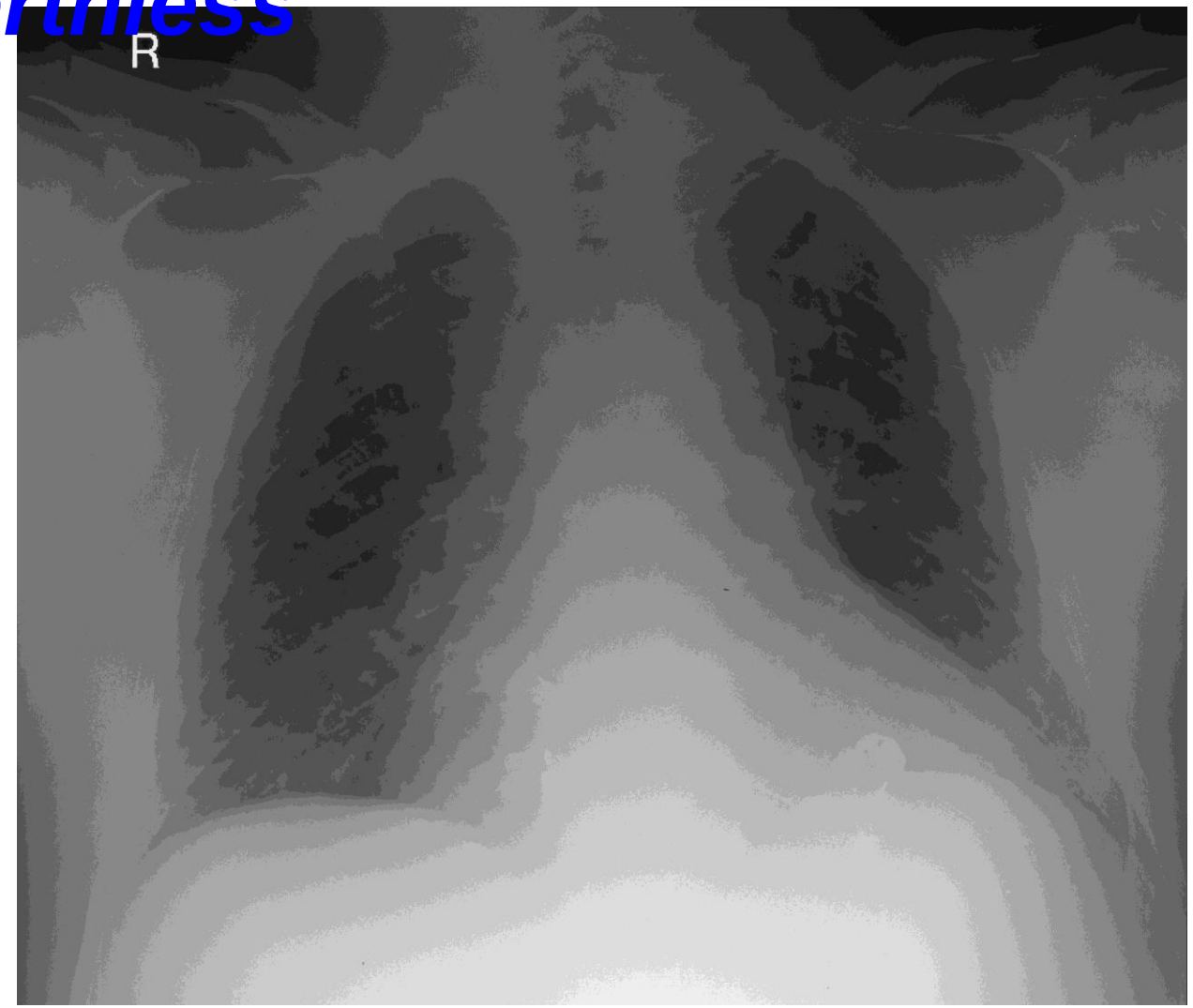
Not all turtles are slow

Chrysemys picta marginata; the diving turtle

47-year-old, shortness of breath and leg swelling for 2 weeks

- Unemployed Berliner, garden colony (*Laubenpieper*)
- No meds, “denies” alcohol intake
- BP 115/60, HR 96/Min, RR 36/Min
- Rales bilateral
- Distant heart sounds, no murmurs, ?S3
- Bowel sounds diminished
- Edema to sacrum
- Suspect CHF

Portable films are next to worthless



Acute labs

- Hb 13 g/dl, Hematocrit 38 vol%
- pH 7.30, $PaCO_2$ 20, PaO_2 105 (mm Hg), HCO_3 10,
- Na 123, K 6.9, Cl 87 (mmol/l)
- Glucose 5.6 mmol/l
- Lactate 14 mmol/l
- Anything life threatening here?

Anything lethal here?

- Acid-base problem?
- Hyperkalemia?
- Hyponatremia?
- Poor oxygen delivery?
- Heart failure? (EF normal; relaxation also OK)
- Just being in our ICU?

The answer is „jawohl“! (Hyperkalemia)

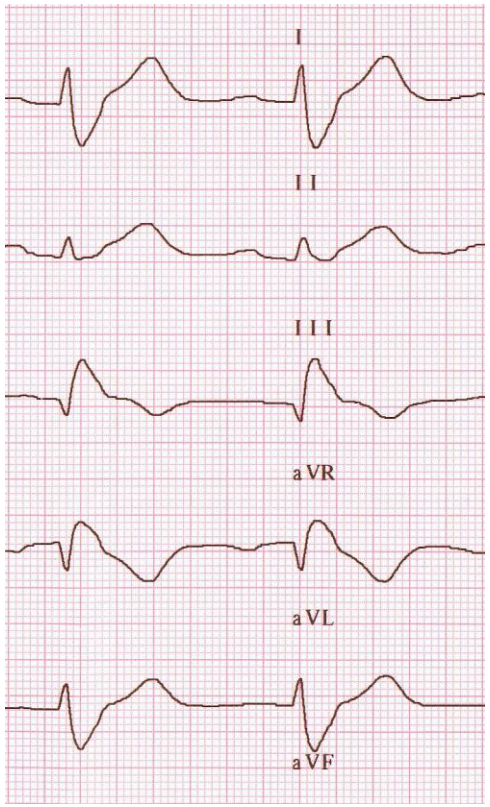
- Assessing heart failure use alveolar gas formula (Sea level)
- What is the alveolar ventilation and how is it measured ($PaCO_2$)?
- PAO_2 = PB-$PH_2$0 x 0.21 = 150 mm Hg
- 150 - ($PaCO_2$)/0.8 [RQ] or $PaCO_2$ x 1.25

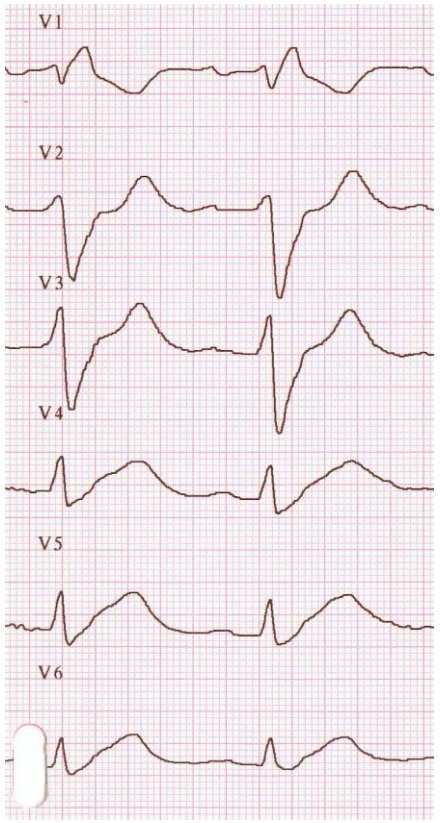
  = 150 - 105 + 25 = 20 mm Hg

  A-a gradient (normal <10 mm Hg).

Laubenpieper has a modest degree of AV mismatch, but O_2 delivery is not a problem.

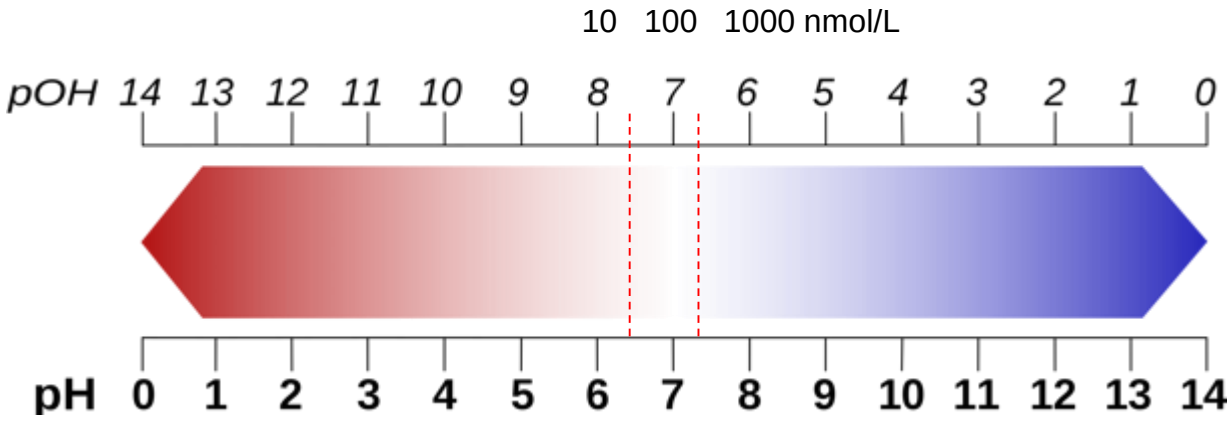
How about Hyperkalemia?

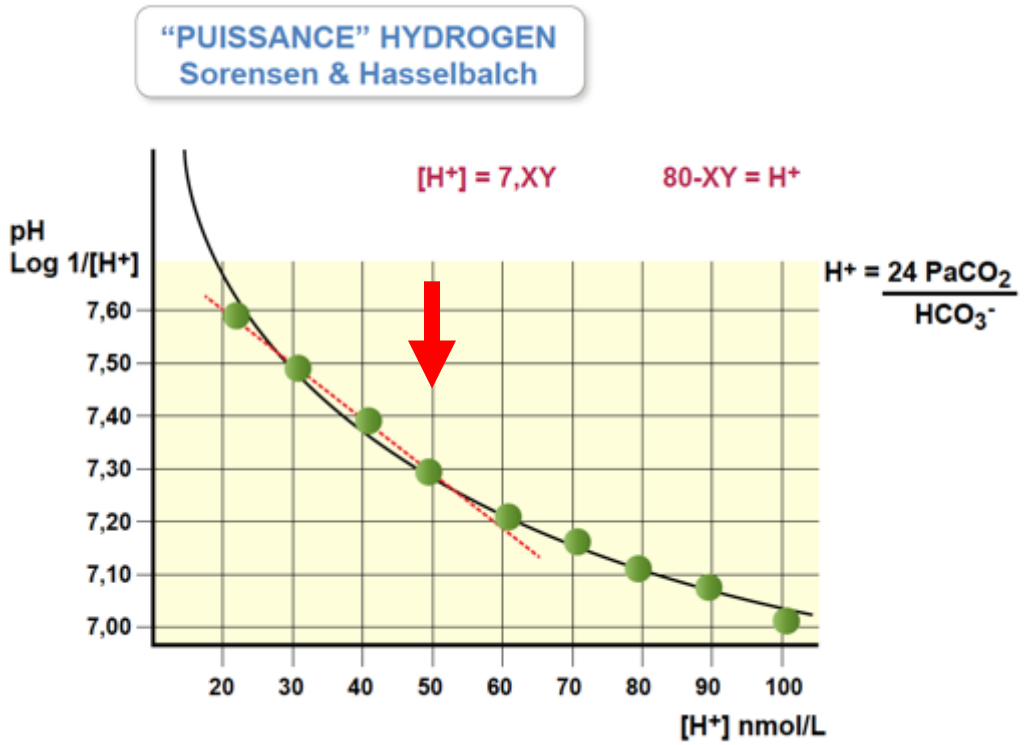




ECG paper speed at 50 mm/sec

The pH was 7.30. What is the [H+] in nanomols per lit





(24 x 20)/10 = 48

Now the nitty-gritty!

- Is there an acid-base problem?
- Acidemia with a low HCO_3 and low $PaCO_2$
- Metabolic Acidosis
- HCO_3 fell by 15 mmol (25 to 10)
- Decrease in $PaCO_2$ was 20 mm Hg
- Metabolic Acidosis, slightly overcompensated ie. respiratory Alkalosis

Is the respiratory compensation appropriate?

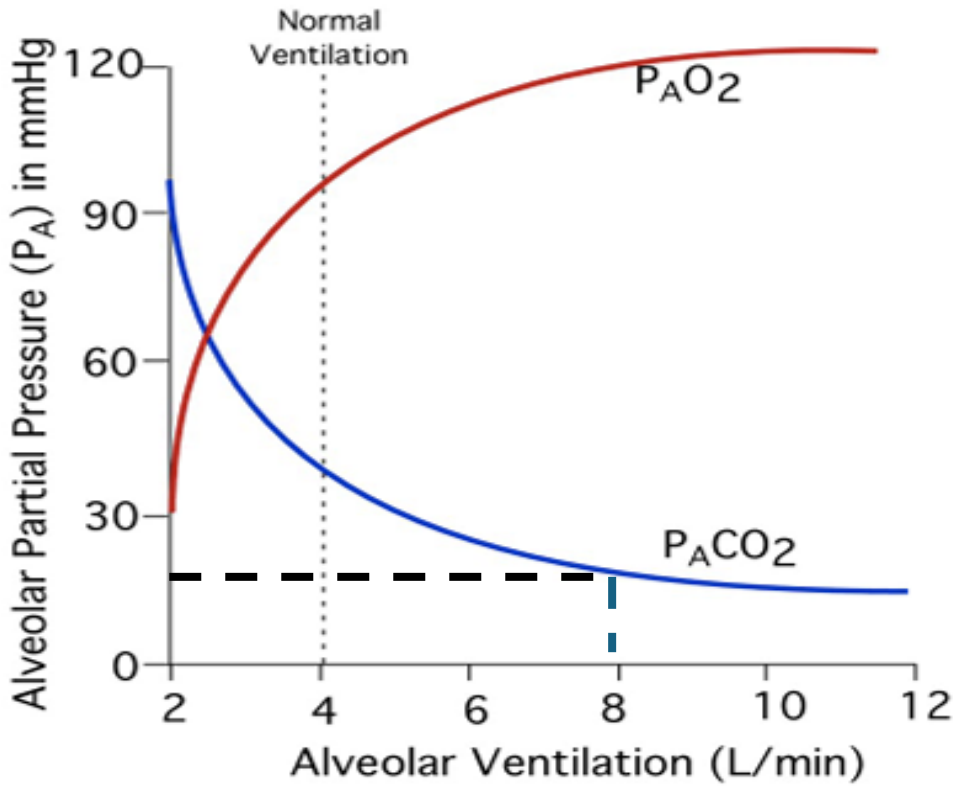
$H = (24 \times PCO_2)/HCO_3$

$PAO_2 = 150\text{-}Pa0_2 + PaCO_2/0.8$

For every mmol(L decrease in HCO_3 PCO_2 should fall by 1 mm Hg.

All derived from Fick's principle

(clearance formulae)

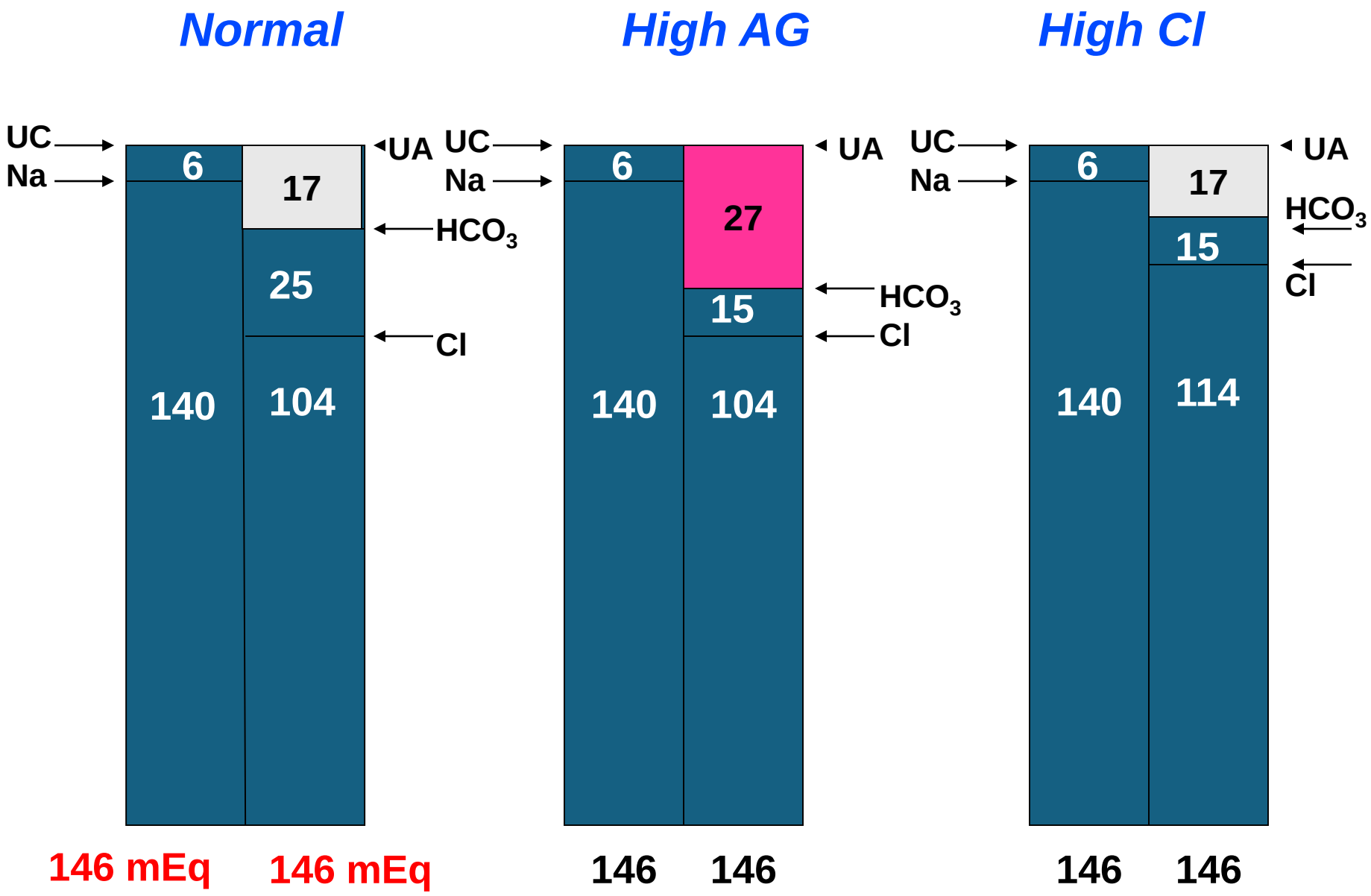


His PO_2 should have been 120, not 105 mm Hg

His $PaCO_2$ should be 26 not 20 mm Hg

Thus, the metabolic acidosis is over compensated, a concomitant respiratory alkalosis.

Metabolic acidosis is caused by gain of [H^+] or loss of [



Laubenpieper has an elevated AG

- AG = Na - Cl - HCO_3 = 26 (12±2)
- AG is 14 mmol/l too high
- Lactate is elevated by 14 mmol/l
- Ahah! For every mmol/l increase in lactate we observe one mmol/l increase in AG
- „Delta“ for „Delta“
- So we have a pure anion-gap metabolic acidosis!

Can we dismiss methanol and ethylene glycol poisoning?

- Calculated Osmo = 2(Na+K) + Glu + Urea
- = 2(129) + 5.6 + 19 = 283
- Difference is only 4 mosm
- Most common cause of increased AG today?

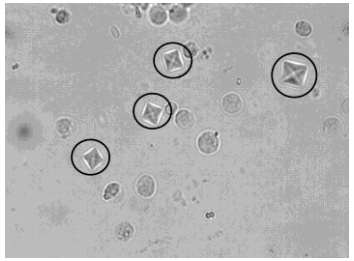
What are "mudpiles"? (Mneumonics) (Or - Kussmaul?)

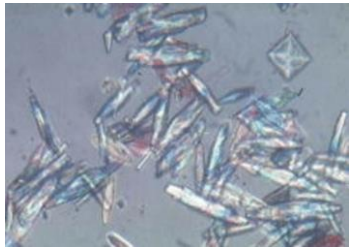
- Methanol; uremia; diabetic ketoacidosis (DKA); paraldehyde, phenformin; iron, isoniazid; lactic; ethylene glycol; salicylates (English)

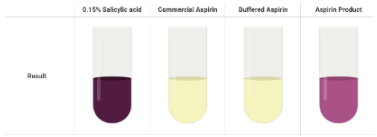
- Kussmaul: Ketoazidose, Urämie, Salizyl-Säure, Metanol, Äthylenglykol, (mehr) Urämie, Laktat (German)

Old fashioned but gave information within seconds

Can his urine tell us anything?







- Sediment for ethylene glycol
- Ferric chloride for acetyl salicylic acid, ketonuria, urea
- Lactate is 100% absorbed and does not appear in urine
- UK, UNa and UCreatinine

Laubenpieper is shipped up to our ICU

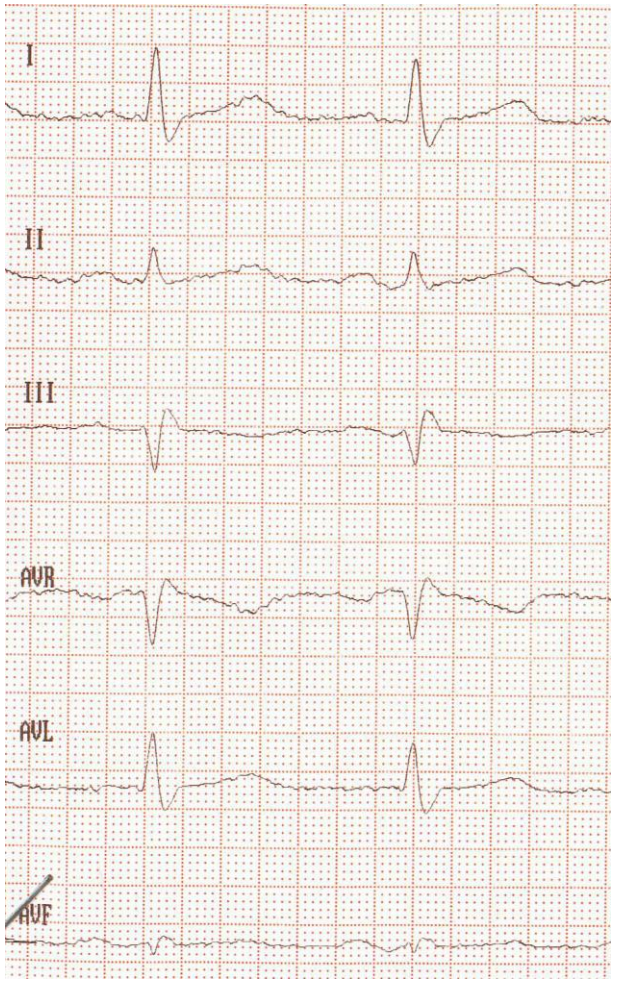
- Leukocytes 16 000/μ^3
- D Dimer 0.48 mg/dl, Trop T 0.05 µg/l
- aPTT 18 sec, ALAT, ASAT, Bilirubin slightly elevated
- Crea 243 µmol/l, Urea 18 mmol/l
- Osmo 287 mosm/l
- Ethanol not detectable

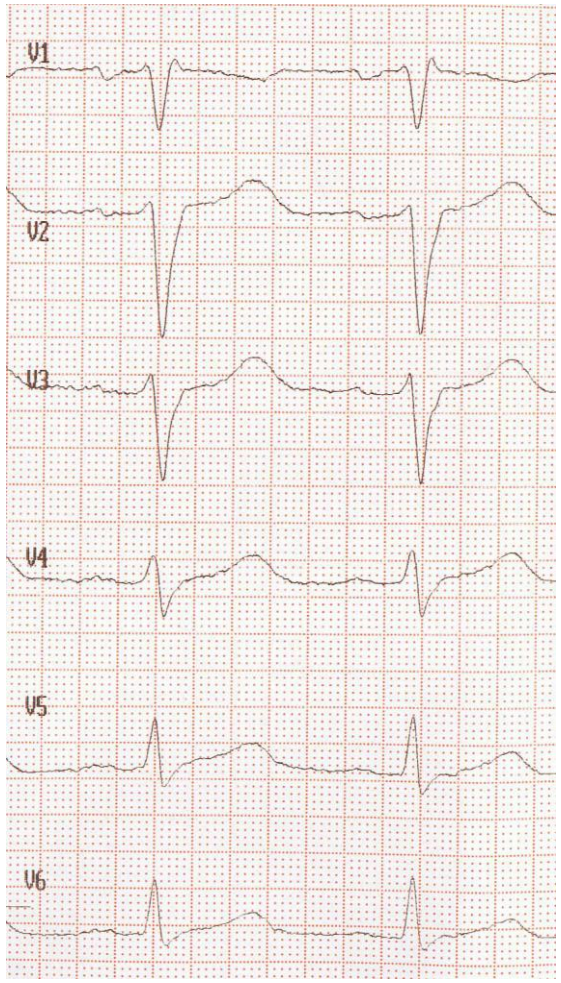
We checked out his urine!

- UNa 10 mmol/l
- UCl 15 mmol/l
- UK 65 mmol/l
- Sp.Grav. 1.030 (What is Uosm??)
- Prot 2+
- WBCs and granulated cylinders
- Ketone not present
- Mneumonics lead us to lactate
- Prerenal acute renal failure?

The potassium switch refers to plasma potassium regulation of the sodium-chloride cotransporter (NCC), which controls distal sodium delivery and therefore potassium secretion. Low extracellular potassium activates NCC by relieving chloride inhibition of With-No-

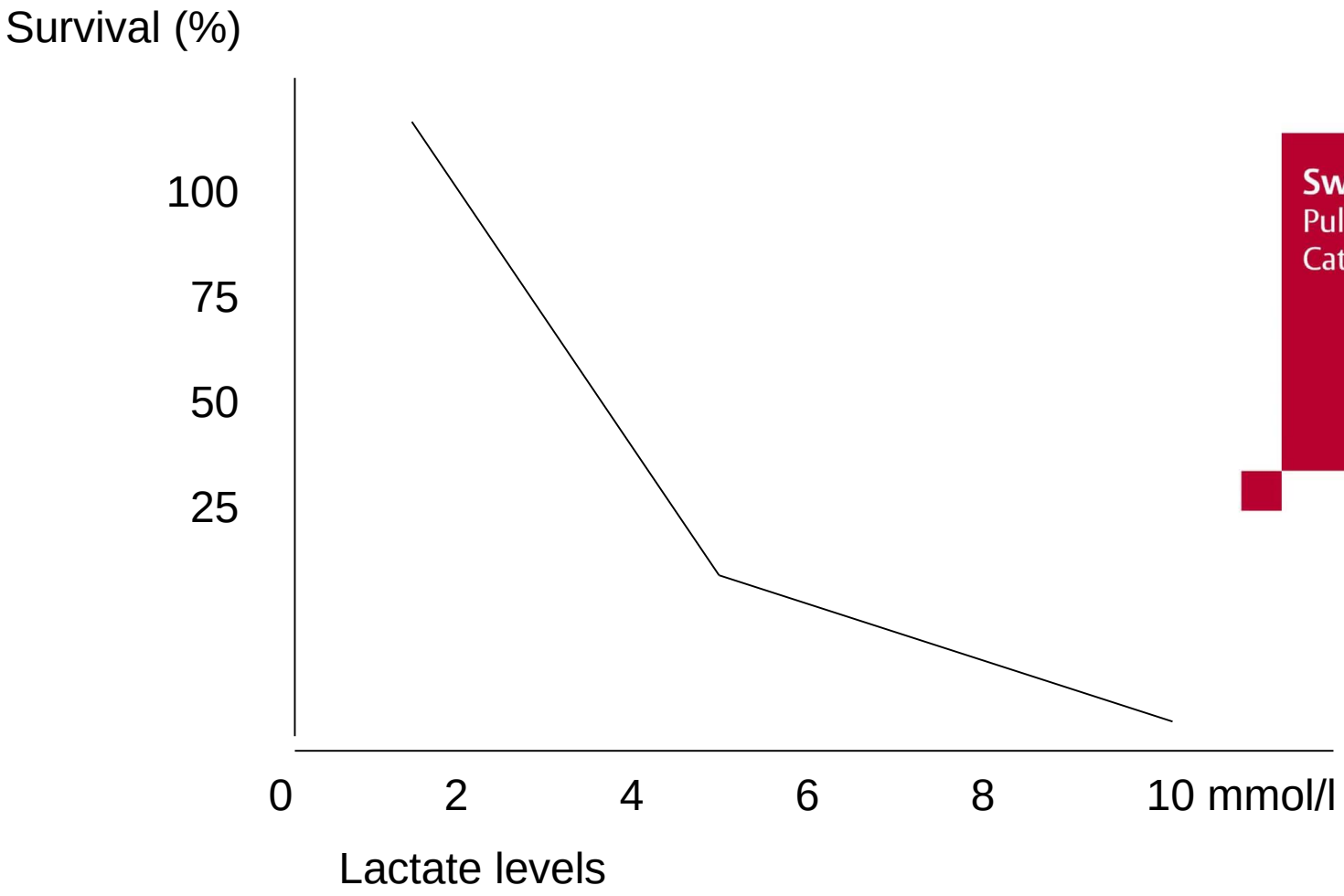
Patient stayed oliguric despite a truck load of furosemide. Hemodialysis was done and fixed his ECG.



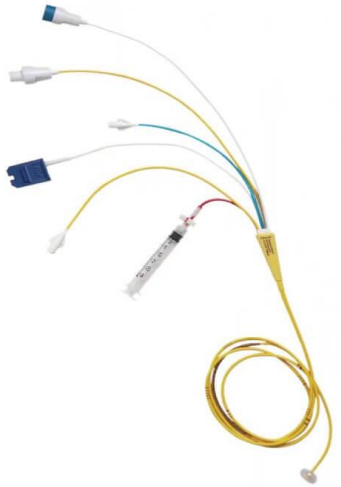


ECG paper speed at 50 mm/sec

Tissue hypoxia - lactate associated with shock (Circulation 1975)

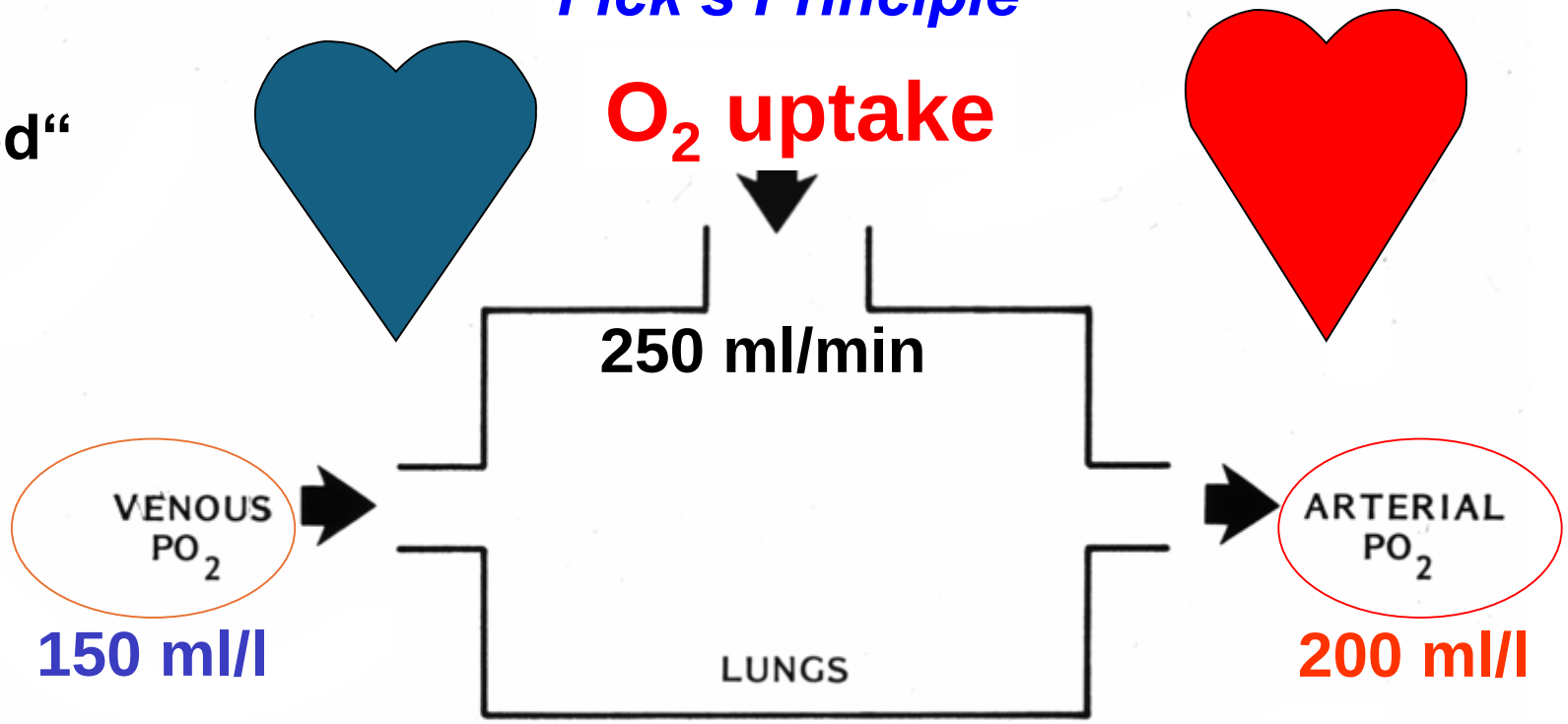


Swan-Ganz
Pulmonary Artery
Catheter



Fick's Principle

„Mixed"



$$\text{C.O. (5 L/min)} = \frac{250 \text{ ml/min}}{CaO_2 \text{ (200 ml/l)} - CvO_2 \text{ (150 ml/l)}}$$

C is "content" i.e. Oxygen content

But Laubenpieper was not in Shock!

- CVP 25 mm Hg
- PCWP 20 mm Hg
- CO 9 l/min
- What was the total peripheral resistance (115/60 mm Hg on admission)?
- What were DO_2, consumption VO_2 and O_2 extraction?
- No Swan-Ganz catheters, unless you can do this!

Total peripheral resistance, Ohm‘s and local resistance, Poiseullie‘s law

Georg Simon Ohm 1789-1854

$E_{Volt} = I_{Amps} \times R_{Ohm}$

$\Delta P_{mmHg} = CO_{L/min} \times R_{Dyn\ Sek/cm^5}$

CO (Q) = ΔP/R
TPR = (ΔP/HZV) x 80

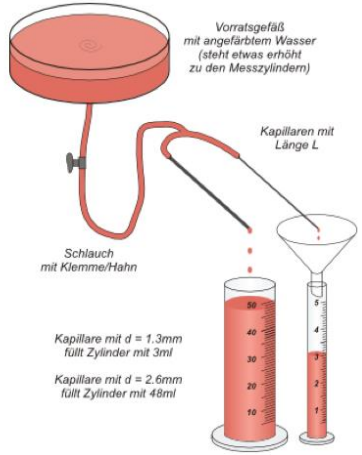
MAP = 70 mm Hg
CO = 9 L/min
LAP = 20 mm HG
Δ P = 50
X 80 = Far lower than normal

336 dyne/cm^{-5}

80 is the „fudge factor“ to convert simple numbers into CGS Units (cm/g/sec) called Dynes

Jean Léonard Marie Poiseuille 1797-1869

$$Q = \frac{\Delta P \times (\pi\ r^4)}{8\ \eta\ l}$$



High output heart failure

- Hb(13 g/dl) x 1.34 = 17.4 ml O_2/dl or 174 ml/l
- CO = 9 l/min
- DO_2 = delivered 174x9=1566 ml/min (O_2 offered per min.)
- VO_2 = consumed DO_2 x (SaO_2 – SvO_2)
- SaO_2 = 100%
- PvO_2 was 60 mm Hg; SvO_2 = 90% (40 mm Hg would be 75%)
- VO_2 = 156.6 ml/min (he utilizes 150 and should use 250)
- O_2ER = extraction 10% (normal O_2ER is 25%)
- Why does the Laubenpieper not utilize O_2?

$Glukose+2ATP+2H_2PO_4 \rightarrow 2Lactate+2ADP+2H_2O$

- Lactate is the end product of anaerobic glycolysis
- Production is 1 mmol/kg/h, circa 2000 mmol/day for our 80 kg Laubenpieper
- Production in skeletal muscle, GI tract, brain and erythrocytes
- The liver uses it (for gluconeogenisis) or for fuel

Glycolysis

Glycogen

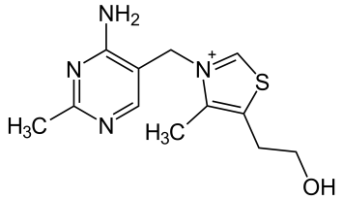
↓ ← Epinephrine

Glucose

↓ ← Alkalosis

2 Pyruvate —LDH→ 2 Lactate + 47 kcal

Tissue hypoxia
Endotoxin
Thiamine deficiency ⊣ PDH complex



(Oxidation) → 673 kcal

(Oxidation) → 652 kcal

(Gluconeogenisis) → Glucose

What leads to O_2 uncoupling?

- Poisoning cytochrome C oxidase
  - Cyanide, CO
- Dinitrophenol
  - Atractyloside (a plant glycoside)
  - Bongkrekic
- Metformin
- Disturbances of PDH
- Endotoxin (sepsis syndrome)
- Thiamine deficiency

Who first described Beriberi?

Nicholas Tulp aus Leyden, 1739
Rembrandt in the
“Anatomy demonstration”

Christiaan Eijkmann, polished rice, Nobel Prize 1929

Laubenpieper received Thiamine

- Within 12 hour Lactate fell to 1 mmol/l
- pH rose to 7.4
- HCO_3 increased to 24 mmol/l
- O_2 extraction was 20%
- Cardiac function improved within 1 week
- Liver and renal function normalized
- Signed out against medical advice

Plasma values (mmol/l) of Chrysemys picta marginata

Prior to hibernation

- Na 117
- Cl 73
- HCO_3 39
- AG 5

- Lactate 4
- K 2
- Mg 2.6
- Ca 3.7

Stuck under water for 5 months

- Na^+ 99
- Cl^- 44
- HCO_3^- 5 Δ34
- AG^- 50 Δ45

- $Lactate^-$ 185 Δ181
- K^+ 10
- Mg^{2+} 12
- Ca^{2+} 59

Reese et al. Respir Physiol. 2001;124(1):43-50.

A physiological lactic acidosis

HCO_3 decease is much lower than would be expected with the lactate increase.
The H^+ Ions were buffered with $CaCO_3$ in the turtle's shell.

Teaching points

- Acid-base problems are not acutely lethal.
- Hyperkalemia can be lethal.
- Swan-Ganz allows metabolic assessments: delivered DO_2 and consumed VO_2.
- AG (like mosm/L) is a clinical tool, not a law of nature.
- Lactic acidosis is today the most common cause of AG acidosis – there are two forms.
- Fick's principle is the key to circulatory, pulmonary, and renal function, as well as to metabolism.