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Acute and Chronic Renal Failure (ARF and CRF)

How to prevent the need for Dialysis:

Protection of Renal Function (Nephroprotection) by Bicarbonate Alkaline Diuresis (BAD), by Bicarbonate Alkaline Polyuria (BAP), by Loop Diuretic-Enhanced Bicarbonate Alkaline Polyuria (LDE BAP)

Summary:

Both, Acute as well as Chronic Renal Failure have in common that the kidneys are unable to eliminate all metabolic end products or waste plus fluids and water in sufficient quantities from the body by formation of adequate amounts of urine. In other words, the kidneys are insufficient in producing enough urine to prevent the life threatening clinical picture of uremia. So far, extracorporeal dialysis procedures were the only means and remedies in order to eliminate all retention products including fluids from the body by way of artificial organ therapy, i e. the artificial kidney. However, since 1976 a scientifically proven, conservative medical alternative has been discovered and developed. By supplying the body and the failing kidneys with adequate amounts of the physiological agent and substance, necessary for adequate renal function, namely sodium-bicarbonate (NaHCO3), the phenomenon of Bicarbonate-Alkaline-Diuresis (BAD), Bicarbonate-Alkaline-Polyuria, or Loop-Diuretic-Enhanced Bicarbonate-Alkaline-Polyuria (LDE-BAP) can be initiated in the patient resulting in the elimination of uremic toxins and fluids in natural ways through the formation of abundant amounts of urine. Therefore, dialysis procedures are **CONTRAINDICATED** as long as the possibility of reaching an adequate renal function, i.e. urine production by inducing BAD, BAP or LDE-BAP has not been tried. This possibility can rapidly be confirmed or excluded by the **prognostic test** further below and applies for both Acute and Chronic Renal Failure. Dialysis procedures are still the ULTIMA RATIO in the presence of rather rare conditions like bilateral necrosis of the renal cortex, Crush-Kidney or Myeloma of the kidney, where renal function is totally abolished. The Non-observation or negligence of the contraindication for dialysis may under jurisdiction be judged as severe malpractice and may be punishable.

The physiological, conservative alternative Therapy

Conservative therapy with sodium bicarbonate (NaHCO3) as an alternative therapy to Dialysis was first described in 1976 (1). Nineteen other publications followed until the year 2000 and over 300 cases of ARF that had been treated conservatively with Sodium bicarbonate in the Center of Nephrology of the Technical University of Munich (TUM) without the use of the Artificial Kidney   have been described (12). Thereby, dialysis-associated mortality had also

been avoided in these cases, and mortality was reduced to what was related only to the underlying illness.

Prevention of Acute Renal Failure (ARF)

The protection of renal function against ARF according to BAD, BAP, LDE-BAP is based on several therapeutic measures aiming to achieve alkaline polyuria as a well-defined goal i.e. the patient starts to excrete urine in increased amounts, at least 100 ml per hour or more than 2400 ml/24 hours. The therapy necessitates the intake or administration of defined amounts of sodium bicarbonate either as tablets by the oral route or by infusion via the intravenous route. The therapeutic procedures should be carried out under medical supervision, if necessary under the conditions of intensive care. Depending on the urgency of the clinical situation, continuous rather than occasional medical supervision by a knowledgeable health-care professional is required. Unfortunately the present situation is characterised by the application of inadequate or ineffective therapeutic attempts with diuretics: C.B. Brown et al (24) followed by clinical deterioration which makes dialysis inevitable. Prophylaxis and Therapy of ARF and CRF as outlined below (1-12) has not generally been accepted. The fascination of an artificial apparatus which for the first time in Medical History was able to replace the function of a natural organ may be one of the reasons for this failure. The former mortality of 100 % from kidney failure was suddenly reduced to 50 to 80 %.

The rotating drum Artificial Kidney machine had been constructed during world-war II by Willem Johan Kolff in the Netherlands . It was successfully used on September 11, 1945 in Kampen Holland on a 67-year old female patient with Acute Renal Failure. She was the first patient to survive ARF. However, since then the mortality of ARF has remained at a level of 50 to 80 % in spite of numerous technical improvements of the Dialysis procedures.

Fascination and fixation on the Artificial Organ concept may have blinded the view regarding the possibility of therapeutic alternatives based on natural physiological principles: An historical overview by H.-G. Sieberth in Steinkopf-Verlag (Intensivmed 37:187-194); “*Geschichtlicher Überblick über die Behandlung des Akuten Nierenversagens in Deutschland* “was still published as late as in the year 2000. This article describes only methods based on the use of various artificial kidney machines for the therapy of Acute Renal Failure.

Mortality of ARF

Numerous publications confirm that the use of extracorporeal Artificial Organ-devices for the therapy of Acute Renal Failure is still at present associated with a mortality of at least 50 to 80 % (1-12). Avoidance of extracorporeal dialysis procedures will therefore by definition eliminate the associated mortality. Therefore, the presently prevailing mortality of ARF due to dialysis procedures is no longer acceptable.

Conservative Protocols:

1) **ORAL PROPHYLAXIS** (If possible - according to basic clinical condition)

RISKS and INDICATION for the Induction of Bicarbonate-Alkaline-Polyuria (BAP)

1. All patients Age over 60 years   i.e. age-dependent decrease of Glomerular filtration rate (GFR)
2. Pre-existing Chronic Renal Failure (CRF): Creatinine > 1.9 mg/dl
3. Electrolyte-Fluid-Acid-Base-Disorders e.g. Dehydration (resulting from fluid losses e.g. Diarrhoea Sweating, Severe Physical Exercise) or Thirst, etc. or overhydration > pulmonary oedema)
4. All patients with only one kidney (solitary or functional)
5. Organ Transplantation e.g. Kidney transplant, Living Donors and Recipients
6. All patients with Systemic Diseases, e.g. Diabetes etc.
7. Pre-Peri-Post-intake or Administration of Nephrotoxic Medication e.g. Antibiotics, Cytotoxic Agents or NSAIDs Exogenous Nephrotoxins, accidental (suicidal): Ethylene glycol Tetracarbonchloride, Herbicides, Mushrooms etc. Pre-Post-Interventions using I.A. or I.V.-Injections or Infusions of Contrast-Media Endogenous: Nephrotoxins e.g. Sepsis, Hemolysis, Rhabdomyolysis, Hyperuricemia, Oxalosis etc.
8. Gravida with Risk of EPH, HELLP or with pre-existing Acute or Chronic Renal Insufficiency
9. Post- Accident Trauma or Multiple Trauma, Burns, etc.
10. Pre- Peri- Post- elective Surgical Trauma
11. Post-Multi Organ-Failure (MOF)

Each Risk 1 through 11 must be considered separately

If   POSSIBLE or AVAILBLE: BLOOD GAS ANALYSIS: Venous, - Arterial in case of Hypoxia   and/or   Hypercapnia)

Oral Use of gastro-resistant 1000 mg tablets Sodium hydrogen carbonate = bicaNormR (FreseniusMedicalCare), Alka-Seltzer-Gold-effervescent-tablets, Sodium-hydrogen-carbonate tablets (Walgreen), Kaiser-NatronR (HOLSTE) or any other NaHCO3 – Preparation available at drugstores either as tablets or powder.

LEADING   PARAMETER   IS   Urine-pH   Optimum pH = 7,5 - 8,0

In case Urine-pH is found **lower than pH 7.5** immediately take 3 tablets or the amount of 3 g of NaHCO3.

Continue until Urine-pH-Optimum is reached. If Creatinine is above 1,9 mg/dl (Patient 70 +/- 20 kg B.W.)   Use Frusemide tablet 40 mg: **Dose/ day = 40 mg x Serum Creatinine**

Avoid low Blood NaCl-levels = Salt Depletion. Therefore, NO LOW-SALT-DIET

MAINTENANCE of BAP:

Continue intake of NaHCO3 until Optimum Kidney Function is reached and maintained

according to the lowering of Serum-Creatinine. Use minimum Frusemide dose / 24 hrs

CONTROLS:

Depending on Clinical Condition e.g. Inpatient / Outpatient:

Blood Gases, Serum Electrolytes including Chloride

Blood Pressure: CAVE Hypotension. In Case of Hypertension low RR may occur.

Diabetics: Blood Glucose CAVE hypoglycemia

URINE Volumes: ml /12 h, ml /24h   (Urine volumes up to 6000 ml/24 h are possible)

BODY WEIGHT,   FLUID BALANCE

URINE pH Testing (Use pH Indicator paper Range: pH 5.6 – 8.0 (Uralyt-UR MADAUS)

Ideally this should be checked on every occasion when urine passed, but at least three times daily is mandatory.

2)   EMERGENCY-PROCEDURE I.V.

RISKS and INDICATION for the Induction of Bicarbonate-Alkaline-Polyuria (BAP)

1. Patients over 60 years i.e. age-dependent decrease of GFR
2. Pre-existing Chronic Renal Failure (CRF):   Creatinine > 1.9 mg/dl
3. Electrolyte-Fluid-Acid-Base-Disorders e.g. Dehydration resulting from losses by nasogastric drainage, diarrhoea, severe physical exercise, etc. or overhydration > pulmonary oedema.
4. All patients with only one kidney (solitary or functional)
5. Organ Transplantation e.g. Kidney- TX, Cadaver- and Living Donors and Recipients
6. Patients with systemic diseases, Diabetes etc.
7. Pre- Peri- Post-intake or Administration of Nephrotoxic Medications e.g. Antibiotics, Cytotoxic Agents and NSAIDs Nephrotoxins exogenous accidental or suicidal e.g. Ethylene-Glycole, Tetracarbonchloride, Herbicides, Mushrooms etc. Pre-Post-Interventions using I.A. or I.V.-Injections or -Infusions of Contrast Media, Nephrotoxins endogenous: e.g.Sepsis, Hemolysis, Rhabdomyolysis, Hyperiuricemia, Oxalosis etc.
8. Pregnancy with Risk of EPH, HELLP or with pre-existing Acute or Chronic Renal Insufficiency
9. Post- Accident Trauma or Multiple Trauma, Burns, etc.
10. Pre Peri or Post- elective Surgical Trauma
11. Peri-Post-Multi-Organ Failure (MOF)

Each Risk of the above must be considered separately

THERAPY

Prepare 100 ml portions each of 1 Mol = 8.4 % NaHCO3 to over-correct or elevate the blood-bicarbonate-level to approx.

28 mMol/l = BE ~ +7 (via Central Venous Access).

Formula: 0,3 x bodyweight (kg) x (BE 7 – BE measured) = mMol or ml 1-molar NaHCO3

Initial Blood Gas Controls: Arterial

CAUTION: Cardio-pulmonary insufficiency, hypoxia, hypercapnia Respirator therapy if indicated

CAUTION: Alkaloses of other origin e.g. hypochloremia, hyperammonemia etc.

IMPORTANT: Na+, K+, Ca++, Cl- Correction to the normal

Subsequent blood-gas-analyses may be venous.

AIM: Blood-BE > 7   Then: loop-diuretic bolus I.V. : Dose: 40 mg Frusemide x Serum-Creatinine

AIM: Key-event: Urine pH > 7.0 + Polyuria: (> 125 ml/h = 2000 to 3000 ml/24h) = BAP

Mandatory controls initially hourly, reducing to 6 and then 3 times daily: Urine-pH, Urine output, fluid balance, blood-gas-analysis, Electrolytes, Creatinine, BUN etc.

MAINTENANCE OF BAP is necessary until the kidney fully recovers – which may be several days or weeks (KOPP's Solution if available)

Major objective is to achieve Urine-pH above 7.

Note: The **Kidney threshold for bicarbonate** is variable and depends on numerous factors such as volume, Potassium, Aldosterone etc. for any given patient and can be as low as BE + 2 mMol/L. Therefore, repeated blood-gas and urine pH-controls are needed:

AIM

1. To identify the lowest possible Blood-BE at which alkaline Urine-pH > 7 can be maintained.
2. To prevent undesired systemic alkalosis.

Loop-diuretic dose per 24 hrs: = identical to starting bolus = 40 mg Frusemide x Serum-Creatinine (continuous infusion)

Polyuria of 3000 to 4000 ml/ 24 hr/ 70 kg man is required:

1. **To obtain adequate uremic waste clearances (diluted urine only)**
2. **To obtain negative fluid balance, if required (e.g. fluid load by intravenous nutrition)**
3. **Fluid and Electrolytes have to be precisely controlled to maintain normal serum levels**

Note: Urine volumes of more than 6000 ml/24 hrs are possible and should be achieved.

Elevated Serum-Creatinine will decrease by approx. 1 mg/dl daily after 1 or 2 days

Prognostic Test

If Bicarbonate Alkaluria or Diuresis (BAD) fails to occur in spite of all attempts according to the protocols, either Oral or Intravenous, this test is a **very early but safe and reliable indicator** that irreversible and almost complete damage has occurred to the kidneys. Extracorporeal procedures may then be planned at a very early stage. Their prognosis will thereby be improved significantly due to the lesser therapeutic impact that is required, e.g. shorter and less intensive dialysis sessions. Transplantation may be indicated, depending upon the primary renal disease or injury, and can also be planned at an early stage.

Physiological Principles

The procedures outlined above induce therapeutic changes of the "Milieu interieur" à la Claude Bernard. The Acid-Base-metabolism is thereby newly adjusted at a slightly elevated alkaline level. Thereby, the homoeostasis of the fluid- and electrolyte metabolism of the organism is also affected.

In the case of ARF and CRF the pertaining parameters are all in a pathological range, i.e. Acidosis. According to the experience of the author, compensation towards neutrality is therapeutically insufficient. Only the establishment of a low degree of Alkalosis by substituting sufficient amounts of Sodium bicarbonate will be successful to instigate urine production as mentioned above. By raising the blood bicarbonate level to 30 mMol/L the renal threshold for bicarbonate will be exceeded and bicarbonate-containing urine will be excreted. This strategy is based on the fundamental work done by Homer W. Smith [13], **Robert F. Pitts [14]**, Ö. Mathisen [15, 16], Jürgen Schnermann [18, 19], Klaus Thurau [21,22] in particular. The administration of increased amounts of Sodium-Bicarbonate into the body by which the Renal threshold for Bicarbonate is exceeded, will immediately be followed by the physiological excretion-mechanism for bicarbonate by the kidneys via an alkaline urine as described by R.F.Pitts [14]; Fig 1.

of lungs and kidneys is reduced. Second, the hydrogen ion concentration of body fluids is no more dependent on the concentration of carbonic acid than on that of bicarbonate ion. Indeed, it is determined by their ratio and therefore is equally dependent on lungs and kidneys.

The thesis will be developed that the tubular secretion of hydrogen ions in exchange for sodium ions is the key mechanism underlying the reabsorption of bicarbonate, the generation of titratable buffer acid and the excretion of ammonium salts. The extent to which this ion exchange mechanism is engaged in each of these processes is determined by the nature and concentration of buffers delivered into the urine in the glomerular filtrate. If the bicarbonate concentration of the filtrate is normal or above normal, the mechanism will be largely engaged in the reabsorption of this anion; little ammonia and titratable acid will be excreted. If the bicarbonate concentration is below normal, the mechanism will be only partially engaged in the reabsorption of this anion, and more titratable acid and ammonia will be excreted. Finally, if the concentrations of all buffers in the filtrate are low or if their pK values are unfavorable (β-hydroxybutyrate and acetoacetate), the buffer deficit will be made up largely by the tubular synthesis and secretion of ammonia into the urine at the sites of hydrogen-sodium exchange.

Renal Reabsorption and Excretion of Bicarbonate

GROSS CHARACTERISTICS

The gross characteristics of the processes of renal reabsorption and excretion of bicarbonate in man are illustrated in Figure 11–1 (1). If ammonium chloride is ingested for several days before an experiment, the plasma concentration of bicarbonate is reduced from a normal value of 26–28 mM/L to about 13–15 mM/L. If sodium bicarbonate is infused slowly, the plasma concentration gradually increases. All bicarbonate filtered through the glomeruli is reabsorbed, and none is excreted until the plasma level attains a value of 26–28 mM/L, which is the so-called renal bicarbonate threshold. As still more bicarbonate is infused and the plas-

Fig. 11–1.—Filtration, reabsorption and excretion of bicarbonate as functions of plasma concentration in normal man. (From Pitts, R. F., Ayer, J. L., and Schiess, W. A.: J. Clin. Invest. 28:35, 1949.)

ma concentration increases above 28 mM/L, a limited amount of bicarbonate, equal to 2.8 mM/100 ml, or 28 mM/L, of glomerular filtrate, is reabsorbed. All filtered in excess of this quantity is excreted in the urine. Processes of reabsorption and excretion of bicarbonate in the dog are essentially similar to those in man, except that the threshold is slightly lower, 24–26 mM/L, and the transport rate slightly less, 2.6 mM/100 ml, or 26 mM/L, of glomerular filtrate (2).

Under normal conditions in man, the plasma concentration of bicarbonate is poised at a value slightly below the renal plasma threshold—perhaps 27 mM/L. If the filtration rate is 125 ml/min, 180 L of plasma are filtered per day, delivering into the tubules some 5,100 mM of bicarbonate. Only 1–2 mM is excreted in 1.5 L of urine of pH 6. Accordingly, more than 99.9% of the filtered bicarbonate is reabsorbed.

If the plasma concentration of bicarbonate were to exceed the renal threshold, owing to the ingestion of bicarbonate or to the metabolism of salts of organic acids, the continued reabsorption of 26–28 mM of bicarbonate per liter of filtrate and excretion of the excess would gradually lower the plasma and interstitial fluid concentrations to the normal range. Excretion would then cease. If there always was an excess of inorganic cations in the diet, as there is in herbivorous animals, the processes of reabsorption and excretion alone would serve to stabilize the bicarbonate ion concentration of the body fluids within the usual limits of normal.

The reabsorption in man of 28 mM of bicarbonate per liter of glomerular filtrate, or in the dog of 26 mM/L, should not be construed as indicating that bicarbonate reabsorption is Tm-limited in the same sense that glucose is. The infusion of bicarbonate in both man and dog progressively increases the filtration rate. Constancy of reabsorption, when plasma concentration exceeds the renal threshold, obtains only if reabsorption is factored by filtration rate, not by time. The teleologic significance of this relationship is evident, even though the mechanism is not. If an ani-

mal with a very labile filtration rate, such as a dog, were to be in bicarbonate balance in the fasting state and if bicarbonate reabsorption were truly Tm-limited in terms of millimoles per minute, the ingestion of a large meal of meat and the attendant increase in filtration rate would rapidly deplete the circulating bicarbonate stores. Actually, an increase in filtration rate is accompanied by no increase in bicarbonate excretion; the increased filtered load is reabsorbed. Because both chloride and bicarbonate exhibit this reabsorptive characteristic and since they are the major anions associated with sodium in the filtrate and tubular urine, it is probable that this characteristic is imposed on them by the sodium reabsorptive mechanism (see Chapter 7).

BICARBONATE REABSORPTIVE MECHANISM

The reabsorption of bicarbonate is depressed and excretion is increased by the administration of a variety of N'-unsubstituted sulfonamide compounds, all of which are inhibitors of the enzyme carbonic anhydrase. This fact suggests that the enzyme plays a key role in the reabsorptive mechanism.

CARBONIC ANHYDRASE.—In 1935, Roughton discovered carbonic anhydrase in red blood cells (3). This enzyme greatly increases the rate of attainment of equilibrium in step 1 of the following reaction:

$$CO_2 + H_2O \underset{1}{\rightleftharpoons} H_2CO_3 \underset{2}{\rightleftharpoons} H^+, HCO_3^-$$

In the absence of enzyme, step 1 is slow. Step 2, on the other hand, is inherently rapid and is uninfluenced by the presence or absence of enzyme. Catalysis by carbonic anhydrase facilitates the rapid conversion of bicarbonate ion into carbon dioxide in the brief interval that any given unit of blood spends in a pulmonary capillary. It likewise facilitates the rapid conversion of carbon dioxide into bicarbonate ion in the tissue capillaries.
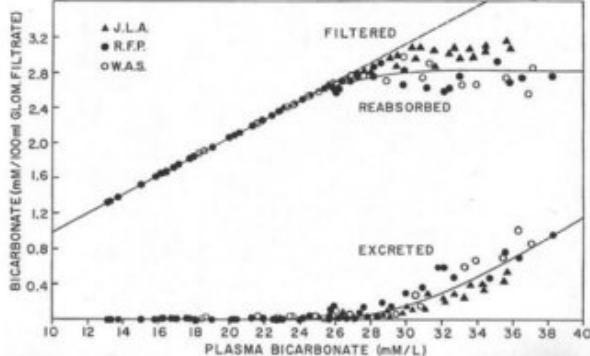
Fig.1

ARF and CRF can be overcome resulting into the Bicarbonate Alkaline-Diuresis (BAD) with a urine- pH between 7.5 and 8.0.

This mechanism always functions, even in the presence of Acute and Chronic Renal Failure and any surplus bicarbonate will be excreted as well as water, electrolytes and retention products as alkaline diuresis (BAD). According to R.F.Pitts (14) increase of bicarbonate in the blood progressively increases the glomerular filtration rate. This increase is mediated by the bicarbonate signal at the macula densa as shown by J. Schnermann (18, 19). The physiological explanation is given by the Tubulo-glomerular feedback mechanism, the "Thurau-Mechanism" (21). The bicarbonate signal at the macula-densa causes a maximum dilatation of the arterial vas afferens of the glomerulus thereby leading to a maximum increase of the glomerular filtration (GFR) in all functioning glomeruli. The filtrate contains abundant amounts of bicarbonate so that all bicarbonate- reabsorption mechanisms in the proximal and distal tubular system are being saturated. Plenty of the intraluminal fluid and an increased filtrate flow will be available for excretion. Thus, the oligo-anuria of the intrarenal vasodilation and the increased blood supply to the tubular system also allows pharmaceuticals e.g. diuretics to reach their cellular target-point in the distal tubular loop and to become active. Enhancement of the Bicarbonate Alkaline Diuresis(BAD) towards BAPolyuria (BAP) due to the action of a distal loop diuretic is thereby made possible. The glomerular filtrate will escape the reabsorption in both the proximal and the distal tubule resulting in the most desired Polyuria (Loop-Diuretic-Enhanced-Polyuria **LDE-BAP**).

The dilatation of the vas afferens of the glomerulus not only increases the glomerular filtration rate (GFR) but also

increases the arterial blood perfusion and oxygenation of the whole tubular system in the renal cortex and renal medulla because it depends on the outflow of blood from the glomerulus via the vas efferens. Anoxic and toxic tubular damages are thereby prevented and the regeneration of tubular damages from ARF is enhanced. The increased rate of intratubular filtrate-flow as a consequence of the increase of the GFR will prevent the tubular reabsorption of any toxin contained in the filtrate into the tubular cells, e.g. hemoglobin, cytotoxic drugs, nephrotoxic antibiotics, contrast-media, biphosphonates etc. In addition, the neutralisation of any positive ions (H+-protonisation) takes place by the negatively charged HCO_3- which is always present. The unified effect of all these mechanisms therefore provides a maximum of Nephro-protection.

Pharmaceutical diuretics or osmo-diuretics are only active at specific loci in the tubular region. They are unable to increase the diminished GFR of ARF and CRF. Due to their tubular blocking effect they result only in an increasing unphysiological salt- and water- diuresis. However, the required elimination of the uremic retention-products remains inadequate and insufficient. As mentioned before, in ARF and CRF the pharmaceutical diuretic drugs cannot reach their target cells in the tubular region due to intrarenal ischemic reduction of blood flow. Therefore any resultant diuresis has no nephron-protective effect. In contrast, the auto-regulatory and physiological Bicarbonate-Alcaline-Diuresis (BAD) or Polyuria is obviously superior to any other form of diuresis. The abundant physiological polyuria leads to the necessary elimination of all uremic retention products and eliminates therefore the need for any extracorporeal procedure or dialysis. The prognosis of ARF and CRF of any origin will therefore be much more favourable. The reported mortality rate of 50 to 80 % associated with the extracorporeal procedures of ARF is therefore eliminated and mortality remains related only to the severity of the specific underlying pathological problem. The prognosis of mortality in ARF, thus treated conservatively, has been reported (9; 10; 11; 12) as between 0% and 20%.

Prevention of the Progression of Chronic Renal Failure (CRF)

The number of publications about the origin and the progression of CRF is plentiful (26; 27; 28). The relative risk (RR) of becoming dependent upon dialysis was significantly reduced in a group treated with supplementation of bicarbonate compared to a control-group receiving no such supplementation (p<0,001), *de-Brito-Ashurst et al. 2009* (26). However, no studies report that the substitution of bicarbonate to the body either orally or intravenously, was carried out in the identical manner as described by Robert F.Pitts in his classical study: *Filtration, reabsorption and excretion of bicarbonate as functions of plasma concentration in normal man; Pitts, R.F., Ayer,J.L. and Schiess, W.A.: J.Clin.Invest.* 28:35, 1949) see Fig 11-1 page 199 in: RENAL REGULATION OF ACID-BASE BALANCE. In none of the cited articles the physiological basis as described by Robert F. Pitts was ever mentioned, nor was it ever employed as a guideline for the prophylaxis and therapy of the bicarbonate deficit of renal acidosis.

In the textbook: PHYSIOLOGY of the KIDNEY and BODY-FLUIDS 3d Edition 1974 Year Book Medical Publishers Inc. 35 East Wacker Drive Chicago by Robert F. Pitts the essential role of Bicarbonate for the physiological function of the kidney is described in detail in the chapter: "*Renal Regulation of Acid Base Balance pp.198-241*. Most deplorable is the fact, that this textbook is unknown to both teachers and students. Let alone that it is used as a guideline for the therapy of renal failure, be it Acute or Chronic.

These fundamental basic principles of Renal Physiology were first applied in 1976 by K.F. Kopp(1). Follow-up publications about further clinical experiences in man and about animal experimental studies on rats (13; 14) appeared until the year 2000 (Selected publications REFS 1-19). In addition, a case report about a non-scheduled animal experiment proved the efficacy of sodium bicarbonate-induced alkaline polyuria (BAP) in a 300 kg bodyweight Circus Tiger. Tiger Mohan was severely bitten in his tail by a jealous fellow tiger followed by ARF due to sepsis and toxicity of Gentamycin-treatment (15). It is the first report worldwide about a feline who recovered from an advanced oliguric Acute Renal Failure (ARF).

Progression of Chronic Renal Failure may have numerous causes. The best know "nephron killer" is hypertension of any origin and Diabetes mellitus type I or type II. In addition, kidney diseases either of genetic, immunological, inflammatory, systemic or urological origin may lead to the irreversible loss of nephrons in the kidney which produce urine. Even if the underlying renal disease can be therapeutically eliminated there remains a persistent factor which will cause the progression of nephron-loss and CRF: that factor is the persistence of chronic acidosis , which is due to a deficit of intra- and extrarenal bicarbonate. So far, this deficit has never been recognized as a promoting factor for CRF nor has it ever adequately been treated.

Nephro-protection using BAP for the prevention of CRF is therefore based on the same physiological principles as for ARF. The elevation of the blood-bicarbonate-level will produce a similar alteration of intra-renal hemodynamics and improve tissue-oxygenation and the cellular biochemistry. Optimised conditions for the functioning and the survival of the remaining nephrons are created and the "vicious circle" of lethal ischemia due to the bicarbonate- deficit is thereby abolished. **The progression of Chronic Renal Failure (CRF) will be prevented and the necessity for long term dialysis can also be prevented - if Bicarbonate-Alkaline-Polyuria (BAP) is started early enough.**

Nephroprotection of organs from potential cadaver donors

Since publication of our paper (25) the possibility of improving the survival of cadaver donor kidneys has not gained any support. The time span in which vital organs suitable for transplantation can be harvested from potential donors is limited to 48 – 72 hours at maximum. After that period the kidneys will undergo lethal changes as in acute renal failure (ARF). Severe shortage of donor organs is the result.

Based on clinical experience the time of viability of kidneys from cadaver donors could be prolonged up until one week until the elective removal could be performed. The time pressure under which the transplant procedure had always to be carried out promptly was thus eliminated. There would be enough time to clarify the important questions e.g. approval from relatives, organ typing, completion of records and notification of recipients etc. As a result, the number of donor-organs suitable for transplantation could be **enhanced significantly.**

Selected Publications about Acute and Chronic Renal Failure (ARF

and CRF)

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