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अंशदायी स्वास्थ्य सेवा स्कीम
CONTRIBUTORY HEALTH SERVICES SCHEME

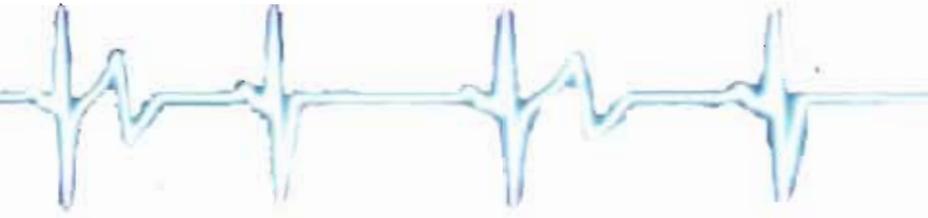


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Maharashtra Medical Council Accredited CMEs conducted at BARC Hospital since the date of accreditation, March 28, 2011

Date	Department	Topic	Speaker
July 8, 2011	Obstetrics & Gynaecology	Cervical Cancer Prevention and Management - Unveiling New Facts	Dr. Mukesh Gupta Dr. Amita Maheshwari
August 26, 2011	Chembur Dispensary	Geriatric Medicine	Dr. Rekha Bhatkhande Dr. H. K. Hase Dr. Bharat Shah
October 14, 2011	ENT	What is New is ENT, Head & Neck	Dr. Prabodh Karnik Dr. Pragnya Parikh Dr. Pankaj Chaturvedi
December 9, 2011	Pediatric	Challenges in Pediatric Infections	Dr. Mamta Manglani Dr. Ira Shah Dr. Anand K. Shandilya
February 3, 2012	Anesthesia	CPCR & Organ Transplant	Dr. Khusrav B. Bajan Dr. Rahul Pandit Dr. Sanjay Nagral
March 30, 2012	Surgical	Palliative Care for life-limiting illness	Dr. Mary Ann Muckaden Dr. P.N. Jain Dr. Sheila N Myatra
June 1, 2012	Medicine	Rheumatology	Dr. Vikram Londhey Dr. Balkrishnan Dr. Sunil Singh
August 3, 2012	Radiology	Non Invasive Vascular Imaging - Role of CT & MRI	Dr. Hemant Telkar Dr. Deepak Patkar Dr. Susheel Kumar
October 5, 2012	Pathology	Update in Laboratory Medicine	Dr. Varsha Vadera Dr. Avinash Phadke Dr. Prema Varthakavi



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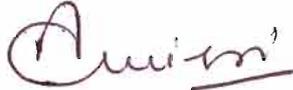
This issue of 'Pulse' focuses on 'Renal disease'. The guest article by Dr. Viswanath Billa has illustrated the objective of BP regulation which is to ensure that enough blood flows to each organ which is physiologically adequate and not injurious. In the physiological aspects, the Pressure Natriuresis Curve and its fundamental correlate to the underlying physiological regulation i.e. increase in salt intake, increase in BP and the role of various regulatory mechanisms like nervous and renal have been explained in detail. In short, the correlation of cardiovascular and renal systems, has been explained clearly. In pregnancy, renal disease can get manifest in gestational hypertension and diabetes. Timing of delivery can prevent the progression of renal disease in such cases. The women with chronic renal disease who opt for pregnancy are at increased risk of rapid deterioration of renal function.

As a part of infection control measures, CDC's core guidelines during dialysis procedures are suggested. In these procedures as there is direct access to the blood stream in haemodialysis and to the closed peritoneal cavity in chronic ambulatory peritoneal dialysis through various tubings/ catheters, the strict compliance with these guidelines shall help to minimize infection related complications.

Lastly, a message for the Resident Medical Officers and the Nursing staff with regard to the generalized care of the hospitalized patients from patient's safety point of view:

- 1. Use of standardized abbreviations and dose designations.*
- 2. Prompt writing of clear, concise and legible admission orders with date and time and the legible signature.*
- 3. Prevention of nosocomial infections by strict adherence to the Infection control practices.*
- 4. Excellent communication among the physicians, nursing staff and the patients/relatives.*

We dedicate this issue of 'Pulse' to our senior colleague, Late Dr. D.K. Jaitley, then Head of Anaesthesiology and Head Medical Division, whose dedication to Medical Division has always inspired us. Dr. Jaitley has given us the opportunity to work for the 'Pulse'.


(Dr. Amrita Misri)

What has Salt got to do with Blood Pressure?

Dr. Viswanath Billa MD, DM

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Consultant Nephrologist and Transplant Physician, Bombay Hospital

A pioneering observation was made by t Nei Ching, in a classic Chinese text, dated 100 BC that linked, for the first time, hypertension and salt intake. In his treatise he refers to hypertension as, "the 'hard pulse' resulting from a high salt intake".

This article attempts to study the data available to date on this subject and current understanding and research that establishes a link between salt as a risk factor to the development of hypertension. In the course of this paper, a systematic analysis of epidemiologic data, evolutionary correlates, physiological correlates and randomized control trials has been done, in an attempt to understand this relationship.

Epidemiologic data:

Lewis Dahl made some seminal observations on salt intake and the prevalence of hypertension in different geographic areas and races, which was published in the American Journal of Clinical Nutrition in 1972. As seen in Fig. 1, he noted that essential hypertension is seen primarily in societies

with average sodium intakes above 100 meq/day (2.3 g sodium); it is rare in societies with average sodium intakes of less than 50 meq/day (1.2 g sodium). These observations do suggest that the development of hypertension requires a threshold level of sodium intake.

The most significant modern epidemiologic research was the INTERSALT Study, which was a worldwide study that tested both within and cross-population prior hypotheses on 24 hour sodium excretion and blood pressure. The relation between these two variables was studied in 10079 men and women aged 20-59, sampled from 52 centres around the world based on a highly standardised protocol and extensive quality control. The results are depicted graphically in the Sodium excretion ranged from 0-2 mmol/24 h (Yanomamo Indians, Brazil) to 242 mmol/24 h (north China). In individual subjects (within centres) it was significantly related to blood pressure. Four centres found very low sodium excretion, low blood pressure, and little or no upward slope of blood pressure with age. Across

the other 48 centres sodium was significantly related to the slope of blood pressure with age but not to median blood pressure or prevalence of high blood pressure. Potassium excretion was negatively correlated with blood pressure in individual subjects after adjustment for confounding variables. As seen in Figs. 2&3 and Table 1, there clearly is a relationship between salt intake and blood pressure in the subjects of this study. Also, the comparative data showing salt consumption and BP between low salt consuming populations versus the rest of the populations studied clearly shows a BP advantage in the low salt consuming populations.

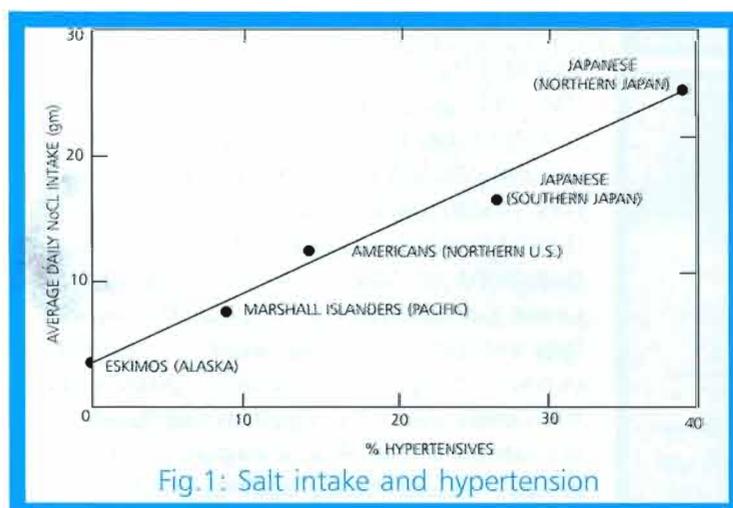


Table 1: Comparison of Four Low Sodium Centres and Remaining 48 INTERSALT Centres

Variables	Yanomamo New Guinea	Xingu	Papua 48 centres	Kenya	Remaining
Lifestyle Factors					
24-hour sodium (mmol-median)	<1	6	27	51	160
Sodium/potassium ratio (median)	<0.01	0.08	0.48	1.8	3.4
BMI	21.2	23.4	21.7	20.8	25.2
Alcohol drinkers (%)	0	0	8.7	30.7	53.0
Blood pressure					
Systolic BP (median)	95.4	98.9	107.7	109.9	118.7
Diastolic BP (median)	61.4	61.7	62.9	67.9	74.0
Hypertensive (%)	0	1.0	0.8	5.0	17.4
Systolic slope with age (mm Hg/10 yr)	-1.1	+0.6	-1.4	+2.4	+5.0

*Systolic blood pressure (BP) of 140 mm Hg or more, diastolic BP of 90 mm Hg or more, or receiving antihypertensive therapy.
BMI, body mass index.

What Dahl published as an observation of salt consumption and blood pressure is fairly congruous to the results of the randomised control trial, INTERSALT.

Why do humans need salt?

Sodium is a vital constituent of the body's ionic composition. In order to maintain extracellular fluid volume, 2500 mEq i.e. 150gm of sodium is necessary. In order to trigger the intracellular action potential 300mEq i.e. 18gm of sodium is required. If salt is essential for life, then why does salt cause disease? Is there a finite threshold of salt consumption that is essential for health and anything beyond this becomes counterproductive to good health?

Salt and Human evolution: We now believe that salt has some causal relation with BP. But we have not been able to establish a mechanistic link between the two. Medicine has historically been concerned with mechanistic or 'proximate' answers to questions of how diseases develop and cause pathology. This approach may not fully explain disease causation. In contrast, evolutionary, or 'ultimate' questions, frequently ask 'why' structures or functions are as they are. A full explanation of a disease should ideally address both.

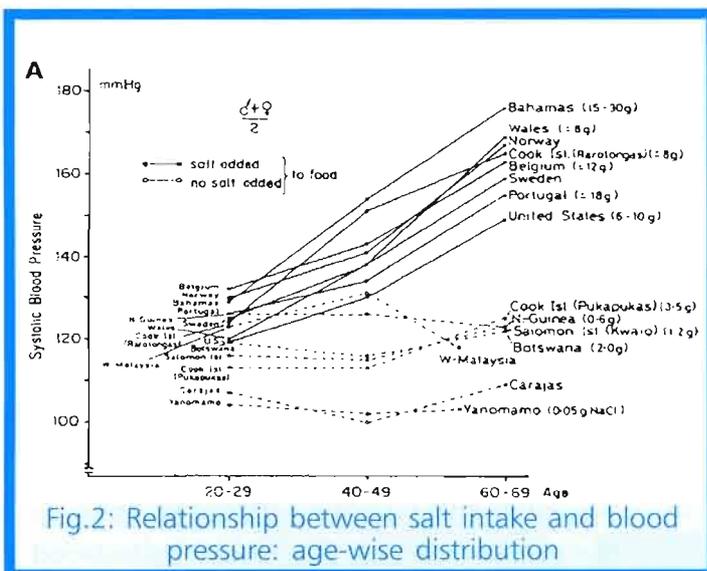


Fig.2: Relationship between salt intake and blood pressure: age-wise distribution

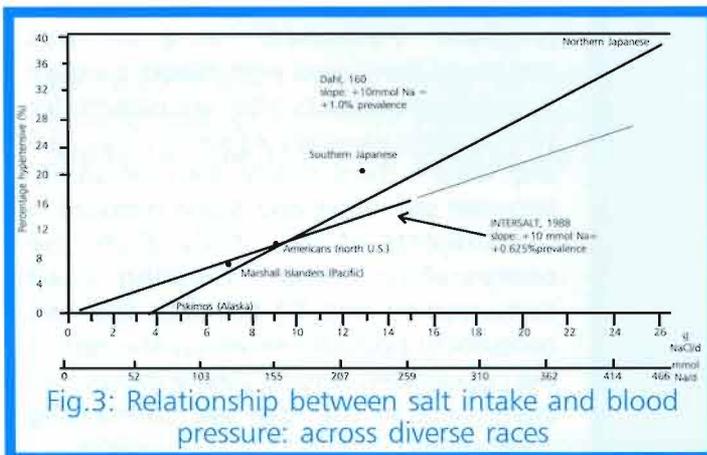


Fig.3: Relationship between salt intake and blood pressure: across diverse races

Life evolved as a unicellular organism. This life form had a simple process for nutrient delivery by diffusion across the cell membrane to provide energy to simple processes of life. As animals evolved, body size increased, and delivery of nutrients to cells came to exceed the range of diffusion. Simple systems capable of supporting cellular metabolism arose, and natural selection went on to shape our staggeringly complex, highly integrated cardiovascular system. In a multicellular organism processes got centralised. There needed to be an organisational structure, no multiplication of responsibility, good communication lines, systems that would deliver input and carry back the output. i.e. a circulatory system. Blood pressure thus became an emergent property of this system. Blood pressure, however, cannot be reduced to the individual elements of the circulation. It is a function of all of them acting in concert; it is an emergent property of the entire system. All hierarchically organized biological systems have higher order emergent functions that depend on, but are not predictable from, the structures and functions of lower levels. Because emergent properties are lost when a system is disaggregated, integrative physiology is critical to understanding blood pressure regulation.

Human beings are believed to have originated in central Africa. In this location, far away from any physical contact to salt in the environment, where diet consisted of what could be gotten by hunting and gathering, sodium conserving genotypes evolved. Since the source of sodium was limited, the body's requirement of sodium was regulated by minimizing losses. As humans migrated out of central Africa, selection pressure for sodium conservation declined in the cooler, wetter climates of the northern latitudes and coastal areas of Africa. However, genetic drift ensured that ancestral sodium-conserving genotypes persisted. If genes originally selected for sodium conservation changed the set point of the renal pressure–natriuresis to a higher blood pressure range when expressed in an environment of sodium abundance, individuals harboring such

genotypes could be at increased risk of developing hypertension. To explain this phenomenon, James Neel proposed the 'thrifty genes' hypothesis. In principle, this hypothesis suggests that any life forms genetic makeup improve an organism's ability to conserve nutritional resources obtained in times of abundance thereby favoring survival during times of want. This ensures reproductive success and the survival of that life form. Thus a changed environment posed a challenge to the genetic framework that was by now programmed to conserve salt. A tradeoff in this scheme of things was the development of hypertension.

Physiological explanation: The fundamental objective of BP regulation is to ensure that enough blood flows to each organ, avoiding competition between organs, adjusting BP to the need of that organism at that time point, and helping keep BP at a level where it is physiologically adequate and not injurious.

Guyton developed a 'Systems Engineering' model or Physiome, which he called 'SAPHIR'—"a Systems Approach for Physiological Integration of Renal, cardiac, and respiratory functions" (Fig.4). The idea behind the Physiome is to see the organism as an integrated system in which each organ plays a role.

He then hypothesised the concept of Hierarchy of Control systems and its contribution to BP regulation. He established a temporal pattern of this and classified them into,

1. short-term (damping), where cardiovascular reflexes regulated blood pressure, mediated by the nervous system
2. intermediate-term (damping) where capillary fluid shifts, delayed compliance of the vasculature, hormonal controls (AngII, AVP) regulated blood pressure.
3. long-term (control), where the kidney manages overall fluid and solute balance, which determines the baseline level of BP. This mechanism had infinite gain.

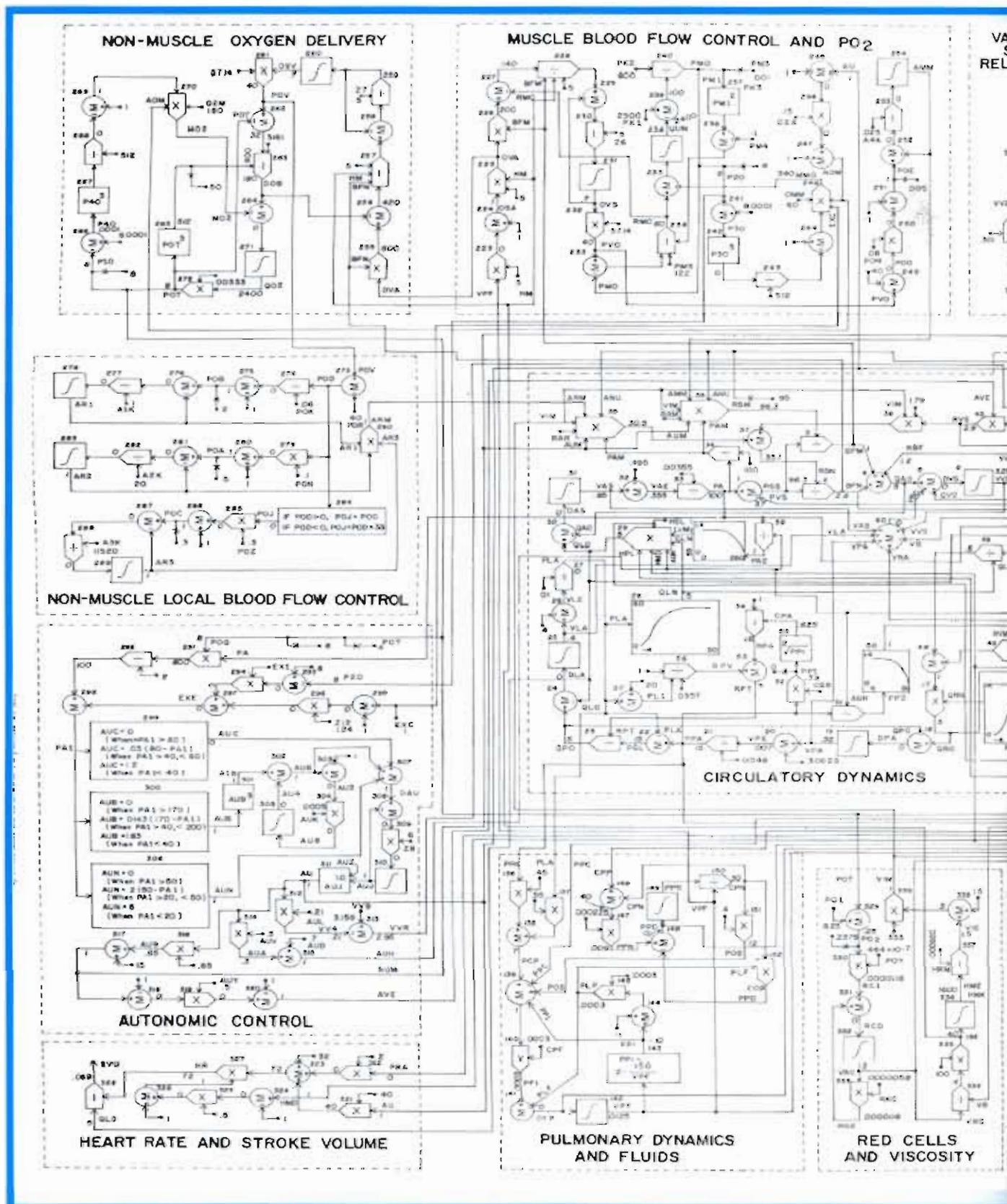


Fig.4: Systems Engineering Model:

AR
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KIDNEY DYNAMICS AND EXCRETION

THIRST AND DRINKING

CAPILLARY MEMBRANE DYNAMICS

ANTIDIURETIC HORMONE CONTROL

ANGIOTENSIN CONTROL

ALDOSTERONE CONTROL

HEART HYPERTROPHY
OR DETERIORATION

TISSUE FLUIDS, PRESSURES AND GEL

ELECTROLYTES AND CELL WATER

"SAPHIR"

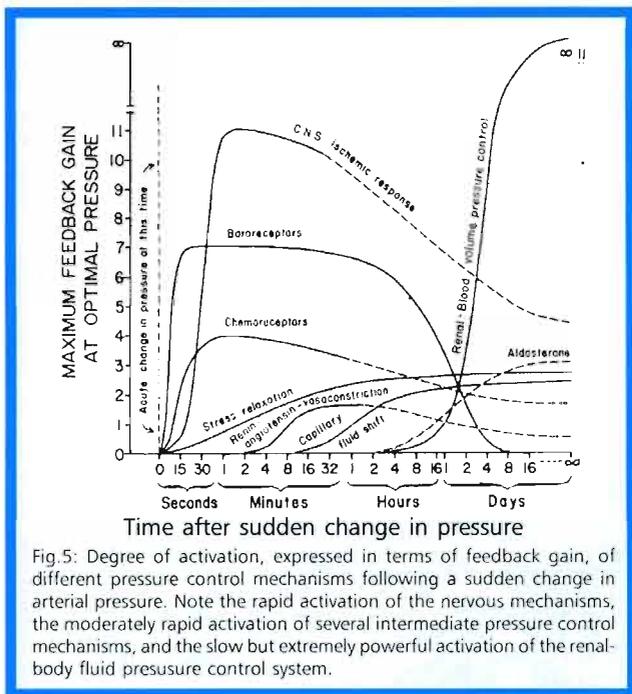


Fig. 5: Degree of activation, expressed in terms of feedback gain, of different pressure control mechanisms following a sudden change in arterial pressure. Note the rapid activation of the nervous mechanisms, the moderately rapid activation of several intermediate pressure control mechanisms, and the slow but extremely powerful activation of the renal-body fluid pressure control system.

This hierarchy of pressure control systems (Fig. 5) very elegantly demonstrates how blood pressure regulatory mechanisms influence BP as a time dependent variable, and how the early responses are quick to react but inefficient, and the late responses are slow to react but more efficient.

The Pressure-Natriuresis Curve is the functional correlate of this underlying physiological regulation (Fig. 6).

An increase in sodium intake shifts the curve to the right ensuring that a similar amount of sodium gets excreted. The tradeoff of this regulatory mechanism is an increase in blood pressure. The curve also depicts the infinite gain feature of the kidney - blood volume - pressure regulator (Fig. 7,8,9). Guyton also used this curve to analyse arterial pressure regulation in several altered functional and pathological states of the kidney such as reduced kidney mass, Goldblatt kidneys and high aldosterone and angiotensin states.

The concept of Salt Sensitivity: This term is the blood pressure responsiveness to variations in Na intake. There is as yet no biochemical nor

clinical criteria for this trait. However several features of this state and factors associated with this state are described in the Tables 2&3.

Randomised control trials to study the association between salt intake and hypertension

There are several ways to determine salt consumption. While dietary recall appears to be a reasonable method, it can be quite erroneous. Measurement of the 24 hr urine excretion of Na is a fairly accurate method to estimate salt consumption and is based on the principle that in a steady state, in health or in disease, salt consumption mirrors salt excretion. (Fig. 10). There have been several formulae devised to

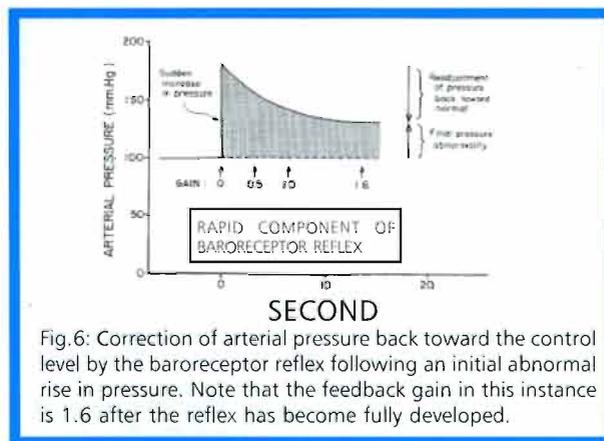


Fig. 6: Correction of arterial pressure back toward the control level by the baroreceptor reflex following an initial abnormal rise in pressure. Note that the feedback gain in this instance is 1.6 after the reflex has become fully developed.

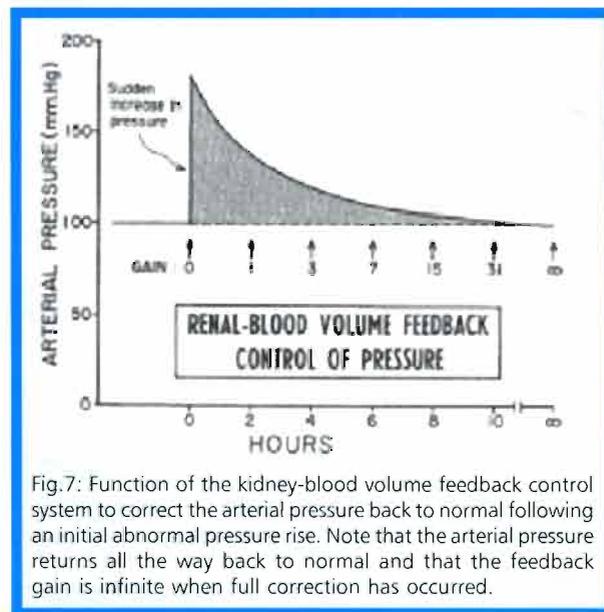


Fig. 7: Function of the kidney-blood volume feedback control system to correct the arterial pressure back to normal following an initial abnormal pressure rise. Note that the arterial pressure returns all the way back to normal and that the feedback gain is infinite when full correction has occurred.

estimate daily salt excretion from a spot urine sodium.

The relation between salt consumption and hypertension has been studied in several animal models.

In Fig.11, salt was added to the usual low Na diet of chimpanzees and the quantitative effect on average BP in this experiment was substantial. With 5 g salt per day, systolic pressure rose 12 mm Hg whereas with a 15 g salt intake the systolic pressure increased by 26 mm Hg. When the experiment was stopped and the original diet was restored, the original low blood pressure was restored.

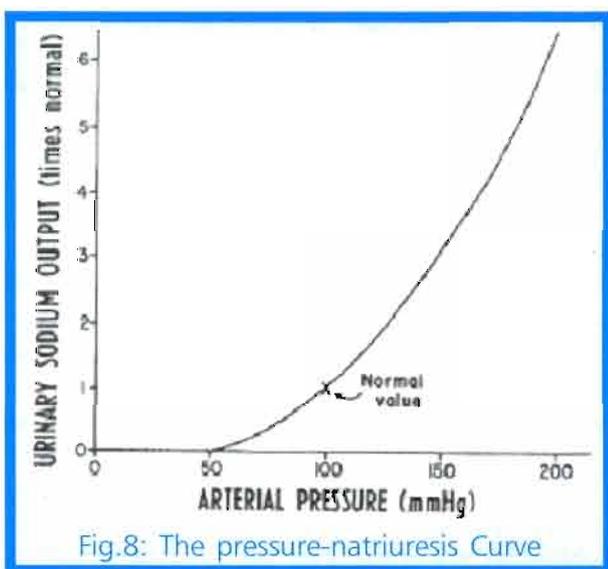


Fig.8: The pressure-natriuresis Curve

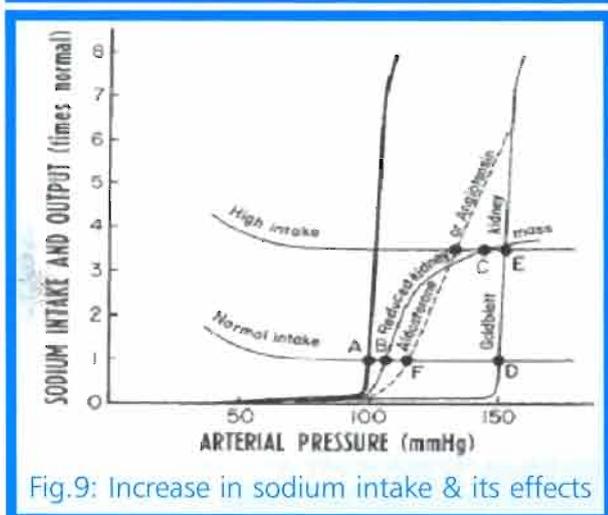


Fig.9: Increase in sodium intake & its effects

Table 2: Features of Salts-Sensitive Hypertension

Epidemiologic fetures

- Black race
- Obesity
- Advanced age
- Diabetes
- Renal dysfunction
- Use of cyclosporine

Clinical features

- Microalbuminuria
- Absence of normal nocturnal decrease in blood pressure
- Absence of modulation of blood flow with sodium loading

The Diet and Systolic Hypertension (DASH) is another powerful study that studied the effect of salt on blood pressure prospectively. (Fig.12). Unlike the other studies done so far, DASH was a Sodium intake study. It attempted to answer several relevant questions by analysing the effect of a usual north American diet as compared to a DASH diet on a little more than 200 subjects in each arm. About 40 percent of these subjects were hypertensive. The DASH diet consisted of fruits, vegetables, and low-fat dairy products, that included whole grains, poultry, fish, and nuts, with only small amounts of red meat, sweets, and sugar-containing beverages. In each arm, 3 subgroups were created with 3.5, 2.3 and 1.2gm sodium respectively. The hypothesis generating questions were,

1. Does reducing the level of sodium from 150 mmol/day (8.7 g of salt) to below 100 mmol/day, lower BP more than reducing the sodium level only to the recommended limit?
2. Does the DASH diet lower the blood pressure beyond the level achievable by simply reducing sodium intake?
3. What is the combined effect of the DASH diet and reduced sodium intake?

The results were interesting. Reducing the sodium intake from the high to the intermediate level

Table 3 Factors associated with sodium retention

- Reduced sodium filtration
 - Decrease in ultrafiltration coefficient
 - Decrease in single-nephron glomerular filtration rate
- Increased sodium reabsorption
 - Increase in vasoconstrictor expression: angiotention II, aldosterone, and hyperactive sympathetic nervous system
- Decrease in vasodilator expression: nitric oxide, kallikrein, dopamine, and vasodilatory prostaglandins
- Altered regulation or altered expression of sodium channels in the renal tubules

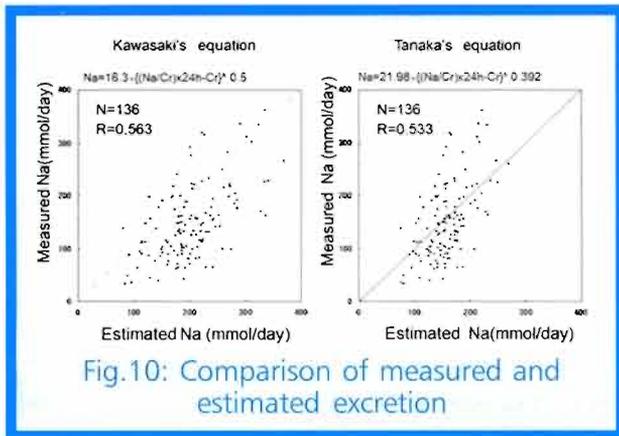


Fig.10: Comparison of measured and estimated excretion

reduced the systolic blood pressure by 2.1 mm Hg ($P<0.001$) during the control diet and by 1.3 mm Hg ($P=0.03$) during the DASH diet. Reducing the sodium intake from the intermediate to the low level caused additional reductions of 4.6 mm Hg during the control diet ($P<0.001$) and 1.7 mm Hg during the DASH diet ($P<0.01$). The effects of sodium were observed in participants with and in those without hypertension, blacks and those of other races, and women and men. The DASH diet was associated with a significantly lower systolic blood pressure at each sodium level; and the difference was greater with high sodium levels than with low ones. As compared with the control diet with a high sodium level, the DASH diet with a low sodium level led to a mean systolic

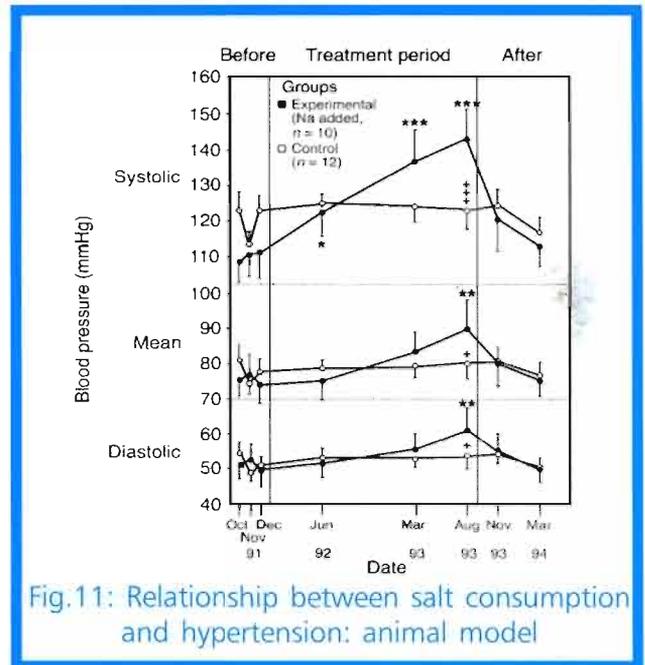


Fig.11: Relationship between salt consumption and hypertension: animal model

blood pressure that was 7.1 mm Hg lower in participants without hypertension, and 11.5 mm Hg lower in participants with hypertension.

Several papers and meta analyses of these studies have come to similar conclusions which have in a scientific manner established credence to the

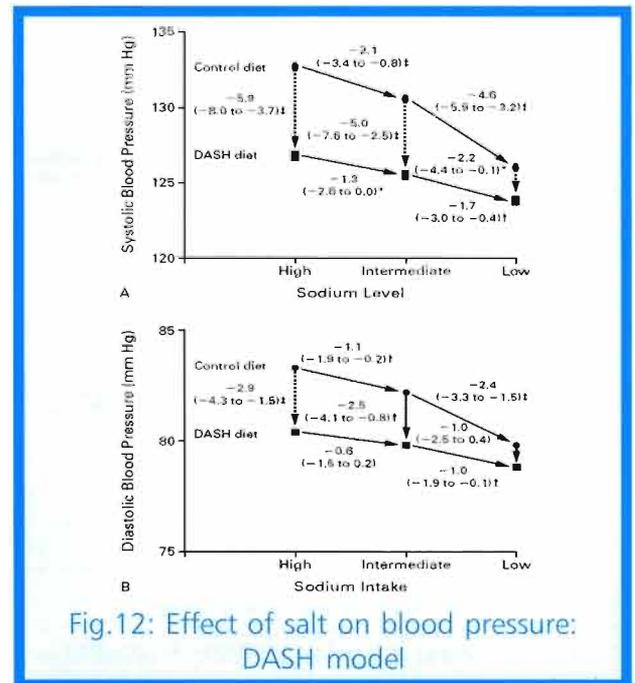
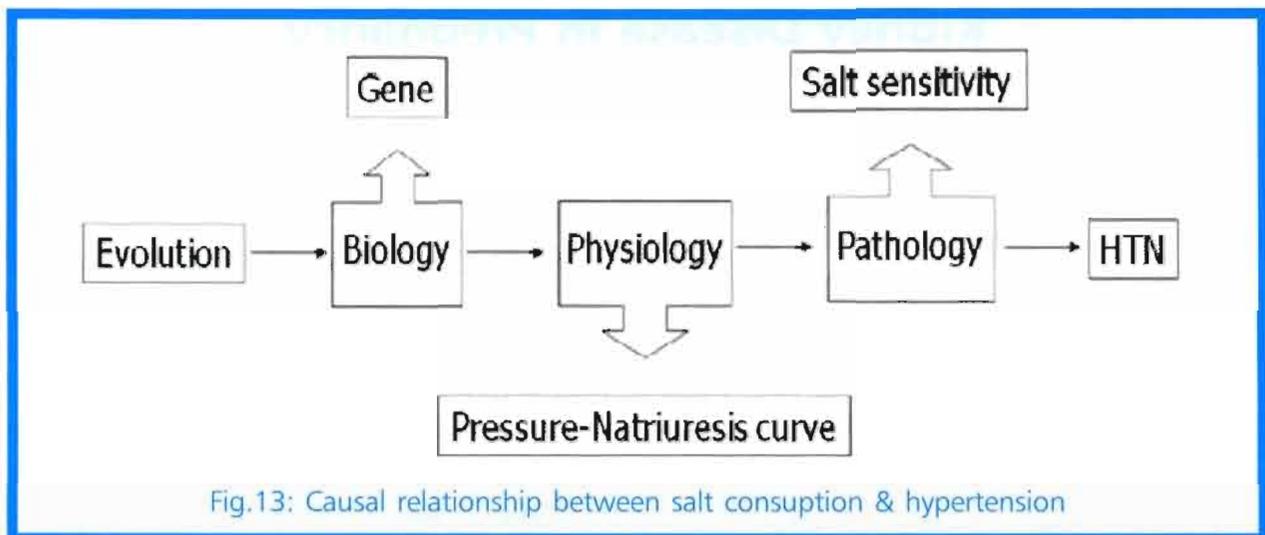


Fig.12: Effect of salt on blood pressure: DASH model



hypothesis that salt consumption is linked to the development of hypertension. Even looking at the output side, drugs that increase sodium loss like the thiazides are potent drugs to control blood pressure.

Seemingly the search for the causal relationship between salt consumption and hypertension by epidemiologic data, evolutionary correlates, physiological correlates, pathological markers and randomized control trials, has come full circle. (Fig.13).

What now remains is how effectively we are able to use this data to implement salt restriction to reduce cardiovascular morbidity and mortality.

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Kidney Disease in Pregnancy

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Introduction

During normal pregnancy, virtually every organ system undergoes anatomical and functional changes. The kidneys also undergo marked haemodynamic, tubular and endocrine changes. A failure of these adaptations in women with renal disease creates a suboptimal environment for fetal development and increases the risk of obstetrics complications. Thus, the understanding of these adaptations plays a major role in obstetric care as they can appreciably alter the criteria for diagnosis and treatment of renal diseases during pregnancy.

Renal Adaptation to Pregnancy

Normally in pregnancy, the kidney length increases from 1 to 1.5 cm, and kidney volume increases by up to 30%. There is physiologic dilatation of the urinary collecting system with hydronephrosis in up to 80% of women, usually more prominent on the right side more likely due to mechanical compression of the ureters between the gravid uterus and the linea terminalis. Hydronephrosis of pregnancy is usually asymptomatic, but abdominal pain, and rarely obstruction, can occur.

Glomerular filtration increases by 40% to 65% due to increase in renal blood flow and is maintained until the middle of the third trimester. The increase in glomerular filtration rate (GFR) results in a physiologic decrease in circulating creatinine, urea, and uric acid levels.

Assessment of Renal Function during Pregnancy

Average serum creatinine decreases from 0.8 mg/dl to 0.5 to 0.6 mg/dl. Hence, a serum creatinine of 1.0 mg/dl reflects renal impairment in a pregnant woman. Blood urea nitrogen (BUN) decreases from an average of 13 mg/dl. Serum uric acid reaches a nadir of 2.0 to 3.0 mg/dl by 22 to 24 weeks. Thereafter, the uric acid level begins to rise, reaching non-pregnant levels by term which is due to increased renal tubular absorption of urate. Pregnant women have normal excretion of an exogenous solute load, and appropriately conserve sodium when intake is restricted. The serum sodium typically decreases by 4 to 5 m mol/l below non-pregnancy levels.

The urinalysis is essentially unchanged during pregnancy, except for occasional glucosuria. These are due to increased filtration with less efficient tubular reabsorption of glucose and aminoacids. There are no significant differences by trimester. Albumin constitutes only a small part of total protein excretion and ranges from 5 to 30 mg/day. Airoidi and Weinstein (2007) concluded that proteinuria exceeding 300 mg/day should be considered abnormal.

Renal disorders in pregnancy:

Renal and urinary tract disorders commonly encountered in pregnancy can be grouped as:

- A) Complications unique to pregnancy-e.g. Diabetes insipidus, Preeclampsia (Gestational Hypertension).

- B) Pregnancy-induced changes predisposing to development or worsening of urinary tract disorders-eg. Markedly increased risk of pyelonephritis.
- C) Diseases preceding pregnancy-e.g. Nephrolithiasis.
- D) Renal diseases associated with systematic illness.

Diabetes Insipidus of Pregnancy

Circulating levels of vasopressinase, an enzyme that hydrolyzes arginine vasopressin, are increased during normal pregnancy. Occasionally, this increase is so pronounced that circulating antidiuretic hormone (arginine vasopressin) disappears, resulting in the polyuria and polydipsia of diabetes insipidus presenting during the second trimester and disappearing after the delivery. Affected women may become dangerously hypernatremic, especially with cesarean section using general anesthesia and/or water restriction in the delivery room. The polyuria can be controlled by the administration of deamino-8-darginine vasopressin (desmopressin [DDAVP]), which is not destroyed by vasopressinase.

Preeclampsia and Hemolysis, Elevated Liver Enzymes, and Low Platelets (HELLP) Syndrome

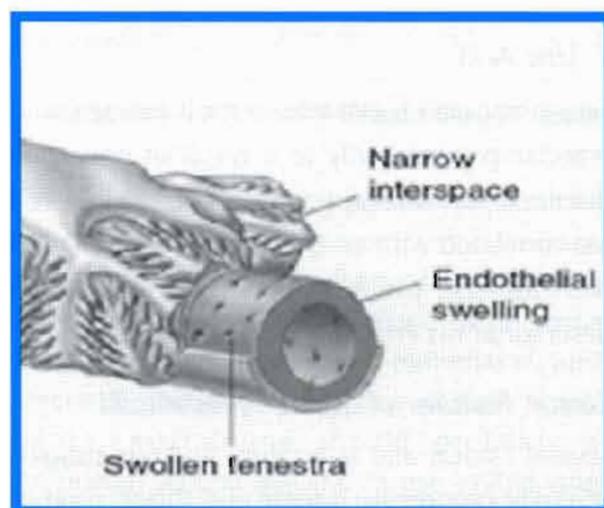
Preeclampsia is a systemic syndrome specific to pregnancy (incidence -3% to 5%), characterized by the new onset of hypertension and proteinuria after 20 weeks of gestation. Several medical conditions are associated with increased preeclampsia risk, including chronic hypertension, diabetes mellitus, renal disease, obesity, and antiphospholipid antibody syndrome.

Renal Changes in Preeclampsia

The pathologic swelling of glomerular endothelial cells, glomerular endotheliosis and loss of the

capillary space is characteristic of preeclampsia as shown in the figure below. There are deposits of fibrinogen and fibrin within and under the endothelial cells, and electron microscopy shows loss of glomerular endothelial fenestrae. Recent studies have shown that mild glomerular endotheliosis also occurs in pregnancy without preeclampsia, especially in gestational hypertension. Both renal blood flow and GFR are low in preeclampsia as compared with normal pregnancy. Renal blood flow decreases as a result of high renal vascular resistance. Although acute renal failure can occur in preeclampsia, typically proteinuria and renal sodium and water retention are the only renal manifestations of disease.

Vascular endothelial changes in Pre-eclampsia



Preeclampsia: Diagnosis and Clinical Features

- Hypertension

For the diagnosis of preeclampsia, hypertension is defined as a systolic blood pressure of 140 mm Hg or higher or a diastolic blood pressure of 90 mm Hg or higher after 20 weeks of gestation in a woman with previously normal blood pressure. Hypertension should be

confirmed by two separate measurements at least 2 hours apart.

- **Proteinuria**

Diagnosis of preeclampsia requires greater than 300 mg protein in a 24-hour urine collection. However, the degree of proteinuria is a poor predictor of adverse maternal and fetal outcomes, thus heavy proteinuria alone is not an indication for urgent delivery.

- **Edema**

It is also recognized to be a feature of normal pregnancy, diminishing its usefulness as a specific pathologic sign. Still, the sudden onset of severe edema, especially edema of the hands and face, can be an important presenting symptom of preeclampsia.

- **Uric Acid**

Serum uric acid is elevated in most women with preeclampsia primarily as a result of enhanced tubular urate reabsorption. Serum uric acid levels are correlated with severity of preeclampsia and with adverse pregnancy outcomes, even in gestational hypertension without proteinuria.

Clinical Features of Severe Preeclampsia

Several clinical and laboratory findings suggest severe or progressive disease and should prompt consideration of immediate delivery.

- Systolic blood pressure >160 mm Hg or diastolic blood pressure >110 mm Hg on two occasions at least 6 hr apart while on bed rest.
- Proteinuria >5 g in a 24-hr urine specimen or
- Dipstick proteinuria +2 or more on two random urine samples at least 4 hr apart.

- Oliguria (<500 ml urine output over 24 hr)
- Severe headache, mental status changes, or visual disturbances
- Pulmonary edema or cyanosis
- Epigastric or right-upper quadrant pain
- Hepatocellular injury (transaminase elevation to at least twofold over normal levels)
- Thrombocytopenia (<100,000 plts/mm³)
- Fetal growth restriction
- Cerebrovascular accident

Eclampsia

It is preeclampsia associated with convulsion not attributed to other causes. Sometimes it can occur without hypertension and proteinuria. Up to one-third of eclampsia occurs postpartum. Radiologic imaging by head computed tomography (CT) or magnetic resonance imaging (MRI) is usually not indicated when the diagnosis is apparent, but typically shows vasogenic edema, predominantly in the subcortical white matter of the parieto-occipital lobes. Eclampsia may cause subtle long-term impairment in cognitive function.

HELLP syndrome

Is an acronym for the syndrome of hemolytic anemia, elevated liver enzymes, and low platelets. It is a severe variant of preeclampsia, although it can occur in the absence of proteinuria. It is associated with increased maternal and neonatal adverse outcomes including eclampsia (6%), placental abruption (10%), acute renal failure (5%), disseminated intravascular coagulation (8%), pulmonary edema (10%), and (rarely) hepatic hemorrhage and rupture.

Maternal and Neonatal Mortality

Maternal death is most often due to eclampsia, cerebral hemorrhage, renal failure, hepatic

failure, pulmonary edema, and HELLP syndrome. Worldwide, preeclampsia is associated with a perinatal and neonatal mortality rate of 10%. Neonatal death is most commonly due to iatrogenic prematurity undertaken to preserve the health of the mother. Fetal growth restriction as a result of impaired uteroplacental blood flow or placental infarction. Oligohydramnios and placental abruption are less common complications.

Management and Treatment of Preeclampsia

- **Timing of Delivery**

In women presenting prior to 24 weeks of gestation, maternal complications and perinatal and neonatal mortality are extremely high (>80%). For this reason, termination is usually recommended. In addition, the presence of non-reassuring fetal testing, suspected abruption placentae, thrombocytopenia, worsening liver and/or kidney function, and symptoms, such as unremitting headache, visual changes, nausea, vomiting, or epigastric pain are generally considered indications for expedient delivery. In preeclampsia presenting between 24 and 34 weeks of gestation without the above severe signs and symptoms, postponing delivery may improve neonatal outcomes.

- **Blood Pressure Management**

Acutely, aggressive lowering of blood pressure can lead to fetal distress or demise, especially if placental perfusion is already compromised. Because of this, antihypertensive therapy for preeclampsia is usually withheld unless the blood pressure rises above 150 to 160 mm Hg systolic or 100 to 110 mm Hg diastolic, above which the risk of cerebral hemorrhage becomes significant. Methyldopa a centrally acting α_2 -adrenergic agonist has the most extensive safety data and appears to have no adverse fetal effects. β

Adrenergic antagonists are effective without known teratogenicity or known adverse fetal effects except atenolol, which has been associated with fetal growth restriction. Labetalol, which result in better preservation of uteroplacental blood flow because of its α -blocking action is used, both as an oral and an intravenous agent. Calcium channel blockers, nifedipine appear to be safe in pregnancy. When hypertension in pregnancy is complicated by pulmonary edema, diuretics are appropriate and effective. Angiotensin converting enzyme ACE inhibitors and angiotensin receptor blockers are contraindicated in the second and third trimester of pregnancy, as they produce renal dysfunction in the fetus, leading to renal dysgenesis, fetal oliguria and oligohydramnios, pulmonary hypoplasia, IUGR, and neonatal anuric acute renal failure (ARF) ultimately leading to death of the fetus.

- **Intravenous Agents for Urgent Blood Pressure Control**

Severe hypertension in pregnancy occasionally requires inpatient management with intravenous agents. Intravenous labetalol is safe and effective. Use of hydralazine is associated with an increased risk of maternal hypotension, maternal oliguria, placental abruption, and low APGAR scores. Hence, hydralazine should probably be considered second-line and its use limited when possible. Nitroprusside carries risk of fetal cyanide poisoning if used for more than 4 hours and is generally avoided.

- **Magnesium and Seizure Prophylaxis**

Magnesium has been widely used for the management and prevention of eclampsia. Magnesium sulfate slows neuromuscular conduction and depresses central nervous system irritability. Women receiving magnesium should be monitored carefully for signs of toxicity,

including loss of deep tendon reflexes, flushing, somnolence, muscle weakness, and decreased respiratory rate. Such monitoring is especially important in women with impaired renal function who have impaired urinary magnesium excretion.

- **Management of HELLP Syndrome**

Among women in the 24- to 34-week gestational window, whose clinical status appears relatively stable and with reassuring fetal status, expectant management is often a viable alternative.

Gestational Hypertension

Gestational hypertension is defined as the new onset of hypertension without proteinuria after 20 weeks of gestation, which resolves postpartum. Gestational hypertension progresses to overt preeclampsia in approximately 10% to 25% of cases. When gestational hypertension is severe, it carries similar risks for adverse outcomes as preeclampsia.

Chronic Hypertension

History of hypertension prior to pregnancy or a blood pressure above 140/90 mm Hg prior to 20 weeks of gestation is suggestive of chronic hypertension. Pregnant women with chronic hypertension have an increased risk of preeclampsia (21% to 25%), premature delivery (33% to 35%), IUGR (10% to 15%), placental abruption (1% to 3%), and perinatal mortality (4.5%).

However, most adverse outcomes occur in women with severe hypertension (diastolic blood pressure >110 mm Hg) and those with preexisting cardiovascular and renal disease. In the absence of underlying renal disease, the new onset of proteinuria (>300 mg/day), usually with

worsening hypertension, is the most reliable sign of superimposed preeclampsia.

Secondary Hypertension in Pregnancy

Causes of secondary hypertension in pregnancy are renal artery stenosis, primary hyperaldosteronism, and pheochromocytoma. Renal artery stenosis should be suspected when hypertension is severe and resistant to medical therapy. Hypertension and hyperkalemia from primary hyperaldosteronism might be expected to improve during pregnancy, as progesterone antagonizes the effect of aldosterone on the renal tubule. Although rare, pheochromocytoma can be devastating when it first presents during pregnancy. This syndrome occasionally is unmasked during labor and delivery, when fatal hypertensive crisis can be triggered by vaginal delivery, uterine contractions, and anesthesia. Maternal and neonatal morbidity and mortality are much better when the diagnosis is made antepartum, with attentive and aggressive medical management. Surgical intervention is typically postponed until after delivery whenever possible.

Approach to Management of Chronic Hypertension in Pregnancy

Blood pressure control should be optimized prior to conception whenever possible, and women should be counselled regarding the risks of adverse pregnancy outcomes, including preeclampsia. Once pregnant, changes in antihypertensive agents may be appropriate and women should be followed closely for signs of superimposed preeclampsia.

Goals of Therapy

Medical treatment should be initiated in women with newly diagnosed chronic hypertension in pregnancy only if there is evidence of end-organ

damage (proteinuria, cardiomyopathy) or the blood pressure exceeds 150 to 160 mm Hg systolic or 100 to 110 mm Hg diastolic.

Similarly, in women already receiving chronic antihypertensive therapy prior to pregnancy, consideration could be given to tapering or discontinuing treatment unless blood pressures exceed these levels.

Acute Kidney Injury in Pregnancy

The most common cause of AKI during pregnancy is prerenal azotemia due to hyperemesis gravidarum or vomiting from acute pyelonephritis. Occasionally preeclampsia, HELLP syndrome, and acute fatty liver of pregnancy are complicated by acute renal failure. Obstetric complications such as septic abortion and placental abruption are associated with severe acute tubular necrosis and bilateral cortical necrosis. Obstructive uropathy is a rare cause of renal failure in pregnancy.

The diagnosis of renal cortical necrosis can be usually be established by CT scan, which characteristically demonstrates hypodense areas in the renal cortex. The treatment of AKI in pregnancy is supportive with prompt restoration of fluid volume deficits, and in later pregnancy, expedient delivery. No specific therapy is effective in acute cortical necrosis except for dialysis when needed. Both peritoneal and hemodialysis have been used during pregnancy, however peritoneal dialysis carries the risk of impairing uteroplacental blood flow. Patients with septicemia, mostly respond to antibiotics and volume resuscitation. Survival is intimately linked with the management and recovery of the AKI.

Obstructive Uropathy and Nephrolithiasis

If clinical suspicion is high (e.g., marked hydronephrosis, abdominal pain, elevated serum

creatinine), a Percutaneous nephrostomy may be needed as a diagnostic and therapeutic trial. If present, obstruction can be managed with ureteral stenting. Circulating levels of 1, 25-dihydroxyvitamin D3 are increased during normal pregnancy, resulting in increased intestinal calcium absorption. Urinary excretion of calcium is also increased, leading to a tendency in some women to form kidney stones. Excessive intake of calcium supplements can lead to hypercalcemia and hypercalcuria. Calcium oxalate and calcium phosphate constitute the majority of the stones produced during pregnancy, presenting with flank pain and lower abdominal pain with hematuria. Premature labor and the risk of infection is increased. Ultrasonography is the preferred method to visualize obstruction and stones. The management of renal calculi is conservative with adequate hydration, analgesics and antiemetics. Thiazide diuretics and allopurinol are contraindicated. Nephrolithiasis complicated by urinary tract infection should be treated with antibiotics for 3 to 5 weeks, followed by suppressive treatment after delivery. Most stones pass spontaneously, but ureteral catheterization and placement of a ureteral stent may be needed. Extracorporeal shockwave lithotripsy has been used during the first 4 to 8 weeks of pregnancy without known adverse consequences to the fetus.

Urinary Tract Infection and Acute Pyelonephritis

Physiologic hydronephrosis predisposes pregnant women to ascending pyelonephritis in the setting of cystitis.

Asymptomatic Bacteriuria is persistent, actively multiplying bacteria within the urinary tract in asymptomatic women.

Incidence during pregnancy varies from 2 to 7 percent. A clean-voided specimen containing

Antimicrobial Agents Used for Treatment of Pregnant Women with Asymptomatic Bacteriuria are as follows:

<p>Single-dose treatment</p> <p>Amoxicillin 3 g</p> <p>Ampicillin 2 g</p> <p>Cephalosporin 2 g</p> <p>Nitrofurantoin 200 mg</p> <p>Trimethoprim-sulfamethoxazole 320/1600 mg</p>	<p>3-day course</p> <p>Amoxicillin 500 mg three times daily</p> <p>Ampicillin 250 mg four times daily</p> <p>Cephalosporin 250 mg four times daily</p> <p>Ciprofloxacin 250 mg twice daily</p> <p>Levofloxacin 250 mg daily</p> <p>Nitrofurantoin 50 to 100 mg four times daily; 100 mg twice daily</p> <p>Trimethoprim-sulfamethoxazole 160/800 mg two times daily</p>
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Other

Nitrofurantoin 100 mg four times daily for 10 days

Nitrofurantoin 100 mg twice daily for 7 days

Nitrofurantoin 100 mg at bedtime for 10 days

more than 10^5 bacteria/ml is diagnostic. Untreated asymptomatic bacteriuria in pregnancy is associated with an increased risk of premature delivery and low birth weight and can progress to overt cystitis or acute pyelonephritis in up to 40% of patients. Acute pyelonephritis is a serious complication presents with fevers, loin pain, and dysuria and can progress to endotoxic shock, disseminated intravascular coagulation, and acute renal failure. Thus, early detection and treatment of asymptomatic bacteriuria is recommended. Urine culture is preferred for screening. Screening for asymptomatic bacteriuria is recommended during the first prenatal visit and is only repeated in high-risk women, such as those with a history of recurrent urinary infections or urinary tract anomalies. If asymptomatic bacteriuria is found, prompt treatment is warranted (usually with a cephalosporin) for at least 3 to 7 days. A follow-up culture 2 weeks after treatment is necessary to ensure eradication of bacteriuria. Suppressive

Treatment failures

Nitrofurantoin 100 mg four times daily for 21 days

Suppression for bacterial persistence or recurrence

Nitrofurantoin 100 mg at bedtime for remainder of pregnancy

therapy with nitrofurantoin or cephalexin is recommended for those patients with bacteriuria that persists after two courses of therapy. Pyelonephritis is usually treated aggressively with hospitalization, intravenous antibiotics, and hydration.

Chronic Kidney Disease and Pregnancy

Women who enter pregnancy with chronic renal disease are at increased risk for rapid decline of renal function and perinatal mortality due to preterm delivery and IUGR.

The physiologic increase in renal blood flow and GFR characteristic of normal pregnancy is attenuated in chronic renal insufficiency. Women with mild renal impairment (serum creatinine less than 1.4), normal blood pressure, and no proteinuria have good maternal and fetal

outcomes, with little risk for accelerated progression toward ESRD or preterm delivery. Initiating pregnancy with a serum creatinine greater than 2.0 mg/dl carries a high risk for accelerated decline in renal function both during and after pregnancy. Among women with a serum creatinine greater than 2.5 mg/dl, over 70% experience preterm delivery, and over 40% experience preeclampsia and terminating pregnancy does not reliably reverse the decline in renal function.

Renal diseases associated with systematic illness

1) Diabetic Nephropathy and Pregnancy

Pregnancy itself does not impact adversely on progression of kidney disease, if kidney function is normal or near normal at the onset. Women with diabetic nephropathy are strongly advised to postpone pregnancy until after renal transplantation, which improves fertility status and fetal outcomes, and does not lead to impaired renal function if allograft function is normal. ACE inhibitors and angiotensin II receptor blockers are contraindicated during pregnancy. It is known that in utero high sugar exposure in the offspring of diabetic mothers leads to impaired nephrogenesis and reduced nephron mass, and this may put the offspring at higher risk for developing renal disease and hypertension in later life.

2) Lupus Nephritis and Pregnancy

With careful planning, monitoring, and management, the majority of patients with SLE—especially those with normal baseline renal function—can complete pregnancy without serious maternal or fetal complications like preeclampsia, preterm birth, IUGR and abortion. Women with lupus should postpone pregnancy until lupus activity is quiescent and immunosuppressives are minimized. Prophylactic therapy with steroids does not appear to prevent a lupus flare during pregnancy.

Pregnancy in chronic dialysis

Current management recommendation in women on chronic dialysis with pregnancy - Increasing the weekly dialysis dose to 20 or more hours per week to improve neonatal outcomes and longer gestations. This is often attained by daily nocturnal dialysis. Medications must be carefully reviewed. Erythropoietin dosing should be adjusted a dose increase of approximately 50% to maintain hemoglobin target levels of 10 to 11 g/dL. Antihypertensive therapy should be adjusted for pregnancy to maintain maternal diastolic pressure at 80 to 90 mm Hg by using methyldopa, labetalol, and sustained release nifedipine. Close monitoring of fetal well-being, in collaboration with an obstetrician, is essential after 24 weeks of gestation as early fetal distress is common.

Pregnancy in the Renal Transplant Patient

Lindheimer and colleagues (2008) and Hou (2003) recommend that women who have undergone transplantation satisfy the following requisites before attempting pregnancy:

1. They should be in good general health for at least 2 years after transplantation.
2. There should be stable renal function without severe renal insufficiency—serum creatinine <2 mg/dL and preferably <1.5 mg/dL, none to minimal proteinuria, no evidence of graft rejection, and absence of pyelocalyceal distension by urography.
3. Absent or easily controlled hypertension.
4. Drug therapy reduced to maintenance levels.

Vaginal delivery is safe, and cesarean section should be performed only for obstetrical indications.

Effect of Pregnancy on Renal Allograft Function

Pregnancy itself does not appear to adversely affect graft function in transplant recipients, provided baseline graft function is normal and significant hypertension is not present.

In general, when pregnancy occurs 1 to 2 years after transplant, the rejection rate is similar to that seen in nonpregnant controls (3% to 4%).

When moderate renal insufficiency is present (serum creatinine >1.5 to 1.7 mg/dl), there is a risk of progressive renal dysfunction, small for gestational age infant and of preeclampsia.

There is increased risk for infections with cytomegalovirus, herpes simplex, and toxoplasmosis. The rate of bacterial urinary tract infections is increased (13% to 40%).

Hypertension affects between 30% and 75% of pregnancies among transplant recipients with risk of Preeclampsia in 25% to 30%. Renal transplant recipients should be managed aggressively, with target blood pressure close to normal—a goal that differs from somewhat higher blood pressure goals in women with hypertension in pregnancy in the absence of a transplant. Agents of choice include methyldopa, nonselective β -adrenergic antagonists (i.e. labetalol), and calcium channel blockers.

Cyclosporine (or tacrolimus) and steroids, with or without azathioprine, form the basis of immunosuppression during pregnancy. Corticosteroids at low to moderate doses (5 to 10 mg/day) are safe. Close monitoring of blood

levels with dosing adjustment are required to avoid risk of acute rejection.

Breast feeding is not recommended in women on immunosuppressive drugs.

Management of Acute Rejection in Pregnancy

Acute rejection should be suspected if fever, oliguria, graft tenderness, or deterioration in renal function is noted.

Biopsy of the renal graft should be performed to confirm the diagnosis.

High-dose steroids remain a mainstay of treatment of acute rejection during pregnancy, with the risk of fetal malformations and maternal infections.

Pregnancy Outcome following Kidney Donation

Recent data suggests that these women have a lower incidence of full-term deliveries and higher risk for fetal loss, gestational diabetes, gestational hypertension, and preeclampsia during pregnancy.

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Renal Cell Carcinoma Imaging

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Abstract:

Objectives: Review the role of imaging in renal cell carcinoma with special focus on contrast enhanced ultrasound imaging.

Methods: The techniques used in evaluation of renal tumors like urography, ultrasonography, CT and MRI are discussed.

Result: Cross sectional imaging has heightened sensitivity of detecting renal masses which may not be clinically apparent. Imaging also helps in characterizing and staging renal masses. On contrast ultrasonography, early and dense persistent enhancement of the lesion compared to rest of the renal parenchyma helps making a confident diagnosis of neoplasm, especially in patients with renal failure and hypersensitivity to iodinated contrast media, where iodinated contrast media are contraindicated and without exposure to radiation.

Conclusion: Imaging has a major role in detecting and staging renal tumours, especially, incidental renal masses.

Introduction

Renal cell carcinoma also known as hypernephroma or Grawitz's tumor, pathologically adenocarcinoma is the most common primary renal malignancy in adults. It accounts for 85% of all malignant renal tumors and about 3% of all diagnosed neoplasms (1).

It is more common in men and is usually in 5th to 7th decades. Most are sporadic; some may be associated with syndromes like von HippelLindau (vHL). Risk factors include smoking, exposure to petroleum and asbestos.

The classic clinical presentation of flank pain, hematuria, and a palpable flank mass is comparatively uncommon (5-10% of cases). However, clinical symptomatology may be quite nonspecific-for example, anorexia, tiredness, weight loss, or fever of unknown origin(2). Other presentations include varicocele formation (from tumor thrombus in the left renal vein or the inferior vena cava [IVC]) and disseminated malignancy. RCC may also present with a variety of paraneoplastic syndromes, such as polycythemia secondary to excessive secretion of erythropoietin, hypercalcemia secondary to factors regulating calcium, and hepatic dysfunction (Stauffer syndrome). Distant metastases may cause symptoms of cough, hemoptysis, bone pain, seizures, etc. Incidentally detected tumors in asymptomatic individuals have been steadily increasing with the dissemination of imaging techniques, including CT, MR, and sonography, accounting for approximately 60% of renal tumors in the 1990s, compared with approximately 10% in the early 1970s (3,4).

Staging Renal Cell Carcinoma (5) Robson's Staging System for Renal Cell Carcinoma

Robson Stage	Disease extent
I	Tumor confined within the renal capsule
II	Tumor spread to perinephric fat or ipsilateral adrenal gland
IIIA	Venous tumor thrombus (renal vein or IVC)
IIIB	Regional lymph node metastases
IIIC	Venous tumor thrombus and regional lymphadenopathy
IV	Direct invasion of adjacent organs outside Gerota's fascia
IVB	Distant metastases

Regional lymph nodes (N)

Stage	Definition
Nx	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in regional lymph node(s)

Distant metastasis (M)

Stage	Definition
M0	No metastasis
M1	Distant metastases

Stage Grouping

Stage I	T1, N0, M0
Stage II	T2, N0, M0
Stage III	T1 or T2, N1, M0
	T3, N0 or N1, M0
Stage IV	T4, any N, M0
	Any T, any N, M1

TNM Staging System for the Kidney

Primary tumor (T)

Stage	Definition
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor 7cm or less in greatest dimension, limited to the kidney
T1a	Tumor 4cm or less in greatest dimension, limited to the kidney
T1b	Tumor more than 4cm but not more than 7cm in greatest dimension limited to the kidney
T2	Tumor more than 7cm in greatest dimension, limited to the kidney
T2a	Tumor more than 7cm but less than or equal to 10cm in greatest dimension, limited to the kidney
T2b	Tumor more than 10cm, limited to the kidney
T3	Tumor extends into major veins or perinephric tissues but not into the ipsilateral adrenal gland and not beyond Gerota's fascia
T3a	Tumor grossly extends into the renal vein or its segmental (muscle containing) branches, or tumor invades perirenal and/or renal sinus fat but not beyond Gerota's fascia
T3b	Tumor grossly extends into the vena cava below the diaphragm
T3c	Tumor grossly extends into the vena cava above the diaphragm or invades the wall of the vena cava
T4	Tumor invades beyond Gerota's fascia (including contiguous extension into the ipsilateral adrenal gland)

Radiological Evaluation

Urography

Urography has been used for many years to diagnose renal tumors. Its sensitivity was 80-85% for masses over 3 cm in size and only 10% for lesions under 3 cm. After the development of cross sectional imaging techniques its role in detection and work up of solid renal masses has decreased and has been replaced mainly by sonography and Uro-CT. Actually it is no more proposed in the detection and characterization of mass-like lesions.

Ultrasound

Gray scale sonography

The echostructure or the echogenicity of the renal carcinoma is correlated to size, vascularization, modality of growth (radial or infiltrative), presence of cystic or necrotic areas. The echographic pattern is finally connected to the echogenicity of the surrounding parenchyma that can be increased or sometimes reduced (6).

The tumor may appear hyperechoic, isoechoic, hypoechoic or of mixed echostructure. Hypoechoic pattern is the most frequent pattern and generally it is related to the hypervascularity or to the internal coagulative necrosis. Hypoechoic pattern is observed in presence of necrotic or hemorrhagic internal areas which are very frequent in major lesions. Anechoic or cystic-like tumors are rare and they can be related to neoplastic transformation of a benign cyst or to acystocarcinoma. Intratumoral or marginal calcifications are observed in about 5-10% of RCC and they appear as spots or focal areas of hyperechogenicity associated with posterior shadowing. Pure isoechoic tumors are rare and they are detected only because they produce a bulging of the renal profile or out grow into the

renal sinus. When the carcinoma is large usually it appears as an inhomogeneous mass with complex mixed echostructure associated to deformation and dislocation of the kidney.

At ultrasonography the differential diagnosis of the renal carcinoma has to be made with some benign tumors and with so called pseudotumors or normal variants of the renal anatomy.

The most common benign tumor is angiomyolipoma (AML) which characteristically appears as a hyperechoic mass well distinct from the adjacent normal parenchyma and without any hypoechoic rim (7,8). In 40% of cases a distant shadowing can be present, which has never been observed in hyperechoic appearing carcinomas. This hyperechogenicity is mainly related to the fatty component of the tumor even if there are AML with limited adipose tissue but still hyperechoic. Any renal hyperechoic mass is very suspicious of AML, but literature data have shown that hyperechogenicity can be observed in 30% of carcinomas, especially in small lesions. For this reason the US diagnosis of AML has to be confirmed by CT or MR on the base of intralesional fat detection.

Oncocytoma, the second most common benign tumor, cannot be differentiated from the carcinoma on the basis of ultrasonography. In some cases a central scar can be demonstrated, but this finding can be observed also in some malignant lesions (7,9).

Color and Power Doppler

The role of Color- and Power-Doppler in the detection of renal carcinomas is still under discussion and the diagnostic gain obtained with these two modalities is limited. The increase of both diagnostic sensitivity and operator diagnostic confidence is limited.

Doppler flow patterns seen in various renal masses has been classified by Jinzaki et al.(10) as follows:

Pattern 0: no vascularization

Pattern 1: small and sparse intratumoral color dots

Pattern 2: penetrating pattern with vessels entering into the mass

Pattern 3: numerous and evident peripheral vessels (peripheral pattern)

Pattern 4: mixed peripheral and penetrating pattern

Pattern 4 is the most common in the RCC, but it is specific because it can be present also in AML and on cocytomas. Masses with sparse spots pattern or only peripheral vascularization are more frequently benign. These Color-Doppler criteria are inadequate to differentiate a benign from a malignant lesion in the clinical practice, but they may only suggest a possible nature of the lesion that requires a pathologic confirmation (11). There are few reports regarding the increase in accuracy in the detection of renal tumors using Color and Power-Doppler imaging associated to gray-scale sonography.

On the other side Color and Power-Doppler technology is very useful in the characterization of pseudotumoral aspects, which are very common in the kidneys (column of Bertin; a dromedary or splenic hump; fetal lobulation; focal areas of hypertrophy). These apparent lesions show a normal vascular distribution of the arteries and veins that resembles that of the normal parenchyma.

Contrast Enhanced Ultrasonography

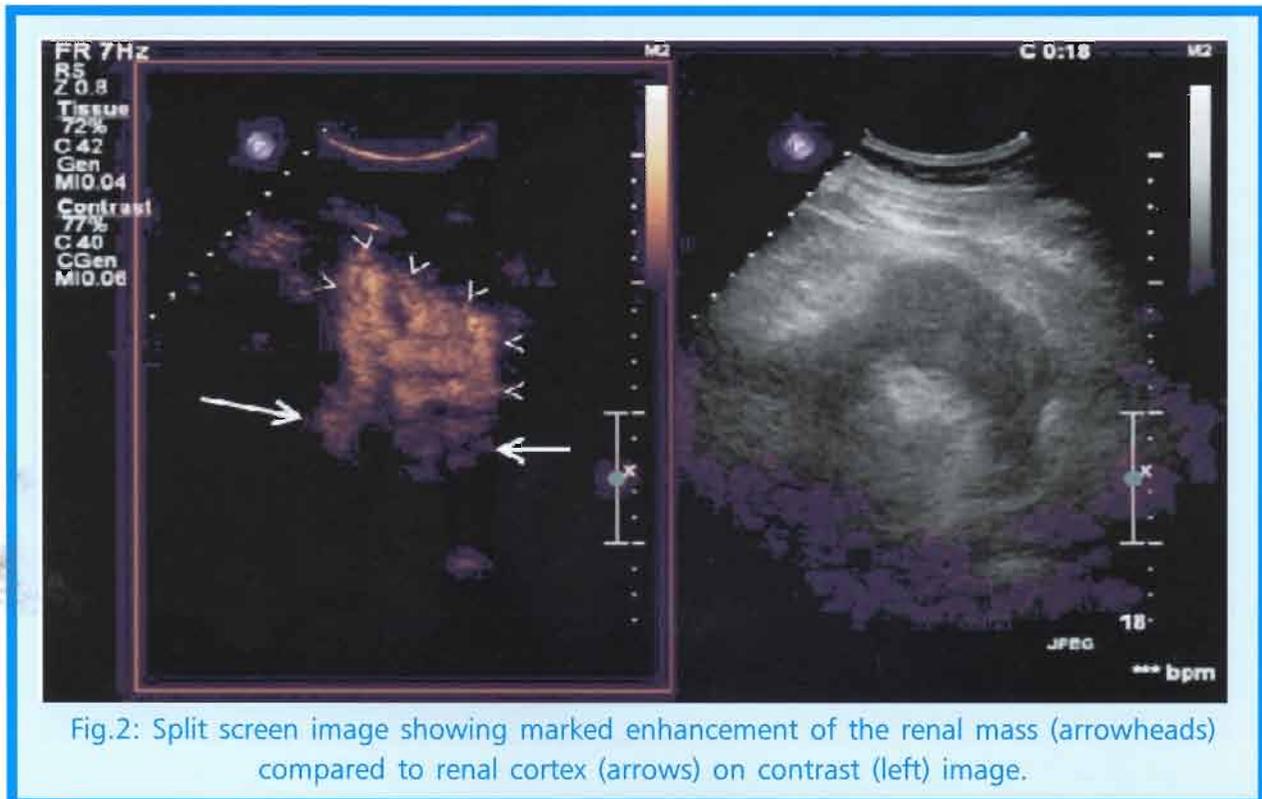
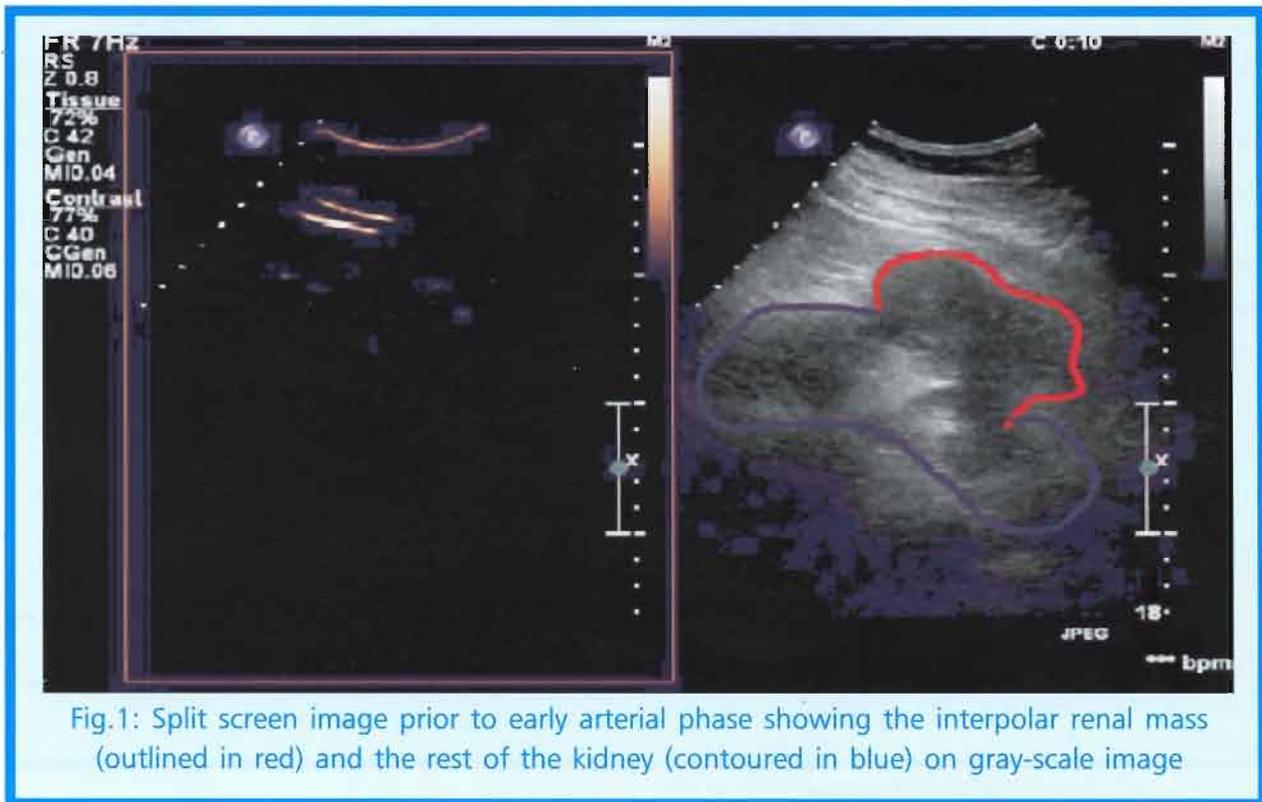
Investigations have shown that contrast-enhanced ultrasound (CEU) may have utility for evaluation of renal masses (12–17). Second-

generation ultrasound microbubble contrast agents are composed of gas-filled lipid microspheres measuring approximately 3-5 μm in diameter that are injected IV. When exposed to low-energy ultrasound, the microspheres resonate and produce an acoustic signal that allows dynamic real-time visualization of tumor vasculature and enhancement characteristics (18). Ultrasound contrast medium has potential advantages over CT and MRI contrast agents in that CEU agents remain intravascular without diffusing into the interstitial space, allow visualization of microvasculature, allow higher temporal resolution of ultrasound than of CT or MRI, and carry no known risk of nephrotoxicity or nephrogenic systemic fibrosis in patients with renal dysfunction (17). The typical contrast agent used in our institute is SonoVue (Bracco SpA, Milan, Italy), which is composed of sulfur hexafluoride gas with a phospholipid shell. The microbubbles are metabolized by the liver (shell component) and the gas is exhaled via the lungs.

Imaging Technique

We use the preset contrast mode on our multipurpose ultrasound machine (iU22, Philips Medical Systems, Bothell, WA, USA) and a curvilinear transducer operating in the frequency range of 2 – 5 MHz which produces images on the basis of maintenance of microbubbles at low acoustic pressure.

A 0.5 ml bolus of SonoVue is injected rapidly followed by a 10 ml saline flush. Continuous timed scanning is started immediately after flushing with saline. Continuous repeated cine loops are acquired simultaneously over a span of about 2 minutes after which no contrast signal was appreciable. Split screen loops are obtained which simultaneously show separate low mechanical index gray-scale and contrast-only images. A very low acoustic pressure (0.05 to 0.09



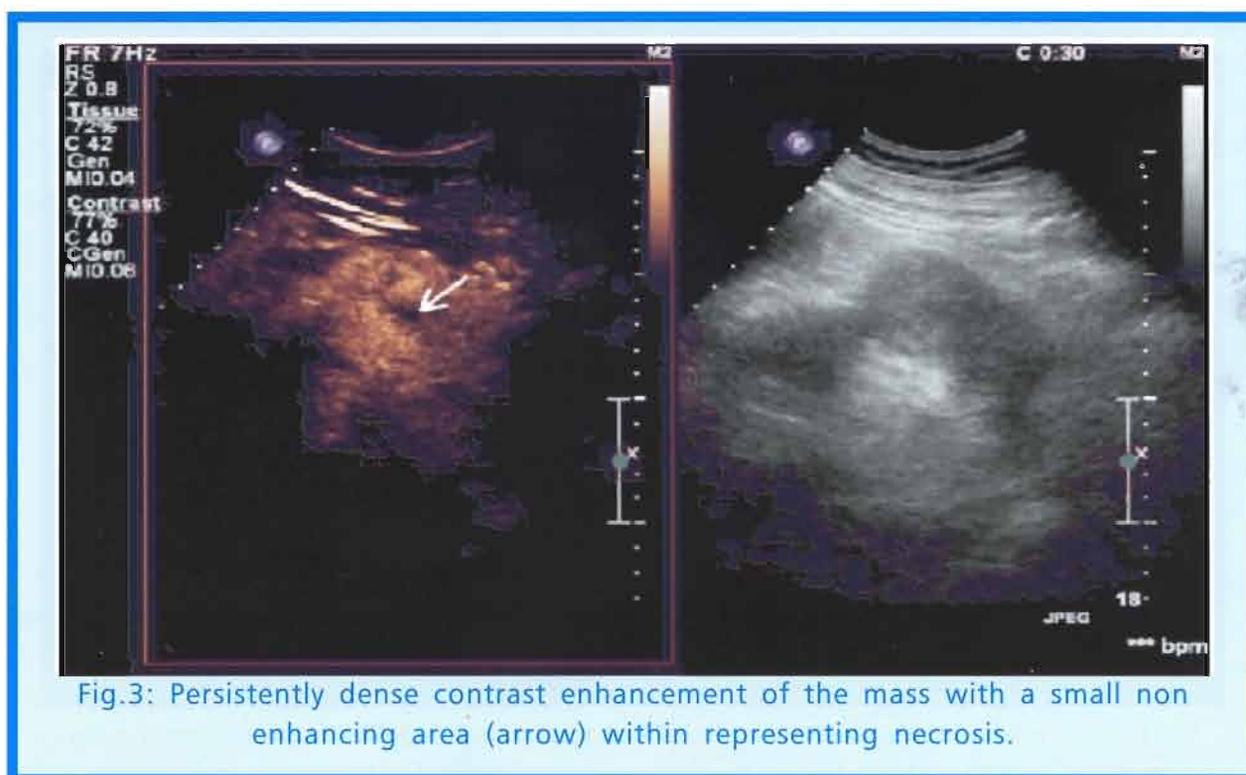


Fig.3: Persistently dense contrast enhancement of the mass with a small non enhancing area (arrow) within representing necrosis.

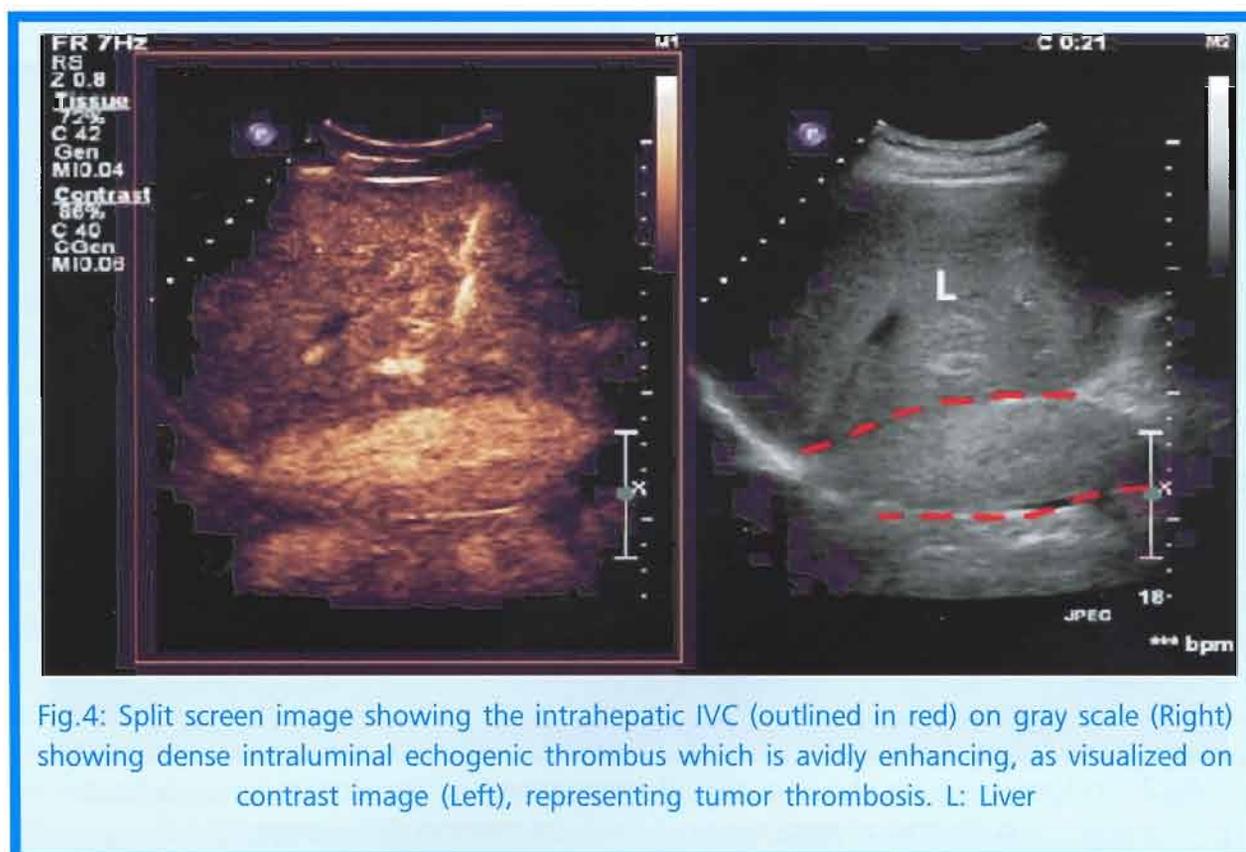


Fig.4: Split screen image showing the intrahepatic IVC (outlined in red) on gray scale (Right) showing dense intraluminal echogenic thrombus which is avidly enhancing, as visualized on contrast image (Left), representing tumor thrombosis. L: Liver

mechanical index, determining a 40- to 50-mPa (derated pressure) is used, with the sound beam focused at the deeper aspect of the region of interest.

Normal Renal Enhancement Pattern on CEUS

The kidney enhances quickly and intensely after SonoVue bolus injection due to the high renal blood flow. Following enhancement patterns are appreciated:

- i. Early arterial phase: Enhancement in the central arteries becomes apparent 10 to 15 s after contrast injection.
- ii. Late arterial or cortical phase: Few seconds later by enhancement of the renal cortex, whereas pyramids remain echo poor.
- iii. Medullary phase: Pyramids gradually fill with contrast until they are isoechoic with the cortex.

On early phase scanning, the kidney becomes hyperechoic in comparison with the liver (right side) or the spleen (left side). Later on, the kidney becomes rapidly hypoechoic if compared with the adjacent parenchyma and especially with the spleen, which shows a very dense and persistent enhancement. The renal-enhancing effect decreases as the general contrast concentration decreases(19). Unlike iodinated contrast media, CEUS microbubbles are blood pool agents and there is no pyelographic phase. (Fig.1-3).

Pseudotumors

CEUS can be helpful in clarifying some potential doubts and sources of misinterpretation of conventional US. A prominent Bertin column, a persistent fetal lobulation, or a dromedary hump can be sometimes misdiagnosed as a renal mass. CEUS can be used to assess renal vascularity, cortical thickness, and pyramid spacing. On CEUS

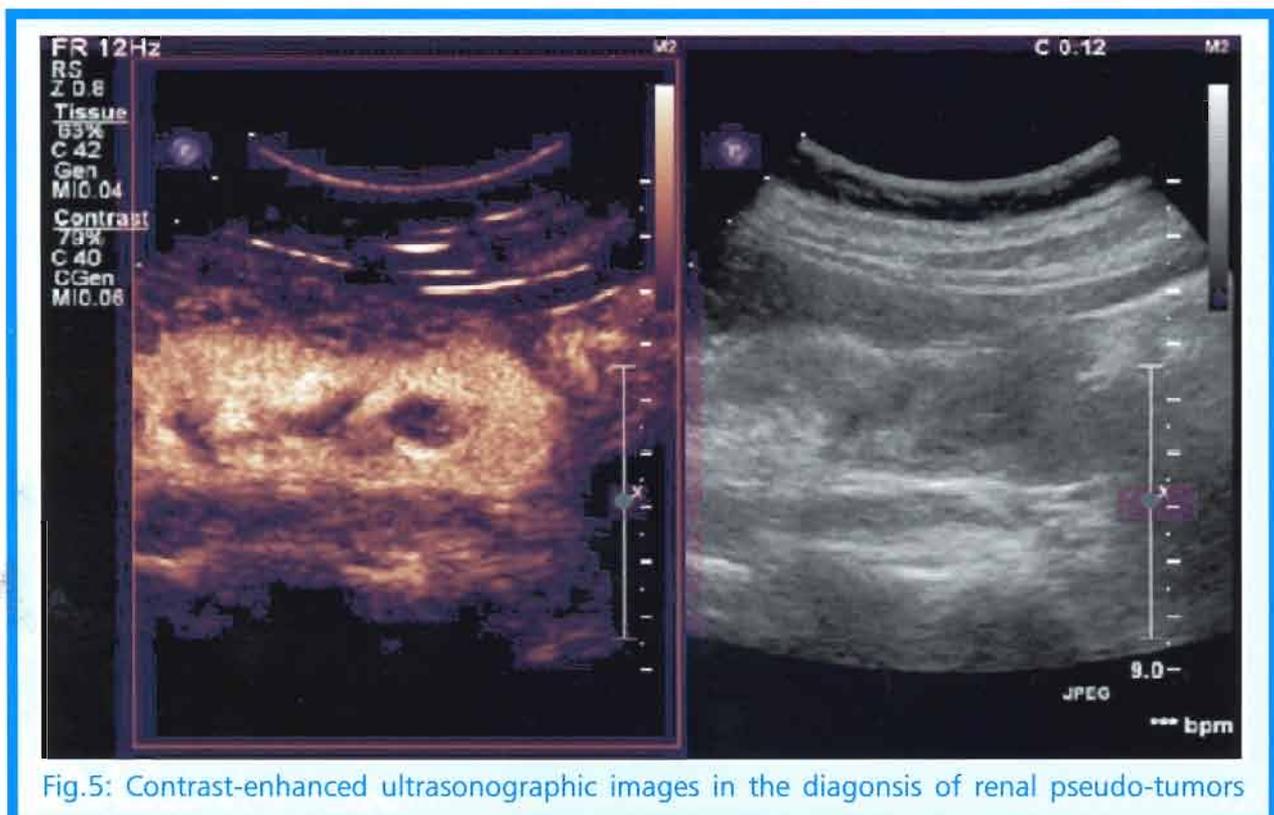


Fig.5: Contrast-enhanced ultrasonographic images in the diagnosis of renal pseudo-tumors

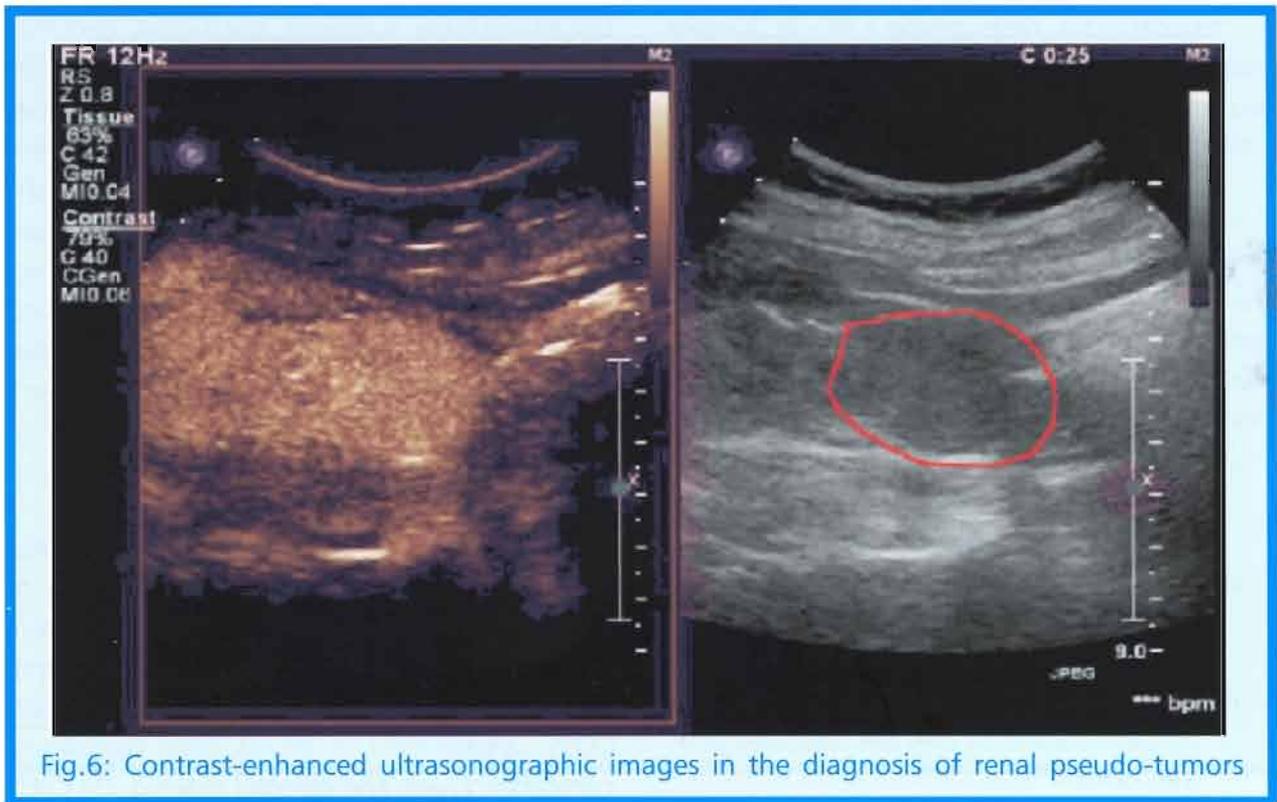


Fig.6: Contrast-enhanced ultrasonographic images in the diagnosis of renal pseudo-tumors

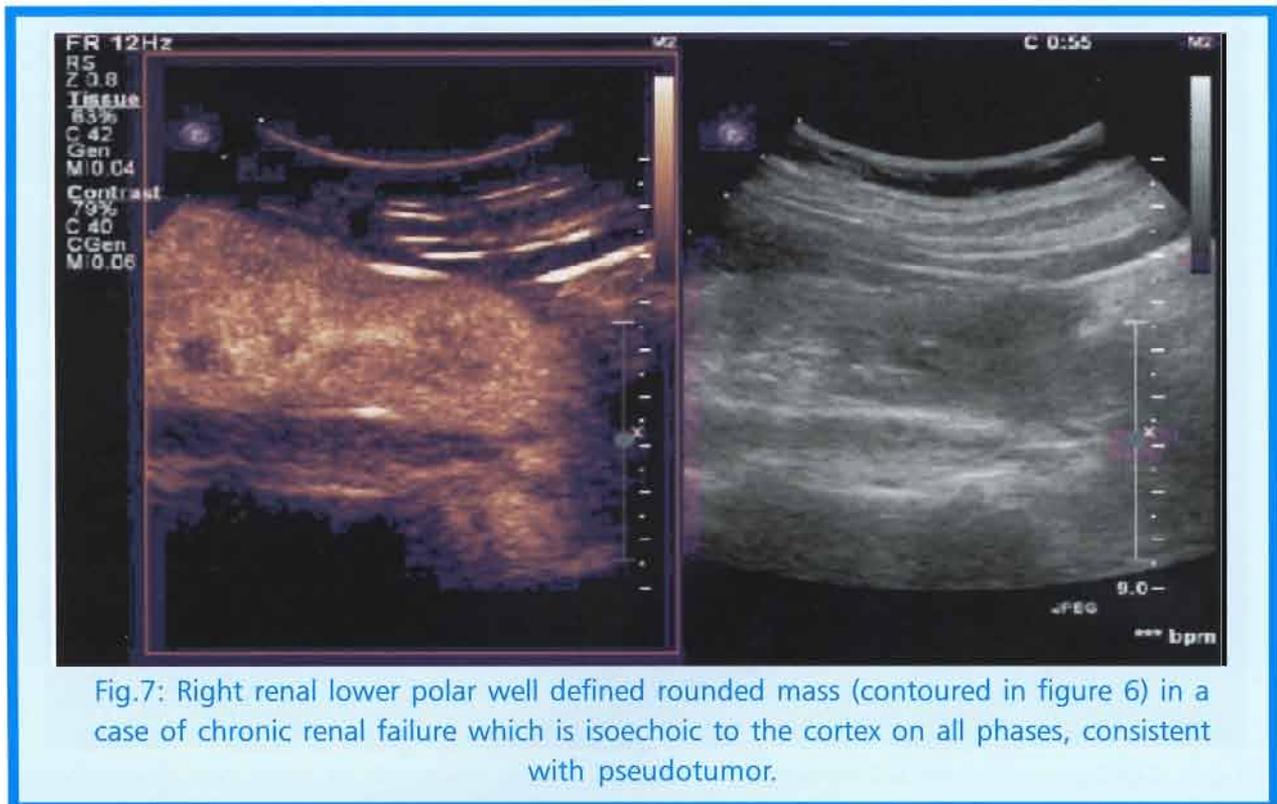


Fig.7: Right renal lower polar well defined rounded mass (contoured in figure 6) in a case of chronic renal failure which is isoechoic to the cortex on all phases, consistent with pseudotumor.

these pseudo-lesions exactly follow the normal enhancement pattern of the renal cortex or the pyramid and can thus be differentiated from a true renal mass lesion (20). (Figs.5,6&7).

Solid Renal Tumors

CEUS has a role in differentiating solid renal masses into benign and malignant. The tumor echogenicity on grey scale, enhancement

patterns, and degree of enhancement at different phases are used to differentiate benign and malignant solid renal mass lesions. CEUS features of early washout, heterogeneous enhancement, and an enhanced peritumoral rim or pseudocapsule favor the diagnosis of RCC (21–23). CEUS can also be used to differentiate between tumour and bland IVC thrombus related to renal cell carcinoma (Fig.4).

Table 1: Bosniak classification of complex renal cysts adapted to CEUS (26)

Type	Description
I	Simple cyst. Benign, with no malignant potential. No further workup.
II	Few thin septations or small amount of peripheral calcification. Weak chance of malignancy. Evaluate cyst enhancement with CEUS. If no enhancement, no further follow-up is needed. If substantial enhancement is observed, assess with CT. Even if CT is negative for enhancement, consider US follow-up.
III	Many thin septations, several thick septations, or a small mural nodule. Intermediate chance of malignancy. Evaluate cyst enhancement with CEUS. If no enhancement is seen, assess with CT and follow with US. If substantial enhancement is seen, consider surgery. Follow-up is mandatory if surgery is not performed.
IV	Many thick septations, large mural nodule, or mural nodularity. Strong chance of malignancy. Evaluate with CEUS. If no sonographic enhancement is seen, assess with CT and follow with US. If substantial enhancement is seen, consider surgery.

Cystic masses

There is over all 39% and more than 50% incidence of renal cyst in patients older than 50 years of age (24). Most of these cysts are incidentally detected. Complex cysts are currently classied according to Bosniak (25). Bosniak classification suggests malignant potential of a cystic mass. This categorization has been based on CT findings (25) but can be efficaciously extrapolated and applied to CEUS (26) (Table 1). Surgery is recommended for IV and III categories, category II and I are benign.

Computed Tomography

MDCT protocol(27)

In general, 100–150 mL of iodinated IV contrast medium is used at a flow rate of 2–3 mL/s. Unenhanced images of the liver and kidneys are obtained with 5-mm collimation in 5-mm increments. Unenhanced images of the kidneys allow detection of calcification or fat in the kidney, enable assessment of contrast enhancement, and assist in characterizing the lesion. IV contrast-enhanced images targeted on the kidneys are obtained in the arterial, late arterial (corticomedullary and portal venous), nephrographic, and excretory phases at 15–30, 45–60, 80–180, and 180 seconds, respectively, after commencement of the IV infusion. Imaging of the liver and the remaining abdominal structures is performed in the portal venous phase.

Unenhanced CT(28)

An initial series of unenhanced scans through the kidneys should be part of every protocol for evaluation of a suspected renal mass; it provides a baseline from which to measure the enhancement within the lesion after the administration of intravenous contrast material. This enhancement characteristic is important in distinguishing hyperdense cysts from solid tumors. Because most renal cell carcinomas have a rich vascular supply, they enhance significantly after administration of contrast material. Enhancement values of more than 12 HU are considered suspicious for malignancy(29).

Most renal cell carcinomas are solid lesions with attenuation values of 20 HU or greater at unenhanced CT (29). Small (≤ 3 -cm-diameter) tumors usually have a homogeneous appearance, while larger lesions tend to be more heterogeneous owing to haemorrhage or necrosis. Calcifications are detected in up to 30% of cases of renal cell carcinoma.

Arteriographic Phase(7)

The arteriographic phase is performed to evaluate the arterial anatomy and it occurs 15-30 s after the contrast injection. It is characterized by the clear visualization of the large and small vessels similar to those obtained with arteriography. It is particularly useful in those cases in which a conservative surgery is planning, because it clearly shows the anatomic distribution of the renal vessels and their relationship with the neoplasm.

Corticomedullary Phase(7,28)

In the cortico-medullary phase the contrast medium is in the glomeruli and in the peritubular capillaries, but it has not arrived in the distal tubular lumina and in the interstitium.

An intense cortical enhancement is observed, while the medulla remains hypodense. RCC are commonly hypodense compared to the cortex and cannot be recognized when they are small. Maximal opacification of the renal veins allows confident diagnosis of venous extension of the tumor which cannot be visible in the prosecution of the study. In small hypervascular tumours with arterio-venous fistulas an early enhancement can be occasionally observed.

Nephrographic Phase

As contrast material filters through the glomeruli into the loops of Henle and the collecting tubules, the nephrographic phase of contrast enhancement begins (30). This phase is best imaged after a scanning delay of at least 80 seconds and lasts up to 180 seconds after the start of injection. In this phase the renal tumors show a relatively less contrast enhancement compared to the normal adjacent tissue. RCC have a rich vascular supply, but lower than normal kidney and a contrast enhancement value of more than 20 HU with respect to the non-contrast scan is considered suspicious for malignancy. When the enhancement is between 10 and 20 HU the diagnostic confidence is lower because these values can be observed in complicated cysts or in cystic carcinomas(31).

Excretory Phase

The excretory phase begins approximately 180 seconds after the initiation of injection of iodinated contrast material. The contrast material is excreted into the collecting system, and as a result, the attenuation of the nephrogram progressively decreases(28). (Fig.8&9).

This phase is occasionally helpful to better delineate the relationship of a centrally located mass with the collecting system and define potential involvement of the calices and renal

pelvis. These data are actually very important when a conservative surgery is planned. Delayed scanning can also be used in lieu of unenhanced scanning to characterize an incidental renal lesion detected on a routine contrast-enhanced CT scan(28).

Multiplanar reformatted and 3D volume rendered presentations of the renal phase images are helpful in allowing visualization of the relationships of structures, particularly for surgeons(28,32,33).

MRI Evaluation

MRI is generally only used when optimal CT cannot be performed, as in the case of a severe allergy to iodinated contrast medium or pregnancy. MRI has similar reported overall staging accuracies to those of CT (34). Its multiplanar capability, however, is particularly useful for delineating the superior extent of tumor in the IVC(2,35,36).

Coronal and axial conventional T1-weighted (TR/TE, 600/60) and axial dual-echo fast spin-echo T2-weighted (6,000/first -echo TE, 136; second-echo TE, 68) fat-suppressed images of the

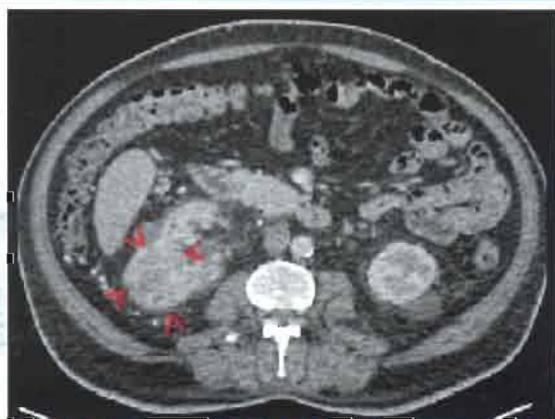


Fig.8: Nephrographic phase shows a well defined rounded heterogeneously enhancing right renal mass (arrowheads).

abdomen are obtained(27). Images supplemented by dynamic contrast-enhanced 3D fast spoiled gradient-recalled echo sequences (FSPGR) help to further delineate the primary tumor and liver lesions and to evaluate any vascular thrombus identified. In particular, tumor, rather than bland, thrombus is indicated by the



Fig.9a

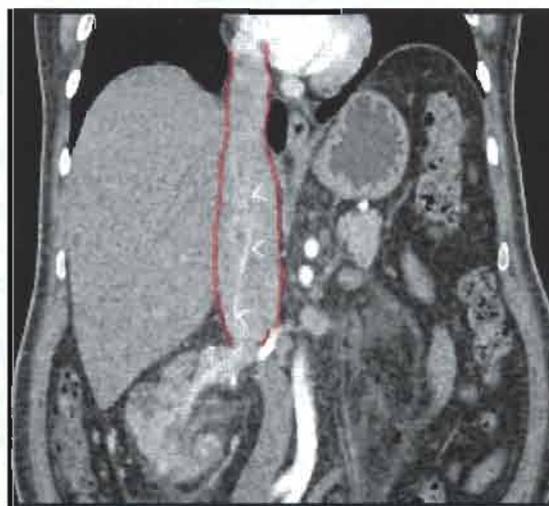


Fig.9b

Axial (Fig.9a) and coronal reformat (Fig. 9b) arterial phase images show abnormally dilated IVC (contoured) with intraluminal thrombus extending from the right renal vein up to the right atrium which shows intramural vascularity (arrowheads), suggestive of tumor thrombus. Same case as in fig.1,2,3,4.

presence of enhancing vessels in the thrombus(27). Multiple dynamic acquisitions can be used to obtain arterial, nephrogenic, and pyelographiclike images (37-40). MDCT with 3D reformations and MRI have similar overall staging accuracies for RCC(41).

Conclusion

Various imaging modalities can be used for evaluation of renal masses. Ultrasonography is the primary modality where an incidental renal mass may come to attention. CT and MRI are the current modalities of choice for preoperative staging of renal masses. Newer imaging techniques like contrast enhanced ultrasound examination offer an advantage of evaluating renal masses, especially, in cases of renal failure where CT and MR contrast media are contraindicated.

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Urological Abnormalities in Children with Urinary Tract Infection

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Introduction

Urinary tract infection (UTI) is a common bacterial infection in infants and children. The presence of UTI may be an indicator of a serious underlying genitourinary abnormality. (1,2). Rapid evaluation and treatment of UTI is important to prevent renal parenchymal damage and renal scarring that can cause hypertension and progressive renal damage. (3). Literature reveals high incidence of abnormalities in the renal tract with vesico-ureteric reflux (VUR) in 30-50% and obstructive uropathies in 1-4%. (4). The management of the patients with UTI does not end only with the treatment but needs further evaluation to diagnose the underlying urological anomalies.

All children with the first UTI should undergo radiological evaluation. The detection of significant scarring, high grade VUR or obstructive uropathy enables the interventions that prevent progressive renal damage in the long term.

Radiological Evaluation includes ultrasonography (USG), dimercaptosuccinic acid (DMSA) renal scan, and Micturating cystourethrography (MCU) performed judiciously.

Ultrasonogram

An ultrasonogram provides information on kidney size, number, and location, presence of hydronephrosis, urinary bladder anomalies and post void residual urine. Ultrasonography should be done soon after the diagnosis of UTI.

Micturating cystourethrography

MCU detects VUR and provides anatomical details regarding the bladder and the urethra. It is recommended 2-3 weeks after the treatment of UTI. Follow up patients with VUR can be performed using direct radionuclide cystography.

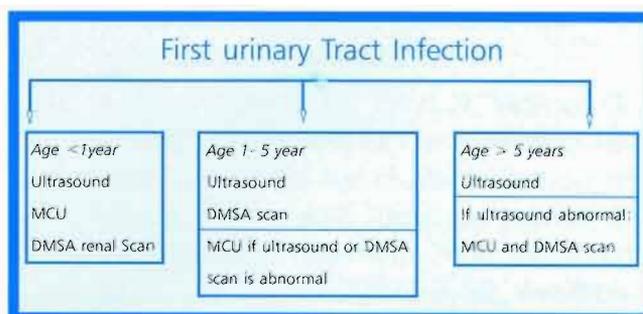
DMSA Renal Scan

DMSA renal scan is a sensitive technique for detecting the renal parenchymal infection and cortical scarring. It should be performed 2-3 months after the treatment.

Choice of Investigation

According to the Guidelines on Revised Statement on Management of Urinary tract infections formulated by the Indian Society of Pediatric Nephrology (5), Radiological evaluation of children after the first episode of UTI is shown in the following figure.

The following figure shows the guidelines for evaluation.



It is recommended that all infants with UTI be screened by ultrasonography, followed by MCU and DMSA scintigraphy. Since older patients

(1 -5 year old) with significant reflux and scars or urinary tract anomalies are likely to show abnormalities on ultrasonography, a MCU is advised in patients having abnormalities on either of the above investigations. Children older than 5 years are screened by ultrasonography and further evaluated only if this is abnormal.

However patients with recurrent UTI at any age should undergo detailed imaging with ultrasonography, MCU and DMSA scintigraphy.

Our Experience:

Following the above guidelines we evaluated 57 cases of UTI in children, in the department of Pediatrics, BARC Hospital.

Aim & Objectives

The Aim of this study was to determine number of patients having underlying urological abnormalities and the specific type of abnormality.

The diagnosis of UTI was based on Signs and symptoms of UTI such as fever, pain in abdomen, dysuria, urinary frequency and urine microscopy showing more than 10 WBCs per high power field of centrifuged urine sample or any growth in the urine specimen.

Table 1 : Age group and sex distribution

Age	Number	Percentage (%)
<1year	12	20.69
1 -5 year	34	58.62
>5year	12	20.69
Total	58	100

Table 2 : Sex incidence

Sex	Number	Percentage
Male	21	36.21
Female	37	63.79
Total	58	100

We observed that majority of the children with UTI were in the age group of 1 -5 years (58.62%). (Table1). Of all cases 36.71% were males and 63.79% were females. The male to female ratio was 1: 1.8 showing female predominance. (Table2).

Symptomatology

In our study, 36.2% children presented with only fever, fever with associated urinary complaints like dysuria, frequency, urgency and pain in abdomen was seen in 52.6%, while 12% cases did not have fever.

Investigations

Urine microscopy was positive for more than 10 pus cells in all the patients. Urine culture done in all the cases was positive in 63.16%. The organism isolated (Table – 3) were E. coli (75%), klebsiella (11.11%), proteus (11.11%) and enterobacter (2.78%).

Table 3 : Organisms isolated from urine cultures

Organism isolated	Number	Percentage (%)
E.coli	27	75
Klebsiella	4	11.11
Proteus	4	11.11
Enterobacter	1	2.78

All patients received appropriate antibiotics for 10 – 14 days to control the infection and underwent full urological investigations.

Radiological Evaluation

All children were subjected to the radiological evaluation as per the Guidelines. Ultrasonography was performed in all children. DMSA scan was performed in 82.57% and 72.41% were subjected to Micturating Cystourethrogram.

Observations

Urological abnormalities were observed in 41.38% cases. Abnormalities were more common (70%) in children less than five years of age.

Table 4 : Type of Urological Structural anomalies in

	Number	Male	Female
Vesicoureteric reflux (VUR)	11	5	6
Posterior urethral valve(PUV)	2	2	-
PU junction obstruction (PUJ)	2	2	0
Ureterocele *	1		1
Calculus with hydronephrosis	1	1	
Bladder neck obstruction with bil hydronephrosis with ureteral dilatation	1		1
Abnormal urethral meatus	1		1
Ectopic kidney	1		1
Bladder dysfunction (post void residue)	2	1	1
Extra renal pelvis	1	1	
Renal scar without other abnormality	1		1
Total	24	11	12

*- had associated VUR.

Ultrasound performed in all cases demonstrated abnormality in 31.03%. The abnormalities detected were hydronephrosis, post void residue, small kidney with scar, calculus with hydronephrosis and ectopic kidney.

DMSA scan revealed renal scarring in 27.7% of cases. Scarring was seen in children secondary to Vesicoureteric reflux. Primary scarring without any abnormality was seen in only one case.

MCU was abnormal in 38.09% of cases. The abnormalities detected on MCU were Vesicoureteric reflux (VUR) in 26.19% (Table -5).

Table 5 : Grades of VUR in children

VUR	Number	Male	Female
Grade 3 and below	7	2	5
Grade 4 and above	5	4	1

The other anomalies detected were Posterior urethral valve (2 cases), Bladder neck obstruction (1 case) and ureterocele (1 case).

After the control of UTI, these children were appropriately managed depending upon the anomaly detected. They are under regular follow up in the Pediatric OPD. Children with VUR are regularly followed up with ultrasonography and renal scan. Children with renal scar are under follow up yearly for growth, hypertension, renal size and function. Those with bowel and bladder dysfunction are managed for the same.

Conclusion

We observed that in children with UTI, urological abnormality was present in

41.38% . Hence even a single confirmed UTI should be taken seriously, especially in young children, due to the potential for renal parenchymal damage. Early intervention to identify and treat them should be carried out so as to prevent serious kidney damage.

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Alarming facts about Kidney failure

- The kidney has a higher blood flow than brain, liver and heart.
- 50 gallons of blood are filtered through 140 miles of tubes and millions of filters within the kidney each day.
- The kidneys continue to perform until they have lost 75-80% of their function.
- Lifestyle related disorders like diabetes and hypertension are important causes of Kidney failure.
- Almost 66% kidney failure occurs due diabetes or hypertension.
- Approximately 7.85 million people suffer from chronic kidney failure in India.
- There were over 1, 50,000 patients were waiting for Kidney transplant in India at the end of 2011.

Renal Disease and Anaesthesia

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Introduction:

The kidneys are responsible for a number of essential functions including water conservation, electrolyte homeostasis, acid base balance, and several hormonal functions. When the kidneys are involved in a disease process, some or all of these functions may be affected. Knowledge of how the kidneys perform these important functions, aids in the understanding of the clinical presentation, signs and symptoms, and treatment of renal diseases.

Renal disease is often discovered incidentally, during a routine medical evaluation though some patients may present with clear evidence of renal dysfunction. Acute as well as chronic renal disease impairs response to anaesthesia and surgery. Certain anaesthetic agents and drugs can induce alteration in renal function.

Relevant Anatomy & Physiology:

Kidneys are paired vital organs. Each kidney consists of approximately a million nephrons, which are the functional units of kidney. As the plasma flows along the nephron, virtually all the fluid and solutes are reabsorbed by a number of active and passive transport systems. The kidneys receive approximately 15% to 25% of total cardiac output, or 1 to 1.25 L of blood per minute through the renal arteries. A unique feature called auto-regulation, maintains renal blood flow when the mean arterial pressure ranges from 60 mm Hg and 160 mm Hg. Interestingly, the kidneys are able to tolerate substantial insults while maintaining adequate function despite this theoretic vulnerability to ischemia.

Renal function tests

Table 1: Tests Used to Evaluate Renal Function

Test	Normal Value
Glomerular Filtration Rate	
Blood urea nitrogen	10–20mg/dL
Serum creatinine	0.7–1.5 mg/dL
Creatinine clearance	110–150mL/ min
Proteinuria (albumin)	<150 mg/day
Renal Tubular Function and/or Integrity	
Urine specific gravity	
Urine osmolality	
Urine sodium excretion	1.003–1.030
Glucosuria	38–1400mOsm/L
Enzymuria	<40 mEq/L
<i>N</i> -Acetyl- β -glucosaminidase	
α -Glutathione- <i>S</i> -transferase	
Factors That Influence Interpretation	
Dehydration	
Variable protein intake	
Gastrointestinal bleeding	
Catabolism	
Advanced age	
Skeletal muscle mass	
Accurate timed urine volume measurement	

Multiple and severe insults are required to cause an injury severe enough to manifest a clinically relevant decrease of renal function. The most common cause of perioperative renal injury is ischemia-reperfusion injury. Drugs like certain antibiotics, radiocontrast dyes, NSAIDs can also impair kidney function (Table 2).

Table 2: Nephrotoxins Commonly Found in the Hospital Setting

EXOGENOUS	ENDOGENOUS
Antibiotics (Aminoglycosides, cephalosporins, amphotericin B, sulfonamide, tetracyclines, vancomycin)	Calcium (hypercalcemia) Uric acid (hyperuricemia and hyperuricosuria)
Anesthetic agents (Methoxyflurane, enflurane) Nonsteroidal anti-inflammatory drugs (Aspirin, ibuprofen, naproxen, indomethacin, ketorolac)	Myoglobin (rhabdomyolysis) Hemoglobin (hemolysis) Bilirubin (obstructive jaundice)
Chemotherapeutic-immunosuppressive agents (Cisplatinum, cyclosporin A, methotrexate, mitomycin, nitrosoureas, tacrolimus) Contrast media	Oxalate crystals Paraproteins

Acute renal failure

This syndrome is a rapid deterioration in renal function that results in retention of nitrogenous waste products (azotemia). It can be divided into prerenal, renal, and post-renal types depending on its cause. Prerenal azotemia results from an acute decrease in renal blood flow. Renal azotemia is usually due to intrinsic renal disease, renal ischemia, or renal toxins. Postrenal azotemia is the result of urinary tract obstruction or disruption. Both prerenal and postrenal azotemia are readily reversible in their initial stages but with time progress to renal azotemia. The course of acute renal failure varies widely, but the oliguria typically lasts for 2 weeks and is followed by a diuretic phase marked by a progressive increase in urinary output. Urinary function improves over the course of several weeks but may not return to normal for up to 1 year.

Chronic renal failure

This syndrome is characterized by a progressive and irreversible decline in renal function over the course of at least 3–6 months. The most common causes are hypertension, diabetes, chronic glomerulonephritis, and polycystic renal disease. The full manifestations of this, often referred to as **uremia** are seen only after the GFR decreases below 25 mL/min. Patients with clearances below 10 mL/min (often said to have end-stage renal

disease) are dependent on dialysis for survival until they receive a successful kidney transplant.

Pathophysiological changes in renal diseases

- 1) Fluid and electrolyte derangement: Usually certain degree of salt and water retention is seen. Patient are unable to compensate for extrarenal fluid losses e.g. diarrhea, vomiting or fever and may develop low blood pressure. Potassium excretion from body is impaired.
- 2) Impaired calcium absorption leads to osteoporosis.
- 3) Anemia
- 4) Increased bleeding tendencies due to impaired function of platelets
- 5) Cardiovascular system: Most of the patients have high blood pressure. Accelerated atherosclerosis may lead to ischemic heart diseases like angina, myocardial infarction.
- 6) Immune function is deranged; hence these patients are prone to infection.
- 7) Gastrointestinal abnormalities: Bleeding in gastrointestinal tract is seen. Delayed gastric emptying leads to anorexia, nausea and vomiting.

- 8) Neurological abnormality:
Peripheral neuropathy characterized by sensory complaints like tingling, numbness, paraesthesia reduced sensations etc are seen in early phases which may later progress to weakness in the muscles of extremities.
- 9) Endocrinal changes: renal failure patients with diabetes may have reduced metabolism of insulin leading to reduced requirement of insulin.

Drug metabolism and renal diseases

With progressive renal disease, drug excretion gets delayed and active metabolite can accumulate in body. Also some drugs may themselves be toxic to kidneys and hence dose adjustment as per renal function (GFR) is required.

Following are alterations seen in patients with renal disease

- 1) Delayed absorption due to delayed gastric emptying
- 2) Distribution of drug in body may be deranged.
- 3) Protein binding of drugs is altered.
- 4) Drugs eliminated by kidneys will have prolonged elimination half life in body.

Anaesthesia in patients with renal diseases

Anaesthesia aims

- Maintain normal blood volume
- Maintain normal BP
- Avoid nephrotoxic drugs
- Avoid drugs which depend mainly on kidneys for elimination

Preoperative evaluation

Patient's medical history: Establish cause of renal failure, duration and need for dialysis. Associated conditions like diabetes, hypertension and heart diseases need to be noted. Conditions associated with renal failure (mentioned above) need to be noted too.

Preoperative laboratory investigations:

- 1) Complete blood count- hemoglobin (low- decreased red blood cell synthesis, increase breakdown of red cells), White blood cell count- raised suggest infection, platelet count.
- 2) Blood glucose level- diabetes is the most common cause for renal impairment.
- 3) Renal function tests- blood urea nitrogen, serum creatinine are raised. Creatinine clearance calculated from creatinine value helps in dose adjustment.
- 4) Serum electrolytes- most commonly serum potassium value are raised.
- 5) Coagulation study- mainly clotting study.
- 6) ECG- for ischemia, arrhythmia or electrolyte dysfunction.
- 7) X ray chest- signs of fluid overload.
- 8) Arterial blood gas- evaluate acid base status.
- 9) Liver function test- if major surgery is planned.

Preoperative optimization:

- 1) Treatment of anemia.
- 2) Evaluation and treatment of associated cardiac diseases.
- 3) Normalize blood pressure.
- 4) Correct serum potassium levels if abnormal.
- 5) Dialysis if evidence of fluid overload- lower limb edema, pleural effusion.
- 6) Control of diabetes.

Preoperative premedication:

- 1) Antihypertensive medication continued.
- 2) Aspiration prophylaxis with an H₂ blocker may be indicated in patients with nausea, vomiting, or gastrointestinal bleeding. Metoclopramide, 10 mg orally or slowly intravenously, may also be useful in accelerating gastric emptying, preventing

nausea, and decreasing the risk of aspiration

- 3) Preoperative use of sedatives should be individualized. Alert patients who are relatively stable can be given sedatives to allay anxiety especially who are having ischemic heart disease.
- 4) Patients on hemodialysis should undergo dialysis during the 24 hours preceding elective surgery.
- 5) The preoperative presence of a coagulopathy may be treated.

Monitoring during surgery and anaesthesia:

Noninvasive monitors-

ECG, noninvasive BP, pulseoximetry, capnography, neuromuscular block, Temperature.

Invasive monitors-

Central venous pressure (fluid status), Arterial line (ABG, invasive BP Monitoring), hourly urine output, blood sugar by finger prick in diabetic patients, nasogastric tube. Pulmonary arterial pressure in selected patients.

General Anaesthesia:

Anaesthesia drugs in renal disease:

Drug class	Safe	Use with caution	Avoid
Induction agents	Propofol	Thiopental sodium, ketamine	
Sedatives		Midazolam, diazepam, lorazepam, alprazolam	
Narcotics	Fentanyl, remifentanyl	Morphine, Alfentanyl	Pethidine
Muscle relaxants	atracurium, cis-atracurium, mivacurium	Vecuronium, Rocuronium, succinylcholine,	doxacurium, pancuronium, pipecuronium, d-Tubocurarine
Analgesics	Paracetamol		NSAIDS

Fluid administration:

Fluid therapy should be cautious in these patients, as these patients can be in fluid overload, and if required central venous monitoring may be done to guide fluid replacement.

Regional Anaesthesia:

Adequacy of coagulation should be considered and the presence of uremic neuropathies excluded before regional anesthesia is performed in these patients. Dose of local anaesthetics may be reduced by 25% because of altered protein binding and lowered seizure threshold.

Post operative pain relief:

Managing postoperative pain is important in these patients. Paracetamol can be used safely in patients with deranged renal function. Non steroidal anti-inflammatory drugs (NSAIDs) are best avoided due to their nephrotoxic potential. Opioids can be used for postoperative pain. Possibility of prolonged half life of these drugs in view of impaired renal excretion especially morphine must be considered. Weak opioids, like tramadol, can be used with dose modification and monitoring. Regional anaesthesia too, in the absence of coagulopathy, can provide adequate pain relief. Hypotension

associated with neuraxial block has to be avoided since it can compromise renal blood flow.

Perioperative problems which can be encountered in patients with renal disease:

- 1) Bleeding- platelet function defect
- 2) Fluid overload
- 3) Hypo/ hypertension
- 4) Inadequate recovery from neuromuscular blocking agents
- 5) Worsening of renal function.
- 6) Difficult intravenous access

Conclusion:

The kidney plays a central role in implementing and controlling a variety of homeostatic functions. Renal dysfunction can occur as a direct result of surgical or medical disease, prolonged

reduction in renal oxygen delivery, nephrotoxin insult, or a combination of these factors. The emphasis in the care of these patients is preservation of the remaining renal function, which is best accomplished by maintaining normovolemia, judicious fluid administration, dialysis with its implications, avoiding nephrotoxic drugs and drug dose reduction to avoid prolong effect. Thus although anaesthesia in patients with renal impairment are challenging, careful approach towards management can result in successful outcome.

References:

- 1) Miller's Anaesthesia, Seventh edition, pg 2105-2134.
- 2) Clinical anesthesiology, G. Edward Morgan, Jr., fourth edition, pg 742-756.
- 3) Clinical anesthesia, Paul G. Barash, sixth edition, pg 1347-1374.

Historical references to Kidney stones

- Hippocrates (470/460 B.C.-380/360 B.C.) makes reference to kidney stones in the famous Hippocratic Oath as follows: "I will not cut persons labouring under the stone, but will leave this to be done by men who are practitioners of this work."
- Louis Napoleon, nephew of Napoleon Bonaparte, lost the Franco-Prussian War of 1870 due wholly or in part from impaired kidney function resulting from kidney stone formation.

Urine Protein Electrophoresis

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In kidneys, the glomerular capillary wall is permeable to substances with molecular weight of 20 kDa or less.¹ A normal adult excretes up to 150 mg/24hr of protein in urine.² Normal urinary proteins consist of about 2/3 plasma proteins and 1/3 protein derived from the urinary tract. Once in filtrate, low molecular weight proteins are reabsorbed and metabolized by the proximal tubule cells. This is most readily seen in two-dimensional electrophoretic map.¹

Proteinuria:^{1,2}

Proteinuria is defined as urinary protein excretion of more than 150 mg per day. Microalbuminuria can be a sign of early renal disease, especially in diabetic patients. In microalbuminuria, 30 to 150 mg protein is excreted per day.

Types of proteinuria:^{1,2}

Proteinuria can be transient (intermittent), orthostatic (relate to sitting / standing) or persistent (always present). In transient proteinuria, protein in urine disappears when the underlying cause is resolved.

In orthostatic proteinuria, protein excretion is normal when the patient is lying down but is increased when a person is sitting or standing. It occurs in approximately 2 to 5 percent of young people, but is unusual in people over the age of 30.

Persistent proteinuria can be further defined as glomerular, tubular or overflow. The most common type is glomerular proteinuria with albumin as the primary urinary protein. This type

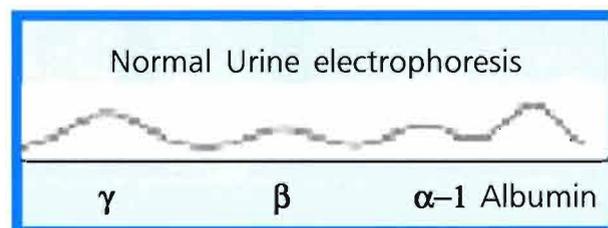
of proteinuria is caused by increased filtration of albumin and other macromolecules across the glomerular basement membrane.

Tubular proteinuria results when malfunctioning tubule cells no longer reabsorb proteins in the filtrate; low molecular weight proteins such as β_2 microglobulin and immunoglobulin light chains dominate over albumin.

In overflow proteinuria, low molecular weight proteins overwhelm the ability of the tubules to reabsorb the filtered proteins. Bence-Jones proteinuria is the classic example of overflow (and also tubular) proteinuria. Quantitative measurement of Bence Jones proteins and determination that they are monoclonal, aid in the diagnosis of various disorders including multiple myeloma – the malignant proliferation of plasma cells.

Urine protein electrophoresis:¹

Urine protein electrophoresis (UPEP) is utilized to detect the type and concentration of various proteins in urine. The test provides information about the location and degree of damage within the nephron. Urine immunofixation electrophoresis (UIFE) helps to determine the type of protein detected by UPEP. Urine electrophoresis should be performed whenever it may be of clinical value to identify the proteins in urine in order to evaluate the nature or extent of renal



damage. But on the other hand, it is important to know that the patient with renal tubular disease may also have protein excretions within the normal range.

A typical pattern of highly concentrated normal urine contains a small amount of albumin and a trace of transferrin, no other discrete peaks are usually visible.

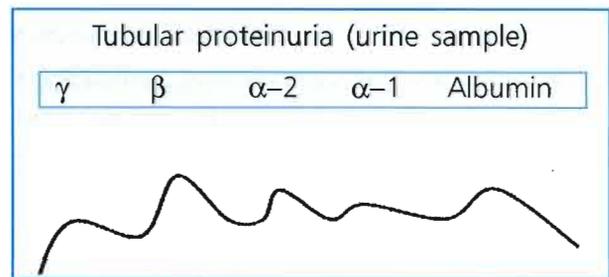
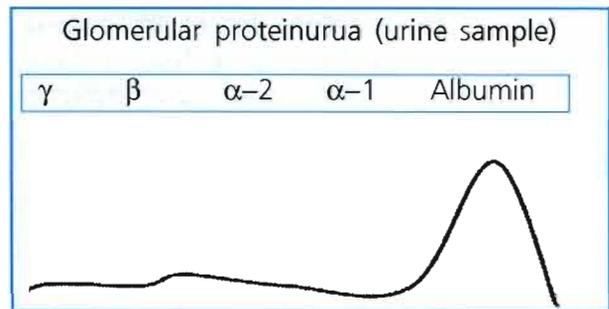
There are several relatively benign conditions which cause significant increase of plasma proteins in the urine. These include pregnancy, exercise, postural hematuria and march hematuria. The patterns in these conditions typically mirror serum electrophoretic pattern.

Trace amount of proteins in urine are important in the monitoring of some disease states. The early stages of diabetic renal disease are monitored by following the excretion of serum albumin. The upper limit of normal for urinary microalbumin is 20-30 mg/day. Urinary microalbumin is typically measured by using low level immunodiffusion plates.

Electrophoretic pattern of urinary proteins:³

- Glomerular proteinuria: albuminuria is hallmark (making up 60 to 90% of total proteinuria)
- Tubular proteinuria: low molecular weight proteins predominate with total urine protein rarely > 2g/d –
 - Impaired tubular reabsorption of low molecular weight proteins, or

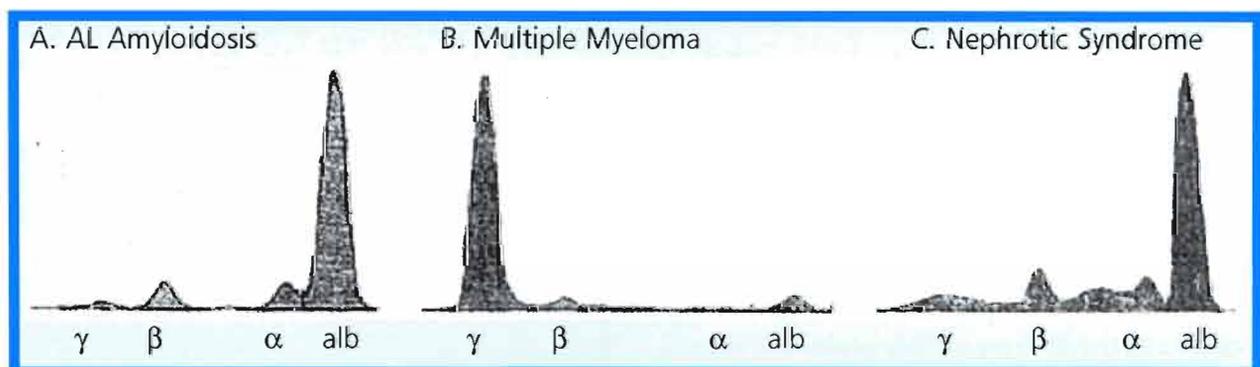
- Overproduction of low molecular weight proteins, such as light chains in myeloma.



- Selective proteinuria expressed as clearance of IgG over clearance of transferrin is reliable indicator of severity and reversibility of abnormalities of glomerular proteinuria; patients with highly selective proteinuria have milder tubulointerstitial damage, improved prognosis and better response to therapy:

Selectivity index (SI) = $\frac{\text{urine IgG}}{\text{serum IgG}} \times \frac{\text{serum transferrin}}{\text{urine transferrin}}$

- $SI \leq 0.10$: Highly selective;
- $SI \geq 0.11$ and $d'' 0.20$: Moderately selective;
- $SI \geq 0.21$: Nonselective.



The presence of any amount of urinary free light chain (Bence-Jones proteins) can be important in the evaluation of patients with monoclonal gammopathies.

The recent "Guidelines for Standard Investigative Workup: Report of the International Myeloma Workshop Consensus Panel 3" states that "both serum and urine should be assessed for monoclonal protein. Agarose gel electrophoresis or capillary zone electrophoresis of serum and urine is preferred to screen for the presence of monoclonal protein."

Although most monoclonal gammopathies can be detected, characterized, and monitored with serum assays, some plasma cell proliferative disorders synthesize and secrete monoclonal free light chain or heavy chain fragments. The products of these clonal plasma cells are relatively small molecular weight and may be readily cleared from blood. To detect and/or monitor these abnormalities, it may be necessary to test urine samples. Monoclonal light chains in patients with diseases such as primary amyloidosis can be detected by serum IFE with a sensitivity of 80 to 85%. Inclusion of urine IFE increases this sensitivity to 90 to 95%.⁴

When to test urine for light chains?¹

The following conditions (to list a few) warrant urine protein electrophoresis:

- 1) Monoclonal protein in serum is > 1.5 g/dL,
- 2) Monoclonal free light chains are detected in serum,
- 3) Hypogammaglobulinemia is present in serum,
- 4) Serum electrophoresis shows nephrotic pattern.

Monoclonal versus Polyclonal Gammopathies:⁵

It is extremely important to differentiate monoclonal from polyclonal gammopathies. Monoclonal gammopathies are associated with a clonal process that is malignant or potentially malignant. In contrast, polyclonal gammopathies

may be caused by any reactive or inflammatory process, and they usually are associated with nonmalignant conditions.

The most common conditions in the differential diagnosis of polyclonal gammopathy are listed in table below:

Differential diagnoses of Polyclonal Gammopathy ⁵	
• Infections	Viral infections, especially hepatitis, HIV infection, mononucleosis and varicella. Focal or systemic bacterial infections, including endocarditis, osteomyelitis and bacteremia Tuberculosis
• Connective tissue diseases	SLE, Mixed connective tissue disorders, Temporal arteritis, Rheumatoid arteritis
• Liver diseases	Cirrhosis, Ethanol abuse, Autoimmune hepatitis, Viral-induced hepatitis, Primary biliary cirrhosis, Primary sclerosing cholangitis
• Malignancies	Solid tumors, Ovarian tumors, Lung carcinoma, Hepatocellular carcinoma, Renal tumors, Gastric tumors
• Hematologic and lymphoproliferative disorders	Lymphoma, Leukemia, Thalassemia, Sickle cell anemia
• Other inflammatory conditions	GI conditions like UC and Crohn's disease, Pulmonary disorders including bronchiectasis, cystic fibrosis, chronic bronchitis, and pneumonitis Endocrine diseases including Grave's disease and Hashimoto's thyroiditis

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- 1) Aigars Brants. Urine protein electrophoresis: Latest Consensus Statements, Recommendations and Testing options. In: newsletter by Sebia Inc., Norcross, GA; *Separation* 2009;1(10):1-2. Downloaded from: www.sebia-usa.com/files/newsletter10-1.pdf
- 2) Richard A. McPherson, Jonathan Ben-Ezra, Shourong Zhao. Basic Examination of Urine. In: Henry's clinical diagnosis and Management by Laboratory methods, 21st ed., W.B.Saunders Comp, 2006
- 3) Mitchell H. Rosner and W. Kline Bolton. Renal Function Testing. *American journal of Kidney diseases* 2006;47(1):174-183.
- 4) A.C. Roden, K.S. Lockington, L.J. Tostrud and J.A. Katzmann. Urine protein electrophoresis and immunoelectrophoresis using unconcentrated or minimally concentrated urine sample. *Am J Clin Pathol* 2008;130:141-145.
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Keep your kidneys healthy and save your heart

- Keeping fit and active
- Keep regular control of your blood sugar level
- Monitor your blood pressure
- Eat healthy and keep your weight in check
- Maintain a healthy fluid intake
- Do not smoke
- Do not take over-the-counter pills on a regular basis
- Check your kidney function if you have one or more of the 'high risk' factors
 - you have diabetes
 - you have hypertension
 - you are obese
 - you or one of your family members suffers from kidney disease
- The kidneys and the heart are closely linked.
- Reduced kidney function and increased protein loss are both important and recently discovered risk factors for heart disease.
- The heart and kidneys also have common risk factors for poor function –smoking, high blood pressure, diabetes and high blood lipids.

Tertiary Hyperparathyroidism Following Chronic Renal Failure – A Case Report

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Introduction

Now a days, patients with chronic renal failure undergoing dialysis are on the rise and therefore cases of secondary hyperparathyroidism are common. However, cases of tertiary hyperparathyroidism are relatively rare. We present here a case of tertiary hyperparathyroidism and discuss the pathophysiology and different treatment option for secondary and tertiary hyperparathyroidism.

Case Report

A 39 yr old male patient, known case of chronic renal failure, was on regular hemodialysis. He had been diagnosed with hypertension at the age of 21 years and his renal biopsy showed chronic proliferative glomerulonephritis. His kidney function had deteriorated gradually and he was put on regular hemodialysis since 24 years of age. He had received a cadaveric renal transplant at the age of 27 yr but had developed severe respiratory tract infection within 6 month of transplant. His immuno-suppressant therapy

was stopped due to severe infection as a life saving measure and thus he ended up with rejection of the transplanted kidney which had to be removed and he was put back on regular hemodialysis thereafter.

He presented with loss of appetite, easy fatigueability and severe bone pain. He was on regular erythropoietin injections, vitamin D and calcium supplements and his hypertension was well controlled with prazosin.

His blood test reports were as follows:

Dexa scan showed severe osteoporosis in entire skeleton with high risk for fracture. Technetium MIBI scan for parathyroid gland uptake showed increased uptake in left lower parathyroid gland. His Technetium pertechnetate and tetrofosmin scan showed increased uptake in right lower parathyroid gland. In view of above, Tertiary hyperparathyroidism with polyglandular hyperplasia was diagnosed.

Test Performed	Normal Range	Patient's values Year wise		
		2005	2006	2007
Serum parathyroid hormone	12 to 72 pg/ml	1823	2627	2120
25 hydroxy cholecalciferol	7.6 to 75 ng /ml	-	-	42.7
Serum calcium	8.5 – 10.5 mg/dl	-	10.2	10.7
Serum Phosphorus	3.5 -5.5 mg/dl	-	6.2	6.3
Serum alkaline phosphatase	30-150U/L	-	-	380
Serum Albumin	3.5 – 5.5 mg/dl	-	-	4.2
Serum creatinine	0.2-1.5mg %	-	-	11.5

He underwent total parathyroidectomy but half of one parathyroid gland was implanted back in the right sternocleidomastoid muscle under general anesthesia. Histopathology of all four parathyroid gland showed hyperplasia of chief cells.

Post operatively, this patient developed severe hypocalcemia due to 'hungry bone syndrome' which was treated with calcium gluconate infusion. He also developed thrombosis of right arterio-venous fistula with right subclavian vein thrombosis which was managed with Inj. Heparin and closure of right arteriovenous fistula.

Gradually, he recovered completely and four years since his surgery, serum parathyroid hormone levels are normal. He does not have any bone pain and his stamina has improved though he is still on regular hemodialysis.

Discussion

The parathyroid glands are four pea-sized glands located on the thyroid gland in the neck. Although their nomenclature seems similar, the thyroid and parathyroid glands are entirely different glands, each producing distinct hormones with specific functions. The parathyroid glands secrete parathyroid hormone, a polypeptide that helps maintain the correct balance of calcium and phosphorous in the body. PTH is involved in the homeostasis of bone metabolism and regulates the level of calcium in the blood, release of calcium from bone, absorption of calcium from the intestine, and excretion of calcium in the urine

The pathophysiology of secondary and tertiary HPT

Chronic renal failure (CRF) causes abnormalities in the renal tubular absorption of phosphate which lead to reduced phosphate excretion and

hyperphosphatemia. Also, renal conversion of 25-hydroxycholecalciferol to 1, 25-dihydroxycholecalciferol which is active form of vitamin D is impaired. Thus it leads to deficiency of active vitamin D resulting in decreased intestinal absorption of calcium and hypocalcemia. Hyperphosphatemia, low vitamin D and hypocalcemia together stimulates increased formation and release of parathyroid hormone. As a consequence of prolonged hypocalcemia, parathyroid chief cell hyperplasia occurs and PTH secretion increases.

Secondary HPT (SHPT) occurs most commonly "secondary" to chronic renal failure (CRF). Hence secondary HPT is frequently referred to as renal HPT. Estimates suggest that as many as 90% of patients with CRF develop this disease by the time hemodialysis is initiated. Other causes of secondary HPT include osteomalacia, rickets, and malabsorption.

Initially, the secretion of parathyroid hormone by hyperplastic chief cells is regulated by negative feedback by calcium acting on calcium receptor located on chief cells. Thus normocalcemia or hypercalcemia suppresses PTH formation. However, as a result of prolonged hypocalcemia and stimulation, chief cells become autonomous and they secrete parathyroid hormone in spite of high level of serum calcium which leads to hypercalcemia and resembles primary HPT. This condition is called "tertiary HPT".

99mTc-sestimibi scintigraphy

Secondary hyperparathyroidism result in hyperplasia of all 4 parathyroid glands. The sensitivity of imaging modalities such as 99mTc-sestimibi scintigraphy and ultrasound is poor in patients with multiple gland disease. This is evident in our case where Technetium MIBI scan and Technetium pertechnetate tetraphosphin

scan showed uptake in different parathyroid gland. However, it is a useful investigation in patients with recurrent hyperparathyroidism where there is a single functioning parathyroid gland in which case accuracy of localization is as high as 95-100%.

Goals of SHPT Treatment

The ultimate goals of treating SHPT are to normalize mineral metabolism, prevention or reversal of osteitis fibrosa cystica and maintenance of bone strength. The markers of calcium (Ca), phosphorus (P), vitamin D and PTH are used as surrogate measures of disease progression.

1. Target range of serum P 3.5–6.0 mg/dl
2. Target range of serum Ca 8.4–10.0 mg/dl
3. Target range of PTH 60-180 pg/ml

In chronic renal failure, bones are resistant to action of parathyroid hormone as a result of uremia. Therefore, they require more than normal level of parathyroid hormone to maintain homeostasis. Excessive suppression of parathyroid hormone in CRF can lead to decreased turnover of bone, called as adynamic bone disease. Therefore, Target range of parathyroid hormone is kept at 2 -3 times normal value in CRF.

Vitamin D therapy

One of the first abnormalities noted on evaluation may be an isolated increase in PTH. If the PTH concentration exceeds the target range, the serum 25 (OH) cholecalciferol concentration should be measured and if that is found to be < 30 ng/ml, then dietary deficiency of Vitamin D is diagnosed and ergocalciferol (vitamin D₂) therapy should be initiated.

If the concentration of 25(OH) cholecalciferol is

> 30 ng/ml and the PTH concentration exceeds the target range, then inadequate conversion of vitamin D to active form secondary to CRF is diagnosed and an activated vitamin D agent should be initiated.

Of the active form of vitamin D, Calcitriol was the first agent available. It has the same structure as endogenous activated vitamin D₃ [1,25 (OH) cholecalciferol] and therefore the same pharmacological actions. It stimulates gut and parathyroid Vitamin D receptors (VDR). Because of its affinity for intestinal VDR, calcitriol has the greatest propensity to increase serum calcium concentrations. It is especially useful when the serum calcium level is less than the mid-point of the target range.

Paricalcitol (19-nor-1,25(OH)₂D₂) and doxercalciferol (1 α -(OH) vitamin D₂) are vitamin D agents that have less affinity for the intestinal receptors and have been shown to cause a lower incidence of hypercalcemia. Therefore, they are the drugs of choice in presence of hyperparathyroidism with hypercalcemia. Doxercalciferol is a vitamin D₂ pro-drug, 1 α (OH) cholecalciferol, and requires activation by hepatic 25-hydroxylase. Therefore, doxercalciferol should not be used in patients with hepatic dysfunction.

Efficacy of therapy for SHPT is generally measured by the degree of suppression of PTH. Active forms of vitamin D appear to provide greater suppression of PTH than doxercalciferol, paricalcitol and cinacalcet.

Dietary phosphate restriction

Hyperphosphatemia generally becomes prevalent as the GFR declines to < 30 ml/min/1.73 m². Dietary phosphate restriction is one of the first interventions recommended to lower serum phosphate concentrations. Foods that are high in phosphate content include dairy products,

meats, beans, dark sodas, beer, and nuts. Many foods that are high in phosphorus are also primary sources of protein, particularly meats. Generally, patients are instructed to reduce their intake of or avoid foods that are high in phosphorus but not high in protein. Examples of foods to avoid include cheese, milk, ice cream, beer, and dark sodas.

Phosphate binding agents

Phosphate binding agents decrease serum phosphate concentrations by binding to dietary phosphate in the gut, forming an insoluble complex that is excreted in the feces. Optimally, these agents are administered with food and are generally taken three times daily with meals. Phosphate binders from different classes may be combined to achieve target concentrations of phosphorus and calcium. In fact, the combined use of a calcium-containing phosphate binder and a non-calcium-containing phosphate binder may reduce the serum phosphorus level while maintaining the calcium concentration. Likewise, the use of one or more non-calcium-containing phosphate binders (e.g., sevelamer hydrochloride) may be needed for patients with hyperphosphatemia with concurrent hypercalcemia.

Calcimimetic agents

It acts by binding to and modifying the calcium sensing receptor (CaR) on the chief cell of the parathyroid gland. This change causes an increased sensitivity of the receptor to serum calcium. Cinacalcet is effective in decreasing PTH concentrations and maintaining calcium and phosphorus concentrations. It can be used in combination with phosphate binders and vitamin D agents. An increase in serum calcium results in rapid diminution of parathyroid hormone (PTH) secretion via activation of the CaR in the parathyroid and enhanced calciuria via activation of the CaR present in the thick ascending limb of

the loop of Henle. Calcimimetics bind to the CaR and result in a marked shift in the calcium response curve, reflecting overactivation of the CaR and resulting in suppression of serum PTH. Optimum dose is 30 to 180mg per day. However, it is known to cause hypocalcemia and hyperphosphatemia as hypercalcemic and a hypophosphatemic effect of parathyroid hormone is absent.

Indications for parathyroidectomy in patients with secondary HPT

Calciphylaxis

Medical observation not possible

Failure of maximal medical management with:
Hypercalcemia, Hypercalcuria

PTH >800 pg/mL

Hyperphosphatemia (with calcium x phosphorus >70)

Osteoporosis

Symptoms: pruritus, pathologic bone fracture, ectopic soft tissue calcifications, bone pain.

Surgical Approach

The most commonly accepted approaches in these patients are

- 1 Subtotal parathyroidectomy - it involves removal of 3 and ½ parathyroid gland with ½ gland is left in situ.
- 2 Total parathyroidectomy with auto transplantation - It involves removal of all 4 parathyroid gland with autotransplantation of ½ of one parathyroid gland into the nondominant forearm or sternocleidomastoid.

Intraoperative parathyroid hormone monitoring (ioPTH)

Studies have shown that ioPTH testing depends on renal function and PTH assay specificity. A 50% drop from the baseline ioPTH is considered

predictive of sufficient parathyroid tissue resection. Depending on the specificity of the assay, an adequate drop in ioPTH levels (>50%) may not be seen for up to 30 minutes after curative resection because of CRF and delayed PTH clearance. Lack of consensus guidelines for ioPTH monitoring in patients with tertiary HPT and skepticism over the potential impact on the overall success rate of parathyroidectomy has led some groups to abandon the routine use of this adjunct.

Radioguided parathyroidectomy

Another state of the art advance that facilitates intraoperative management of patients with secondary and tertiary HPT is application of radioguided techniques. Patients are injected with 10 mCi of ^{99m}Tc-sestamibi approximately 1 to 2 hours before surgery. A gamma probe is then utilized to identify parathyroid glands intraoperatively.

Minimally invasive parathyroidectomy (MIP)

During the last two decades, several techniques for minimally-invasive parathyroidectomy have been developed, including open approaches (open minimally-invasive parathyroidectomy), Endoscopic parathyroidectomy, minimally invasive video-assisted parathyroidectomy (MIVAP). The term "minimally invasive" should be reserved to a procedure that allows the surgeon to perform a traditional operation through an access that minimizes the trauma of surgical exposure and dissection. Open MIP indicates parathyroid procedures performed through a small incision, usually less than 2.5-3 cm.

Endoscopic parathyroidectomy (EP)

Total EP was first described by Gagner in 1996. It is carried out entirely under a steady gas flow, using a 5 mm endoscope introduced through a central trocar and two or three additional trocars

for needlescopic instruments. All endoscopic techniques are characterized by continuous CO₂ insufflation or mechanical external retraction to maintain the operative space for dissection and trocar positioning.

Minimally - invasive video - assisted parathyroidectomy (MIVAP)

MIVAP was firstly described by Miccoli et al. A small (1.5-2.0 cm) skin incision is performed between the cricoid cartilage and the sternal notch, in the midline. The thyroid lobe is separated from the strap muscles with small conventional retractors (Farabeuf retractors), which are also used to maintain the operative space. At this point, the endoscope (5 mm, 30°) and the small surgical instruments are introduced through the single skin incision without using any trocar. After identification, the affected parathyroid gland is bluntly dissected under endoscopic vision by using dedicated spatulas and a spatula shaped aspirator.

Anaesthesia in CRF and SHPT patients

Administering general anesthesia to an anuric patient on hemodialysis is a challenge and has its own attendant risks. Nephrotoxic agents and drugs which depend entirely on the kidneys for their elimination such as diclofenac, aminoglycosides, pancuronium etc should be avoided. Patients need pre-operative hemodialysis which increases the risk of coagulation abnormalities. Therefore heparin free hemodialysis is preferred. Often, dehydration post dialysis leads to hypotension especially after induction of anesthesia. Incidences of fluid overload, congestive cardiac failure and delayed emergence from anesthesia are higher in such patients as also post operative hypocalcemia, laryngeal spasm and tetany and need for post operative ventilatory support.

Hungry bone syndrome

The postoperative hypocalcemia probably results from acute reversal of the PTH-induced contribution of bone resorption to maintain the serum calcium concentration. In the high turnover state associated with hyperparathyroidism, PTH increases bone formation and resorption with a net efflux of calcium from bone. Sudden withdrawal of PTH in such patients causes an imbalance between osteoblast-mediated bone formation and osteoclast-mediated bone resorption and perhaps other changes affecting calcium fluxes, leading to a marked net increase in bone uptake of calcium, phosphate and magnesium and thus causing severe, persistent and prolonged hypocalcemia.

Conclusion

Thus, HPT is a complex and challenging condition. Metabolic parameters such as calcium, phosphate, PTH, and vitamin D must be maintained within target ranges to prevent bone disease and extraskeletal calcification, decrease cardiac disease risk, and maintain homeostasis of other body systems. Additionally, all of these parameters need to be controlled simultaneously to be successful.

Control of calcium and phosphorus during treatment

Further reading

- Secondary and Tertiary Hyperparathyroidism: state of art surgical management. Susan C. Pitt *Surgical Clinics of North America*, volume 89, (2009) 1227–1239
- Minimally invasive video - assisted parathyroidectomy (MIVAP) for secondary hyperparathyroidism: report of initial experience, Piero F. Alesina, *The American Journal of Surgery* (2010) 199, 851–855
- Evaluation of Hypercalcemia in Relation to Hyperparathyroidism, Phillip K. Pellitteri, *Otolaryngologic Clinics of North America* - Volume 43, Issue 2 (April 2010)
- Clinical Practice Guideline for the Management of Secondary Hyperparathyroidism in Chronic Dialysis Patients, Guideline Working Group, Japanese Society for Dialysis Therapy, *Therapeutic Apheresis and Dialysis* volume 12(6):514-525(2008)

Low calcium
Low phosphorus
Treatment
Calcium Carbonate
High doses of Vitamin D

Low calcium
High Phosphorus
Treatment
Calcium carbonate
Low dose of Vitamin D

High Calcium
Low Phosphorus
Treatment
Sevelamer
Cinacalcet
Low dose of Vitamin D or
Doxercalciferol, Paricalcitol

High Calcium
High Phosphorus
Treatment
Sevelamer
Low dose of Vitamin D or
Doxercalciferol, Paricalcitol
Consider Parathyroidectomy

Infection Control Measures

Dr. Amrita Misri, Convener Infection Control Committee

CDC's Core Interventions for Dialysis Blood Stream Infection Prevention

What Healthcare Providers Can Do:

1. Chlorhexidine for skin antisepsis: Use an alcohol-based chlorhexidine (>0.5%) solution as the first line agent for skin antisepsis, particularly for central line insertion and during dressing changes. Povidone-iodine, preferably with alcohol, or 70% alcohol are alternatives.
2. Catheter hub cleansing: Cleanse catheter hubs with an appropriate antiseptic after the cap is removed and before accessing.
3. Antimicrobial ointment or chlorhexidine-impregnated sponge dressing: Apply bacitracin/gramicidin/polymyxin B ointment or povidone-iodine ointment to catheter exit sites during dressing change OR use a chlorhexidine-impregnated sponge dressing.

What Healthcare Institutions Can Do:

1. Surveillance and feedback using National Health Safety Network: Conduct monthly surveillance for Blood stream infections and other dialysis events and enter National Center for Emerging and Zoonotic Infectious Diseases events into CDC's National Healthcare Safety Network. Calculate facility rates and compare to rates in other facilities using NHSN. Actively share results with front-line clinical staff.
2. Hand hygiene surveillance: Perform monthly hand hygiene audits with feedback of results to clinical staff.
3. Catheter care/ vascular access observations: Perform quarterly audits of vascular access care and catheter accessing to ensure adherence to recommended procedures. This includes aseptic technique while connecting and disconnecting catheters and during dressing changes. Share results with front-line clinical staff.
4. Patient education/engagement: Provide standardized education to all patients on infection prevention topics including vascular access care, hand hygiene, risks related to catheter use, recognizing signs of infection, and instructions for access management when away from the dialysis unit.
5. Staff education and competency: Provide regular training of staff on infection control topics, including access care and aseptic technique. Perform competency evaluation for skills such as catheter care and accessing at least every 6-12 months and upon hire.
6. Catheter reduction: Incorporate efforts (e.g., through patient education, vascular access coordinator) to reduce catheters by identifying barriers to permanent vascular access placement and catheter removal.

Paper Publications / Presentations / Achievements

Department of Pediatrics

Publication:

Topic: Herpes zoster in a healthy immunocompetent two year old child

Authors: Dr. Sangeeta P. Sawant, Dr. Alpa Amin, Dr. Santosh Kumar

Journal: Pediatric Infectious Disease, Journal of The Indian Academy of Pediatrics Infectious disease Chapter, 2012. Vol: 4, No.1. Pg.13-14.

Department of Obstetrics and Gynaecology

Achievements:

- Dr. Amrita Misri, Head of Unit and in-charge Surgical Services, was conferred Fellowship by Indian College of Obstetricians & Gynaecologists (FICOG) at 55th All India Congress, Banaras on January 29, 2012.

Paper Presentations

- Title: Role of pelvic organ prolapse quantification system in uterovaginal prolapse
Authors: Dr. N. Mishra, Dr. Misri, Dr. Joshi, Dr. S. Prabhu, Dr. V. Jadhav.
Presented by: Dr. Nigamanada Mishra
Venue: 55th All India Congress, Banaras.
Date: 28-29 January 2012.
- Title: Diagnostic Accuracy of Hysteroscopy in evaluation of PM bleeding
Authors: Dr. Shilpa Singh, Dr. Bahadur Rao, Dr. N. Mishra, Dr. D.P. Joshi, Dr. S.R. Prabhu, Dr. Amrita Misri
Presented by: Dr. Shilpa Singh (DNB student)
Venue: 40th Annual Conference of Mumbai Obstetrics & Gynecological Society, Juhu.
Date: January 7-8, 2012.
- *Paper bagged Ashok Mehra Endoscopy Prize.*
- Title: Role of Hysteroscopy in evaluation of Post menopausal bleeding
Authors: Dr. Shilpa Singh, Dr. Bahadur Rao, Dr. N. Mishra, Dr. D.P. Joshi, Dr. S.R. Prabhu, Dr. Amrita Misri
Presented by: Dr. Shilpa Singh (DNB student)
Venue: "The Prize Symposium celebrating the Talent within" by MOGS held at Masina Hospital, Mumbai.
Date: 19th February, 2012.

Clinical Meetings Conducted at BARC Hospital January 2012 - October 2012

DATE	Department	TOPIC
January 27, 2012	Gynaecology & Obstetrics	Role of hysteroscopy in evaluation of post menopausal bleeding
February 10, 2012	Medicine	Tuberculosis: Management Dilemma
February 24, 2012	Surgical	Good Prescription Practices in Gastroenterology
March 09, 2012	Pathology	Approach to Diagnosis of Multiple Myeloma
April 13, 2012	Radiology	Interesting Cases 1. Renal Artery Stenosis 2. Acrania
April 27, 2012	Paediatrics	Common Dermatological Problems in Childhood
May 11, 2012	Vashi Dispensary	1. Case of breast carcinoma in male patient 2. Case of alopecia universalis in female patient
May 18, 2012	Medicine	Cardiology
May 25, 2012	Psychiatry	Eating Disorders
June 08, 2012	ENT	Cochlear Implants - our experience
June 22, 2012	Ophthalmology	LASIK
July 06, 2012	Medicine	ABC of Sleep Disorders
July 13, 2012	Anaesthesia	Acute Pain Management
July 20, 2012	NPCIL	1. Radiation: Part of our life 2. Relationship of Cancer and Radiation 3. NPCIL Employees' Health Profile
July 27, 2012	Gynaecology & Obstetrics	Pregnancy Hypertension
August 10, 2012	Orthopedics	Surgical Management of Rheumatoid-Deformities
August 24, 2012	Mandala Dispensary	Study of Anaemia at mandala Dispensary
September 14, 2012	Medical	Final Evaluation of Jaundice
September 28, 2012	Surgical	Breast Cancer Screening in CHSS women
October 12, 2012	Psychiatry	Conversion Disorder

Chief Editor

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