BY INVITATION

ACUTE RENAL FAILURE SOME NEW THOUGHTS

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A CHANGING DISEASE

Acute Renal Failure (ARF) is an interesting multi-faceted disease condition which has changed its clinical expression considerably during the last two decades. This change was neither spontaneous nor rapid. It was a gradual change induced by the development of man's destructive power due to more effective weapons on the one hand and an improvement in the healing power of the physician in the field, on the other.

Medicine has learned to prevent certain conditions which have classically caused ARF. Severe or prolonged hypovolemic shock or dehydration, especially after blood or fluid loss following injury or an operative procedure are such examples. This is done by early and adequate replacement and by using drugs which would increase or maintain the renal blood flow. Medicine has also learned to treat ARF early when it is still in its incipient stages. This is done by the use of dopamine, an agent which increases renal blood flow by its dopaminergic action on the renal arterioles, or by the single use of hypertonic mannitol which is also known to improve renal circulation during renal cortical ischemia and to improve renal function, provided that ARF is not already established. These procedures can prevent ARF from occuring, thus saving the patient from entering into genuine ARF (i.e. established acute tubular necrosis) with its much dreaded high mortality statistics.

As expected, ARF is associated with wars! The Germans recognized it at the end of the first World War and named it 'Vasomotor Nephropathy', because of the lack of gross histological lesions in the kidneys (1). ARF was faced once more in World War II, but this time in the form of the so-called 'Crush Syndrome', a term coined by Bywaters (2) because it was often observed in patients who had large masses of their muscle crushed by debris of bombed buildings in the massive bombardments of London. In one study in World War II, 40% of the severely wounded developed ARF with a fatality rate of 90% among the severely oliguric ones (3). In another study, 18.6% of deaths from battle injuries in Army Hospitals had renal lesions (4). In this study, the term 'Hemoglobinuric Nephrosis' was coined. In 1950 it was named Acute Tubular Necrosis (ATN) (5), because of the marked tubular damage

observed in the severe cases which came to necropsy. Teschan et al and Smith et al (3, 6) were impressed by this disease as an important cause of illness and death in initially surviving combat casualties and called it 'Post-traumatic Renal Insufficiency'. It was met during the Korean War in 1951 in wounded soldiers, especially those who had lost blood and were in shock or hypotension with delayed fluid or blood replacement. It was there that a special 'Research Team' attempted early evacuation of the wounded and early dialysis by artificial kidneys placedat the'Renal Insufficiency Centre' in Wonju, Korea, 25 miles south of the battle line. They clearly showed that they were able to decrease mortality from about 80%-90% to about 53% by dialysis, and that the majority of deaths in the wounded treated by dialysis was attributable to complications of the original injury rather than uremia or the renal insufficiency itself (6).

Much has been learned about ARF in the war in Vietnam. Early evacuation and treatment by fluid and blood replacement together with definitive surgery prevented the development of ARF in the milder cases. ARF was therefore seen only in the severely wounded, especially in soldiers with multiple injuries and more so after abdominal wounds and surgery. Mostly a combination of several episodes rather than a single etiologic factor tended to precipitate ARF, both at the time of trauma and in the post-traumatic course (7). Early and frequent hemodialyses were discovered to reduce both morbidity and mortality (7) as was suggested earlier by Teschan et al (8). At this time and later in the Middle East conflicts in 1967 and 1973, it was observed that the severe injuries were associated with post-traumatic pulmonary insufficiency.

Presently, ARF following blood loss and shock in countries with well developed medical facilities has become rare. Its place was gradually taken by the ARF caused by nephrotoxins, such as aminoglycosides e.g. gentamicin given alone in high doses or in a combination with cephalosporins, or cytoxic drugs such as cis-platinum. In the present war in Lebanon, ARF was virtually absent on the Israeli side and occurred only in those with such severe multiple injuries that they can be considered to be a terminal event. This can be attributed to very early evacuation and intensive therapy given to the very badly wounded while still in the field.

During these years cadaveric kidney transplantation became an accepted form of therapy. In this condition, ARF in the form of ATN is met frequently if the kidneys are taken rather late i.e. if they have been subjected to long periods of warm ischemia. Attempts at reducing the incidence of ARF in donor kidneys included many maneuvres amongst which there was the perfusion of the kidney with a solution containing phenoxybenzamine at the time of harvesting, which was later found to be of no value. Mannitol administered to the prospective donor is thought to improve the renal circulation. The most useful maneuvre is actually the reduction of the ischemia time, both warm and cold, to a minimum. Needless to say, the heart-beating cadavers kept on the respirator form a better group of kidney donors, with respect to ATN.

Recently non-traumatic rhabdomyolysis has emerged as a more frequently reported clinical entity associated with ARF (9).

PREVENTION AND THERAPEUTIC MEASURES

The preventive measures which we have learned to apply are adequate hydration, early replacement of blood and fluid loss as well as the use of such drugs as may result in an increase in RBF, for example, small doses of dopamine. The use of mannitol as a single dose in the few patients who are caught at the incipient stage of their ARF, when the Urine/Plasma osmolality ratio was still above 1.0 (i.e. about 1.2 to 1.4) proved to be very useful (10). The use of furosemide in the early stages of ARF is debatable. Numerous authors do not agree that fuoresmide is able to prevent or even ameliorate ARF. It seems to be useful only in those whose ARF has a cardiogenic cause. In hypovolemia and in shock kidneys, furosemide may even result in further renal vasoconstriction. Injection of furosemide into the renal artery of patients with ARF, failed to improve renal function as assessed by urine output or serum creatinine during 4 days following its injection (11).

Recently certain therapeutic maneuvres were tried on humans to alleviate ARF in man. At the Chiba University Hospital in Japan, ATP.MgC12 was infused in patients with ARF in order to replenish intracellular ATP which is known to decrease considerably following ischemia (12). The syringe was surrounded with ice and the infusion was carried out gradually to prevent significant decreases in blood pressure. To achieve the same purpose different solutions of amino acids were given i.v. at different stages of ARF. Kopp and Thul (13) proposed that sodium bicarbonate, when administered in sufficient amounts to alkalinize the urine, accelerated recovery. These latter procedures still await further investigation and confirmation.

ABOUT PATHOGENESIS:

The pathogenesis of ARF was not easy to investigate in humans. Bull et al (5) using the Fick principle with PAH, came to the conclusion that during the oliguric phase, the RBF through the renal parenchyma was grossly reduced. They concluded that the oliguria of ARF is due to persisting renal ischemia. Soon it was found that this method is not acceptable, and a method independent of renal excretion and urine flow is needed. Conn et al (14), using nitrous oxide, found that a reasonable amount of RBF continues in ARF. Since the RBF is reduced only to about one third of normal in both the oliguric and the diuretic phases of ARF and since the amount of RBF is not inconsistent with considerable glomerular filtration, Munck (15) concluded that renal insufficiency in ARF cannot be due to ischemia alone. Hollenberg et al (16) studied 20 patients with ARF by the xenon washout technique. They found that the early rapid component in the xenon washout curve, which is supposed to represent cortical perfusion, is absent. They concluded that in ARF there is a preferential renal cortical ischemia. This was shown to occur in the hepatorenal syndrome in which, despite severe derangements of renal function, histological abnormalities are minimal (17, 18). Furthermore, kidneys taken from these patients and transplanted, resume normal kidney function in the recipient (19). These observations show that most cases of ARF in the hepatorenal syndrome are functional in nature. This, together with other studies of the renal circulation with indocyanine green and 51Cr EDTA (20) lend further support to the findings that renal cortical ischemia is an important event in the development of decreased filtration in ARF.

Recently, evidences for a reduction in the glomerular coefficient of filtration, Kf, were reported both in humans (21) as well as in experimental animals (22, 23). It was suggested that the reduction in Kf reflects a decrease in the total glomerular capillary filtering surface area as a result of mesangial cell contractility (23).

Much work has been done to elucidate the pathogenesis of the failure of filtration in the experimental animal especially in the rat. The classical major mechanisms in the development and maintenance of this failure of filtration are: preglomerular vasoconstriction, tubular obstruction, tubular leakage and the specific glomerular membrane pathology leading to decrease in Kf (glomerular capillary ultrafiltration coefficient).

The immense work of Oken et al (24), Flanigan and Oken (25) and Ayer et al (26) showed that at least in the early

phases of ARF, there is indeed cortical vasoconstriction which initiates a severe decrease in GFR, probably because of a lack in adequate filtration as a result of vasoconstriction. However, the intrarenal injection of vasodilators of all sorts including the alpha-adrenergic blocker phenoxybenzamine, did not improve the GFR (27). Thurau et al tried to explain the mechanisms which maintain the low GFR in ARF differently. In short, they accuse the ischemia of the proximal renal tubule to cause a decrease in Na+ reabsorption at the proximal tubule, resulting in a high concentration of NaCl at the distal tubule and the macula densa. High concentration of NaCl at the macula densa results in high intrarenal renin. This is taken to be responsible for the vasoconstriction. A vicious circle develops in which there is a continuing glomerular vasoconstriction, further ischemia and inability to reabsorb Na adequately, allowing more NaCl to reach the macula densa, and resulting in higher renin secretion and further vasoconstriction. Thus, the decreased GFR is maintained by this sodium chloride-sensitive tubulo-glomerular feedback mechanism at the level of the JGA (28, 29)., which is dependent on the intrarenal reninangiotensin system. This is thought by Thurau to be a protective mechanism, preventing tremendous losses of volume which would have occurred in the presence of inadequate proximal tubular reabsorption. Thurau and Boyland even called it "acute renal success" (30). This mechanism was thought to be due to the activation of the renin-angiotensin system inside the kidneys. However, many attempts to interfere with the renin-angiotensin system within the kidneys (31, 32), including the administration of antibodies to renin did not improve or prevent the ARF.

To justify the hypothesis that intrarenal renin and angiotensin II formation are nevertheless the responsible agents for the glomerular vasoconstriction, Thurau and his group bring the following arguments: angiotensin II is located in high concentrations in the same cells of the JGA which also synthesize renin at the glomerular vascular pole. The major site of action of intrarenally formed angiotensin II may be intracellular. Cell membranes form a barrier for such substances as antibodies, receptor blocking agents or converting enzyme inhibitors. These agents cannot reach the interior of the cell. Therefore, they cannot stop the vasoconstrictor action of the intracellular angiotensin II. Thus, it is not surprising that the use of these substances was unable to prevent ARF.

Beta-adrenergic blockade by the administration of propranolol brought about a significant amelioration of experimental ARF. This was observed in the ischemic type of ARF in the rat, following unilateral nephrectomy and renal artery clamping of the remaining kidney for 70 minutes (33, 34). A similar amelioration in ARF was obtained also by oxprenolol, metoprolol and practolol (35). The failure of function in this model of unilateral nephrectomy and renal artery obstruction was found to be due to tubular obstruction. The proximal intratubular pressure increased from a mean of 11.5 + 1.6 mm Hg to a mean of 31.2 + 5.3 mm Hg one to three hours after the renal artery occlusion, and total renal vascular resistance was doubled (36, 37). This was confirmed by Tanner and Sophasan (38). Chevalier and Finn (39) also found that propranolol reduced the severity of the ischemic type of ARF. This was associated with a significant decrease in proximal intra-tubular pressure (to about 18 mm Hg). The improvement of ARF is not due to hemodynamic changes nor to changes in the renin-angiotensin system as was shown by Solez et al (40). The significant improvement in inulin clearance in the propranolol treated rats occurred without commensurate increase in RBF and suggested attenuation of intratubular obstruction by the drug (40). They concluded that while the precise mode of action of propranolol is unclear it may involve metabolic effects in tubular cells resulting in less cellular damage.

An important point to keep in mind is the fact that in ARF, the RBF returns almost to normal in the ischemic models and is not very low in other models while the severely decreased GFR is maintained (22, 41, 42). Alpha-adrenergic blockers or other vasodilators were unable to reverse the filtration failure. Furthermore, there are theraputic maneuvres which are able to improve ARF which cannot be related to hemodynamic changes. In the nephrotoxicity models of ARF the primary lesion is at the tubular cell level while the renal vasoconstriction is a secondary phenomenon. All these point to the importance of renal tubular cell injury as an initiator of the pathological events which may lead to whole kidney failure.

One of the major functions of the renal tubular cell is the reabsorption of sodium, which is the driving force for the reabsorption of water and other filtered substances. There is a direct relationship between oxygen consumption and sodium reabsorption. This is an energy requiring process which is supplied by chemically bound energy in the form of ATP and the ATP-hydrolyzing enzyme Na.K.ATPhase. Mitrochondrial structure and function are essential for the formation of cellular energy. The tubular-cell membrane damage following ischemia or nephrotoxicity will alter mitrochondrial function. As a consequence, tubular insufficiency occurs. The sequence of plasma-cell-membrane injury and dysfunction (permeability changes and active transport mechanisms) and the mitochondrial insult (cellular energy supply) is not known. There are evidences that the proximal tubular cells are preferentially affected. In contrast, the distal tubular cells can maintain integrity and function for a longer period of time (43).

The study of ATP depletion in ischemic tissue in vivo was recently advanced by the use of nuclear magnetic resonance i.e. 31P NMR (44-46). The severe depletion of intracellular ATP following ischemia is taken to be as a result of mitochondrial dysfunction. This occurs in both the ischemic and the nephrotoxic models of ARF (47-49). The infusion of ATP.MgC12 after the release of the clamps following bilateral renal artery occulsion, prevented the development of kidney failure almost completely. This protection did not occur after the infusion of MgC12 alone or ADP or AMP. MgC12. The authors conclude that this protection is not due to the vasodilatory effect of ATP. MgC12, but is most probably due to the fact that the infused ATP has crossed the cell membranes to provide high-energy phosphate which promotes tubular-cell healing (50).

The favorable results obtained in accelerating the recovery of ARF with the administration of ATP. MgC12 as a cellular energy supply procedure, favors the pathogenetic importance of this mechanism.

In our laboratory we have studied cellular responses to ischemia following uninephretomy and contralateral renal artery clamping for 70 minutes in rats. A significant rise in cAMP was observed during the first 2 minutes of ischemia. The administration of propranolol did not influence this rise in cAMP. Later during the ischemia, the cAMP decreased to about 60-80 percent of the pre-ischemic levels and returned to normal after only 30 minutes of declamping and reflow. Renal tubular beta adrenergic receptors as determined by direct tissue binding were not altered by the ischemia. Thus it is unlikely that this is a result of beta adrenergic agonistic effect (51).

Elevated cellular cAMP were linked with augmented Ca++ influx into the cell via the slow voltage-sensitive channels (52). High intracellular Ca++ was indeed found in ARF and the administration of the calcium blocker verapamil improved ARF (53).

Different humoral and vasoactive substances were found to modulate glomerular ultrafiltration coefficient. Some of these stimulate glomerular cyclic nucleotide formation. Dibutyryl cyclic AMP was found to reduce Kf(23). However, dibutyryl cyclic AMP promotes intrarenal

angiotensin II formation (54) which was found to act on specific mesangial cell receptors to produce mesangial cell contraction and a decrease in glomerular capillary filtration surface area (53).

Other biochemical cellular events were described in ARF. Molecular defect in maleic acid (55), decreased protein synthesis following fungal toxins such as Amanitin (56), peroxidation of membrane lipids and important diminution of the total renal glutathione content (49) and important changes in tissue phospholipid content during toxicity (57).

CONCLUDING REMARKS

In summary, recent data indicate that following different etiological insults which cause ARF, important cell-membrane and intracellular pathobiochemical events will determine cell function and survival. Different tubular functions will be altered and different tubulo-glomerular feedback mechanisms will determine the degree of failure of filtration and eventually the resultant clinical picture of whole kidney failure. Therefore, the therapeutic approach should aim at making the renal cells more resistant to the disturbances in cell energy supply and should attempt to offer the background for accelerated cellular recovery.

REFERENCES

1. Oken DE: Nosologic considerations in the nomenclature of acute renal failure. Nephron 1971; 8:505-510.
2. Bywaters EGL, Joekes AM: The artificial kidney: its application in the treatment of traumatic anuria. Proc Roy Soc Med 1948; 41:420-426.
3. Teschan PE, Smith LH, Abernathy RS, Davis JH, Gray DM, Howard JM, Johnson KE, Klopp E, Mundy RL, O'Meara MP, Rush BF: Post-traumatic renal insufficiency in military casualties. I. Clinical characteristics; in Battle Casualties in Korea. Vol IV Post-Traumatic Renal Insufficiency. Ed John M Howard. Army medical Service Graduate School. Walter Reed Army Medical Center. Washington DC. US Government Printing Office 1955. Pp7.
4. Mallory TB: Hemoglobinuric nephrosis in traumatic shock. Am J Clin Path 1947; 17:427-443.
5. Bull GM, Joekes AM, Lowe KG: Renal funtion studies in acute tubular necrosis. Clin Sci 1950; 9:379-404.
6. Smith LH, Post RS, Teschan PE, Abernathy RS, Davis JH, Gray DM, Howard JM, Johnson KE, Klopp E, Mundy RL, O'Meara MP, Rush BF: Post-traumatic renal insufficiency in military casualties. II Management, Use of an artificial kidney, Prognosis in Battle Casualties in Korea vol IV. Post-Traumatic Renal Insufficiency. Ed. John M Howard. Army Medical Service Gradual School. Walter Reed Army Medical Center. Washinton DC, US Government Printing Office 1955 Pp 31.
7. Whelton A, Donadio JV: Post-traumatic acute renal failure in Vietnam. The John Hopkins Medical Journal 1969; 124:95-105.
8. Teschan PE, Baxter CR, O'Brien TF, Freyhof JN, Hall WH: Prphylactic hemodialysis in the treatment of acute renal failure. Ann Intern Med 1960; 53: 992-1016.
9. Koffler A, Freidler RM, Massry SG: Acute renal failure due to non-traumatic Rhabdomyolysis. Ann Intern Med 1978; 85: 23-28.
10. Eliahou HE, Bata A: The diagnosis of ARF. Nephron 1965; 2:287-295.
11. Epstein M, Schneider NS, Befeler B: Effect of intrarenal furosemide on renal function and intrarenal hemodynamics in acute renal failure. Am J Med 1975; 58:510-516.
12. Hirasawa H, Odaka M, Soeda K, Sato H, Recovery of renal function and reversal of renal cellular edema with ATP-MgC12 following 90 minutes of renal ischemia; in Acute Renal Failure, Ed. H Eliahou. John Libbey, London, 1982 Pp248.
13. Kopp KF, Thul GM: Prophylaxis and emergency treatment of acute renal failure by acute intravenous bicarbmate loading; in Acute Renal Failure, Ed. H Eliahou John Libbey, London 1982 Pp181.
14. Conn HL Jr, Wilds L, Helwig J: Study of renal circulation, tubular function and morphology, and urinary volume and composition in dogs following mercury poisoning and transfusion of human blood. J Clin Invest 1954; 33:732-741.
15. Munck O: Renal Circulation in acute renal failure. Blackwell Scientific Publications, Oxford 1958.
16. Hollenberg NK, Epstein M, Rosen SM, Basch RI, Oken DE, Merrill JP: Acute oliguric renal failure in man: Evidence for preferential renal cortical ischemia. Medicine 1968; 47:455-474.
17. Epstein M, Berk DP, Hollenberg NK, Adams DF, Chalmers TC, Abrams HL, Merrill JP: Renal failure in patient with cirrhosis; the role active vasoconstriction. Am J Med 1970; 49:175-185.
18. Epatein M: Hepatorenal syndrome: current concepts of pathogenesis; in Acute Renal Failure, Ed. H Eliahou, John Libbey. London 1982, Pp219.
19. Koppel MH, Coburn JW, Mims MM, Goldstein H, Boyle JD, Rubini ME: Transplantation of cadaveric kidneys from patients with heptorenal syndrome. Evidence for the functional nature of renal failure in advanced liver disease. New Engl J Med 1969; 280:1367-1371.
20. Reubi FC, Vorburger C, Tuckman J: Renal distribution of volumes of indocyanine green, (51Cr) EDTA and 24Na in man during acute renal failure after shock. Implications for the pathogenesis of anuria. J Clin Invest 1973; 52:223-235.
21. Myers BD, Carrie BJ, Yee RR, Hilberman M, Michaels AS: Pathophysiology of hemodynamically mediated acute renal failure in man. Kidney International 1980; 18:495-504.
22. Cox JW, Baehler RW, Sharma H, O'Dorisio T, Osgood RW, Stein JH, Ferris TF: Studies on the mechanism of oliguria in a model of unilaternal acute renal failure. J Clin Invest 1974; 53:1546-1558.
23. Ichikawa I, Schor N: Humoral regulation of glomerular filtration rate. In vivo evidence. Proc 8th International Congress of Nephrology, Athens, 1981. Pp 109-115.
24. Oken DE, Arce ML, Wilson DR: Glycerol-induced hemoglobinuric acute renal failure in the rat. I. Micropuncture study of the development of oliguria. J Clin Invest 1966; 45:724-735.
25. Flanegan WJ, Oken DE: Renal micropuncture study of the development of anuria in the rat with mercury-induced renal failure. J Clin Invest 1965; 44:449-457.
26. Ayer G, Grandchamp A, Wyler T, Truniger B: Intrarenal hemodynamics in glycerolo-induced myohemoglobinuric acute renal failure. Circul Res 1971; 29:128-135.
27. Eliahou HE, Brodman RR, Friedman EA: Adrenergic blockers in ischemic acute renal failure; in Proc of Conference on Acute Renal Failure. Eds EA Friedman HE Eliahou. DHEW Publication No. (NIH)74-608, 1973. Pp265.
28. Thurau K, Schnerman J, Nagel W, Horster M, Wahl M: Composition of tubular fluid in the macula densa segment as a factor regulating the function of the juxtaglomerular apparatus. Circul Res 1967; 20/21 Suppl 2: 79-89.
29. Thurau K: Nature of autoregulation of renal blood flow. Proc of 3rd International Congr Nephrology, Washington, 1966. Vol I, Pp162-173. Basel, New York. Karger.
30. Thurau K, Boylan JW: Acute renal success: the unexpected logic of oliguria in acute renal failure. Am J Med 1976; 61:308-315.
31. Brown JJ, Gavras H, Kremer D, Lever AF, McGregor J, Powell-Jackson JD, Robertson IS: Renin and acute renal failure; in Proc of Conference on Acute Renal Failure. Eds EA Friedman HE Elaihou. DHEW Publication No. (NIH)74-608, 1973. Pp57.
32. Flamenbaum W, Kotchen TA, Oken DE: Effect of renin immunization on mercuric chloride and glycerol-induced renal failure. Kidney International 1972; 1:406-412.
33. Iaina A, Solomon S, Eliahou HE: Reduction in severity of acute renal failure in rats by beta adrenergic blockade. Lancet 1975; 11:157-159.
34. Eliahou HE, Iaina A, Soloman S, Gavendo S: Alleviation of anoxic experimental acute renal failure by beta adrenergic blockade. Nephron 1977; 19:158-166.
35. Orndorff MH, Hathaway S, Solomon S, Iaina A, Eliahou HE: B-Blocking agents in acute renal failure. Proc West Pharmacol Soc 1978; 21:209-213.
36. Finn WF, Arendshorst WJ, Gottschalk CW: Pathogenesis of oliguria in acute renal failure. Circul Res 1975; 36:675-681.
37. Arendshorst WJ, Finn WF, Gottschalk CW: Pathogenesis of acute renal failure following temporary renal ischemia in the rat. Circul Res 1975; 37:558-568.
38. Tanner GA, Sophasan S: Kidney pressures after temporary

renal artery occlusion in the rat. Am J Physiol. 1976; 230: 1173-1181.
39. Chevalier RL, Finn WF: Effects of propranolol on post-ischemic acute renal failure. Nephron 1980; 25:77-81.
40. Solez K, D'Agostini RJ, Stawowy L, Freedman MT, Scott WW Siegelman SS, Heptinstall RH: Beneficial effect of propranolol in a histologically appropriate model of post-ischemic acute renal failure. Am J Path 1977; 88-163-185.
41. Conger JD, Schrier RW: Renal hemodynamics in acute renal failure. Ann Rev Physiol 1980; 42:603-614.
42. Tanner GA, Sloan KL, Sophasan S. Effects of renal artery occlusion on kidney function in the rat. Kid International 1973 4:377-389.
43. Mason J, Beek F, Dorge A, Rick R, Thurau K: Intracellular electrolyte composition following renal ischemia. Kid International 1981; 20:61-70.
44. Bailey JA, Seymour AML, Radda GK: A 31P-NMR study of the effects of reflox on the ischemic rat heart. Biochem biophys Acta 1981; 637:1-7.
45. Chan L, Ledingham GG, Dixon JA, Radda GK, Ross BD Acute renal failure: A proposed mechanism based upon 31P nuclear magnetic resonance studies in the rat. In: Acute renal failure. Ed. HE Eliahou. John Libbey Comp Ltd. London, 1982. Pp35-41.
46. Koretsky AP, Strauss W, Basus V, Murphy J, Bendel P, James T, Weiner MM: Feasibility of 31P NMR to study metabolic effects of renal ischemia in vivo. In: Acute renal failure. Ed. HE Eliahou. John Libbey Comp Ltd. London 1982. Pp 42.
47. Schrier RW, Arnold PE, Burke TJ: Alterations in mitochondrial respiration and calcium movements in norepinephrine-induced acute renal failure: Modification by mannitol. In: Acute renal failure. Ed. Eliahou HE. John Libbey Co Ltd. London. 1982. Pp21-22.
48. Weinberg JM, Humes HD: Mechanisms of gentamicin-induced dysfunction of renal cortical mitochondria. Arch Biochem Biophys 1980; 205:222-231.
49. Phaller W, Gstraunthaler G, Deetjen P: Biochemical aspects of cell injury in acute renal failure. In: Acute renal failure. Ed. Eliahou HE. John Libbey Co Ltd. London 1982. Pp25.
50. Siegel NJ, Glazier WB, Chaudry IH, Gaudio KM, Lytton B, Baue AE, Kashgarian M: Enhanced recovery from acute renal failure by the postischemic infusion of adenine nucleotides and magnesium chloride in rats, Kidney International 1980; 17:338-349.
51. aina A, Goldfarb D, Serban I, Gavendo S, Kapuler S, Eliahou HE, Thurau K. Renal cellular responses to ischemia; in Acute Renal Failure. Ed HE Eliahou. John Libbey, London, 1982. Pp 50.
52. Tsen RW: Cyclic AMP and contractile activity in the heart. Adv. Cyclic Nucleotide Res. 1977; 8:364-420.
53. Burke TJ, Arnold PE, Grossfield PD, Schrier RW: Effect of calcium membrane inhibition on norepinephrine-induced acute renal failure; in Acute Renal Failure. Ed HE Eliahou. John Libbey, London. 1982, Pp239.
54. Hofbauer KG, Konrads A, Schwarz K, Werner J: Role of cyclic AMP in the regulation of renin release of the isolated perfused rat kidney. Klin Wochschr 1978; 56 (Suppl I):51.
55. Silverman M: The mechanism of Maleic acid nephropathy: Investigations using brush border membrane-vescicles. Membr Bioch 1981; 4:63.
56. Lampe KF. Toxic fungi. Ann Rev Pharmacol Toxicol. 1979; 19:85-104.
57. Knauss TC, Weinberg JM, Humes HD: Changes in tissue phospholipid content during developing nephrotoxicity; in Acute Renal Failure. Ed HE Eliahou, John Libbey, London 1982. Pp23.