Problems of Calcification of Dialysis Fluid with Acidification of 3 mmol/l Acetate

Thomas Ryzlewicz MD

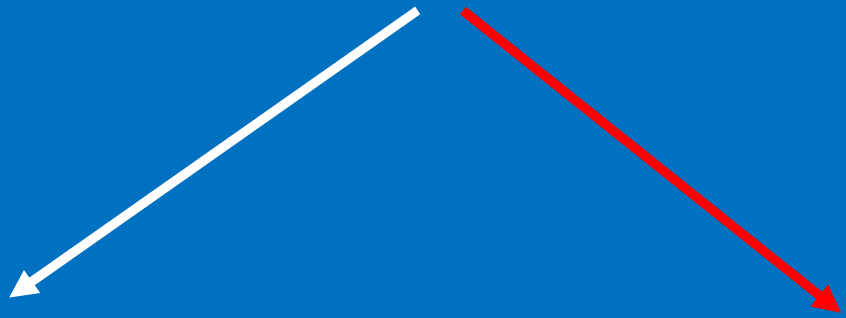
How did we deal with lemons➔

when we use acetate for acidification?

why acidification?

- Mammals and Man produce a great deal of CO_2-Gas ➔ transported in Blood as HCO_3^- and eliminated via the lungs by diffusion
- This is driven by metabolism (37°C, motion, function of the body)
- CO_2 40 Torr = 1.2 mmol/l acidifcation

what is the Problem of Bicarbonate Dialysis?



with Acetate Dialysis (1965-1978) you *never* have a Problem with Calcification - there is only the exceeding of the metabolic capacity of the Liver

in Bicarbonate Dialysis you have the alternative between Calcification or CO_2 Overload

Problem: short time of HD Treatment (> 12 – 24 h per one week with 168 h of living) ➔ Buffer Concentration was set to 32 mmol/l

Acidification in Bicarbonate Dialysis - but how?

Acidification and its relation to pH?

$$pH \downarrow \sim \frac{HCO_3^-}{pCO_2}$$

Addition of acid → partial transformation from $HC\bar{O}_3$ to CO_2

→ That is how the solubility of calcium, magnesium & bicarbonate can be achieved

how the acidification bicarbonate-dialysis was achieved?

- W. Kolff (1943): acid Na^+-phosphate
- N. Alwall (1945): carbogen-gas
- since 1978 3 mmol/l acetate
- in France 4 or 5 mmol/l acetate

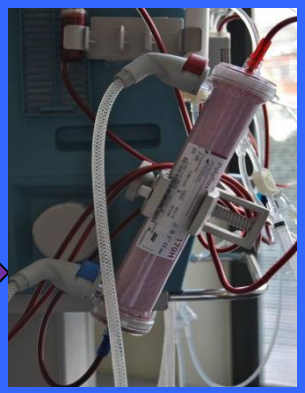
➔ ***Perhaps French doctors are better!***

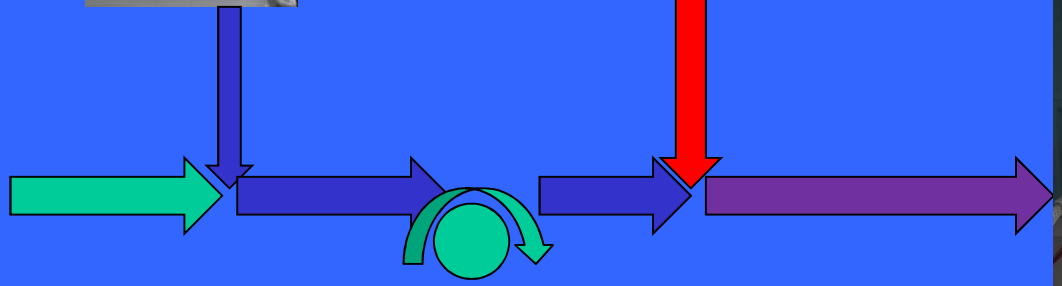
No, they aren‘t (!): COLD & weaning from Respirator

A-Component
3 mmol/l Acetate

BiCart

High-Flux





pH 7.2
pCO_2 85

Treatment

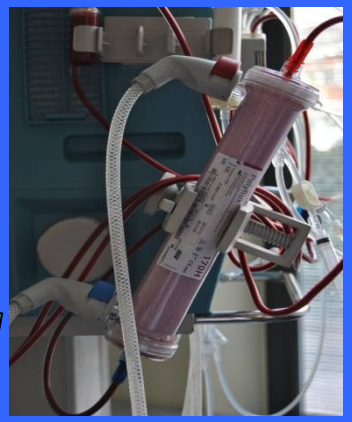
Permeation

De-Air

Dialysis-
Fluid

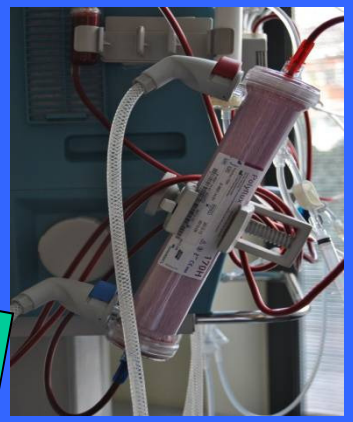
and Calcification

Dialyzer as Oxygenator (for Exchange of CO_2)



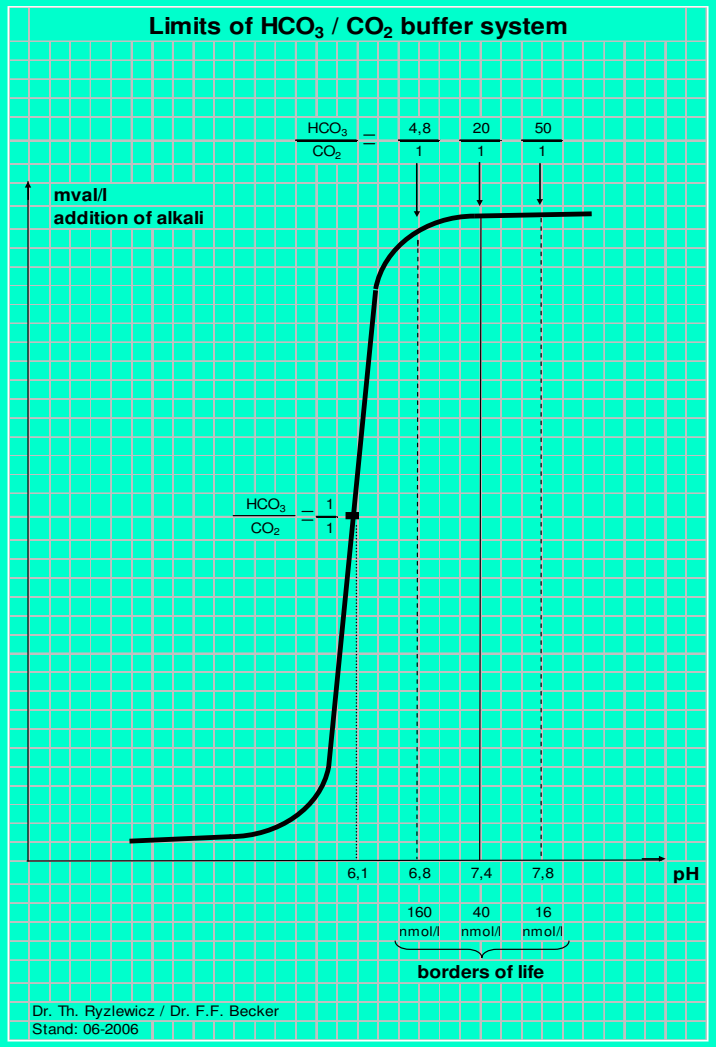
pCO_2 85 mm Hg
3 mmol/l acid

Calcification

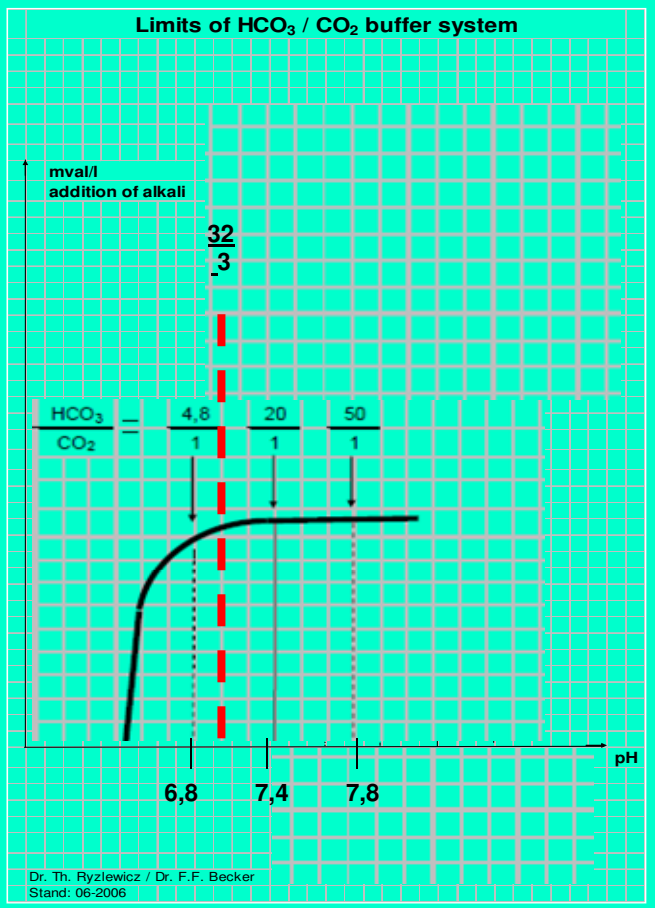


pCO_2 100 – 130 mm Hg
4 to 5 mmol/l acid

Problems for COLD-Patients, as well as for ICU-Patients being on a respirator



Henderson-Hasselbalch's Equation



Henderson-Hasselbalch‘s Equation

. . . and after the treatment . . .

. . . the monitor
must be de-scaled
immediately . . .

the patient . . .
however,
cannot be de-scaled

the coefficients of solublility . . .

- are known and defined at 20℃ and 25℃
- for 37℃ they are NOT KNOWN(!)
- Sodium-bicarbonate is soluble (8.4 % or ~ 9 % as BiCart)
- the solubility of Na-bic is dependent on the temperature

the coefficients of solubility . . .

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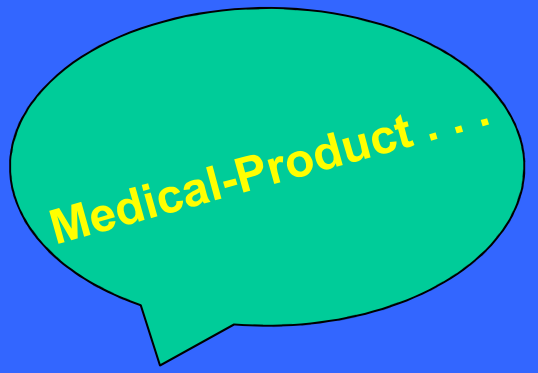
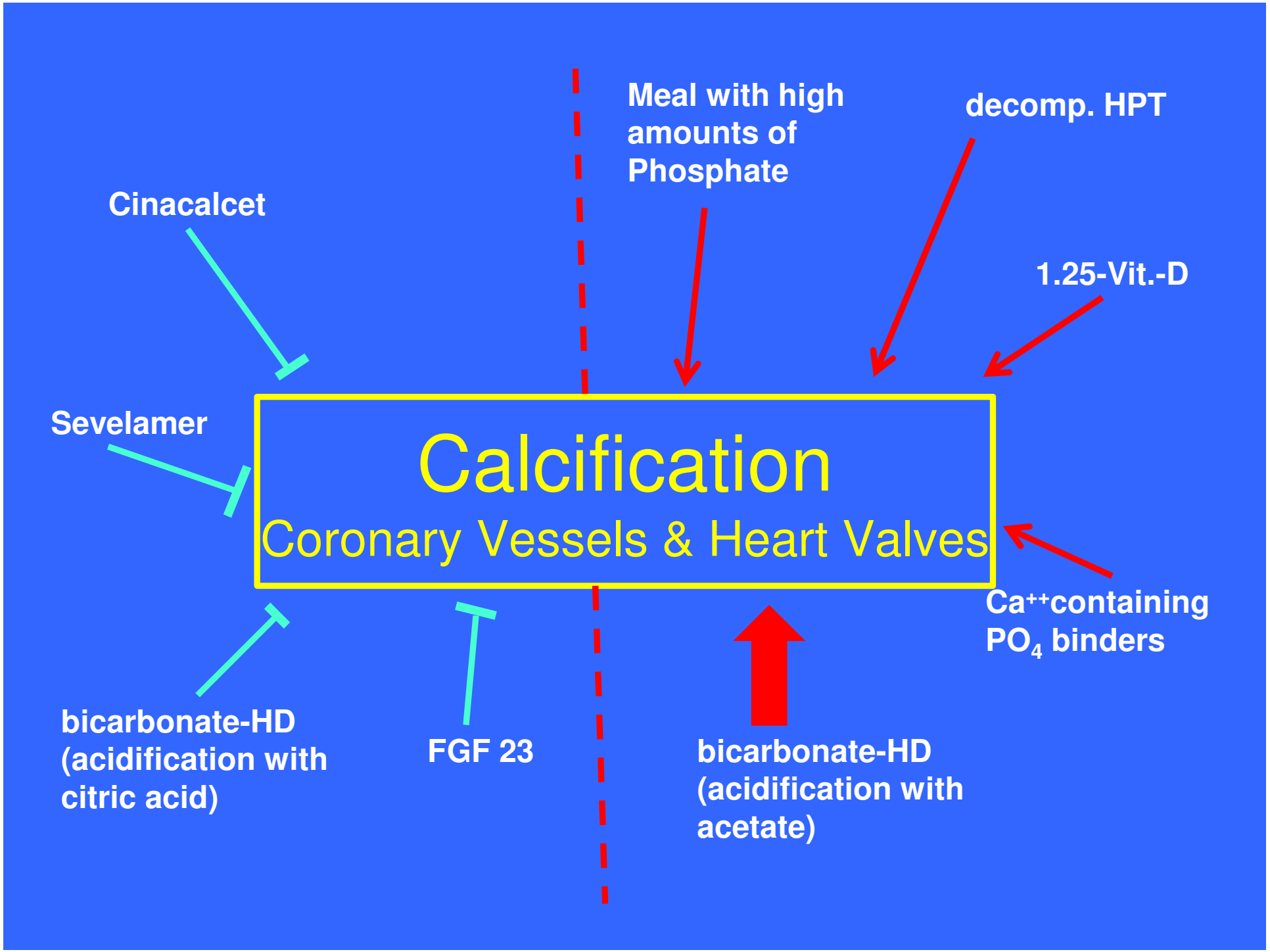
as a drug this prescription of the dialysis fluid of today never would be allowed




Meal with high amounts of Phosphate
decomp. HPT
Cinacalcet
1.25-Vit.-D
Sevelamer
Calcification
Coronary Vessels & Heart Valves
Ca++containing PO4 binders
bicarbonate-HD (acidification with citric acid)
FGF 23
bicarbonate-HD (acidification with acetate)

Clearance 15 ml/min: when does the calcification begin?

CKD-4: phosphate-elimination will be improved by FGF 23

➔„no phosphate binders“ and „no calcification“

CKD-5: same as CKD4
Now bicarbonate dialysis is started (acetate-acidification)

➔calcification:
➔now the patient needs . „phosphate binders“

the chalenge of acidification with acetate: „calcification or too high pCO_2“

the Solution: acidification with citric acid

Why?

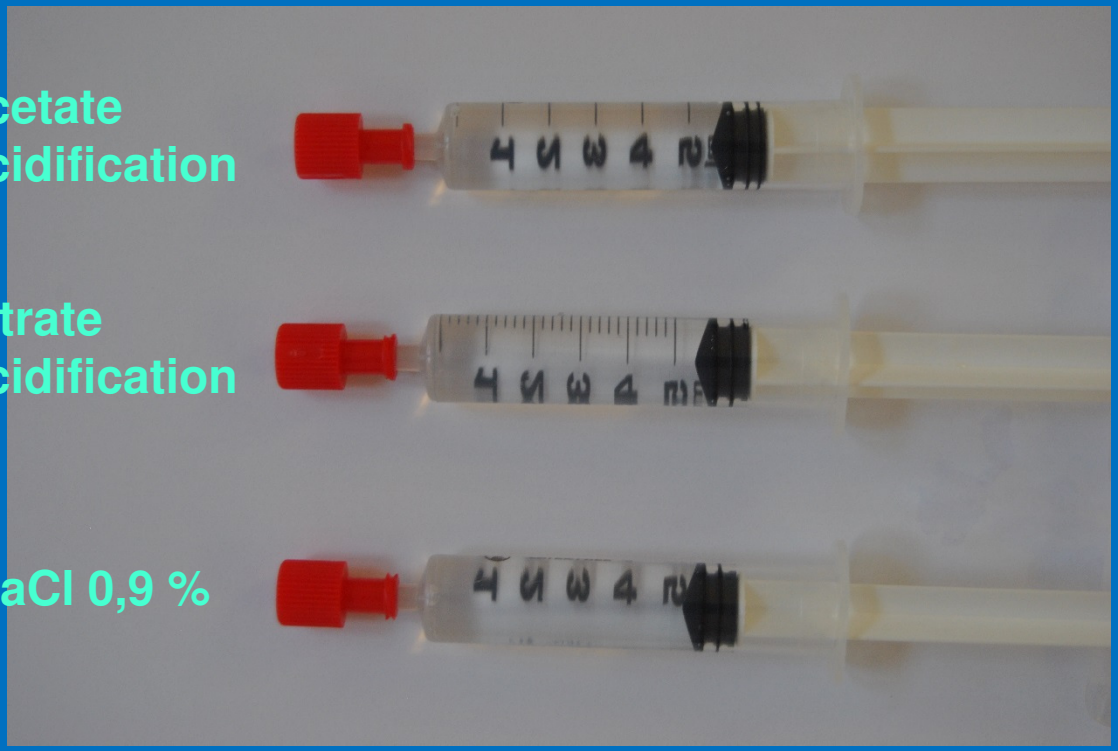
with the same power of acid & CO_2 production nothing will calcify because Ca^{++} is *disguised* in the chelate lattice

Transparency of a Solution

Acetate Acidification

Citrate Acidification

NaCl 0,9 %



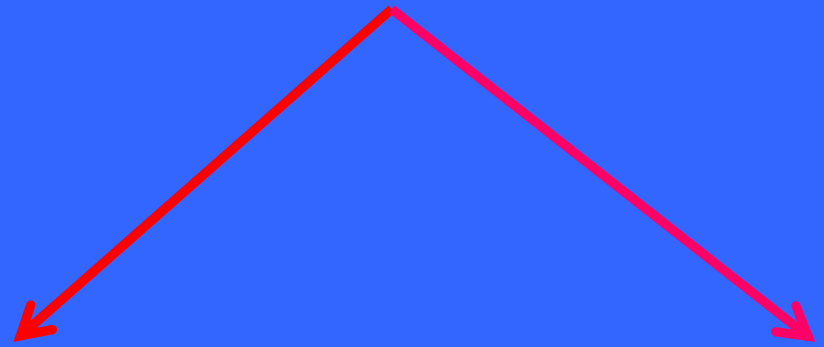
Laymen & Patients see the difference

Nephrologists didn‘t see this

BfArM ignores this

Acidification with Citric Acid

Acidification with Citric Acid



Select Bag Citrate 1.0 mmol/l Citric Acid	Citrasate 0.8 mmol/l Citric Acid & 0.3 mmol/l Acetate

	3.0 mmol/l Acetate	4/5 mmol/l Acetate	0.8 mmol/l Citric Acid 0.3 mmol/l Acetate (MTN)	1.0 mmol/l Citric Acid Gambro
Problem	Calcification	high pCO_2	./.	./.

Survey of the different possibilities for acidification

what should be taken into account when acidifying with citric acid?

- NOTHING will calcify (neither the patient nor the monitor)
- Ca^{++} in the dialysis fluid must be raised a little (Citric Acid – after having passed the dialysis membrane – will bind a smaller part of Ca^{++})
- so measurement of Ca^{++} after switching the dialysis fluid is reasonable for the first time
- the dosage of heparin can be reduced to 50 %

Is there a problem of communication when acidifying with citric acid?

Indeed, this exists:

the acidification with citric acid is *not well understood by many doctors*.

nevertheless, a discussion concerning the concentration of *Ca^{++} in the dialysis fluid* is continued . . .

why is the acidification with 1.0 mmol/l citric acid a good concept?

Do it right the first time! **(RH Herbst)**

- no further elevation of pCO_2
- no calcification at all
- good anti-thrombogenic effect (< Heparin)

equal acidification with 3.0 meq/l

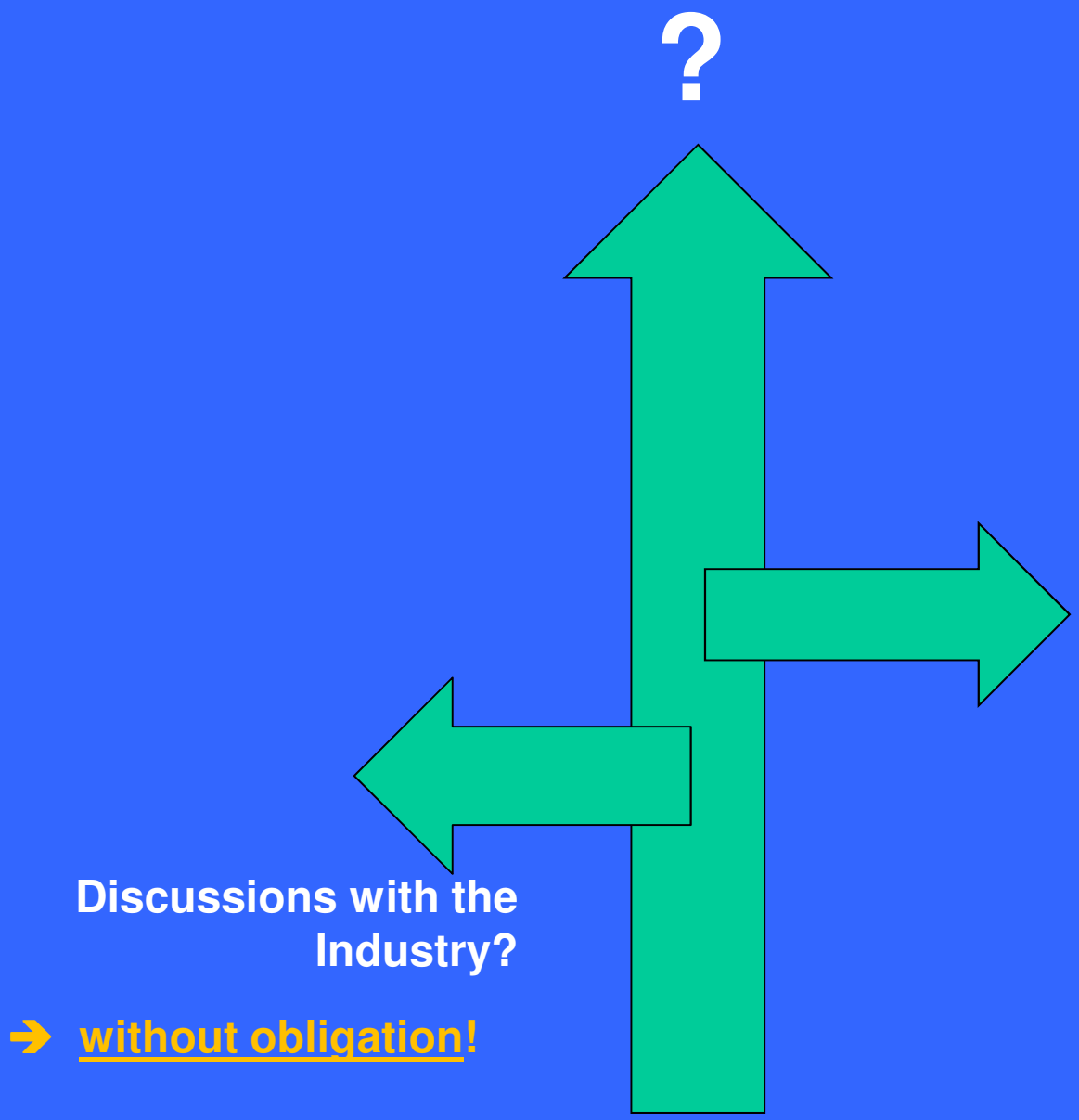
Acetate

- here only one principle is working:
  - a (smaller) part of bicarbonate will be transformed into CO_2

Citric Acid

- at first the same effect as with acetate
- second effect by disguising Ca^{++} and Mg^{++} by the chelate lattice of citric acid ➔ product for solubility of Ca^{++} x citrate and Mg^{++} x citrate will <u>not</u> be reached

Strategy



Lecture / Congress?

➔ without obligation!

Discussions with the Industry?

➔ without obligation!

Acidification with Citric Acid

3 possibilities

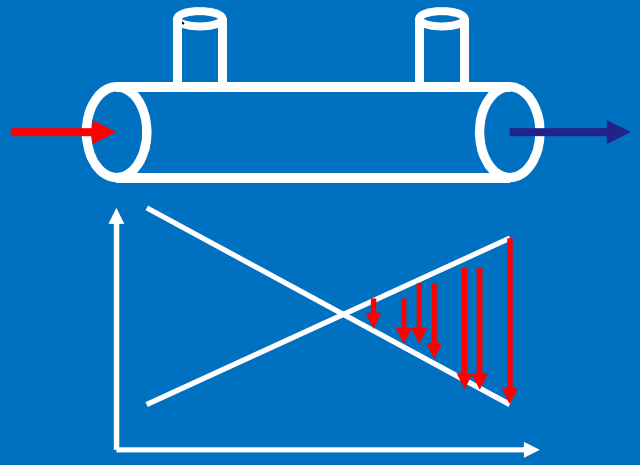
- Study
- Prohibition of the 3 mmol/l acetate-acidification (> BfArM)
- one concerned Patient (> chemist)
- Information of the doctor doesn‘t work here ➔ the theme is too complicated!

why a Chemical Evaluation is necessary?

- the Problem of Calcification with 3 mmol/l Acetate Acidification is a Problem of **Solublitiy**
- this never can be judged in a qualified way by Physicians
- there does exist the Prescription with 1 mmol/l Citiric Acid without any Calcification
- the Medical Authority BfArM Institute ingnored the Chemical Evaluation without a serious reason

Steps to reach a Chemical Evaluation:

- Oct. 2012 Letter to BfArM Institute Germany
  Result: Referrence Number, Proposal to discuss this at DGN
- Dec. 2013 Letter of a Medical Lawyer
  ➔ no Result(!)
- May 2014 Letter to the German Minister of Health (> Supervision of the BfArM)
- May 2014 Report to FDA (> VMDR & 3500A)



Conclusion

Backfiltration 8 ltr.
or online-HDF up to 30 ltr.

Calcifying Fluid

2 well known
Chemists . . .

. . . did not mention the
Calcification with
Acetat-Acidification . . .

. . . related with
Dialysis Industry

BfArM Institute
Medical Product

. . . refuses a Chemical
Evaluation

Everything is
allowed with a
Medical Product

FDA is involved (> VMDR & 3500 A for Chemical Evaluation)

We have to say what we think

We have to do what we say

What we do should reflect this

Alfred Herrhausen

1930 - 1989