reported that systemic anticoagulation was achieved by intravenous administration of a priming dose of heparin at the dose rate 75 to 80 IU/kg and continuous heparinization during dialysis at the rate of 50 to 60 IU/kg/hour into the extraceporeal circuit.

2.6.6 Efficacy of hemodialysis

Hemodialysis was found to be both effective and efficient means to control many of the metabolic disturbances of acute uremia. Biochemical and

metabolic upsets could be normalised in hours. Plasma creatinine, urea nitrogen, phosphorus and potassium concentrations and plasma osmolality were normalised or nearly so with five hours of hemodialysis therapy. Elevated serum potassium concentrations, a frequent cause of death in uremic animals, could be lowered to safe ranges one hour after the start of dialysis. Nephrectomised dog was kept alive in satisfactory health for 26 days with alternate day hemodialysis (Cowgill and bovee, 1975).

Macdougall *et al.* (1977) reported a reduction in plasma urea from 76 m mol/L on day 4 to 37 m mol/L on day 7 corresponded to a fall in plasma creatinine from 964 m mol/L to 619 μ mol/L during hemodialysis. After the dialysis therapy the dog recovered completely and lived for months.

DiBartola *et al.* (1985) have proved that dogs with ethylene glycol poisoning could be maintained by hemodialysis for long periods. Hyperkalemia and hyponatermia were corrected by dialysis and serum osmolality also brought back to normalcy after dialysis.

Takeda(1992)reported that the extraction rate of blood urea nitrogen and creatinine were 13 to 32.1 per cent and 13.3 to 31.3 per cent, respectively when the blood flow rates were 35 to 50 ml/min with 0.1 to 0.5 M^2 dialyzers. When the flow rates were 17 to 100 ml with 0.5 to 1.5 M^2 dialyzers, the extraction rate of blood urea nitrogen and creatinin were 9.6 to 61.3 per cent and 8.8 to 82.4 per cent, respectively.

2.6.7 Complications

Gourley *et al.* (1973) observed a shock like phenomenon characterized by vomiting and collapse occuring during dialysis which responded to 5 to 10 per cent intravenous glucose administration and careful control of blood flow through dialyzer. The value of glucose administration was attributed to its action in countering the tissue catabolism and its effect on keeping potassium within the cell. Without the use of glucose infusion it was not possible to dialyse a dog effectively. Hemolysis was the another complication occured during dialysis. It was due to the osmolality difference between dialysate and uremic plasma, causing hemolysis by relative hypotonicity. By increasing the osmolality of the dialysate to 325 mosm dialysis without hemolysis was achieved. Cowgill and Bovee (1975) reported that any procedure incorporating extracorporeal circulation of blood was subjected to certain technical difficulties and patient risk. Potential patient's risk occured in haemodialysis included haemorrhage, hypotension, hemolysis and embolism.

2.7 PERITONEAL DIALYSIS

The possibility of dialysis using the peritoneal membrane arose at the time when intraperitoneal infusion was used for fluid replacement just as intravenous infusion (Ganter, 1923).

Peritoneal dialysis makes use of the peritoneum as a dialysing membrane. A fluid with an electrolyte content similar to that of plasma is infused into the peritoneal cavity where diffusion takes place between the fluid

and the blood. The fluid is then withdrawn bringing with it some of the toxic waste products of metabolism (Jackson, 1964).

Parker *et al.* (1972) reported that urea and potassium are small molecules and diffused more rapidly through the peritoneum than creatinine and phosphate. In one hour, equilibrium for that fluid exchange is 98 per cent complete for urea and potassium and 60 to 80 per cent complete for creatinine and phosphate.

Nalph *et al.* (1977) stated that solute clearance in peritoneal dialysis was dependent on the molecular size of the substances involved, pore size of the peritoneum, volume, temperature, flow rate of the dialysate and the dialysate composition.

Peritoneal dialysis clears middle molecules (Molecular weight 300 t0 1500 dalton) more efficiently than hemodialysis does (Brown *et al.*, 1978).

Thornhill (1981) reported that continuous ambulatory peritoneal dialysis (CAPD) had proved to be an effective therapeutic modality for short and long term support for dialysis dependent renal failure in dog and cat by making use of a new peritoneal access catheter that efficiently drains the abdominal cavity.

2.7.1 Dialysate

The dialysis fluid is usually an isotonic solution containing 1.5 per cent dextrose and possessing the electrolyte content similar to that of the extracellular fluid. However, by addition of more dextrose (upto 7 per cent) hypertonic solution can be produced which is stated to be more efficient in

removing waste materials. Glucose is added to vary the osmolality of the solution and to provide some calories which help to prevent further catabolism of tissue protein. The choice of the tonicity of the solution depend upon the degree of hydration of the patient and the degree of uremia present. Hypertonic solutions will remove more waste products from the blood. They should be used with caution, since they will cause water to move from extracellular fluid into the dialysate and the resultant electrolyte imbalance may be dangerous to the dog. A solution of 4.5 per cent dextrose will accomplish rapid reduction of blood urea nitrogen and simultaneous administration of 1.5 per cent dextrose intravenously will assume proper hydration of the patient (Jackson, 1964).

Gross and Macdonald (1967) stated that temperature of the dialysate could effect the intercellular pore size of the peritoneum until the fluid was warmed by body heat. Dialysate warmed to a temperature of 37°C resulted in a 35 per cent greater clearance of urea and creatinine than a dialysate temperature at 20°C.

Thornhill (1981) developed a physiologicaal solution containing concentration of dextrose (1.5 to 4.25 per cent) for osmotic extracellular fluid removal. It did not contain urea, creatinine and other non-protein nitrogenous wastes.

In emergency, lactated Ringer's solution could be used by the addition of 1.5 per cent glucose to adjust the osmolality and sufficient sodium lactate (2G/L) to increase the sodium to physiological levels (Parker, 1981; Crisp *et al.*, 1989).

2.7.2 Procedure

Kirk (1957) administered warm dialysate solution into the peritoneal cavity through a 16 or 18 gauge needle under aseptic condition for the purpose of peritoneal dialysis in a dog. Depending on the size of the dog the volume of the fluid injected was 400 to 2000 ml. After two hours the solution was withdrawn. The rinsing or lavage procedure was repeated two or three times a day for three or four days.

According to Jackson (1964) the success of the technique depends upon removal of fluid in amounts approximating those injected. An area 2 to 3 inches posterior to the umbilicus slightly to the right of the midline was prepared aseptically for peritoneal dialysis. The bladder was emptied prior to the start of the procedure. A 12 gauge hypodermic needle was inserted with a pushing motion into the peritoneal cavity under local analgesia. The previously warmed dialysis fluid was administered through the tubing until the abdomen was moderately distended. Depending on the size of the dog and obesity, the volume of fluid required was 700 to 1500 ml. Then the needle was left in place, the tube clamped off and dog held in place for 30 minutes. After 30 minutes the fluid was drained out and measured. In severe cases of uremia dialysis was performed twice daily. However, in many cases, once a day was sufficient to keep the animal compensated.

Tabotabo *et al.* (1970) chosen the same site on the abdomen as that of previous author and the needle used was a 16 gauge hypodermic. Volume of fluid injected was 500 to 750 ml depending on the size of the animal and dwelling time was 45 minutes.

Osborne *et al.* (1972) used commercial peritoneal dialysis catheters and dialysate solutions meant for human patients. The catheter was moistened with heparin to prevent occlusion of the catheter with fibrin. The dwelling time maintained was 30 to 60 minutes. Patients with severe uremia required five or more exchanges per day in order to control signs.

Multiperforated polythene catheter was passed into the peritoneal cavity and the fluid administered was at the rate of 70 to 100 ml/kg body weight (Maruthy, 1982).

The dog was confined in lateral recumbency during dialysis. Heparin was infused at the rate of 250 units/L to prewarmed commercially available dialysis fluid. The abdominal tunic was punctured by using a trocar of 4 mm diameter and the catheter was pushed inside (Dighe *et al.*, 1990).

Clement (1991) performed peritoneal dialysis using commercially available dialysis fluid and the catheter meant for human being (Peritocat catheter). A nick was made with 11 size surgical blade on the abdomen 3 cm behind the umbilicus slightly on the right side on the mid-line under local analgesia. A sterile 15 gauge needle was introduced through the nick and about 200 ml of fluid was administered into the peritoneum. Then the needle was removed and the catheter with stylet was pushed into peritoneal cavity. The stylet was withdrawn and the catheter was secured in its place by purse string sutures. The dialysis fluid was again administered into the peritoneum and allowed to dwell for 30 to 45 minutes. After the dwelling time the fluid was removed through the catheter. This cycle was repeated 3 to 4 times according to the uremic status of the animal.

Crisp *et al.* (1989) reported that fifteen dogs were dialyzed using a column disk catheter and 10 dogs and 2 cats were dialyzed by use of free floating feeding catheters. All the catheters were surgically inplanted under general anaesthesia. Ringer's lactate with 1.5 per cent dextrose was used as dialysis fluid. Heparin at the rate of 1000 IU/L was added to the dialysate solution. The number of exchange per day was tailored to each animal's needs and varied from 6 to 24 exchanges/day using a continuous ambulatory peritoneal dialysis system. The volume of dialysate per exchange was approximately 40 ml/kg body weight.

Thornhill *et al.* (1984) reported that a bilaterally nephrectomized dog was successfully supported with peritoneal dialysis for 54 days using a radially new design of access catheter (immobilized disk) and an automated peritoneal dialysis machine.

2.7.3 Efficacy

Kirk (1957) stated that intermittent peritoneal lavage was a practical clinical procedure which could be used as a temporary substitute for the excretory functions of the kidney. By repeated peritoneal lavage for two to three times a day in a uremic dog, a concentration of blood urea nitrogen of 275 mg/100 ml could be cleared and the recovered lavage solution had a concentration 225 mg/100 ml of urea.

Jakson (1964) recorded that by intermittent peritoneal dialysis in four different types of uremic cases, the blood urea nitrogen level was brought down from 135 mg to 40 mg/di after two days of dialysis; from 180 mg to 100 mg/dl

after 8 days of dialysis; from 380 mg to 70 mg/dl after 7 days of dialysis and from 160 mg to 45 mg/dl after 4 days of dialysis respectively. Serum creatinine was recorded in two cases only and it was lowered from a level of 5.13 mg to 1.52 mg/dl after fifth day of dialysis and from 3.75 mg to 0.75 mg/dl after eighth day of dialysis, respectively.

Tabotabo *et al.* (1970) reported that peritoneal dialysis has successfully eleminated the accumulated toxic products in the blood of uremic patients. A high blood urea nitrogen level of 61.5 mg per cent was lowered to 36.9 mg per cent after 4 hours of dialysis. On subsequent dialysis it was again reduced to 20.8 mg per cent. Uremic symptoms like anorexia, retching and vomiting have declined after peritoneal dialysis.

Parker (1981) recorded that equilibrium of urea and potassium was 98 per cent complete by the end of the first hour and over 90 per cent complete after the first 40 minutes. Therefore for these substances it was of little value to leave the dialysate in the abdomen for longer than half an hour. Creatinine and phosphate molecules are larger than urea and diffuse at slower rate. Consequently 80 per cent equilibrium level was not reached until the end of the first hour and equilibration did not occur until after two hours and he opined that a period between 40 minutes and one hour was optimal for removing urea, potassium, creatinine and phosphate.

A bilaterally nephrectomized dog was remained active and alert for 54 days with a stabilized blood urea nitrogen of 30 to 40 mg/dl and a serum creatinine concentration of 4 to 6.5 mg/dl by ambulatory peritoneal dialysis (Thornhill *et al.*, 1984).

Crisp *et al.* (1989) recommended that peritoneal dialysis, although associated with a high complication rate, was a successful technique for reducing azotemia in dogs with acute and chronic renal failure. A clearance rate at the range of 15.13 per cent to 64.68 per cent for blood urea nitrogen and a range of 27.74 per cent to 56.16 per cent of serum creatinine was recorded in peritoneal dialysis in acute and chronic renal failures.

2.7.4 Complications

Ribot *et al.* (1966) reported that the complications of peritoneal dialysis were moderate to severe haemorrhage, fever, peritonitis, positive or negative water balance and hypokalemia.

As in man the major complication in the dog was peritonitis. Although the incidence of peritonitis was higher, when the peritoneum was punctured repeatedly for dialysis, infection of peritoneal membrane still is recognized as one of the leading causes for peritoneal dialysis failure (Thornhill and Riviere, 1983).

Thornhill *et al.* (1984) observed that the problems encountered in peritoneal dialysis were peritonitis, anorexia, and significant loss of protein. Protein loss coupled with anorexia resulted in a catabolic state in animals.

The most common complication of peritoneal dialysis was hypoalbuminemia and peritonitis (Crisp *et al.*, 1989).

Materials and Methods

CHAPTER III

MATERIALS AND METHODS

The study was conducted in the Department of Clinical Medicine and Therapeutics, Madras Veterinary College, Madras over a period of nine trimesters. Dogs which were attending the small animal clinic of Madras Veterinary College Hospital with renal failure and the experimental dogs selected from the Madras city corporation lethal chamber were utilised for this study.

3.1 DESIGN OF STUDY

3.1.1 Classification of animals

3.1.1.1 Experimental animals

Thirty apparently healthy non-discript adult dogs were subjected to experimental studies. They were divided into three groups based on the type of dialysis therapy.

Group A - six animals control group

Group B - twelve animals hemodialysis group

Group C - twelve animals peritoneal dialysis group.

3.1.1.2 Clinical cases of uremia

Twelve dogs suffering from uremia brought to the Madras Veterinary College Hospital were taken up for this study. They were divided into two groups based on the type of dialysis.

Group 1 - Six animals - hemodialysis

Group II - Six animals - peritoneal dialysis.

3.2 PARAMETERS STUDIED

The following parameters were studied in both experimental and clinical cases.

3.2.1 Clinical Examination

3.2.2 Pathological constituents of urine

3.2.3 Hematology

Hemoglobin (Hb)

Packed cell volume (PCV)

Total Erythrocyte count (TEC)

Total Leucocyte count (TLC)

Differential Leucocyte count (DLC)

3.2.4 Blood biochemistry

Serum Urea

Serum Creatinine

Serum Total Protein

Serum Sodium

Serum Potassium

Serum Chloride

3.3 OUTLINE OF CASE STUDY

3.3.1 Experimental Study

Thirty apparently healthy non-descript dogs selected from the corporation lethal chamber, Madras were divided into three groups, viz., group A-6 animals as control; group B-12 animals for hemodialysis and group C-12 animals for peritoneal dialysis. They were kept under observation for 10 days and subjected to routine physical examination (Boddie, 1969) as well as laboratory investigation with special reference to uremia (Appendix-1). Ethylene glycol was administered orally at the dose rate of 6.6 ml/kg body weight to 15 dogs (Kersting and Nielson, 1966) and Mercuric chloride solution (2%) was administered intravenously at the dose rate of 2 mg/kg body weight to the other 15 animals (Srinivasan, 1990) for the induction of uremia. The animals were subjected to close observation and the following parameters were studied: urinalysis, hematology and blood biochemical profile. When the uremia developed the groups B and C were subjected to dialysis. Hemodialysis was performed in twelve animals of group-B and peritoneal dialysis in twelve animals of group-C. Hemodialysis was repeated after the third day of first dialysis, where as peritoneal dialysis was carried out on alternate days. Pre and post-dialysis urinalysis, hematology and blood biochemistry were conducted. The six animals of group A were not subjected to dialysis. They

were treated only by supportive therapy until their death. Supportive therapy was given to all the 30 animals and it comprised of parenteral administration of Ampicillin sodium @ 20 mg per kg body weight, balanced electrolyte solution and vitamin-B complex.

3.3.2 Clinical study

Ailing animals presented to the small animal clinic, out patient/in patient ward of medical unit, Madras Veterinary College, Hospital were screened for the presence of uremia. Based on the history, physical examination (Boddie, 1969) and laboratory investigation (appendix-1) renal uremic cases were identified and 12 dogs of different breeds suffering from renal uremia were taken up for the clinical study. Hemodialysis/peritoneal dialysis were carried out in these animals with 6 animals for each therapy. Pre and post-dialysis urinalysis, hematology and blood biochemistry were conducted as in cases of experimental study. Supportive therapy was carried out in all the animals.

3.4 HEMODIALYSIS

Hemodialysis is a process by which an extracorporeal system is utilized to provide semipermeable membrane through which dialysis can occur. It incorporate five separate essential components. These include;

1. The patient
2. Dialysis control unit which controls the extracorporeal circulation and supplies and regulates the flow and temperature of the dialysate solution.

3. The Dialyzer
4. Blood tubings and canula for access to the patients vascular system which carry blood from the patient to the dialyzer and back to the patient.
5. The Dialysis control unit.

3.4.1 Dialysis control unit

Dialysis control unit control the extracorporeal circulation and regulate the supply, flow and temperature of the dialysate solution. Cobe centry system-2 (Cobe Laboratories, Lakewood, U.S.A.) (Plate 1) was the Dialysis control unit, used in this study. The dialysis control unit mix the dialysate concentrate with heated aerated water to the desired proportion (1 part of dialysate concentrate to 34 part of water) for the proper functioning of the unit. The mixed dialysate was continuously monitored and controlled for temperature and conductivity. The machine was provided with a blood pump (a peristaltic pump) which can be set at different speeds to alter the rate of blood flow through the dialyzer. The pump switches off automatically and stops the blood flow if the monitoring system detects any fault. Heparin was infused into the blood circuit through a Heparin pump at a rate of 50 IU/Kg/hr for anticoagulation. Blood pressure in the extracorporeal circulation was monitored by the machine. The unit was also provided with an ultrafiltration facility which allowed the operator to efficiently and accurately calculate, predict and control the fluid removal from the patient during dialysis. A monitoring equipment was also incorporated in the control unit to correct technical errors. The monitoring equipment has two types of indication for proper dialysis.

1. An audio visual alarm, which alert the operator for safety and
2. A built in fail-safe component by which the instrument fail to operate in case of any defect in the system.

3.4.2 Dialyzer (artificial kidney)

The dialyzer (artificial kidney) used in the present study was 0.8 m^2 Hollow Fiber Dialyzer (Senko Medical Instruments, Japan) (Plate 2). It comprised of 10000 to 20000 hollow fibers made up of cuprophan enclosed in a cylinder case made up of polycarbamate. Each hollow fiber had a length of 185 mm with a surface area of 0.8 m^2. The wall thickness of the fiber was 8μ, internal diameter was 200 μ and the total priming volume (blood compartment) of the kidney was 47 ml.

The arterial and venous connections (Port) of the dialyzer were fixed on either end of the kidney and it was indicated by red color and blue color, respectively. The blood from the patient enters into the dialyzer through the arterial port and leavesthe kidney, through the venous port. The inlet and outlet for dialysate fluid was also provided on either end of the kidney.

The dialysate fluid was made to circulate outside the hollow fibers in the dialyzer in an opposite direction to that of blood, (counter current) for enhanced driving force for waste exchange. During dialysis the dialyzer was fixed in a vertical position on the stand attached to the machine with the arterial port (red color) on the upper side. The dialyzer can be reused several times if properly cleaned and sterilized with 1.5 per cent formalin.

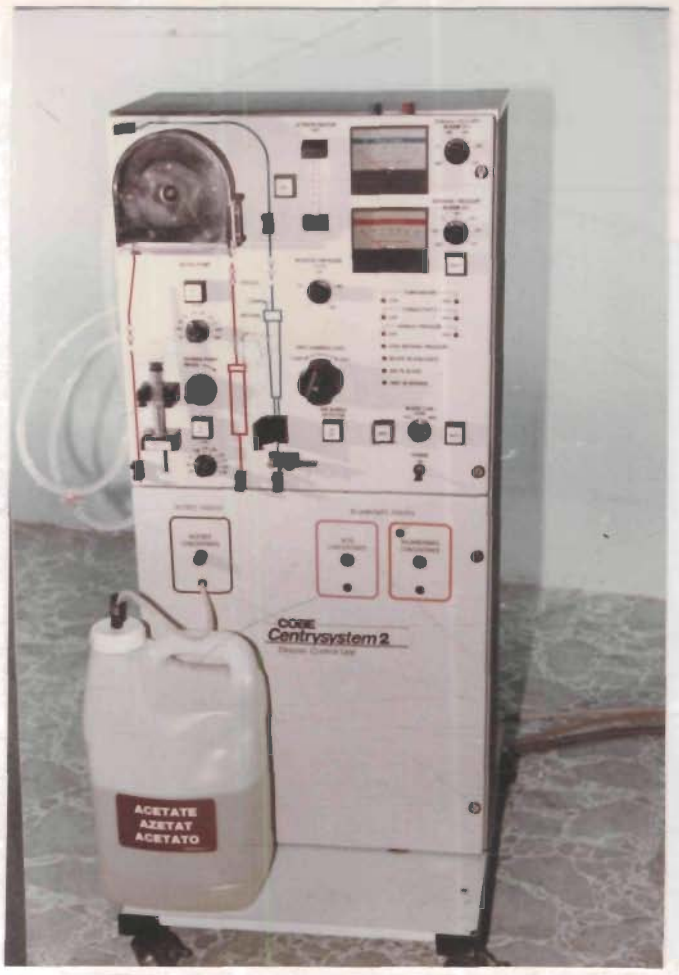


Plate 1. Hemodialysis control unit

Plate 2. Dialyzer (artificial kidney)

3.4.3 Blood tubing and cannula

For establishing the extracorporeal circulation pediatric blood tubing (Hemaflo-Cobe) was used in the present study. For canulation of blood vessels 18 gauge intravenous canula (Venflow-Sweden) was used (Tani 1993).

The blood tubing for hemodialysis comprised of an arterial and a venous tube which could be identified by red and blue color on the tip of the tubes, respectively. The arterial tube was connected between the patient and the inflow port (red color) of the dialyzer and venous tube between the patient and outflow port (blue color) of the dialyzer. The arterial tube was passed through the slots of blood pump and other slots meant for it and venous tube was passed through its respective slots on the machine. After passing through the kidney, the blood was collected in a bubble trap with a filter for clots on the venous line (venous pressure was monitored at the bubble trap) and returned to the patient. Any infusion that may be necessary could be given into either arterial line before the kidney or the venous line at the bubble trap.

3.4.4 Dialysate solution

The concentrated dialysate solution used for the present study was prepared by dissolving analytical grade reagent salts in deionized water. Since tap water used for diluting the concentrate dialysate by the machine, the concentration of electrolytes in the tap water was determined before the preparation of dialysate concentrate. Sodium and Potassium of the tap water was estimated by Emission Flame Photometry; calcium by EDTA Titrimeteric method; Chloride was estimated by Argentimetric method and Magnesium

was determined by Gravimetric method (Rand *et al.*, 1976). The electrolyte concentration of the tap water used for the present study was : sodium 67.40 mEq/L, Potassium 4.2 mEq/L, Calcium-4 mEq/L, magnesium 2 mEq/L and chloride 18.99 mEq/L.

Based on the electrolyte composition of the tap water the concentration of the dialysate concentrate was computed and prepared. The final concentration of the dialysate circulating through the kidney used in this study had the following concentration.

Sodium	145	mEq/L
Potassium	4.2	mEq/L
Chloride	112	mEq/L
Calcium	4	mEq/L
Magnesium	2	mEq/L
Acetate	38-40	mg/L
Glucose	100	mg/L
Osmolality	325	m osm.

Dialysate solution (water and electrolytes) was prepared as a concentrate solution and kept in a 10 litre container infront of the machine. The concentrate dialysate was made to enter into the proportionating pump of the machine through a tube connecting the machine and the container. The concentrate dialysate was mixed with tap water by the proportionating pump at a proportion of 1:35, thereby the concentration of diluted dialysate was

almost equal to the electrolyte composition of the extracellular fluid of the patient and it was made to circulate through the dialyzer. The dialysate fluid travelling through the dialysate line of the machine enter the kidney through the venous dialyzer port (blue color) and left the kidney through the arterial dialyzer port (red color). The dialysate solution coming out from the artificial kidney after dialysis was drained out from the artificial kidney. Approximately 500-600 ml of used dialysate was drained out per minute.

3.4.5 Dialysis

Hemodialysis was performed on twelve experimental and six clinical cases of uremia during this study (Plate 3).

The dialysis control unit was switched on after connecting the water supply and drainage hose into the appropriate position. The dialyzer was fixed on a vertical position on the stand in such a way that the arterial port (red color) of the artificial kidney was on the upper side. Blood tubes and dialysate lines were connected to the respective ports on the kidney and the different slots of the machine. Priming of the dialyzer and blood tubes was done by running normal saline through them.

The patient was restrained on lateral recumbency by sedating the animal by intramuscular administration of xylazine hydrochloride at the dose rate of 2 mg/kg body weight.

For systemic anticoagulation a priming dose of Heparin sodium was administered intravenously at the dose rate of 75 IU/kg body weight. Five

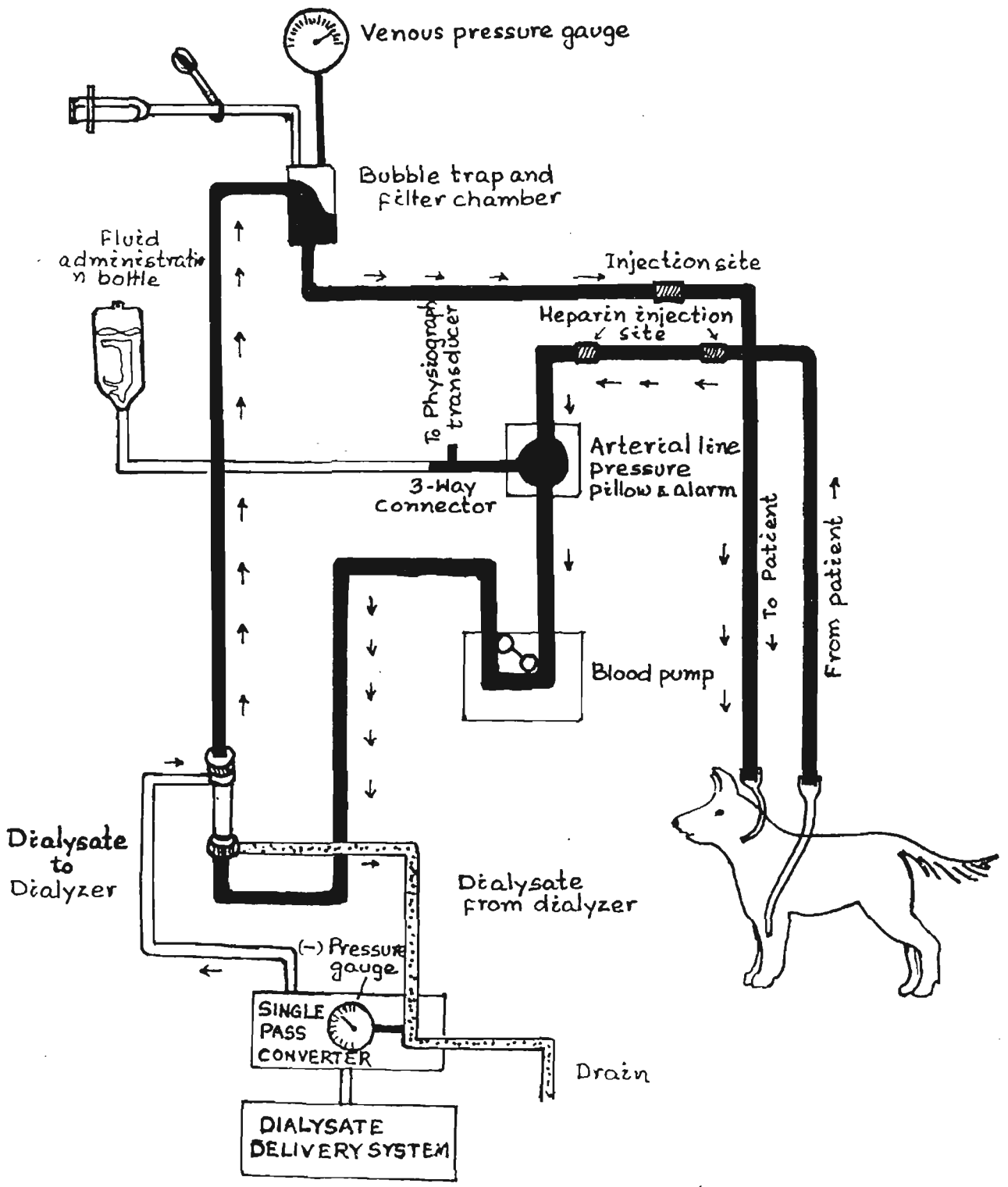
millilitre of Heparin sodium was taken in the syringe attached to the Heparin pump of the machine and the rate of discharge of Heparin into the extracorporeal circulation during dialysis was adjusted to 50 IU/Kg/h (Tani 1993).

The blood access was established by inserting 18 gauge intravenous canula into the jugular vein and cephalic vein under asceptic precautions and it was clamped. The arterial line (red color) was connected to the canula of the jugular vein and venous line (blue color) to the cephalic vein. The clamps were released and simultaneously the blood pump and Heparin pump were started. The speed of the blood flow was adjusted to 5-10 ml/kg/min by regulating the blood pump knob (Tani 1993). The blood was flowed from the jugular vein to the artificial kidney, dialysed there and returned back to the patient through the cephalic vein (Fig.2). Dialysis was continued for 3 to 4 hours depending on the uremic status of the animal. At the end of the dialysis the blood supply from the jugular vein was clamped and the blood remaining in the extracorporeal circulation was allowed to enter to the patient completely by rinsing the extracorporeal circuit with normal saline. After that the intravenous canulas were removed and the puncture wound was sealed. Patients body weight, temperature, pulse, respiration etc. were recorded and clinical materials were collected before and after dialysis.

3.5 PERITONEAL DIALYSIS

In peritoneal dialysis, the patient's own peritoneum which invests most of the abdominal organs and lines the inner surface of the abdominal wall serve as a semipermeable exchange surface. Dialysate was delivered to the

Fig. 2 DIAGRAM OF BLOODFLOW AND DIALYSATE FLOW THROUGH THE SYSTEM



(Dhein, 1981)

abdominal cavity through a peritoneal catheter, allowed to remain for a prescribed time and is then removed. Dialysate to be a physiological solution contains electrolytes and dextrose almost equal to the extracellular fluid of the dog.

3.5.1 Procedure

The peritoneal dialysis in the present study was carried out as per the technique described by Osborne *et al.* (1972), Parker (1981) and Clement (1991).

In the present study dialysis was performed in 12 experimental and 6 clinical cases of uremia.

The urinary bladder of the patient was evacuated by catheterization or by cystocentesis if it was found to be distended. The peritoneal dialysis fluid was warmed to 37°C and 500 IU of heparin was infused into the bottle. The peritoneal dialysis administration set was connected to the dialysate bottle and it was kept ready at a sufficient height on a drip stand. The longer tube of the peritoneal administration set was connected to a drainage bottle and it was kept closed and placed below the table. The shorter tube of the administration set was connected to the tube provided with the catheter. The fluid was allowed to run through the tube to evacuate the air from the tube and to prevent the entry of air into the peritoneum which would interfere with the retrival of the dialysate.

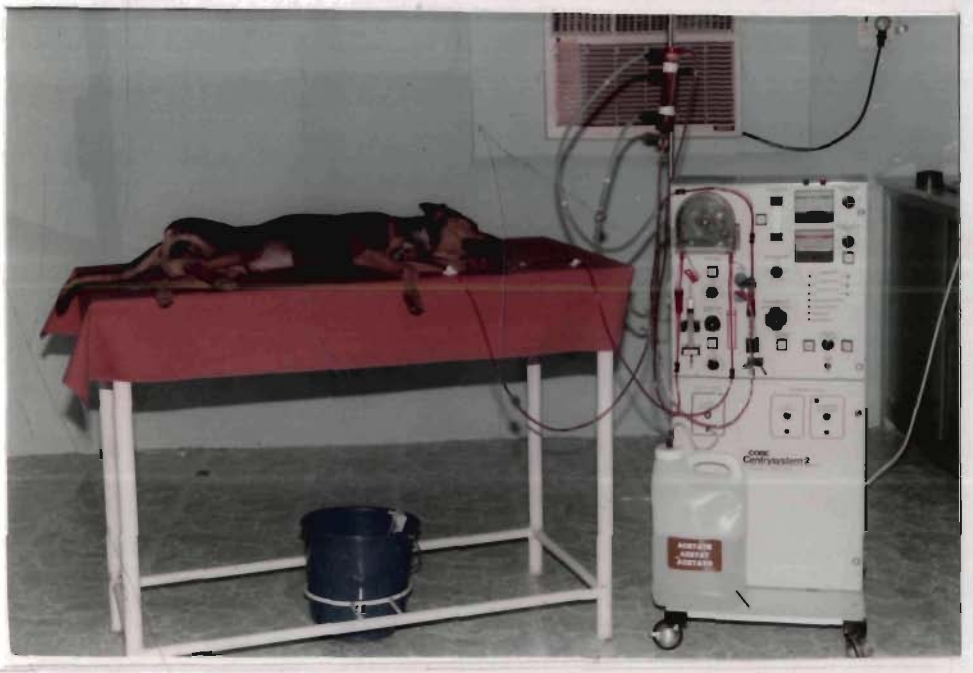


Plate 3. **Hemodialysis in progress**

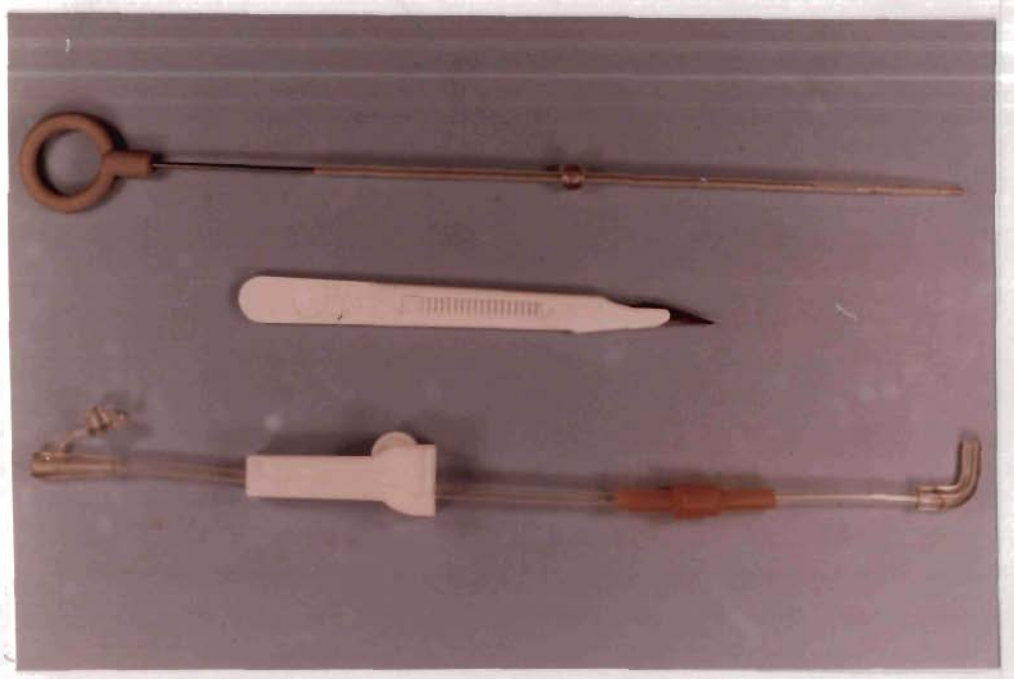


Plate 4. **Peritoneal dialysis catheter**

The patient was prepared as if for abdominal surgery with hair clipped from the abdomen. The skin is scrubbed and an antiseptic was applied over the abdomen. The animal was restrained on the table on dorso-ventral position. Local anaesthetic was instilled 3 cm behind the umblicus slightly on the right side, one or two centimeter away from the midline. Then a nick made with a 11 size surgical blade at the prepared site.

A sterile 15 gauge needle was introduced through the nick. Care was taken to ensure to avoid puncturing the visceral organs. The dialysate fluid was allowed to pass into the peritoneal cavity through the needle. After administration of 100-200 ml of dialysate fluid the needle was removed and the peritoneal catheter with stylet (Peritocat) was introduced into the abdomen (Plate 4). The stylet was withdrawn after placing the catheter into the peritoneum and pushing it to the right iliac fossa.

The catheter was secured in its place by putting purse string suture around it (Plate 5 & 6). Then the fluid administered was evacuated immediately through the outlet to check for any obstruction due to the presence of blood clots. The dialysate was again administered into the peritoneum and allowed to dwell for 30-45 min. After the dwelling time the fluid was removed through the catheter. This cycle was repeated 3 or 4 times according to the uremic status of the animal. After the evacuation of last cycle 250 mg of Ampicillin sodium was administered into the peritoneum and the nick was closed by mattress sutures. Patient's body weight, temperature, pulse, respiration etc. were recorded and clinical materials were collected before and after dialysis for the study of the parameter chosen in this study. The dialysis

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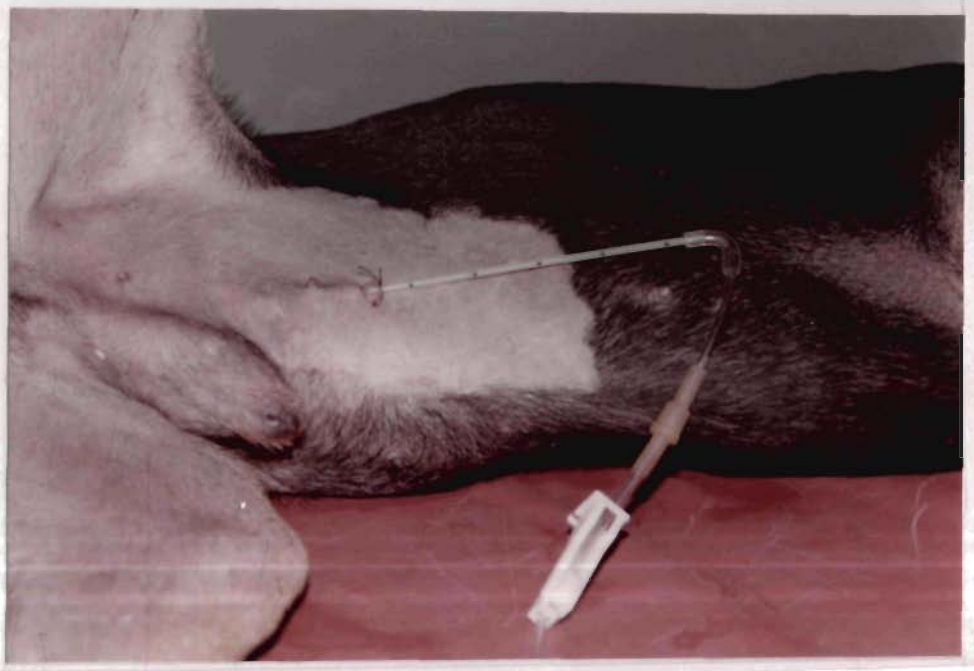


Plate 5. **Introduction of catheter into the peritoneal cavity**

Plate 6. **Peritoneal dialysis in progress**

was again repeated on alternate days. The composition of the commercially available dialysate fluid used in the present study is given below :

Each 100 ml of dialysate contains:

Dextrose anhydrous	1.70 g
Sodium chloride	0.556 g
Sodium Acetate	0.476 g
Calcium chloride	0.023 g
Magnesium chloride	0.152 g
Sodium Metabisulphite	0.015 g

Concentration of m mol/L approximately :

Sodium-130, Calcium-1.5, Magnesium 0.75 Chloride 100 , and Bicarbo
(as acetate).

3.6 COLLECTION OF CLINICAL MATERIALS

Urine was collected from the uremic animals by manual compression of abdomen or catheterization or by cystocentesis depending on the situation.

For hematological examination 5 ml of blood in a vial containing anticoagulent (EDTA) and for blood biochemistry 10 ml of blood for the separation of serum from all the uremic animals were collected (Benjamin 1985).

3.7 EXAMINATION OF CLINICAL MATERIALS

3.7.1 Pathological constituents of Urine

The urine samples collected from the uremic animals were tested for color, reaction, protein, glucose, bile salts, bile pigments and sediments (Coles, 1986).

3.7.2 Hematological examination

Hematological examination including hemoglobin, packed cell volume, total erythrocyte count, total leucocyte count and differential leucocyte count were carried out as per the method of Schalm *et al.* (1975).

3.7.3 Blood biochemistry

Serum urea was determined by Diacetyl monoxime method of Marsh *et al.* (1965). The serum creatinine was estimated by Alkaline picrate method of Bonses and Taussky (1945). Total serum protein was estimated by modified biuret method of Allan *et al.* (1949). Sodium and Potassium in the serum was analysed by Emission Flame Photometry as described by Oser (1965) and serum chloride was estimated by Mercuric Nitrate method of Schales and Schales (1941). The results obtained in conventional units from various laboratory analysis were converted to international units (SI) as per Kaneko (1983).

3.8 STATISTICAL ANALYSIS

The data collected was analysed and reported as per Snedecor and Cochran (1967).

Results

CHAPTER IV

RESULTS

A total of thirty apparently healthy dogs were utilized for the experimental induction of uremia and subsequent dialysis experiments. Out of them twelve dogs were taken for performing hemodialysis and another twelve for peritoneal dialysis. The remaining six dogs were maintained as control group, after induction of uremia. The nephrotoxic agents viz. mercuric chloride and ethylene glycol were used for the induction of uremia with six animals each in hemodialysis and peritoneal dialysis groups and three animals each in control group. After induction of uremia, statistically significant difference did not observe in the clinical, biochemical and hematological parameters between the mercuric chloride induced uremia and ethylene glycol induced uremia (Table 1-3). Hence the data obtained from all the experimentally induced uremic cases were pooled together and analysed statistically for discussion.

Sick animals attending the small animal clinic (medical unit) of Madras Veterinary College Hospital with signs of uremia were utilized for the clinical study. A total of twelve uremic cases were identified and taken up for study and they were divided into two groups. Hemodialysis and petitoneal dialysis were performed in six dogs from each group.

The results obtained during the study were analysed statistically, wherever applicable. Further significant observations related to the

Table 1

Mean ± SE values of hemogram and erythrocytic indices in experimental uremia induced by mercuric chloride and ethylene glycol

Parameters	Uremia induced by mercuric chloride	Uremia induced by ethylene glycol	t value
Hemoglobin (g/dl)	12.22 ± 1.48	12.62 ± 1.38	0.1827
Packed cell volume (per cent)	38.8 ± 1.20	41.86 ± 0.89	0.1537
Total erythrocyte count ($10^6/\mu l$)	6.14 ± 0.72	6.74 ± 0.46	1.0212
Mean corpuscular volume (mcv) (fl)	63.19 ± 1.82	62.11 ± 1.42	0.1427
Mean corpuscular hemoglobin (mch) (pg)	19.90 ± 1.41	18.92 ± 1.08	1.0121
Mean corpuscular hemoglobin concentration (mchc) (per cent)	31.49 ± 0.94	30.15 ± 1.04	0.4212

Table 2

Mean ± SE values of leucogram in experimental uremia induced by mercuric chloride and ethylene glycol

Parameters	Uremia induced by mercuric chloride	Uremia induced by ethylene glycol	t value
Total leucocyte count (per μl)	17420.82 ± 1240.20	18012.67 ± 1236.28	0.1682
Neutrophil (per μl)	14064.23 ± 1120.30	14598.52 ± 1040.30	0.1721
Lymphocyte (per μl)	2750.8 ± 127.5	2786.32 ± 138.42	0.2872
Monocyte (per μl)	356.48 ± 38.51	360.32 ± 42.40	0.0212
Eosinophil (per μl)	254.4 ± 28.28	268.23 ± 32.25	0.1241

Table 3

Mean ± SE values of biochemical parameters of blood in uremia induced by mercuric chloride and ethylene glycol

Parameters	Uremia induced by mercuric chloride	Uremia induced by ethylene glycol	t value
Serum urea (m mol/l)	32.16 ± 0.56	35.80 ± 0.39	1.96
Serum creatinine (μ mol/l)	416 ± 44.15	420.82 ± 28.04	0.8146
Serum urea/creatinine ratio	18.45 ± 1.22	21.42 ± 0.28	1.280
Serum total protein (g/l)	55.34 ± 0.89	57.26 ± 0.24	0.1566
Serum sodium (m mol/l)	139.33 ± 2.20	141.83 ± 0.59	0.1201
Serum potassium (m mol/l)	6.0 ± 0.29	5.77 ± 0.15	1.9542
Serum chloride (m mol/l)	100.13 ± 3.61	102.53 ± 1.73	0.0393

hemodialysis procedure and its usefulness as a therapeutic measure is also presented.

4.1 INCIDENCE

The total number of dogs that were brought to the small animal clinic (medical unit) of Madras Veterinary College Hospital, irrespective of the disease were taken from the hospital records over a period of three years (1990-1992). Total number of dogs brought to the hospital during this period were 36,312 and only 753 (2.07 per cent) were having clinical and laboratory evidence of uremia. Among them 470 (62.41 per cent) animals were male dogs and 283 (37.59 per cent) were females dogs (Fig.3). Out of 753 uremic dogs, 602 animals (79.94 per cent) were in the age group of about 8 years and remaining 151 dogs were less than eight years of age.

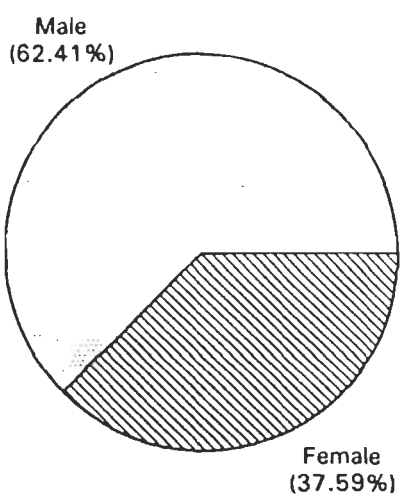
4.2 CLINICAL SIGNS

In experimentally induced uremia, clinical signs were manifested from the second day after inductions. Important signs observed were loss of appetite, depression, oliguria/anuria, vomiting, melaena, dehydration and altered gait. After dialysis therapy most of the clinical signs disappeared considerably and the animals were moderately bright and alert. In control animals the clinical signs aggravated as the days advanced and all the dogs died between 7th and 10th day of induction.

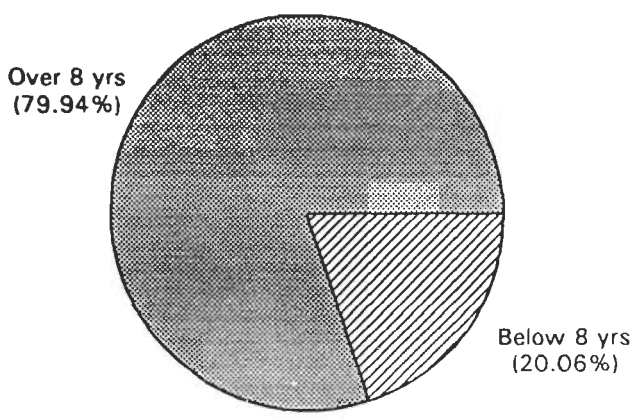
In clinical cases of uremia, important signs were frequent vomiting, haemorrhagic enteritis, ulcers in the buccal mucosa, loss of appetite,

FIG. 3

PARTICULARS SHOWING INCIDENCE OF UREMIA IN MALE AND FEMALE DOGS



PARTICULARS SHOWING INCIDENCE OF UREMIA IN DIFFERENT AGE GROUPS OF DOGS



polyurea/oliguria, polydipsia and depression. After dialysis therapy there was improvement in the clinical signs.

4.3 PATHOLOGICAL CONSTITUENTS OF URINE

Urine analysis for the presence of the pathological constituents like protein, glucose, bile salts, bile pigments and urinary sediments were carried out on urine samples obtained from the experimental and clinical cases of uremia. However, the pathological constituents of urine pertinent to the renal disease like protein and sediment are presented.

Proteinuria of moderate degree (++) was observed in all the experimental and clinical cases of uremia (Fig.4) Microscopic examination of urinary sediments revealed occurrence of pus cells and granular casts in both experimental and clinical cases of uremia (Fig.4). In addition moderate degree of crystalluria was also evident in all the experimental cases. However, it was found that dialysis did not have any affect on the pathological constituents of urine in experimental and clinical cases.

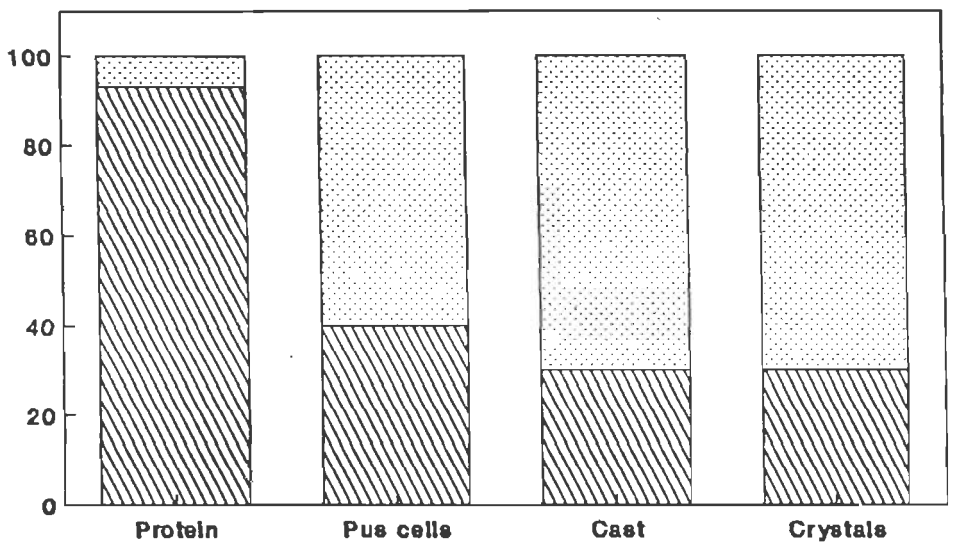
4.4 HEMATOLOGY

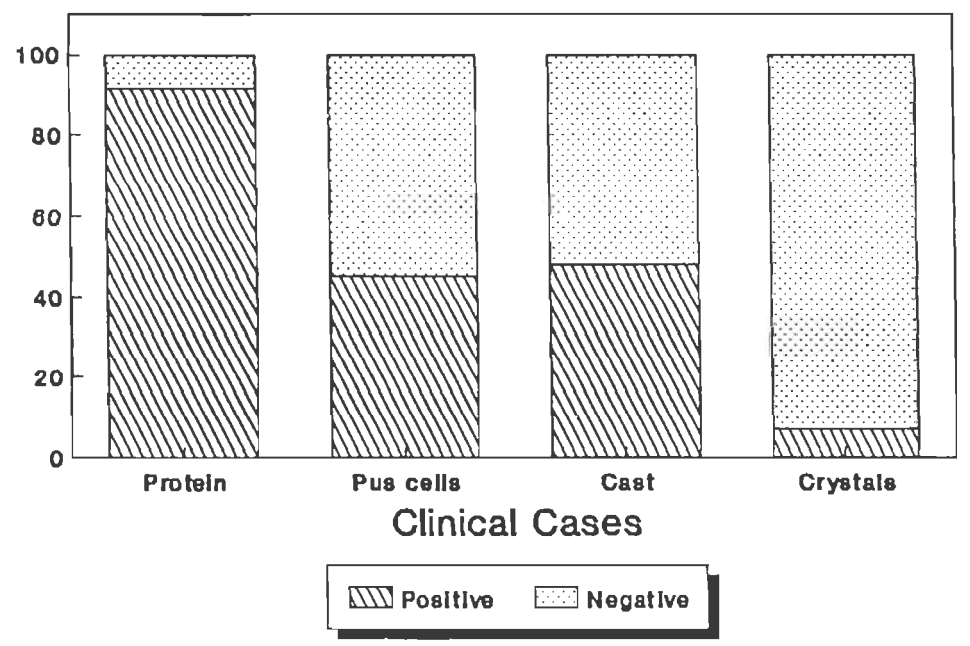
4.4.1 Group-A - Control animals

The mean values of hemogram, erythrocytic indices and leucogram in experimentally induced uremic animals were given in the Tables 4 and 5. The pre-induction mean values of hemogram were presented in Table 4. The mean values of these parameters except packed cell volume did not differ significantly between pre-induction and post-induction of uremia. Packed cell

FIG. 4

PARTICULARS SHOWING THE OCCURRENCE OF PATHOLOGICAL CONSTITUENTS OF URINE IN CANINE UREMIA (%)





volume increased from the pre-induction value of 36.83 ± 1.03 per cent to 40.33 ± 0.47 and 44.33 ± 0.47 per cent on 4th and 7th day, respectively of post induction of uremia making a significant increase at each stage. A slight elevation of hemoglobin and total erythrocyte count corresponding to the rise in packed cell volume were also observed which was statistically not significant.

The pre-induction mean value of total leucocyte count 12241.67 ± 1140.20/μl was elevated significantly to 17716.16 ± 1010.36/μl and 19916.67 ± 3085.58/μl on 4th and 7th day of post induction, respectively. The neutrophil count was also significantly increased from the pre-induction value of 8713.52 ± 1420.11/μl to 14232.80 ± 1020.4/μl and 16331.12 ± 1471.81/μl on 4th and 7th day of post induction, respectively. The lymphocyte, monocyte and eosinophil values did not show any significant difference between pre and post-induction period of uremia (Table 5).

4.4.2 Group B - Hemodialysis

The mean values of hemogram, erythrocytic indices and leucogram of experimentally induced uremic animals which were treated by hemodialysis are furnished in tables 6 and 7. The mean values of these parameters before induction of uremia were within the normal range of dogs. The mean values of packed cell volume was increased significantly to 40.08 ± 1.28 per cent during uremia and decreased to 36.01 ± 1.28 per cent after hemodialysis. Corresponding changes were also observed in the levels of hemoglobin and total erythrocyte count, before and after dialysis, which were statistically not significant. The pre-induction mean value of erythrocytic indices, viz. mean

Table 4

Mean ± SE values of hemogram and erythrocytic indices in experimentally induced uremia (control group)

Parameters	Pre-induction	4th day of induction	7th day of induction	F value
Hemoglobin (g/dl)	11.30 ± 1.23	12.42 ± 0.76	13.5 ± 0.74	2.201
Packed cell volume (per cent)	36.83 ± 1.03[a]	40.33 ± 0.47[b]	44.33 ± 0.47[c]	4.26*
Total erythrocyte count ($10^6/\mu l$)	5.68 ± 0.61	6.44 ± 0.25	7.0 ± 0.37	2.101
Mean corpuscular volume (mcv) (fl)	64.84 ± 1.90	62.62 ± 2.52	63.32 ± 1.82	1.928
Mean corpuscular hemoglobin (mch) (pg)	19.89 ± 1.2	19.28 ± 0.92	19.29 ± 2.2	2.012
Mean corpuscular hemoglobin concentration (mchc) (per cent)	31.68 ± 0.93	30.79 ± 0.48	30.53 ± 1.51	1.729

* Significant at 5% level ($p < 0.05$)

Table 5

Mean ± SE values of leucogram in experimentally induced uremia (control group)

Parameters	Pre-induction	4th day of induction	7th day of induction	F value
Total leucocyte count (per μl)	12241.67 ± 1140.20[a]	17716.16 ± 1010.36[b]	19916.67 ± 3085.58[a]	7.38**
Neutrophil (per μl)	8713.52 ± 1420.11[a]	14232.80 ± 1020.4[b]	16331.12 ± 1471.81[c]	8.83**
Lymphocyte (per μl)	2897.48 ± 124.5	2887.4 ± 301.8	2987.4 ± 402.33	2.005
Monocyte (per μl)	367.23 ± 42.81	357.48 ± 32.11	358.32 ± 43.20	1.828
Eosinophil (per μl)	267.23 ± 36.11	260.32 ± 4.28	268.32 ± 36.26	1.721

** Significant at 1% level ($p < 0.01$)

Table 6

Mean ± SE values of hemogram and erythrocytic indices before and after hemodialysis in experimentally induced uremia

Parameters	Pre-induction	Before dialysis	After dialysis	F value
Hemoglobin (g/dl)	11.29 ± 0.68	12.37 ± 0.75	11.31 ± 0.56	2.02
Packed cell volume (per cent)	35.88 ± 1.72[a]	40.08 ± 1.28[b]	36.01 ± 1.28[a]	3.81*
Total erythrocyte count ($10^6/\mu l$)	5.48 ± 0.58	6.0 ± 0.62	5.5 ± 0.41	2.011
Mean corpuscular volume (mcv) (fl)	65.53 ± 1.62	64.87 ± 5.12	65.34 ± 2.33	1.767
Mean corpuscular hemoglobin (mch) (pg)	20.95 ± 0.62	20.52 ± 0.78	21.36 ± 1.10	2.020
Mean corpuscular hemoglobin concentration (mchc) (per cent)	32.26 ± 0.75	32.29 ± 0.81	31.92 ± 0.37	1.562

* Significant at 5% level ($p < 0.05$)

Mean values bearing the same **superscript do not differ** significantly.

Table 7

Mean ± SE values of leucogram, before and after hemodialysis in experimentally induced uremia

Parameters	Pre-induction	Before dialysis	After dialysis	F value
Total leucocyte count (per μl)	12925.29 ± 2690.87[a]	17112.5 ± 1348.25[b]	17178.34 ± 2294.09[b]	6.98**
Neutrophil (per μl)	9687.79 ± 1478.76[a]	13877.5 ± 1665.59[b]	13869.76 ± 1825[b]	6.388**
Lymphocyte (per μl)	2623.41 ± 268.63	2616.83 ± 314.12	2673.7 ± 208.21	2.016
Monocyte (per μl)	377.47 ± 80.43	372.83 ± 58.94	379.08 ± 53.81	1.718
Eosinophil (per μl)	247.43 ± 34.16	249.25 ± 81.63	255.24 ± 91.57	1.920

** Significant at 1% level ($p < 0.01$)

Mean values bearing same superscript do not differ significantly.

corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC) were 65.53 ± 1.62 fl, 20.95 ± 0.62 pg and 32.26 ± 0.75 per cent, respectively. The mean values of erythrocytic indices did not differ significantly between pre-induction, before and after dialysis (Table 6).

The mean values of total lucocyte and neutrophil before induction of uremia were 12925.29 ± 2690.87/μl and 9687.79 ± 1478.76/μl, respectively. A significant increase in the mean values of these parameters to 17112.5 ± 1348.25/μl and 13877.5 ± 1665.59/μl, respectively were recorded during uremia. Hemodialysis did not show any significant effect on the leucogram (Table 7).

The mean values of hemogram, erythrocytic indices and leucogram of clinical cases of uremia are furnished in Tables 8 and 9. The mean values of hemoglobin, packed cell volume and total erythrocyte count were 9.1 ± 0.76 g/dl, 28 ± 1.64 per cent and 4.5 ± 0.19 million/μl, respectively during uremia and from these values the mean values of mean corpuscular volume, mean corpuscular hemoglobin and mean corpuscular hemoglobin concentration were computed as 63.44 ± 2.14 fl, 21.72 ± 4.5 pg and 32.42 ± 1.48 per cent, respectively. The mean values of total leucocyte, neutrophil, lymphocyte, monocyte and eosinophil count were 14725 ± 1293.5/μl, 11156.33 ± 1083.44/μl, 2838.337 ± 173.92, 458.83 ± 68.30 and 273.5 ± 50.82, respectively. Hemodialysis did not show any significant effect between before and after dialysis values. However the normal values of erythrocytic indices and lower values of hemoglobin, packed cell volume and total erythrocyte count indicated

Table 8

Mean ± SE values of hemogram and erythrocytic indices, before and after hemodialysis in clinical cases of uremia

Parameters	Apparently healthy control	Before dialysis	After dialysis	F value
Hemoglobin (g/dl)	11.30 ± 1.23^a	9.1 ± 0.76^b	9.0 ± 1.73^b	3.82*
Packed cell volume (per cent)	36.83 ± 1.03^a	28 ± 1.64^b	26.2 ± 1.28^b	3.69*
Total erythrocyte count ($10^6/\mu l$)	5.68 ± 0.61^a	4.5 ± 0.19^b	4.53 ± 0.34^b	3.70*
Mean corpuscular volume (mcv) (fl)	64.84 ± 1.90	63.44 ± 2.14	63.65 ± 1.89	1.892
Mean corpuscular hemoglobin (mch) (pg)	19.89 ± 1.2	21.72 ± 4.15	20.78 ± 2.48	2.320
Mean corpuscular hemoglobin concentration (mchc) (per cent)	31.68 ± 0.93	32.42 ± 1.48	32.84 ± 2.07	1.928

* Significant at 5% level ($p < 0.05$)

Mean values bearing the same **superscript do not differ** significantly.

Table 9

Mean ± SE values of leucogram, before and after hemodialysis in clinical cases of uremia

Parameters	Apparently healthy (control)	Before dialysis	After dialysis	F value
Total leucocyte count (per μl)	12241.67 ± 1140.20[a]	14725 ± 1293.5[b]	14716.69 ± 1274.21[b]	3.82*
Neutrophil (per μl)	8713.52 ± 1420.11[a]	11156.33 ± 1083.44[b]	11159.83 ± 899.52[b]	4.72*
Lymphocyte (per μl)	2897.48 ± 124.5	2838.33 ± 173.72	2820 ± 387.12	2.626
Monocyte (per μl)	367.23 ± 42.81	458.83 ± 68.36	457.67 ± 49.67	1.828
Eosinophil (per μl)	267.23 ± 36.11	273.5 ± 50.82	284.83 ± 40.68	1.802

* Significant at 5% level ($p < 0.05$)

Mean values bearing same superscript **do not differ significantly.**

the presence of a normocytic normochromic anaemia in clinical cases of uremia (Table 8).

4.4.3 Group C - Peritoneal dialysis

The mean value of hemogram and erythrocytic indices of experimentally induced uremic animals which were treated by peritoneal dialysis are furnished in table 10. The mean values of packed cell volume increased to 41.25 $\pm$ 2.33 per cent in uremia and it significantly decreased to 37.52 $\pm$ 2.34 per cent after peritoneal dialysis. There was no significant difference between the mean values of packed cell volume after dialysis and before induction of uremia, suggesting that the peritoneal dialysis was effective in correcting the dehydration. The other parameters of hemogram did not show any significant effect due to uremia or peritoneal dialysis.

The mean values of leucogram of this group of animals are given in Table 11. The pre-induction values of total leucocytes and neutrophils were 13040.54 $\pm$ 1650.7/μl and 9896.83 $\pm$ 1569.85/μl, respectively and it was significantly elevated to 17175 $\pm$ 2108.38/μl and 14094.33 $\pm$ 1391.58/μl, respectively during uremia. Peritoneal dialysis did not show any significant effect on any of the parameters of leucogram.

The mean values of hematological parameters recorded in the clinical cases of uremia are given in table 12 and 13. The mean values of hemoglobin, packed cell volume and total erythrocyte count were found to be significantly decreased to 9.4 $\pm$ 0.85 g/dl, 29.5 $\pm$ 0.89 per cent and 4.67 $\pm$ 0.42 million/μl, respectively due to uremia. The normal values of erythrocytic indices

Table 10

Mean ± SE values of hemogram,and erythrocytic indices, before and after peritoneal dialysis in experimentally induced uremia

Parameters	Pre-induction	4th day of induction	7th day of induction	F value
Hemoglobin (g/dl)	11.85 ± 0.97	12.7 ± 0.82	11.9 ± 0.82	1.572
Packed cell volume (per cent)	36.53 ± 4.12[a]	41.25 ± 2.33[b]	37.52 ± 2.34[a]	3.812*
Total erythrocyte count ($10^6/\mu l$)	6.01 ± 0.82	6.49 ± 0.71	6.15 ± 0.81	1.729
Mean corpuscular volume (mcv) (fl)	61.24 ± 1.28	62.21 ± 1.29	61.69 ± 0.72	1.025
Mean corpuscular hemoglobin (mch) (pg)	20.21 ± 2.24	21.05 ± 2.42	19.69 ± 1.32	1.642
Mean corpuscular hemoglobin concentration (mchc) (per cent)	33.36 ± 1.51	33.46 ± 1.72	32.51 ± 1.42	1.782

* Significant at 5% level ($p < 0.05$)

Mean value bearing the same superscript do not differ significantly.

Table 11

Mean ± SE values of leucogram, before and after peritoneal dialysis in experimentally induced uremia

Parameters	Pre-induction	Before dialysis	After dialysis	F value
Total leucocyte count (per μl)	13040.54 ± 1650.7[a]	17175.00 ± 2108.38[b]	17325.25 ± 4352.29[b]	6.528**
Neutrophil (per μl)	9896.83 ± 1569.85[a]	14094.33 ± 1391.58[b]	14218.75 ± 1507.08[b]	6.427**
Lymphocyte (per μl)	2558.85 ± 272.4	2500.51 ± 291.81	2514.17 ± 246.21	1.721
Monocyte (per μl)	325.7 ± 100.35	329.97 ± 61.32	335.92 ± 76.9	1.852
Eosinophil (per μl)	260.8 ± 58.6	253.00 ± 78.63	263.00 ± 68.65	1.225

** Significant at 1% level ($p < 0.01$)

Mean values bearing same superscript do not differ significantly.

(Table 12) and lower value of hemoglobin, packed cell volume and total erythrocyte count indicated the presence of a normocytic, normochromic anemia in the clinical cases of uremia. Peritoneal dialysis did not show any significant effect on the hemogram and erythrocytic indices of uremic animals.

The mean values of total leucocyte and neutrophil count were found to be significantly elevated in clinical cases of uremia than apparently healthy control animals, suggestive of leucocytosis and neutrophelia. Peritoneal dialysis did not have any significant effect on the leucogram in clinical cases of uremia (Table 13).

4.5 BLOOD BIOCHEMISTRY

4.5.1 Group A - Control animals

The mean values of biochemical parameters of the control animals are furnished in Table 14. The values of serum urea, creatinine, urea/creatinine ratio and total serum protein before induction of uremia were 6.88 $\pm$ 1.11 mmol/L, 98.14 $\pm$ 7.48 μmol/L, 16.32 $\pm$ 1.04 and 57.33 $\pm$ 0.94 g/L, respectively. After induction of uremia, the serum urea level was increased significantly to 33.82 $\pm$ 2.16 m mol/L and 64.13 $\pm$ 5.66 m mol/L on 4th and 7th day of induction respectively. Serum creatinine was increased to 418.73 $\pm$ 23.5 μmol/L and 480.5 $\pm$ 39.24 μmol/L and urea/creatine ratio was elevated to 19.90 $\pm$ 2.14 and 33.8 $\pm$ 2.89, on 4th and 7th day of induction, respectively. There was no significant changes in the mean values of total serum protein.

Mean value of serum sodium, potassium and chloride were also found to be altered after induction of uremia. Serum potassium level was

Table 12

Mean ± SE values of hemogram and erythrocytic indices, before and after peritoneal dialysis in clinical cases of uremia

Parameters	Apparently healthy control	Before dialysis	After dialysis	F value
Hemoglobin (g/dl)	11.30 ± 1.23^a	9.4 ± 0.85^b	9.3 ± 0.75^b	3.72^*
Packed cell volume (per cent)	36.83 ± 1.03^a	29.5 ± 0.42^b	27.3 ± 0.72^b	3.68^*
Total erythrocyte count ($10^6/\mu l$)	5.68 ± 0.61^a	4.67 ± 0.42^b	4.83 ± 0.31^b	3.78^*
Mean corpuscular volume (mcv) (fl)	64.84 ± 1.90	64.56 ± 1.92	61.65 ± 0.89	1.782
Mean corpuscular hemoglobin (mch) (pg)	19.89 ± 1.2	20.48 ± 1.45	19.85 ± 2.72	2.420
Mean corpuscular hemoglobin concentration (mchc) (per cent)	31.68 ± 0.93	32.40 ± 2.48	32.64 ± 1.89	1.852

* Significant at 5% level ($p < 0.05$)

Mean values bearing the same superscript do not differ significantly.

Table 13

Mean ± SE values of leucogram, before and after peritoneal dialysis in clinical cases of uremia

Parameters	Pre-induction	Before dialysis	After dialysis	F value
Total leucocyte count (per μl)	12241.67 ± 1140.20[a]	14325 ± 1534.04[b]	14316 ± 1270.02[b]	6.532**
Neutrophil (per μl)	8713.52 ± 1420.11[a]	11460 ± 938.09[b]	11488.48 ± 815.53[b]	6.427**
Lymphocyte (per μl)	2897.48 ± 1245	2148.75 ± 330.06	2118.72 ± 339.16	1.821
Monocyte (per μl)	367.23 ± 42.81	429.75 ± 60.77	426.17 ± 76.47	1.528
Eosinophil (per μl)	267.23 ± 36.11	288.50 ± 57.86	284.32 ± 57.26	1.762

* Significant at 5% level ($p < 0.05$)

Mean values bearing same superscript do not differ significantly.

Table 14

Mean ± SE values of biochemical parameters of blood in experimentally induced uremia (control group)

Parameters	Pre-induction	4th day of induction	7th day of induction	F value
Serum urea (m mol/l)	6.88 ± 1.11[a]	33.82 ± 2.16[b]	64.13 ± 5.66[a]	66.35**
Serum creatinine (μ mol/l)	98.14 ± 7.48[a]	418.73 ± 23.5[b]	480.5 ± 39.24[c]	66.90**
Serum urea/creatinine ratio	16.32 ± 1.04[a]	19.90 ± 2.14[a]	33.8 ± 2.89[b]	7.82**
Serum total protein (g/l)	57.33 ± 0.94	56.75 ± 2.08	55.5 ± 2.45	0.4129
Serum sodium (m mol/l)	142.50 ± 1.19[a]	140.29 ± 1.22[a]	136.66 ± 0.98[b]	6.69*
Serum potassium (m mol/l)	4.25 ± 0.12[a]	5.88 ± 0.15[b]	6.37 ± 0.14[c]	62.32**
Serum chloride (m mol/l)	103.1 ± 1.12[a]	101.17 ± 1.5[a]	96.15 ± 1.13[b]	4.91*

* Significant at 5% level ($p < 0.05$)

* Significant at 1% level ($p < 0.01$)

Mean values bearing the same **superscript do no differ** significantly.

significantly increased to 5.88 ± 0.15 m mol/L and 6.37 ± 0.14 m mol/L or 4th and 7th day of induction, respectively. Though mean values of serum sodium and chloride were decreased even by the 4th day of induction, a significant decrease to the level of 136.66 ± 0.98 mmol/L and 96.15 ± 1.13 mmol/L, respectively were noticed by the 7th day of induction. By the 7th day of induction all the animals were azotemic hyperkalemic, hyponatremic and hypochloremic.

4.5.2 Group B - Hemodialysis

The mean values of biochemical parameters pertaining to experimentally induced uremic animals which were used for hemodialysis experiments are furnished in Table 15. After induction of uremia (before dialysis) the mean values of serum urea and cratinine were significantly elevated to 33.99 ± 2.58 mmol/L and 507.56 ± 22.02 μmol/L, respectively. There was slight increase in the ratio of serum urea/creatinine, which was not significant. After hemodialysis the mean values of serum urea and creatinine decreased significantly to 11.49 ± 1.65 m mol/L and 234.42 ± 17.3 μmol/L, respectively and it did not differ significantly with that of pre-induction values. The mean values of serum urea/creatinine ratio was also decreased significantly to 12.04 ± 0.78 and after dialysis. It decreased even beyond the pre-induction value and differed significantly with that value. The total serum protein levels did not vary significantly after induction of uremia and after hemodialysis.

The pre-induction mean values of serum sodium, potassium and chloride were were presented in Table 15. The serum levels of sodium and chloride were found to be slightly decreased after induction of uremia and after dialysis

Table 15

Mean ± SE values of biochemical parameters, before and after hemodialysis in experimentally induced uremia

Parameters	Pre-induction	Before dialysis	After dialysis	F value
Serum urea (m mol/l)	7.16 ± 0.89[a]	33.99 ± 2.58[b]	11.49 ± 1.65	71.05**
Serum creatinine (μ mol/l)	110.78 ± 16.51[a]	507.56 ± 22.02[b]	234.42 ± 17.3[a]	19.62**
Serum urea/creatinine ratio	14.86 ± 2.61[a]	16.48 ± 2.07[b]	12.04 ± 0.78[c]	3.68*
Serum total protein (g/l)	56.78 ± 0.04	55.73 ± 0.20	56.13 ± 2.3	0.56
Serum sodium (m mol/l)	141.69 ± 0.72	138.84 ± 0.01	141.83 ± 0.87	2.87
Serum potassium (m mol/l)	4.32 ± 0.21[a]	6.48 ± 0.32[b]	4.8 ± 0.51[a]	42.48**
Serum chloride (m mol/l)	103.08 ± 3.26	99.32 ± 2.7	103.11 ± 3.28	0.75

* Significant at 5% level ($p < 0.05$)

** Significant at 1% level ($p < 0.01$)

Mean values bearing same superscript do not differ significantly.

it has become normal. But these changes were not statistically significant. The mean vlaues of serum potassium increased significantly to 6.48 ± 0.32 m mol/L after induction of uremia and decreased significantly towards the normal value of 4.8 ± 0.51 m mol/L after dialysis. The mean value of potassium did not differ significantly from that of pre-induction value after hemodialysis (Table 15).

In clinical cases of uremia, the mean values of serum urea, creatinine and urea/creatinine ratio were 37.92 ± 2.79 m mol/L, 430.16 ± 67.8 μmol/L and 22.72 ± 4.37, respectively. These values were found to be elevated significantly than the mean values of apparently healthy control animals indicating uremia (Table 16). After dialysis the mean values of these parameters were decreased significantly to 19.64 ± 1.89 m mol/L, 235.75 ± 20.98 μmol/L and 19.87 ± 1.02, respectively. There was no significant changes in the levels of serum total protein before and after hemodialysis.

The mean value of serum sodium and chloride before and after hemodialysis did not vary significantly in clinical cases of uremia, however a slight increase in the levels of these electrolytes could be observed after dialysis. The elevated serum potassium level of 6.37 ± 0.14 m mol/L observed in uremic animals was significantly reduced to 4.37 ± 0.14 m mol/L after hemodialysis (Table 16).

4.5.3 Group C - Peritoneal dialysis

The mean values of biochemical parameters pertaining to the experimentally induced uremic animals which were utilized for peritoneal dialysis experiments are given in Table 17. The pre-induction mean values of

Table 16

Mean ± SE values of biochemical parameters before and after hemodialysis in clinical cases of uremia

Parameters	Apparently healthy (control)	Before dialysis	After dialysis	F value
Serum urea (m mol/l)	6.88 ± 1.11[a]	37.92 ± 2.79[b]	19.64 ± 1.89[c]	28.68**
Serum creatinine (μ mol/l)	98.14 ± 7.48[a]	430.16 ± 67.8[b]	235.75 ± 20.98[c]	18.42**
Serum urea/creatinine ratio	17.32 ± 1.04[a]	21.72 ± 4.37[b]	19.8 ± 1.02[a]	3.68*
Serum total protein (g/l)	57.33 ± 0.94	52.33 ± 0.94	52 ± 0.92	1.5873
Serum sodium (m mol/l)	142.50 ± 1.19	140.48 ± 0.72	142.47 ± 1.23	1.8242
Serum potassium (m mol/l)	4.25 ± 0.12[a]	6.37 ± 0.14[b]	4.37 ± 0.14[a]	9.58**
Serum chloride (m mol/l)	103.1 ± 1.12	101.16 ± 2.66	103.75 ± 1.15	2.14

* Significant at 5% level ($p < 0.05$)

** Significant at 1% level ($p < 0.01$)

Mean values bearing same superscript do not differ significantly.

serum urea, creatinine, urea/creatinine ratio and total serum protein were within the normal range for dogs. The levels of serum urea, creatinine and urea/creatinine ratio were increased significantly to 32.33 ± 2.55 m mol/L, 439.65 ± 30.18 μmol/L, 18.55 ± 3.3, respectively after induction of uremiaa. After peritoneal dialysis the mean values of these parameters decreased significantly to 15.46 ± 1.88 m mol/L, 257.72 ± 16.45 μmol/L and 15.37 ± 2.91, respectively. The mean value of serum urea and creatinine after peritoneal dialysis still differed significantly from that of pre-induction value. The mean values of serum urea/creatinine ratio also decreased significantly after dialysis and this value did not differ significantly from that of pre-induction value. The level of total serum protein reduced significantly after peritoneal dialysis. This value significantly differed from that of pre-induction value indicating loss of serum total protein during peritoneal dialysis (Table 17).

The levels of serum sodium and chloride did not vary significantly during the different stages of this study, however a mild increase of these electrolytes were noticed after peritoneal dialysis. The mean value of serum potassium was increased significantly to 5.82 ± 0.28 m mol/L after induction of uremia and it decreased significantly to 4.53 ± 0.18 m mol/L after peritoneal dialysis. This value did not vary significantly from that of pre-induction value (Table 17).

The mean values of biochemical parameters in clinical cases of uremia before and after peritoneal dialysis are furnished in Table 18. The levels of serum urea, creatinine and urea/creatinine ratio in clinical cases of uremia were 40.49 ± 9.67 m mol/L, 439.09 ± 74.55 μmol/L, 23.63 ± 4.28, respectively

Table 17

Mean ± SE values of biochemical parameters of blood, before and after peritoneal dialysis in experimentally induced uremia

Parameters	Pre-induction	Before dialysis	After dialysis	F value
Serum urea (m mol/l)	6.73 ± 1.23[a]	32.33 ± 2.55[b]	15.46 ± 1.88[c]	46.58**
Serum creatinine (μ mol/l)	113.16 ± 15.98[a]	439.65 ± 30.18[b]	257.72 ± 16.45[c]	48.18**
Serum urea/creatinine ratio	15.68 ± 0.54[a]	18.55 ± 3.3[b]	15.37 ± 2.91[a]	3.84*
Serum total protein (g/l)	56.13 ± 2.19[a]	55.07 ± 2.19[a]	48.63 ± 1.88[b]	5.29*
Serum sodium (m mol/l)	141.21 ± 2.26	139.04 ± 1.26	142.33 ± 1.55	0.36
Serum potassium (m mol/l)	4.49 ± 0.43[a]	5.82 ± 0.28[b]	4.53 ± 0.18[a]	13.23**
Serum chloride (m mol/l)	102.95 ± 2.49	100.96 ± 1.24	103.63 ± 2.69	0.81

* Significant at 5% level ($p < 0.05$)

** Significant at 1% level ($p < 0.01$)

Mean values bearing same superscript do not differ significantly.

and it was found significantly elevated than the mean values of apparently healthy control animals, indicating uremia. After dialysis these parameters were decreased significantly to 19.64 ± 1.89 m mol/L, 297.23 ± 66.15 μmol/L and 16.82 ± 1.28, respectively. The mean values of serum urea and creatinine after dialysis varied significantly from that of apparently healthy control dogs. But there was no significant difference in the mean value of serum urea/creatinine ratio. Total serum protein level was decreased significantly from 53.7 ± 0.13 g/L to 47.7 ± 0.14 g/L after peritoneal dialysis.

The values of serum sodium and chloride before and after dialysis did not differ significantly. Whereas the elevated serum potassium level of 6.01 ± 0.34 m mol/L decreased significantly to 4.95 ± 0.09 after peritoneal dialysis (Table 18).

4.6 EFFICACY OF HEMODIALYSIS V/s PERITONEAL DIALYSIS

The mean values of the percentage of clearance of serum urea, creatinine and potassium during hemodialysis were found to be 60.19 ± 1.74 per cent, 45.05 ± 3.34 per cent and 27.71 ± 2.07 per cent, respectively. With respect to peritoneal dialysis these values were 47.94 ± 2.46 per cent, 36.88 ± 2.08 per cent and 20.65 ± 1.65 per cent, respectively. These clearance rates did not differ significantly between hemodialysis and peritoneal dialysis, however a higher rate of clearance was observed in hemodialysis (Table 19).

Table 18

Mean ± SE values of biochemical parameters before and after peritoneal dialysis in clinical cases of uremia

Parameters	Apparently healthy (control)	Before dialysis	After dialysis	F value
Serum urea (m mol/l)	6.88 ± 1.11[a]	40.49 ± 9.67[b]	19.64 ± 1.89[c]	26.86**
Serum creatinine (μ mol/l)	98.14 ± 7.48[a]	439.09 ± 74.55[b]	297.23 ± 66.15[c]	17.52**
Serum urea/creatinine ratio	16.32 ± 1.04[a]	23.63 ± 4.28[b]	16.82 ± 1.28[a]	3.72*
Serum total protein (g/l)	57.33 ± 0.94[a]	53.7 ± 0.13[a]	47.7 ± 0.14[b]	4.7281*
Serum sodium (m mol/l)	142.50 ± 1.19	140.44 ± 0.89	142.2 ± 2.43	1.6242
Serum potassium (m mol/l)	4.25 ± 0.12[a]	6.01 ± 0.34[b]	4.95 ± 0.09[a]	8.72**
Serum chloride (m mol/l)	103.1 ± 1.12	101.52 ± 2.21	102.22 ± 2.48	2.08

* Significant at 5% level ($p < 0.05$)

** Significant at 1% level ($p < 0.01$)

Mean values bearing same superscript do not differ significantly.

Table 19

Mean ± values of clearance rate of serum urea, creatinine and potassium during hemodialysis and peritoneal dialysis in experimental and clinical cases of uremia (in percentage)

	Hemodialysis	Peritoneal dialysis	t value
Serum urea	60.19 ± 1.74	47.94 ± 2.46	1.8494
Serum creatinine	45.05 ± 3.34	36.88 ± 2.08	1.8244
Serum potassium	37.71 ± 2.07	20.65 ± 1.65	0.1395

4.7 OBSERVATIONS DURING DIALYSIS

4.7.1 Technical aspects

Hemodialysis was successfully carried out in 18 uremic patients. For creating extracorporeal circulation, cannulation of jugular vein and cephalic vein with the use of 18 or 19 gauge intravenous canula was found to be more suitable in the dogs. A minimum body weight of 10 kg was found necessary for the continuous flow of blood through the extracorporeal circulation. The blood flow rate maintained in this study (5-10 ml/kg body weight per minute) was suitable for dogs. For systemic anticoagulation the dosage of heparin used in this study was sufficient to maintain anticoagulation through out the dialysis process.

4.7.2 Efficacy of dialysis

All the experimental cases of uremia in the present study were treated for a period of one week by dialysis. Hemodialysis was done two times in a week at an interval of 3 days and peritoneal dialysis was carried out on 3-4 times in a week on alternate days. Treated animals, recovered from the uremic crisis by the end of the dialysis therapy, and later lived upto 2 to 3 weeks.

In clinical cases all the animals showed marked improvement after hemodialysis/peritoneal dialysis therapy, but 9 out of 12 clinical cases died due to the chronic nature of renal damage.

4.7.3 Economic aspects of dialysis

Hemodialysis control unit is costing about the Rs. 2.5 lakhs. The cost of a dialyzer (artificial kidney) was Rs.600/-. The artificial kidney could be reused upto 9-10 times by proper sterilization. So the cost of the kidney for each dialysis was about Rs.60/- and the other expenses for dialysis, such as cost of canula, heparin and dialysate were found to cost Rs.60/-. Hence the average total expenditure for one hemodialysis was found to be Rs.125/-.

In case of peritoneal dialysis the cost of catheter was Rs.175. It was also used several times after sterilization. The cost of dialysate, heparin etc. was found to cost around Rs.60. Hence each peritoneal dialysis was costing on an average Rs.100/-.

Discussion

CHAPTER V

DISCUSSION

Hemodialysis or peritoneal dialysis represent the supportive therapy for renal failure and uremia which remain unresponsive to conservative therapeutic procedures. The purpose of such therapy is to maintain the normalcy of body fluids and support the patient's life while the failing kidneys repair and assume functional capabilities. The superior efficacy of hemodialysis compared to peritoneal dialysis is well recognized in human medicine. Until recently technical and economic factors restricted the development and use of hemodialysis in veterinary practice. To study the efficiency and economy of modern artificial kidneys, an investigation on the feasibility of hemodialysis in experimental and clinical cases of renal failure in canine was undertaken.

5.1 INCIDENCE

Renal disease is one of the most common diseases of dogs and in any renal dysfunction, uremia is a common consequence (Tabotabo *et al.*, 1970, Murray *et al.*, 1971). Cowgill and Spangler (1981) opined that the renal failure is the recognized cause of morbidity and mortality in geriatric dogs. It is more prevalant in aged animals. Low (1981) reported that the incidence of renal problems was 1.8 per cent of hospital admission in dogs. Incidence of confirmed cases of renal diseases was about 1.1 per cent of clinical admissions in dogs (Doxey, 1983). The incidence of clinical cases of primary uremia recorded in this study was 2.07 per cent of hospital admissions at Small

animal clinic (medical unit) of Madras Veterinary College hospital. The present findings concurred with that of Doxey (1983).

Wright *et al.* (1976) recorded nephritis in ten male dogs and six female dogs. Arunkumar (1976) also observed the incidence to be more in male than females. Viswanathan (1988) found that males were more vulnerable than females. Srinivasan (1990) observed major incidence of renal disease in males similar to the earlier findings. The observation of this study on the sex predisposition to renal diseases revealed more incidence in males (62.41 per cent) than females (Fig.3).

Biewinga and Gruys (1986) reported nephritis in dogs aged from one to fourteen years. Center *et al.* (1987) recorded glomerulonephritis in forty one dogs whose age ranged from two months to eighteen years. However, Srinivasan (1990) reported that 52 per cent of the dogs affected by primary chronic renal inefficiency were in the age group of two to five years and 36 per cent in more than 10 years of age. The observation with respect to the age of the clinical cases of uremia under this study were in agreement with Srinivasan (1990).

5.2 CLINICAL SIGNS

Tabotabo *et al.* (1970) reported that anorexia, reteching, vomiting, arching of the back and straining were the common signs of uremia in dogs. Clinical signs of uremia might vary from patient to patient. Dehydration vomiting, hemorrhagic ulcerative gastritis, diarrhoea due to enterocolitis polyuria, polydipsia, oliguria, ulcers in the oral mucous membrane and

progressive degenerative anaemia were the different signs of uremia (Osborne *et al.*, 1972; Bush 1972; Macdougall *et al.*, 1977). The clinical signs observed in the experimentally induced uremia and clinical case of uremia were in agreement with previous authors.

5.3 PATHOLOGICAL CONSTITUENTS OF URINE

In this study varying grades of proteinuria was evident (Fig.4) as 93.33 per cent in experimentally induced uremia and 91.7 per cent in clinical cases of uremia. Chew and DiBartola (1986) reported that pathological renal proteinuria might result from failure of tubular absorption of protein, tubular secretion of protein and protein leakage from the damaged tubular cells. This might be attributed to the occurrence of moderate degree of proteinuria in 93.33 per cent of experimental and 91.7 per cent of clinical cases of uremia. However, Jackson (1964) opined that abnormalities in the urine merely serve to indicate the presence of kidney damage, but do not offer any quantitative measure of the extent of damage nor do they necessarily suggest uremia.

On microscopical examination of the urinary sediment in this study revealed frequent occurrence of pus cells (Fig.4), cylindruria and crystalluria. Krawice (1986) reported that 0-5 pus cells and/or red blood cells could normally be present in urine under high power microscopic examination. McCaw *et al.* (1984) opined an increase in pus cells in the urine indicating inflammation some where in the urinary system. This study revealed frequent occurrence of pus cells in the urine of 40 per cent of experimental and 45 per cent of clinical cases of uremia indicating the presence of inflammatory process.

Casts are often the first indication of renal disease (Fleming *et al.*, 1989). The presence of casts in the urine usually indicated a pathological change in the kidney. Presence of casts observed in the 30 per cent of experimental and 48 per cent of clinical cases of uremia in this study was conformative of pathological changes in the kidney (Fig.4).

Crystals in the sediment of urine have no clinical significance, Calcium oxalate and hippuric acid may be present but are less common. Large number of calcium oxalate in the urine of animals with renal failure may suggest ethylene glycol toxicity (Coles, 1986). Large number of crystals observed (30 per cent in experimentally induced renal failure and 7 per cent in clinical cases of renal failure) in the present study (Fig.4) were in agreement with the observation of Coles (1986).

5.4 HEMATOLOGY

5.4.1 Hemogram

After statistical analysis the mean $\pm$ SE values of hemogram and erythrocytic indices of control and dialysis group of animals were furnished in Tables 4,6,8,10&12.

Schalm *et al.* (1975) reported the following hemogram values for dogs. Total erythrocyte count - 5.5 to 8.5 million/μl, hemoglobin 12 to 18 g/dl and packed cell volume 37 per cent to 55 per cent. Dhanapalan (1987) recorded the mean values of hemogram in non-descript dogs as total erythrocyte count 6.10 $\pm$ 0.29 million/cu.mm, hemoglobin - 11.20 $\pm$ 0.36 g/dl and packed cell volume -36 $\pm$ 0.55 per cent. The hemogram and erythrocytic indices of

apparently healthy animals (before induction of uremia) observed in the present study (tables 4, 6, & 10) were in agreement with the above authors.

In experimental animals after induction of uremia there was significant elevation of packed cell volume (tables 6 & 10) indicating dehydration as a result of frequent vomiting and diarrhoea in uremia. This finding concurred with the observation of Chew and DiBartola (1986) who reported an elevation of packed cell volume in uremic cases. The elevated packed cell volume was found to be decreased significantly after hemo/peritoneal dialysis (Tables 6 and 10). In hemodialysis it could be due to the effect of fluid administered through out the period of hemodialysis procedure, where as in peritoneal dialysis some amount of fluid might be absorbed from the dialysate to the body through the peritoneal membrane and thus corrected the dehydration.

In clinical cases of uremia the mean value of total erythrocyte count, hemoglobin and packed cell volume were found to be significantly lower than the apparently healthy animals (Tables 8 & 12) which was suggestive of a normocytic normochromic anaemia. These observations were in agreement with the findings of Osborne *et al.* (1972), Schalm *et al.* (1975) and Finco (1980) who have reported non-regenerative normocytic normochromic anaemia often associated with chronic renal diseases. From the above findings in the present study it could be presumed that clinical cases utilized for the dialysis experiments were of chronic renal failures. These parameters could be considered as a supportive parameter along with the other kidney function tests to differentiate the acute/chronic renal failure in field conditions. Contrary to the findings on packed cell volume subsequent to dialysis in

apparently healthy animals (before induction of uremia) observed in the present study (tables 4, 6, & 10) were in agreement with the above authors.

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experimental cases, there were no significant changes on packed cell volume in clinical cases of uremia after dialysis. Since there was no elevated packed cell volume before dialysis and further the dehydration could be a prominent feature of acute renal failure than with chronic renal failure.

5.4.2 Leucogram

Schalm *et al* (1975) reported the leucogram values of dogs as: total leucocyte count-6000-17000/μl, neutrophil-3000-15000/μl, lymphocyte 1000-4800/μl, monocyte 150-1350/μl and eosinophil - 100-1250 μl; According to Nambi (1993) leucogram values of non-descript dogs were: total leucocyte count 12875 $\pm$ 2374 cu.mm, neutrophil - 9680 $\pm$ 1697 cu.mm, lymphocyte 2650 $\pm$ 686 cu.mm, monocyte 371 $\pm$ 87 cu.mm, and eosinophil 174 $\pm$ 80 cu.mm. The leucogram values of apparently healthy animals (before induction of uremia) observed in the present study (Tables 7, 9 & 11) were in agreement with the above authors.

After induction of uremia there was significant elevation of total leucocyte and neutrophil count indicating acute inflammatory reaction in the body as a result of experimental induction of kidney damage. These findings concurred with the observations of Osborne *et al*. (1972). DiBartola *et al*. (1985) and McCaw *et al*. (1989) who have reported leucocytosis and neutrophilia in clinical uremia. Similar type of reaction was also observed in clinical cases of uremia (Tables 9 & 13) even though it was lower than experimental cases, was in full agreement with the above authors.

With regard lymphocyte, monocyte and eosinophil there was no change either due to uremia or dialysis in both experimental and clinical cases of uremia.

5.5 BLOOD BIOCHEMISTRY

5.5.1 Serum urea

The mean values of serum urea in experimental and clinical cases of uremia were presented in Tables 14 to 18. The results indicated that there was a significant elevation of blood urea values before dialysis.

Jackson (1964) reported the normal values of blood urea as 6.64 mmol/L or less and in uremia the blood urea level ranged from 13.28 mmol/L to 63.08 mmol/L. English *et al* (1980) recorded the normal blood urea level as 3 to 7.5 mmol/L. According to Srinivasan (1990) the blood urea level in chronic renal insufficiency and experimentally induced renal insufficiency were 28.14 $\pm$ 2.54 mmol/L and 20.57 $\pm$ 2.30 mmol/L, respectively. The blood urea of apparently healthy animals (before induction of uremia), experimentally induced uremic cases and clinical cases of uremia observed in this study were in agreement with the findings of above authors. After dialysis there was significant reduction of blood urea in both experimental and clinical cases of uremia. Cowgill and Bovee (1975) recorded that plasma urea concentration was normalized or nearly so within five hours of hemodialysis therapy. Macdougall (1977) reported a reduction of plasma urea from the level of 76 mmol/L to 37 mmol/L during hemodialysis. The reduction in the levels of blood urea observed in the present study (Tables 15 & 16) were similar with the reduction observed by above authors. In clinical cases of uremia the serum

urea level did not reach normalcy contrary to the experimental cases of uremia. In clinical cases of uremia dialysis could be done only once and that would be the reason for the insufficient reduction of serum urea. From this it could be presumed that single hemodialysis was not sufficient for the complete removal of serum urea from the body.

Tabotabo *et al.* (1970) reported that a high blood urea level of 22.14 mmol/L was lowered to 13.28 mmol/L after 4 hours of dialysis. On subsequent dialysis it was again lowered to 7.49 mmol/L. Crisp *et al.* (1989) observed that serum urea concentration ranging from 39.21 mmol/L to 100.8 mmol/L was reduced to the rang of 26.78 mmol/L to 33.84 mmol/L by continuous ambulatory peritoneal dialysis. The mean $\pm$ SE values of serum urea in experimental and clinical cases of uremic animals after peritoneal were found to be decreased significantly, but did not reach to normal values as occurred in hemodialysis of experimentally induced uremia. From this observation it could be proved that even though the blood urea level was lowered by both dialysis procedures, hemodialysis was more efficient for clearing the abnormal concentration of urea from the blood.

5.5.2 Serum creatinine

Finco (1980) stated that normal creatinine level in dog was usually in the range of 70-160 μmol/L and above 180 μmol/L was indicative of reduced glomerular filtration rate. Srinivasan (1990) reported the serum creatinine values in chronic renal insufficiency and experimentally induced renal insufficiency as 403.10 $\pm$ 63.64 μmol/L and 302.33 $\pm$ 53.04 μmol/L, respectively. Sandhya (1992) recorded the normal creatinine level in non-descript dogs as

96.36 ± 6.19 μmol/L. The mean ± SE values of serum creatinine observed in the apparently healthy (before induction), experimentally induced and clinical cases of uremia are presented in tables 14 - 18. These values are quite comparable to above authors.

After hemodialysis the serum creatinine level lowered significantly both in experimental (from 507.56 ± 22.02 to 234.42 ± 17.3 μmol/L) and clinical cases (from 430.16 ± 67.8 to 235.75 ± 20.98 μmol/L) of uremia and the percentage of serum creatinine reduction was 53.81 per cent and 45.19 per cent in experimental and clinical cases respectively. Macdougall (1977) reported a reduction of plasma from 964 μmol/L to 619 μmol/L (35.7 per cent clearance) during hemodialysis. In experimentally induced uremia the serum creatinine level lowered to normalcy (table 15) after hemodialysis, where as it did not occur in clinical cases (table 16). The reduction of serum creatinine values observed in the present study was in agreement with Macdougall *et al.* (1979), however a higher percentage of clearance of serum creatinine was observed in the present study than that observed by the above authors.

After peritoneal dialysis serum creatinine was lowered significantly both in experimental and clinical cases of uremia but it did not reach to the normal level as observed in hemodialysis of experimentally induced uremia. Jackson (1964) reported that serum creatinine level was lowered from a level of 453.49 μmol/L to 134.37 μml/L after 5 days of dialysis and from 31.5 μml/L to 66.8 μml/L after 8 days of dialysis. Chisp *et al.* (1989) stated that the serum creatinine values were lowered from the range of 663-2062.37 μml/L to 488.85-863.67 μml/L after peritoneal dialysis (clearance rate ranged from

26.40-58 per cent). In the present study the serum creatinine level reduced from 439.65 ± 30.18 μmol/L to 257.72 ± 16.45 μmol/L in experimentally induced uremia and from the mean value of 439.09 ± 74.55 μml/L to 297.23 ± 66.15 μml/L in clinical cases of uremia. The rate of extraction of serum creatinine was 41 per cent and 32 per cent respectively in experimental and clinical cases. The reduction of serum creatinine levels noticed in the present study were within the range reported by Jackson (1964) and Crisp *et al.* (1989).

5.5.3 Serum urea/creatinine ratio

According to Kaneko (1988) the urea/creatinine ratio of dog is 10-20:1. Higher ratios are seen after feeding of a proteinaceous diet or in uremic toxicities, where as low ratio in starvation and liver diseases. The mean value of urea/creatinine ratio obtained in the apparently healthy animals (pre-induction value) were within the range from 14.86 ± 2.61 to 17.32 ± 1.04. After induction it was increased to the range of 16.48 ± 2.07 to 19.90 ± 2.14. (tables 14,15 & 17). The increase in the urea/creatinine ratio observed in the experimentally induced uremia were not gone beyond the normal ratio of 10-20:1 on the 3rd day of induction (before dialysis), where as it has increased to 33.8 ± 2.87 on the 7th day of induction in control animals. (table 14). From this observation it can be presumed that even though the increase in serum urea/creatinine ratios were within the normal range of 10-20:1, the increase observed during every stage of induction of uremia in this study were corresponding to the degree of kidney damage and uremia. In clinical cases the serum urea/creatinine ratio were 21.72 ± 4.37 and 23.63 ± 28 in hemodialysis and peritoneal dialysis groups, respectively (Tables 16 and 18). These values

were in agreement with Kaneko (1988) suggestive of uremic toxicities in clinical cases.

After dialysis serum urea/creatinine ratio decreased significantly in both experimental and clinical case of uremia. In experimentally induced uremia which were treated by hemodialysis, the serum urea/creatinine ratio was found to be lowered significantly to 12.04 $\pm$ 0.78, even beyond the preinduction value of 14.86 $\pm$ 2.61 (Table 15). This might be explained by the observation made by Dosseter (1966) that during hemodialysis urea diffused more rapidly into the dialysate than did creatinine and thus altered the ratio significantly. This phenomenon did not occur in clinical cases of uremia, because of insufficient dialysis.

5.5.4 Serum total protein

Serum total protein values in apparently healthy (before induction of uremia) animals, experimentally induced uremia and clinical cases of uremia were presented in Tables 14-18. Although there was no statisticallly significant change in total serum proteins, there was a slight decerase of serum proteins in clinical cases of uremia. Wiseman *et al.* (1980) stated that serum protein levels were reduced in a wide variety of diseases including the various types of glomerulonephritis, amyloidosis and nephrosis. They explained that total serum protein levels were reduced due to urinary protein loss. Srinivasan (1990) reported low protein levels of 52.4 $\pm$ 2.2 g/L and 55.8 $\pm$ 3.0 g/L in chronic renal insufficiency and experimentally induced renal insufficiency. The lower level of serum total protein observed in the present study is in agreement with Wiseman *et al.* (1980) and Srinivasan (1990). The moderate

degree of proteinuria observed in the present study might be the reason for the low level of serum protein in clinical casesof uremia (table 14 & 18).

The mean values of serum total protein in clinical cases of uremia (Tables 16 and 18) were found to be lower than the mean values of experimentally induced uremia (tables 15, 17). The clinical cases under the present study were suffering from chronic nature of renal problem as evident from the normocytic normochromic anemia and all the animals had moderate degree of proteinuria since long time and that could be the reason for the development of hypoproteinemia in clinical cases of uremia as opined by Wiseman *et al.* (1980). The concurrent occurrence of proteinuria and hypoproteinemia observed in the clinical casesof the present study might be considered as a parameter to differentiate acute/chronic renal failure. However a more detailed well designed study is required to give an authenticated suggestion about this aspect.

After hemodialysis there was no significant change in the serum protein levels, where as peritoneal dialysis resulted in significant loss of serum protein in the experimental and clinical cases of uremia (Tables 17 & 18). These findings concurred with the protein loss observed during peritoneal dialysis by Thornhill (1984) and Clement (1991). They have explained that it could be due to the large pore size of the peritoneal membrane which allowed the passage of substances with higher molecular weight like protein. In case of hemodialysis, protein having high molecular weight could not pass through the small proes of the membranes of the dialyser (Dhein 1981). Ash (1981) reported that large proteins and blood cells were rejected while small

molecules such as urea and creatinine cross easily through the membrane pores of dialyzer.

5.5.5 Serum sodium and chloride

Hoe and O Shea (1965) stated that the plasma concentration of the electrolytes sodium and chloride are likely to be altered at some stage in the course of acute renal failure. DiBartola *et al.*(1985) reported hyponatremia (120-139 mmol/L) and hypochloremia (90 - 120 mmol/L) in acute renal failure in dogs. The mean value of serum sodium and chloride were found to be altered significantly on the 7th day of induction of uremia (Table 14). In experimental and clinical cases of uremia there was reduction in the levels of sodium and chloride before dialysis (Tables 15 - 18) which was not significant statistically. The changes observed in the experimentally induced and clinical cases of uremia were in agreement with the above authors. After dialysis the serum levels of sodium and chloride were found to be normal in experimental and clinical cases of uremia. The dialysate used in both hemodialysis and peritoneal dialysis had the normal concentration of electrolytes as that of blood. Hence there was no net change of the concentration of these electrolytes in the blood. However slight reduction of sodium and chloride observed before dialysis were corrected by diffusion of these electrolytes from dialysate to the blood, a net transfer of electrolytes from the higher concentration in the dialysate to the lower concentration of blood (Dhein 1981).

5.5.7 Serum potassium

The mean values of serum potassium were found to be increased significantly at every stage of the experimentally induced uremia and clinical cases of uremia (Tables 14 - 18). Pits (1968) stated that the plasma concentration of potassium was usually elevated from the normal value of 4.3 $\pm$ 0.8 mmol/L in acute renal failure. Hyperkalemia in dogs has been reported following the release of potassium from cells as a result of protein catabolism and acidosis (Bush, 1972). An elevated potassium level of 5-6 mmol/L to 8-9 mmol/L was reported in acute renal failure (DiBartola *et al.*, 1985). After dialysis the serum levels of potassium were decreased significantly in both experimentally induced uremia and clinical cases of uremia. There was no significant difference in the extraction of potassium between hemodialysis and peritoneal dialysis. In both cases elevated serum potassium was brought back to normalcy after dialysis, since potassium diffuses very rapidly through the membranes than any other substances. Cowgill and Bovee (1975) recorded that elevated serum potassium levels, a frequent cause of death in uremic animals, could be lowered to safe levels one hour after the start of hemodialysis. Parker (1981) recorded that equilibrium of potassium was over 90 per cent complete after the first 40 minutes and 98 per cent by the end of the first hour. The equilibration of potassium to the normal level occurred in the present study concurred with the findings of the above authors. Both dialysis could be considered as equally good for the alleviation of hyperkalemia, the most potent life threatening factor during the uremic crisis.

5.6 EFFICACY OF HEMODIALYSIS V/S PERITONEAL DIALYSIS

Efficacy of dialysis is assessed from the rate of extraction of common uremic toxins taking place during dialysis. Rate of extraction of uremic toxins in the present study is furnished in table 19.

Takeda (1993) reported the extraction rate of blood urea nitrogen and creatinine were 9.6 to 61.3 percent and 8.8 to 82.4 per cent, respectively when the flow rate of blood was 17 to 100 ml with 0.5 to 1.5 M^2 dialyzer. In the present study the dialyzer used was 0.8 M^2 and the blood flow speed was maintained at the rate of 5-10 ml/kg/minute. However the rate of extraction observed in the present study (urea - 60.19 $\pm$ 1.74 and creatinine 45.45 $\pm$ 3.34) is in the range of rates reported by the above author.

In case of peritoneal dialysis Crisp *et al.* (1989) recorded a clearance rate of 15.13 percent to 64.68 per cent for blood urea nitrogen and a range of 27.74 per cent to 56.16 per cent for serum creatinine. The extraction rates obtained in the present study were 47.94 $\pm$ 2.46 and 36.88 $\pm$ 2.08, respectively for blood urea and creatinine and this was in agreement with the extraction rates reported by Crisp *et al.* (1989).

When compared the values of rate of extraction between hemodialysis and peritoneal dialysis, there was no significant difference between their efficacy in respect to the extraction of uremic toxins. However a higher rate of extraction of uremic toxins were observed in the hemodialysis experiments. Moreover in hemodialysis, the mean values of serum urea and creatinine were found to be decreased significantly to the normal level after dialysis, whereas

in peritoneal dialysis it did not reach to the normal level. In peritoneal dialysis there was loss of plasma protein during dialysis, which was not observed in the hemodialysis. Hence hemodialysis could be considered superior to peritoneal dialysis with respect to the extraction of uremic toxins and retention of plasma proteins.

5.7 OBSERVATIONS DURING DIALYSIS

5.7.1 Technical aspects

Hemodialysis could be performed in this study without much complications by proper cannulation and preparation of suitable dialysate for the dog species. Cannulation was done by using intravenous canula commonly used in human beings, which can be reused if properly sterilized. Even for repeated dialysis there were no complications with the use of intravenous canula. There was no need for the preparation of arterio-venous shunt for hemodialysis as reported by Dhein (1981).

The dialyzer used in the present study was a pediatric dialyzer (0.8 M^2) and it has given satisfactory clearance during dialysis. For canine patients still small dialyzers are preferable as the total blood volume will be less when compared to human beings.

For systemic anticoagulation heparin was administered at the rate of 75 IU/kg body weight as a priming dose and it was maintained by continuous infusion of heparin at the dose rate of 50 IU/kg per hour. With this dosage level no untoward effects were observed during dialysis and after dialysis.

5.7.2 Efficacy of dialysis

All the experimental and clinical uremic animals were recovered from the uremic crisis after hemo/peritoneal dialysis. In experimentally induced uremia, all the animals lived upto 1-2 weeks after dialysis, but subsequently died due to existing renal damage hence the survival rate was zero. In clinical cases survival rate was 25%. All the animals in this study were suffering from either acute toxic nephritis or chronic renal diseases, and they were not considered ideal patients for hemodialysis. The ideal patient for hemodialysis in veterinary medicine would be an acute oliguric and uremic dog as reported by (Dhein 1981).

5.7.3 Economic aspect of hemodialysis

The initial expenditure for the installation of hemodialysis unit was very high, Rs.2.5 lakhs. For each hemodialysis in the present study the expenditure was around Rs.125 and for peritoneal dialysis it was around Rs.100/- so costwise there was not much difference between hemodialysis and peritoneal dialysis. Since peritoneal dialysis was to be performed more frequently the overall cost of the peritoneal dialysis for a course of therapy was equal to hemodialysis. But with regard a efficacy hemodialysis was found to be superior to peritoneal dialysis for clearing the uremic toxins.

Summary

CHAPTER VI

SUMMARY

A study on "Hemodialysis in canine uremia" was conducted to assess the feasibility and efficacy of hemodialysis in uremia and it was compared with peritoneal dialysis. The study included 30 experimental and 12 clinical cases of uremia. Experimental induction of uremia was carried out by oral administration of ethylene glycol at the dose rate of 6.6 ml/kg body weight or intravenous administration of mercuric chloride at the dose rate of 2mg/kg body weight each in 15 number of dogs. Hemodialysis was performed in 12 experimentally induced uremia and 6 clinical cases of uremia. Like wise peritoneal dialysis was also carried out in equal number of animals. Six experimentally induced uremic animals were maintained as control without any dialysis.

The following characters were taken for the study in experimental and clinical cases

a. Incidence

b. Clinical signs

c. Pathological constituents of urine

d. Hematology - hemogram and leucogram

e. Blood biochemistry - serum urea, creatinine, total protein, sodium, potassium and chloride.

The following were the significant observations of this study.

Incidence of uremia among the clinical cases brought to the small animal clinic (medical unit) of Madras Veterinary College Hospital during the period of 3 years (1990-1992) was 2.07 per cent. Among them 62.41 per cent were male and 37.59 per cent were females. 79.94 per cent of dogs affected with renal failure were above eight years and the remaining dogs were less than 8 years of age.

Important clinical signs observed in experimentally induced uremia were loss of appetite, depression, oliguria/anuria, vomiting, melaena, dehydration and altered gait. In clinical cases of uremia the signs were frequent vomiting, haemorrhagic enteritis, ulcers in the buccal mucosa, polyuria/oliguria, polydipsia and depression.

The abnormalities in the urine merely served to indicate the presence of kidney damage, and did not offer any quantitative measure of the extent of kidney damage and uremia. Dialysis did not show any significant effect on the pathological constituents of urine.

In experimental animals after induction of uremia there was significant elevation of packed cell volume which indicated dehydration as a result of frequent vomiting and diarrhoea. After hemodialysis and peritoneal dialysis the packed cell volume was brought to the normal level. The normocytic normochromic anaemia observed in the clinical cases of uremia was suggestive of the chronic nature of the clinical cases. The erythrocytic indices could be considered as a supportive parameters along with other kidney

function tests to differentiate the acute/chronic renal failure in field conditions. Leucocytosis and neutrophilia observed in this study was suggestive of inflammatory reactions in the body both in experimental and clinical cases of uremia. Dialysis did not have any effect on the leucogram of uremic animals.

Serum urea, creatinine and serum urea/creatinine ratio were found to be significantly elevated in experimentally induced and clinical cases of uremia. After hemodialysis and peritoneal dialysis, the serum urea, creatinine and urea/creatinine ratio were lowered significantly. However hemodialysis was found to be more efficient for clearing the uremic toxins, since a higher clearance rate was observed for both experimentally induced uremia and clinical cases of uremia during hemodialysis.

Serum protein level did not change significantly in experimentally induced uremia. However a slight reduction in the serum protein was observed in clinical cases of uremia which was attributed to the presence of proteinuria since long time due to chronic nature of renal damage in clinical cases. The concurrent occurrence of proteinuria and hypoproteinemia observed in the clinical cases might be considered as a parameter to differentiate acute/chronic renal damage.

During peritoneal dialysis there was significant loss of plasma protein leading to hypoproteinemia. This phenomena did not occur in hemodialysis group of animals.

The concentration of serum sodium and chloride did not alter significantly during the uremic state both in experimental and clinical cases.

However a slight reduction noticed before dialysis was found to be corrected after dialysis by diffusion of these electrolytes from the dialysate to the blood during dialysis both in hemodialysis and peritoneal dialysis.

The serum concentration of potassium was significantly elevated in experimental and clinical cases of uremia. Hyperkalemia was found to be quickly corrected both in hemodialysis and peritoneal dialysis as potassium diffused very rapidly through the dialyzing membranes. Both dialysis techniques could be considered equally good for the alleviation of hyperkalemia, the most potent life threatening factor during uremic crisis.

Hemodialysis could be performed in this study without much complication by proper cannulation and preparation of suitable dialysate with the facilities available in the laboratory. Blood access was made by intravenous cannulation instead of creating arterio-venous shunt surgically. Systemic anticoagulation was also done successfully and there was no further bleeding after dialysis under the dosage used in the present study.

All the experimental and clinical cases recovered from the uremic crisis after dialysis, but subsequently died due to the underlying toxic nephropathy/chronic renal failure. Economically hemodialysis was costlier than peritoneal dialysis, but with regard to the efficacy hemodialysis was found to be superior. Peritoneal dialysis needsto be performed daily or alternate days, where as hemodialysis needsto be done once in 3 or 4 days.

The following conclusions were derived from this study.

1. The hemodialysis can be safely and effectively used in canine practice for alleviating uremic crisis.

2. It is found superior to peritoneal dialysis for clearing uremic toxins.

3. It is also found that total serum protein level did not lower significantly after hemodialysis where as in peritoneal dialysis there was loss of serum protein.

4. Hemodialysis requires lesser time than peritoneal dialysis. Peritoneal dialysis is to be performed daily or alternate days. The stress due to frequent manipulation of the patient is minimum in hemodialysis and also the man hours required to bring the animal to the hospital is less when compared to peritoneal dialysis.

5. From the experience in this study and reviewing the literature on hemodialysis, it is found that hemodialysis can also be used as an emergency therapy in poisoning cases of the dogs, if the poison is dialysable.

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APPENDIX 1

Proforma for Case Study

Serial No. : Clinical/Experimental

Case No. :

Name & Address of the Owner :

Description of the Dog

Breed : Sex **Age:**

Colour : Body **Wt.**

Owners Complaint :

History

Present :

Past :

Diet :

General Clinical Examination

General appearance and behaviour

Body condition

Condition of skin and coat

Respiration

Abdomen

Posture

Gait

Abnormal acts

Visible Mucous **Membrane**

Temperature

Pulse

Systemwise Examination

Digestive System :

Circulatory System :

Urogenital System :

Nervous System :

Lymphatic System :

Locomotor System :

Laboratory Investigation

Urine : Specific Gravity
Colour
Protein
Glucose
Bile Pigments
Sediments

Blood

Haematology Haemoglobin
P.C.V. L%
R.B.C. M%
W.B.C. E%
Blood Parasites B%

Biochemistry Blood Urea
Serum Creatinin
Serum Total Protein
Serum Potassium
Serum Sodium
Serum Chloride

Diagnosis

Prognosis

Therapy Hemodialysis
Peritoneal dialysis

Results

Remarks

APPENDIX 2

Analysis of Variance for the hemogram and erythrocytic indices in experimentally induced uremia (Control Groups)

Source of Variations	df	Hb		PCV		TEC		MCV		MCH		MCHC	
		MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value
Treatment	2	7.065	2.201	49.339	4.26	3.027	2.101	43.380	1.928	24.264	2.012	18.405	1.729
Error	15	3.210	-	11.582	-	1.441	-	22.500	-	12.060	-	10.645	-

Analysis of Variance for leucogram in experimentally induced uremia (Control Groups)

Source of Variations	df	TLC		N		L		M		E	
		MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value
Treatment	2	197909.46	7.38	115878.07	8.83	220375.36	2.005	58874.46	1.828	90210.96	1.721
Error	15	26817	-	13429	-	109912.09	-	32267.04	-	52417.76	-

APPENDIX 3

Analysis of Variance for the hemogram and erythrocytic indices before and after hemodialysis experimentally induced uremia

Source of Variations	df	Hb		PCV		TEC		MCV		MCH		MCHC	
		MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value
Treatment	2	5.01364	2.02	40.24122	3.81	3.388535	2.011	56.66	1.767	23.29	2.020	19.134	1.562
Error	15	2.482	-	10.562	-	1.685	-	32.07	-	11.33	-	12.25	-

Analysis of Variance for the hemogram before and after hemodialysis experimentally induced uremia

Source of Variations	df	TLC		N		L		M		E	
		MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value
Treatment	2	142867.62	6.98	79278.27	6.388	19911.63	2.016	45445.57	1.718	81254.52	1.920
Error	15	22365.20	-	12410.50	-	9876.80	-	26452.60	-	42320.06	-

APPENDIX 4

Analysis of variance for hemogram and erythrocytic indices, before and after hemodialysis in clinical cases of uremia

Source of Variations	df	Hb		PCV		TEC		MCV		MCH		MCHC	
		MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value
Treatment	2	9.04576	3.82	36.41292	3.69	6.6674	3.70	54.209	1.892	25.984	2.320	20.884	1.928
Error	15	2.3680	-	9.8680	-	1.8020	-	28.652	-	11.200	-	10.832	-

Analysis of variance for leucogram before and after hemodialysis in clinical cases of uremia

Source of Variations	df	TLC		N		L		M		E	
		MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value
Treatment	2	72260.34	3.82	48335.44	4.72	26813.17	2.626	44899.88	1.828	75703.10	1.802
Error	15	18916.32	-	10240.56	-	10210.65	-	24562.30	-	42010.60	-

APPENDIX 5

Analysis of variance for the hemogram before and after peritoneal dialysis in experimentally induced uremia

Source of Variations	df	Hb		PCV		TEC		MCV		MCH		MCHC	
		MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value
Treatment	2	2.944356	1.572	47.123944	3.812	3.202108	1.729	23.210	1.025	20.198	1.642	18.582	1.782
Error	15	1.873000	-	12.362	-	1.852000	-	22.640	-	12.301	-	10.428	-

Analysis of variance for leucogram before and after peritoneal dialysis in experimentally uremia

Source of Variations	df	TLC		N		L		M		E	
		MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value
Treatment	2	141244.25	6.528	78796.94	6.427	17572.27	1.721	45578.28	1.852	39391.35	1.225
Error	15	22320.52	-	12260.30	-	10210.50	-	24610.30	-	32156.20	-

APPENDIX 6

Analysis of variance for the hemogram before and after peritoneal dialysis in clinicals cases of uremia

Source of Variations	df	Hb		PCV		TEC		MCV		MCH		MCHC	
		MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value
Treatment	2	11.1042	3.72	45.448	3.68	7.63938	3.78	57.95	1.782	31.508	2.420	18.957	1.852
Error	15	2.9850	-	12.350	-	2.0210	-	32.52	-	13.02	-	10.236	-

Analysis of variance for leucogram before and after peritoneal dialysis in clinical cases of uremia

Source of Variations	df	TLC		N		L		M		E	
		MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value
Treatment	2	145795.55	6.532	77177.34	6.427	18580.84	1.821	49304.28	1.528	43175.38	1.762
Error	15	22320.20	-	12008.30	-	10203.65	-	32267.20	-	24503.62	-

APPENDIX 7

Analysis of variance for biochemical parameters of blood in experimentally induced uremia (Control Groups)

Source of Variations	df	BU		CR		BU/CR		PROTEIN		SODIUM		POTASSIUM		CHLORIDE	
		MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value
Treatment	2	970.25	66.35	187562.17	66.90	73.766	7.82	3.79	0.41	43.61	6.69	11.64	62.32	157.171	4.91
Error	15	14.62	-	2803.62	-	9.433	-	9.20	-	6.52	-	0.18	-	32.012	-

Analysis of variance for biochemical parameters of blood before and after hemodialysis in experimentally induced uremia

Source of Variations	df	BU		CR		BU/CR		PROTEIN		SODIUM		POTASSIUM		CHLORIDE	
		MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value
Treatment	2	1018.08	71.05	20616.54	19.62	34.2976	3.68	4.9034	0.56	24.168	2.87	7.92252	32.48	23.715	0.75
Error	15	14.32	-	5602.32	-	9.32	-	8.7560	-	8.421	-	0.18650	-	31.620	-

APPENDIX 8

Analysis of variance for biochemical parameters of blood in clinical cases of uremia

Source of Variations	df	BU		CR		BU/CR		PROTEIN		SODIUM		POTASSIUM		CHLORIDE	
		MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value
Treatment	2	372.406	28.68	95827.47	18.42	45.93	3.68	24.3238	1.5873	16.839	1.8242	1.7278	9.58	68.949	2.14
Error	15	16.420	-	5202.36	-	12.48	-	15.324	-	9.231	-	1.1803	-	32.100	-

Analysis of variance for biochemical parameters of blood before and after peritoneal dialysis in experimental cases of uremia

Source of Variations	df	BU		CR		BU/CR		PROTEIN		SODIUM		POTASSIUM		CHLORIDE	
		MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value
Treatment	2	680.99	46.58	234941.09	48.18	43.15	3.84	86.41	5.29	4.55	0.36	2.42	13.23	26.414	0.81
Error	15	14.62	-	4876.32	-	11.24	-	16.33	-	12.63	-	0.18	-	32.61	-

APPENDIX 9

Analysis of variance for biochemical parameters before and after peritoneal dialysis in clinical cases of uremia

Source of Variations	df	BU		CR		BU/CR		PROTEIN		SODIUM		POTASSIUM		CHLORIDE	
		MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value	MSS	F Value
Treatment	2	385.7096	26.86	57210.33	17.52	38.54	3.72	86.911	4.7281	20.497	1.62	1.44	8.72	64.89	2.08
Error	15	14.3600	-	3265.43	-	10.36	-	18.382	-	12.620	-	0.16	-	31.20	-