Bicarbonate is an anion with problems of heavy solubility. In mammalians and humans, bicarbonate is the transport form of produced CO2. In the lungs, this bicarbonate will re-transform into CO2 by carbo-anhydrase for ventilation. So an acidification with physically solved gas CO2 had implemented with the amount of 4 % of the total alkali bicarbonate (> Homer W. Smith, “From Fish to Philosopher”, 1953). With bicarbonate 24 mmol/l and CO2 1,2 mmol/l (= 40 mm Hg), there is not calcification with Ca++ und Mg++ ions in humans at all. Kolf had set the bicarbonate concentration in his prescription to 32 mmol/l, because of the shorter treatment time with dialysis in relation to one week living (= 168 hours), in order to treat the metabolic acidosis. The former ways of acidification had been not sufficient concerning calcification (Koll: acid sodium phosphate – Alwall: carbogen gas (5 % CO2)). In 1978, 3 mmol/l acetate had introduced in bicarbonate dialysis fluid. With the reintroduction of bicarbonate in the prescription of dialysis fluid again (1978), the calcification accompanies the dialysis. Because of the calcification of the monitors, a descaling procedure for the monitors was necessary after every treatment. The patients however received no descaling . . .

In the end of the 1970-ies, there was the cry of shortening the treatment time of dialysis (> B.H. Scribner, square-meter-hour-hypothesis). Surfaces of dialyzers become big and bigger and blood flow had raised, in order to reach the same Kt/V of the former long-term treatment. This critical behaviour neglected, that the very most dialysis centres had over-run the metabolic capacity of the liver for acetate metabolism (> in his first profession, Shaldon had been hepatologist . . .).

In 2007, a new prescription of dialysis fluid appeared with an exchanged mode of acidification, citrate 0,85 mmol/l (ART group, Seattle). First thought was, to replace the RCA (Regional Citrate Anticoagulation, done in the ICU’s). Whenever this target of replacing Heparin as the single anti-coagulating drug failed, it is a very interesting prescription of acidification of dialysis fluid, as there is no calcification at all in this dialysis fluid. The ART prescription consists of 0,85 mmol/l citrate and 0,3 mmol/l acetate. This had fixed in patents. The small amount of 0,3 mmol/l acetate is not so important. In 2012, a second prescription with citrate appeared, Citrate 1,0 mmol/l. Comparing this new citrate acidification (1,0 mmol/l) with the classical acetate acidification (3 mmol/l): Citrate is a threefold base, so 1,0 mmol/l is equivalent to 3 mval/l. This means, that the amount of produced CO2 derived of bicarbonate buffer, will be exact the same like the acidification with 3,0 mmol/l acetate. The essential is, that there is a second principle of working inside, the chelate ligature. This chelate ligature of citrate disguises the both problematic cat-ions of solubility in the dialysis fluid, Ca++ und Mg++. So, they both are present in the dialysis fluid, but they cannot take part tocalcify.

What is the problem with citrate acidification? This second principle of working, the chelate ligature, will not well understood by Medical Doctors, as this requires some chemical knowledge. Medical opinion leaders will complain the well-known calcification of coronary vessels and heart valves of CKD-5 patients, but the usual haemodialysis has its own problem of calcification even in the prescription! - The same problem is inside in the Medical Authorities: They had casted also with its own problem of calcification even in the prescription! - The same problem is inside in the Medical Authorities: They had casted also with the usual haemodialysis has its own problem of calcification even in the prescription! - The same problem is inside in the Medical Authorities: They had casted also with the usual haemodialysis has its own problem of calcification even in the prescription! - The same problem is inside in the Medical Authorities: They had casted also with the usual haemodialysis has its own problem of calcification even in the prescription! - The same problem is inside in the Medical Authorities: They had casted also with the usual haemodialysis has its own problem of calcification even in the prescription! - The same problem is inside in the Medical Authorities: They had casted also with the usual haemodialysis has its own problem of calcification even in the prescription! - The same problem is inside in the Medical Authorities: They had casted also with the usual haemodialysis has its own problem of calcification even in the prescription! - The same problem is inside in the Medical Authorities: They had casted also with the usual haemodialysis has its own problem of calcification even in the prescription! - The same problem is inside in the Medical Authorities: They had casted also with the usual haemodialysis has its own problem of calcification even in the prescription! - The same problem is inside in the Medical Authorities: They had casted also with the usual haemodialysis has its own problem of calcification even in the prescription! - The same problem is inside in the Medical Authorities: They had casted also with the usual haemodialysis has its own problem of calcification even in the prescription! - The same problem is inside in the Medical Authorities: They had casted also with the usual haemodialysis has its own problem of calcification even in the prescription! - The same
What will remain? An interested Nephrologist or a Dialysis Provider will be the best option in order to reach the dialysis fluid without any calcification, the citrate acidification. We will not wait until the Medical Societies and Medical Authorities will have finally understood this problem of chemical solubility, as it is a real clinical problem!

Naturally, the problems of calcification of CKD-5 patients have several different reasons, e.g. secondary hyperparathyroidism, nutrition intake of protein and phosphate or reduction of the FGF-23 principle. With this background, there is the medical obligation, to avoid any further reason for calcification.

An important point: When switching to citrate acidification, the concentration of Ca++ should slightly elevated in order to prevent a hypo-calcaemic reaction of the patient, as a smaller part of the patient’s Ca++ will bound by citrate. For example, instead of Ca++ 1,25 mmol/l (3 mmol/l acetate), Ca++ 1,5 mmol/l should use with citrate.

Smaller points: Toxicity of citrate. In former times, RCA had done with 30% citrate as regional anticoagulation in case of bleeding problem. The known danger was the metabolic alkalosis, due to the three-fold buffer precursor citrate additional to the bicarbonate concentration of 32 mmol/l. One third of this total dosage had run into the patient, up to 450 mval. This was an over-treatment with alkali and not a specific effect of citrate. RCA today will done in most cases with 4% citrate (in pre-dilution mode). With this set-up, citrate levels will reach about 10 mmol/l in the patient’s blood today. For successful anticoagulation with citrate as the single anticoagulating drug, a level between 4 – 6 mmol/l is the target. With citrate acidification, the reached level of citrate will be about 1 mmol/l. - Taking-up these citrate levels, there will be a partial effect of anticoagulation in the citrate acidification. Different studies had shown a possible reduction of Heparin up to 50% bolus and 50% of the continued dosage of Heparin (H. Wolf, Ahrenholz). A dialysis with citrate acidification needs for anticoagulation a second principle, e.g. a disorder of the patient’s anticoagulation or the half dosage of Heparin. - Stimulation of the MPO (Myeloperoxidase): In the ART prescription, there will be today 0,3 mmol/l acetate inside. This is a reduction of two ten-potencies, when comparing with the acetate dialysis of Shaldon. In this set-up, there will be no effect of acetate on the MPO. - Kt/V will be slightly higher with citrate acidification in comparison to the classical acetate acidification, due to the additional anticoagulation effect of citrate. - Citrate will metabolized quantitative in high turn-over mode in the Krebs cycle, as this is the oxidative metabolism (> proven by the Calcium gap smaller than 0,2 %):

\[ Ca^{++} \text{ GAP} = (\text{total Ca}^{++} \text{ post - total Ca}^{++} \text{ pre}) - (\text{ion Ca}^{++} \text{ post - ion Ca}^{++} \text{ pre}), \text{Gabutti).} \]

Conclusion

Several curious points you will observe:

1. The Medical Authorities had casted with Medical Doctors. They do not ask a chemist for consulting concerning the problem of chemical solubility of the classical dialysis concentrate of bicarbonate dialysis (acidification with 3 mmol/l acetate). Moreover, there absolutely no existing vigilance for Medical Products.

2. Medical Societies and their Opinion Leaders are also Medical Doctors, who do not really assess the problem of chemical solubility of the classical dialysis concentrate. This remains the duty of a chemist. Therefor the Medical Societies complain the clinical calcification problems of the CKD-5 patients.

3. Lectures by a chemist to this theme are seldom. When these will presented, the context will only deal with the smaller points concerning the extent (Kt/V, IL concentration, MPO activation). The best of them will report concerning the reduction of Heparin dosage. - Nearly all chemists, who are involved in the production of dialysis fluid, had employed by the companies. There are conflicts of interests: Not to damage a running product (> the classical bicarbonate dialysis prescription). It is not a deficit of knowledge of them . . .

4. It remains to the interested doctors and interested dialysis providers, to switch to the citrate based dialysis concentrates in order to prevent the important additional effect of calcification by the wrong bicarbonate dialysis prescription. The citrate based dialysis concentrates are licensed and available on the market. We should not wait "ad calendas graecas" until Medical Societies or Medical Authorities will awake . . .