Some peculiar blood gas analyses

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Woman, 68 years

Admitted for hip pain, hip prosthesis two years earlier

Clin exam: remarkable for a temp 38,5°C

Was taking carbamazepine, phenytoin and phenobarbital for epilepsy

WCC 12,000, CRP 125 mg/lit

Blood cultures grew *Staphylococcus aureus*

Twelve days later

Treated with Floxapen 6x 2 gr IV

Was found on a monday morning twelve days after admission: obtunded, tachypneic, tachycardic and hypotensive

Transfer to ICU

- pH: 7,24
- pCO_2: 22 mmHg
- paO_2: 87 mmHg
- HCO_3: 9,6 mMol/L
- Cl :90 meq/lit
- Na: 128 mmol/lit
- Lactate 2,5 mmol/mL

Normal renal function

Dip stick + ketones

Primary abnormalities in acid-base

	pH	PCO_2	HCO_3^-
Metabolic acidosis	↓↓	↓	↓↓
Metabolic alcalosis	↑↑	↑	↑↑
Respiratory acidosis	↓↓	↑↑	↑
Respiratoiry alcalosis	↑↑	↓↓	↓

Expected compensations

Metabolic acidosis: $PCO_2 = 1.5 \times [HCO_3^-] + 8 (\pm 2)$

Metabolic alcalosis: $PCO_2 = 0.7 \times ([HCO_3^-] - 24) + 40$

Acute respiratory acidosis: $[HCO_3^-]$ increase 1 mmol/lit for every 10 mmHg rise in pCO_2

Chronic respiratory acidosis: $[HCO_3^-]$ increase 3 mmol/lit for every 10 mmHg rise in pCO_2

Acute respiratory alcalosis: $[HCO_3^-]$ decrease 2 mmol/lit for every 10 mmHg decrease in pCO_2

Chronic respiratory alcalosis: $[HCO_3^-]$ decrease 4

In case of metabolic acidosis…

- Expected pCO_2 = 1.5 * HCO_3^- + 8 +/- 2 (Winter's formule)
- = 1.5 * 4,7 + 8
- = 22 mmHg

- Complete secondary adaptive response within 12-24 hours

- Other easier formula: Expected pCO_2 = HCO_3^- + 15

High anion gap metabolic acidosis

Ketonen	GOLD MARRK
Uremie	glycols, 5-oxoproline,
Salicylaten	L-lactate, D-lactate
Methanol	methanol, aspirin,
Aldehyde	renal failure,
Lactaat	rhabdomyolysis
Ethyleen glycol	keto-acidosis

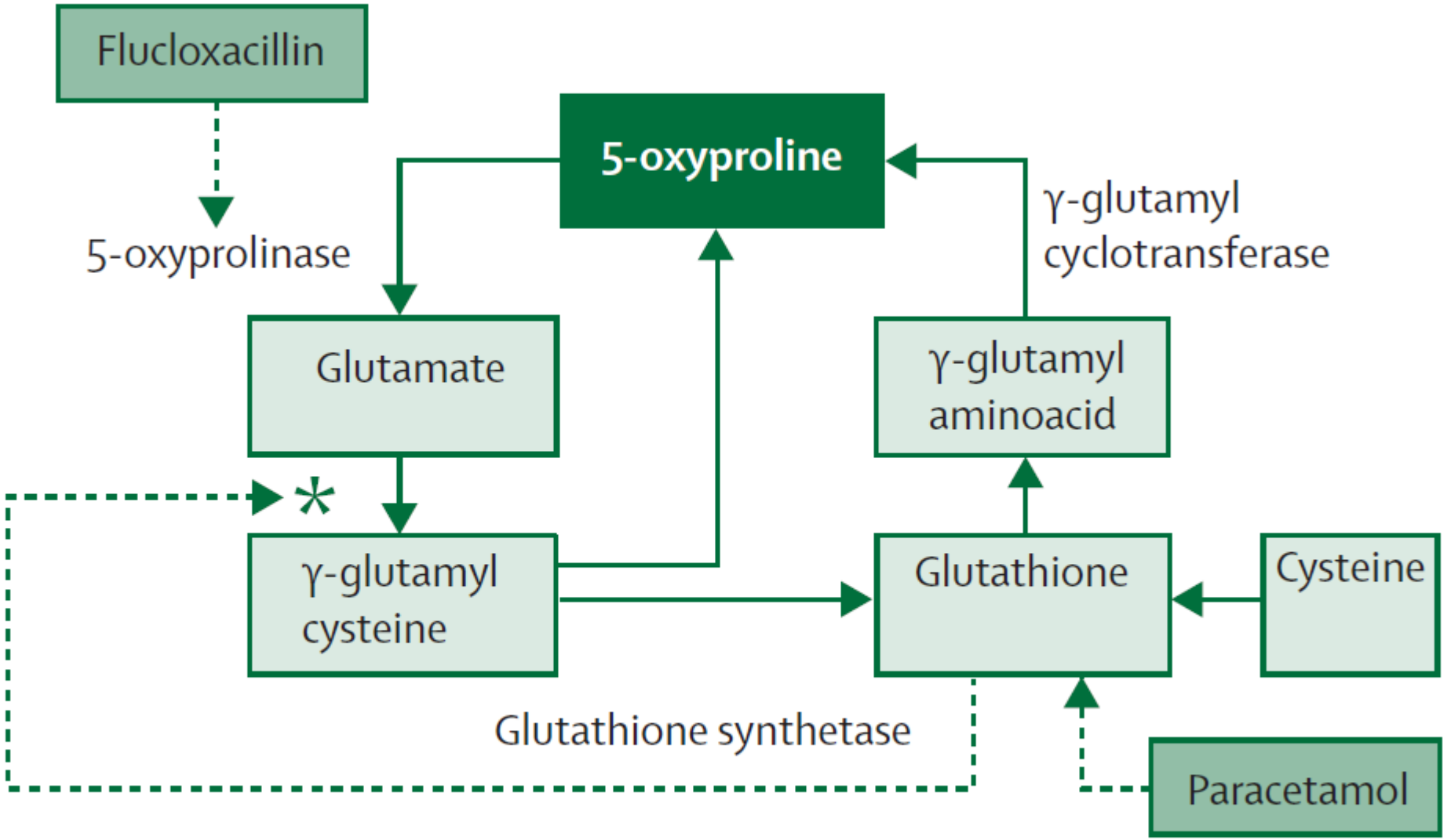


Figure: **The γ-glutamyl cycle**

Pyroglutamic aciduria or oxoprolinuria

- Rare cause of high anion gap metabolic acidosis
- Think of it in any patient who is malnourished and/or receives paracetamol and flucloxacillin
- Stop offending agents, administer calories
- Consider treating with N-acetylcystein

Young man found unresponsive

pH = 7,23, pCO_2 22 mmHg, bicarbonate 9 mmHg, pO_2 139 met O2 28%.

No fever, GCS 12/15 RR 23/min, euvolemic

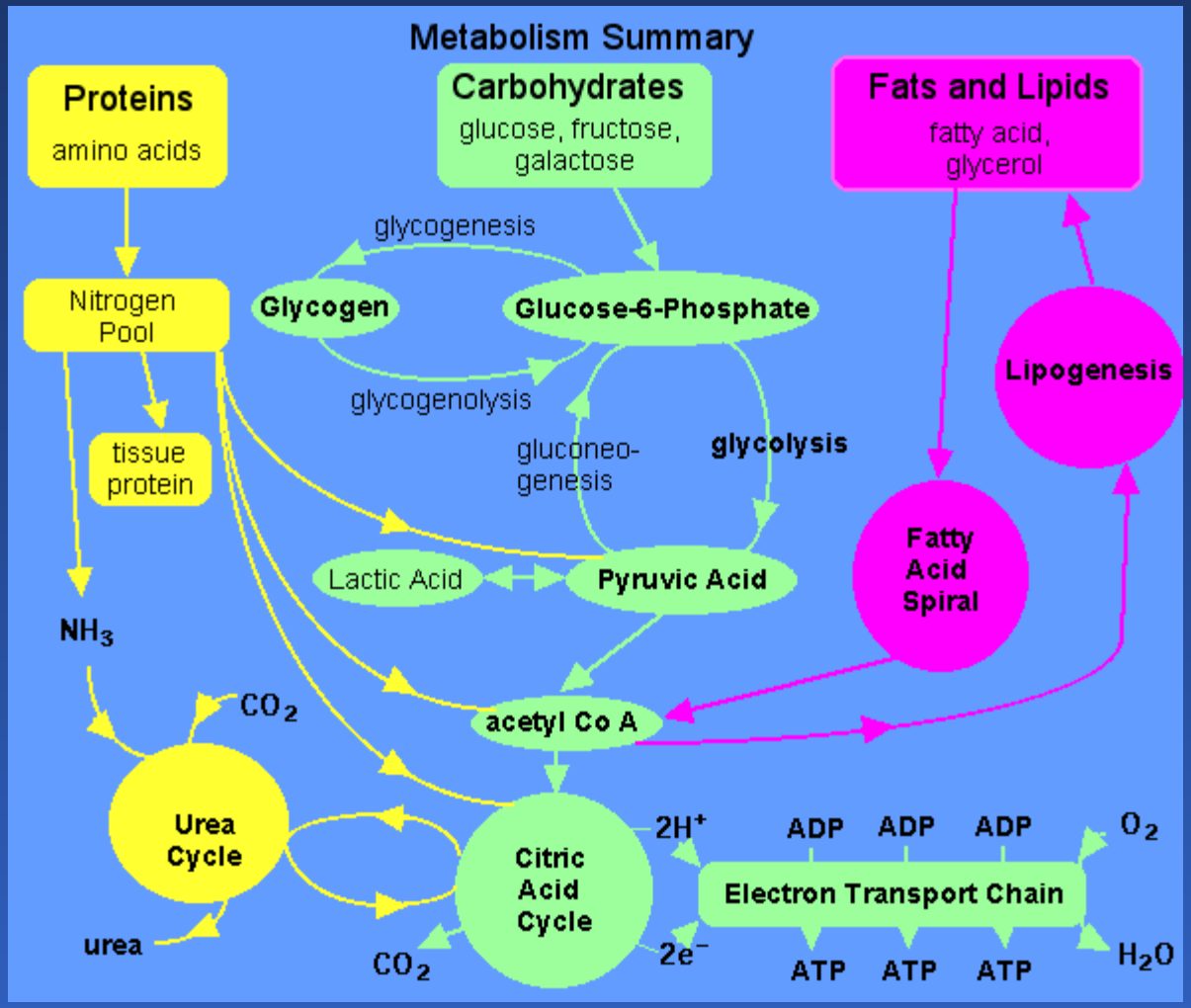
Leukocytosis (16,000 WBC, N 81%)
Sodium 140 meq/lit
Chloride 77 meq/lit
Potassium 3,4 meq/lit
Bicarbonate 9 meq/lit
Creatinin 1,4 mg/dl
Urea 55 mg/dl
Plasma ketones = trace

ECG "sinus tachycardia, 130/min"

Anion gap

Anion gap = 140 -77-9= 54

Lactate 17 mmol/lit


Metabolism Summary
Proteins
amino acids
Carbohydrates
glucose, fructose, galactose
Fats and Lipids
fatty acid, glycerol
glycogenesis
Nitrogen Pool
Glycogen
Glucose-6-Phosphate
Lipogenesis
glycogenolysis
tissue protein
gluconeo-genesis
glycolysis
Fatty Acid Spiral
Lactic Acid
Pyruvic Acid
NH3
CO2
acetyl Co A
Urea Cycle
Citric Acid Cycle
2H+
ADP ADP ADP
O2
Electron Transport Chain
urea
CO2
2e−
ATP ATP ATP
H2O

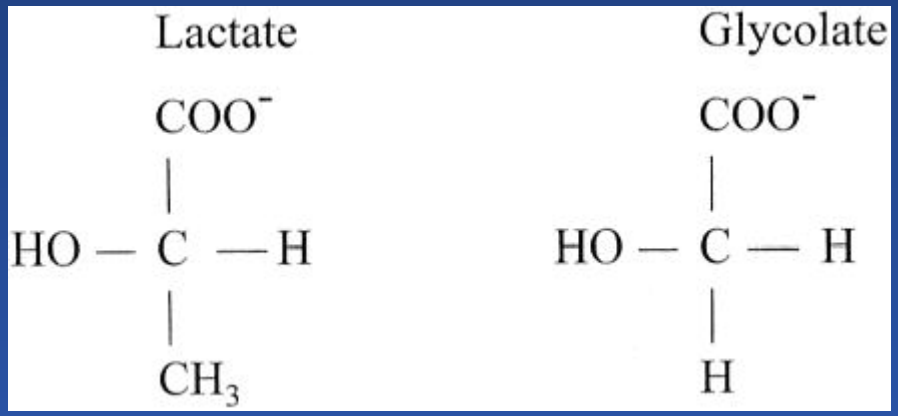
Etiology van lactic acidosis

- Increased lactate production by increase in anaerobic metabolism (epilepsy), by decreased oxygen delivery (shock, carbon monoxide, hypoxia)
- Primary problem of decreased lactate clearance (acute severe liver failure, severe septic shock
- Increased glycolysis (phaechromocytoma, psychogenic hyperventilation)
- Other type B cases not related to tissue hypoxia (glucophage, antiretrovirals, diprivan, thiamin deficiency, lymphoma)

If you are confronted with a high anion metabolic acidosis and the cause is not very obvious from the beginning (no reason to think of lactic acidosis or ketoacidosis), then measure the osmolal gap

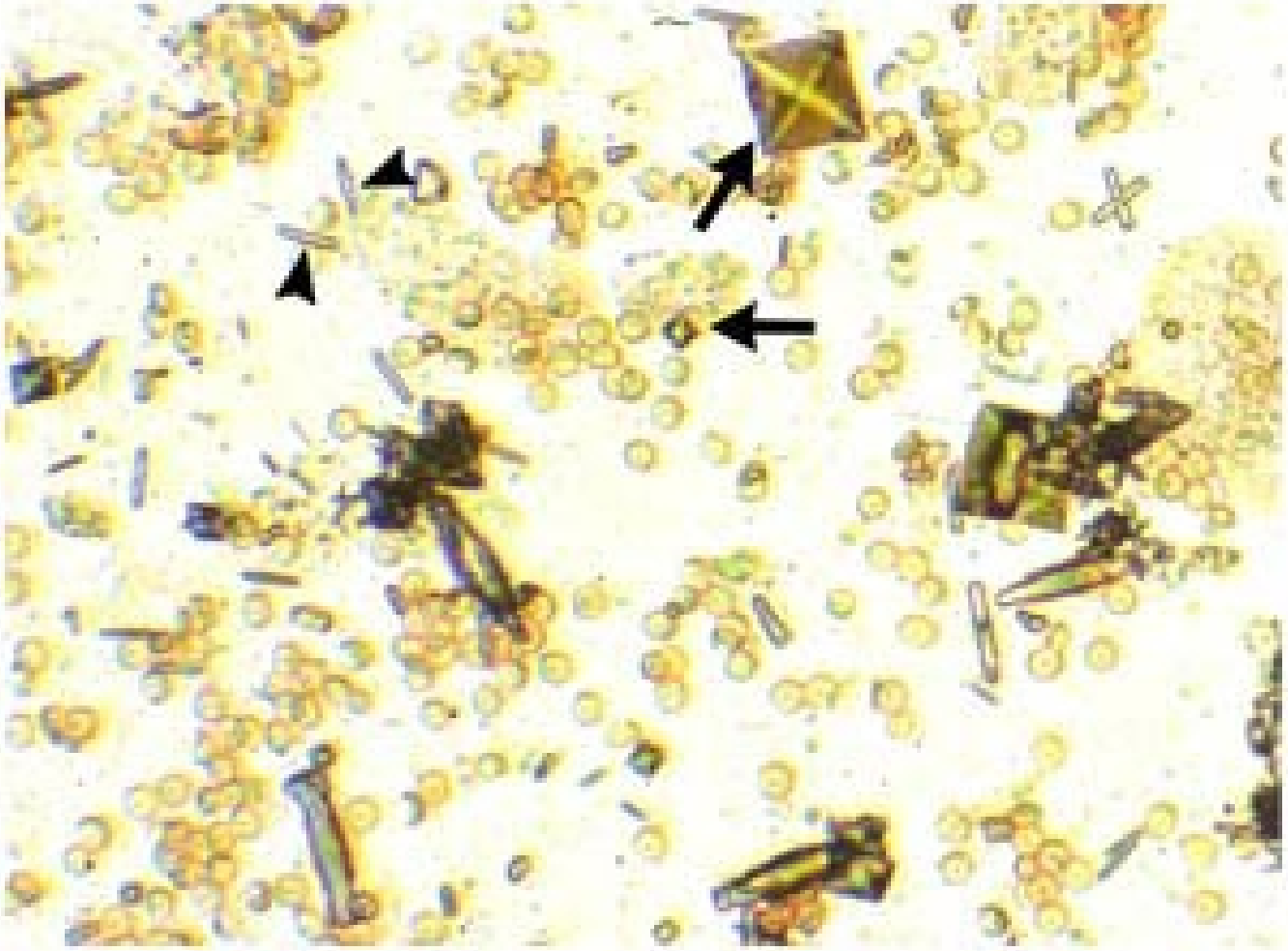
- Serum osmolality = 336 mosm/kg (nl 275-290 mosm/kg)
- Measured osmolality = 2 x Na + glucose/18 + ureum/6= 301 mosm/kg
- Osmolar gap = 35

Falsely elevated lactate on blood gas machine
Normal level when measured in the lab

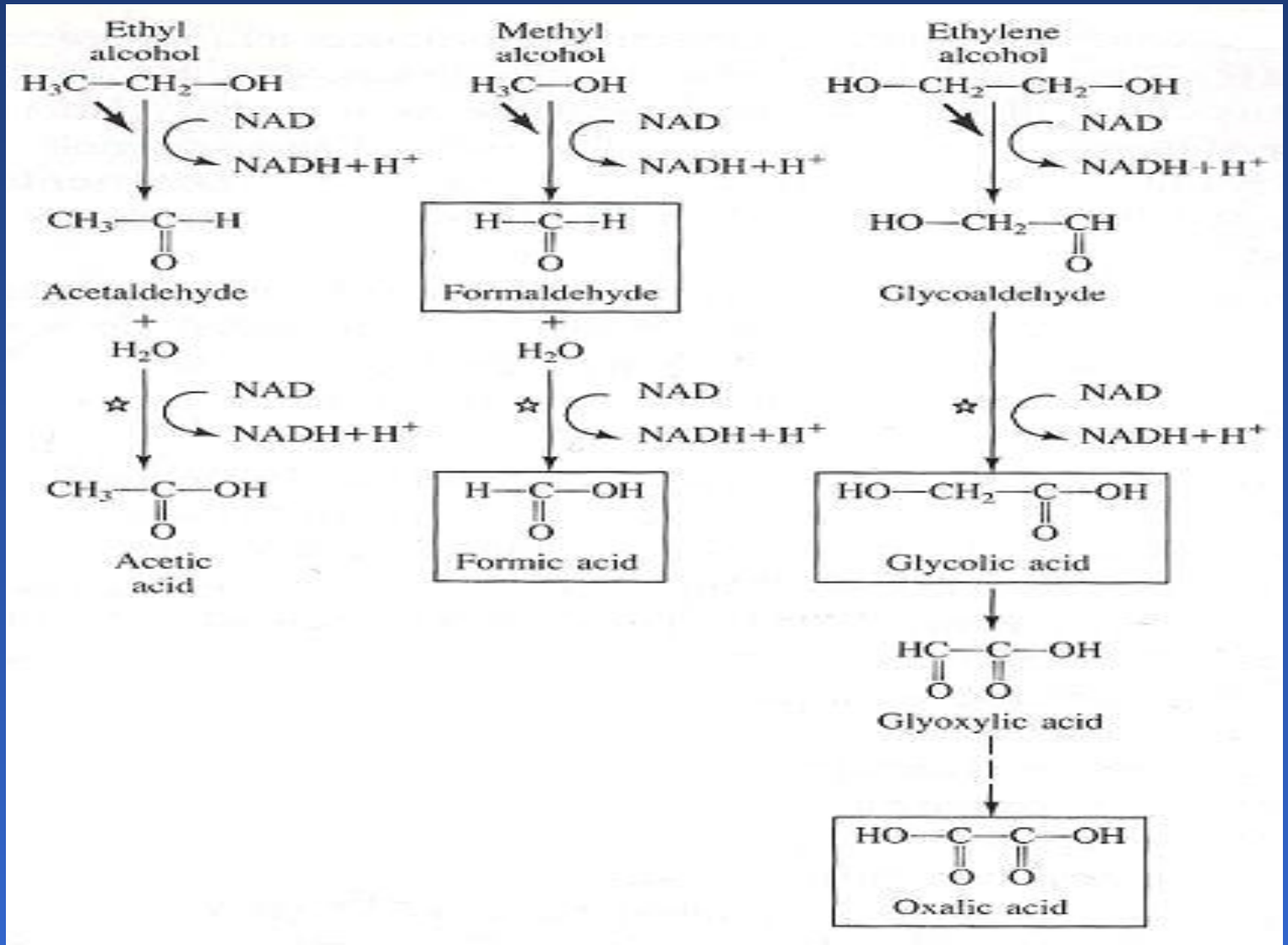


Point-of-care: lactate oxydase

Plasma sample: "lactate gap"



Ethyleen glycol intoxication



Ethyleen glycol intoxication

- High anion gap metabolic acidosis
- Osmolal gap
- Loss of consciousness
- Needle shaped crystals in the urine
- Lactate gap

Ethyleen glycol intoxication: treatment

- Ethanol infusion 0.6 g/kg loading dosis, 100-200 mg/kg/hour
- Hemodialysis
- Thiamine and pyridoxine supplements
- Fomepizole as antidotum

49-year old lady

- Referred for low oxygen saturation by the pre-operative clinic
- Was scheduled for curettage, hysteroscopy and possible resection of uterin fibroids (heavy menstrual bleeding despite treatment with medroxyprogesterone acetate)
- On baseline blood results: iron-deficient anaemia

Past medical history

- Tonsillectomy 28 years ago
- Tubal ligation 7 years ago

- Coughing and cyanosis were noted in the recovery room after tubal ligation
- Hypertension, mild asthma
- Treatment: Selozok, Brufen, Ferrogradumet, Duovent, Seretide

Clinical examination and baseline preop assessment

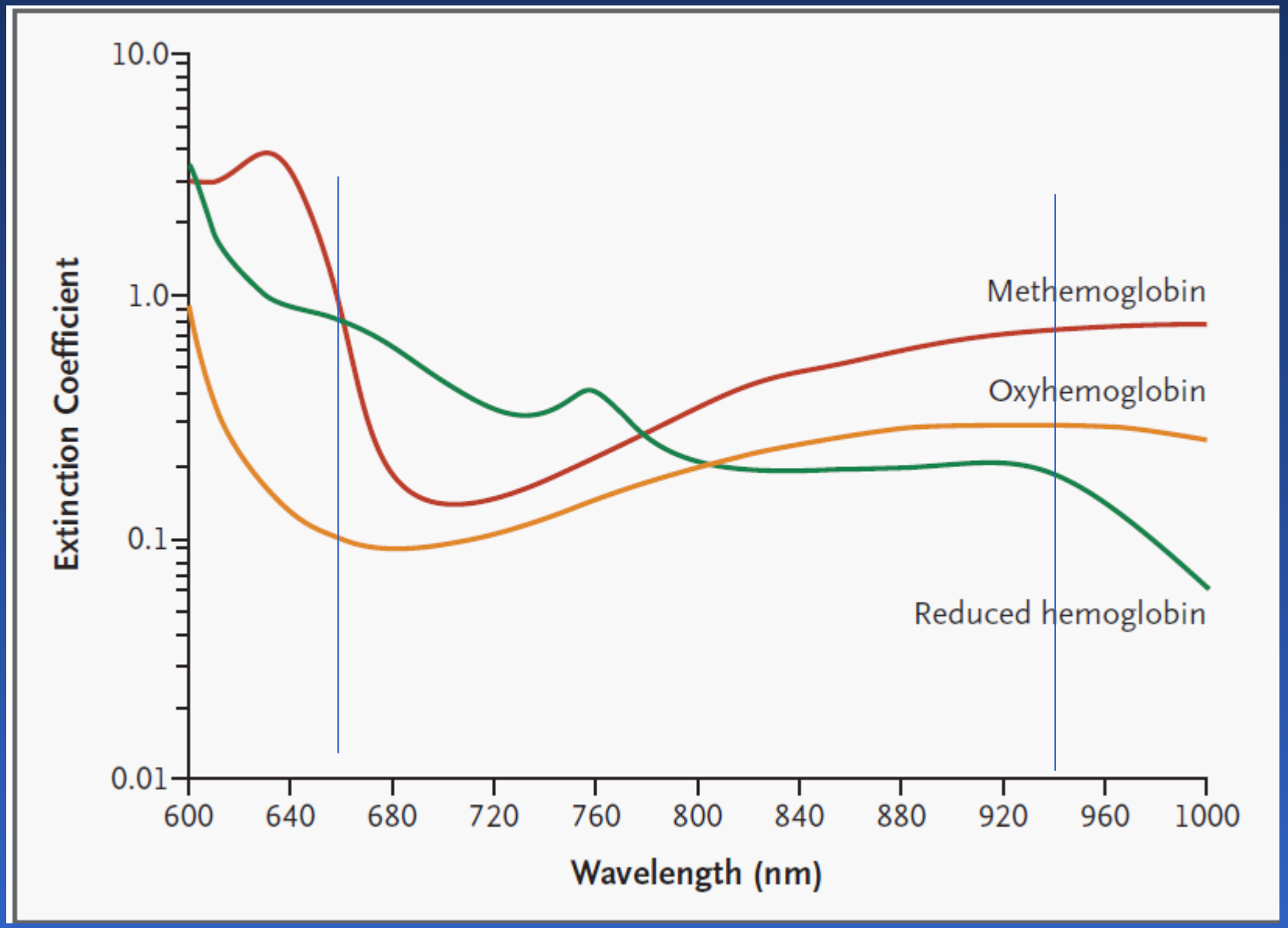
- Blood pressure 160/80 mmHg
- Heart rate 97/min
- Respiratory rate 24/min
- Slightly prolonged expiration and wheezing
- **Pulse oximetry 93%,** increased to 98% with O_2
- Normal ECG, chest X-ray and baseline blood tests
- Pulmonary function tests: normal
- Ultrasound heart: no shunt

Causes of low oxygen saturation on pulse oximetry

- Hypoxemia due to hypoventilation, mismatching of ventilation and perfusion, right-to-left shunting and diffusion abnormalities
- Abnormal hemoglobin variants
- Methemoglobinaemia
- Sulfhemoglobinaemia
- Intravenous dyes
- Blue nail polishes

Limitations of pulse oximetry

- It does not directly measure oxygen saturation
- It measurs light absorbance of blood components
- Two wavelengths of light (660 nm, red and 940 nm, infrared) are emitted
- Oximeter calculates the mean light absorbances of the two wavelengths, which are compared with values obtained from healthy volunteers (varying degrees of hypoxemia)


10.0
1.0
0.1
0.01
Extinction Coefficient
600
640
680
720
760
800
840
880
920
960
1000
Wavelength (nm)
Methemoglobin
Oxyhemoglobin
Reduced hemoglobin

You need to draw a blood sample

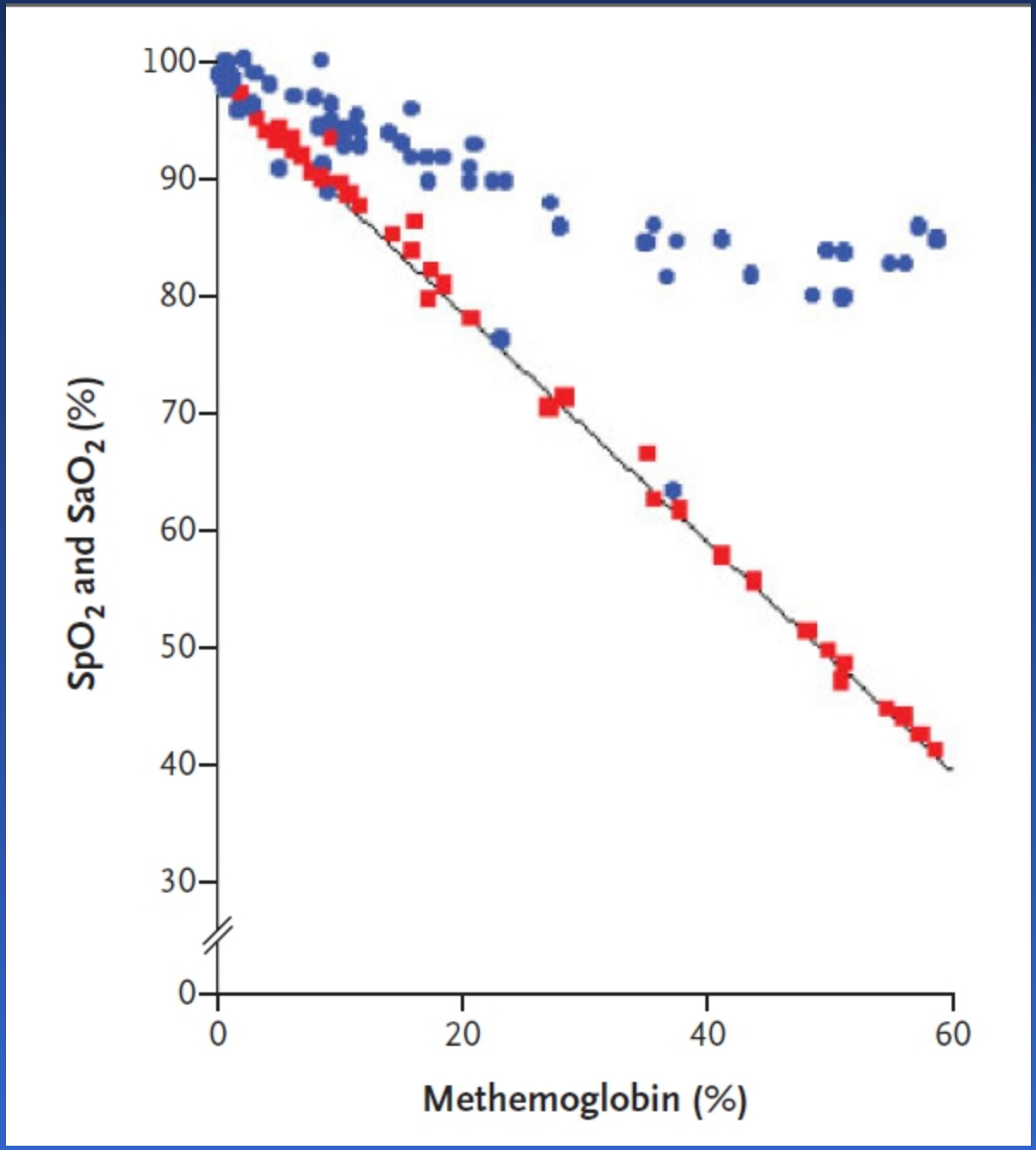
- Hemoglobin 12.5 gr per dl
- SpO_2 94%
- Fract sat 89%
- SaO_2 98%
- pH 7.43
- pO_2 98 mmHg
- pCO_2 33 mmHg

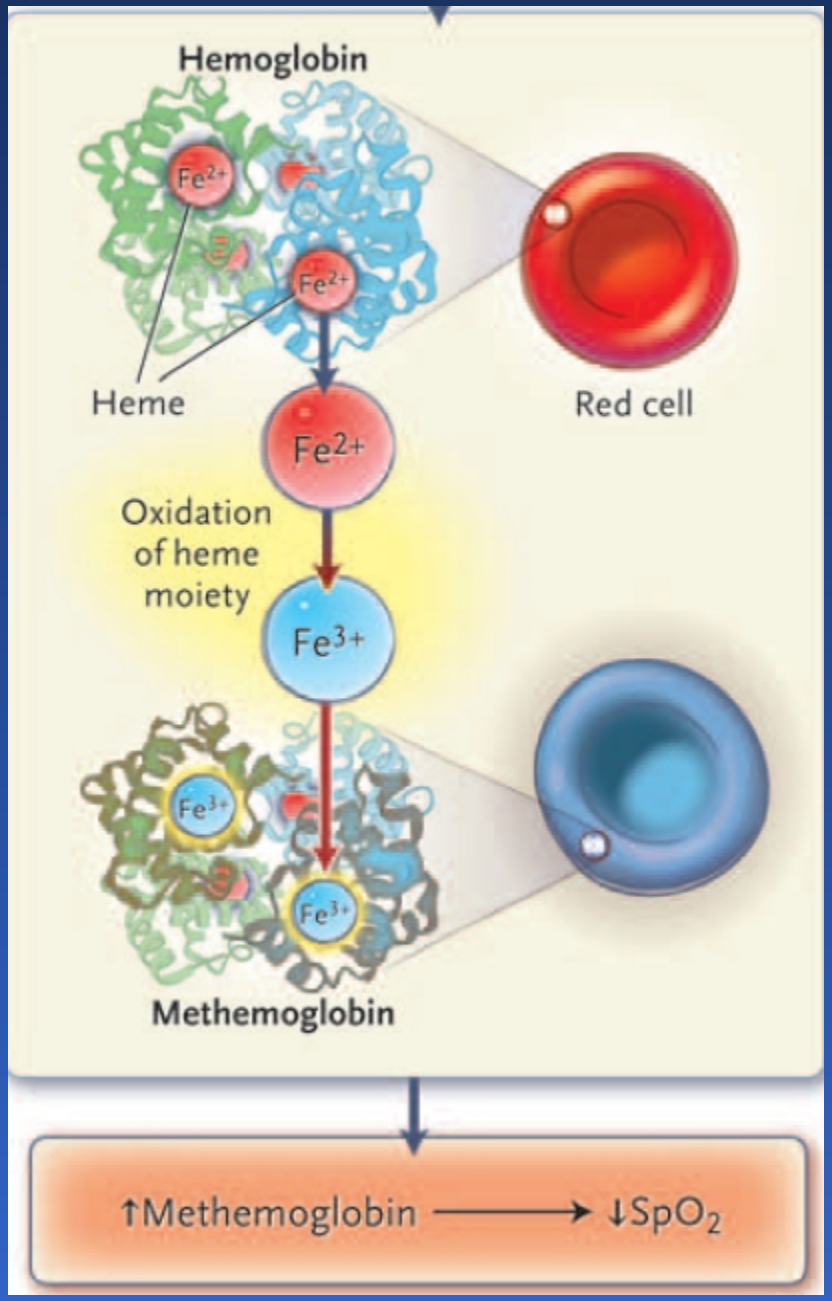
Term	Formula
Oxygen saturation by pulse oximetry (SpO_2)	$k \times (AC_{660}/DC_{660})/(AC_{940}/DC_{940}) + b$
Functional saturation of oxygen (SaO_2)	$[HbO_2]/([HbO_2] + [\text{reduced Hb}])$
Fractional saturation†	$[HbO_2]/([HbO_2] + [Hb] + [COHb] + [metHb]) =$ $[HbO_2]/[\text{total Hb}]$

SpO_2 = pulse oximetry: a diode on the oximeter probe emits two wavelengths (660 nm, 940 nm, It measures absorbance at each wavelength, The absorbance of deoxygenated hemoglobin is different than oxygenated hemoglobin and this is true for both wavelengths,

SaO_2 = in blood gas analysis: measured from pH, temperature and paO_2

Fractional saturation on a co-oximeter = blood gas analysis: multiple wave length spectrophotometers, measures fraction of hemoglobin, oxygenated hemoglobin, methemoglobin and carboxyhemoglobin


100
90
80
70
60
50
40
30
0
0
20
40
60
SpO2 and SaO2 (%)
Methemoglobin (%)

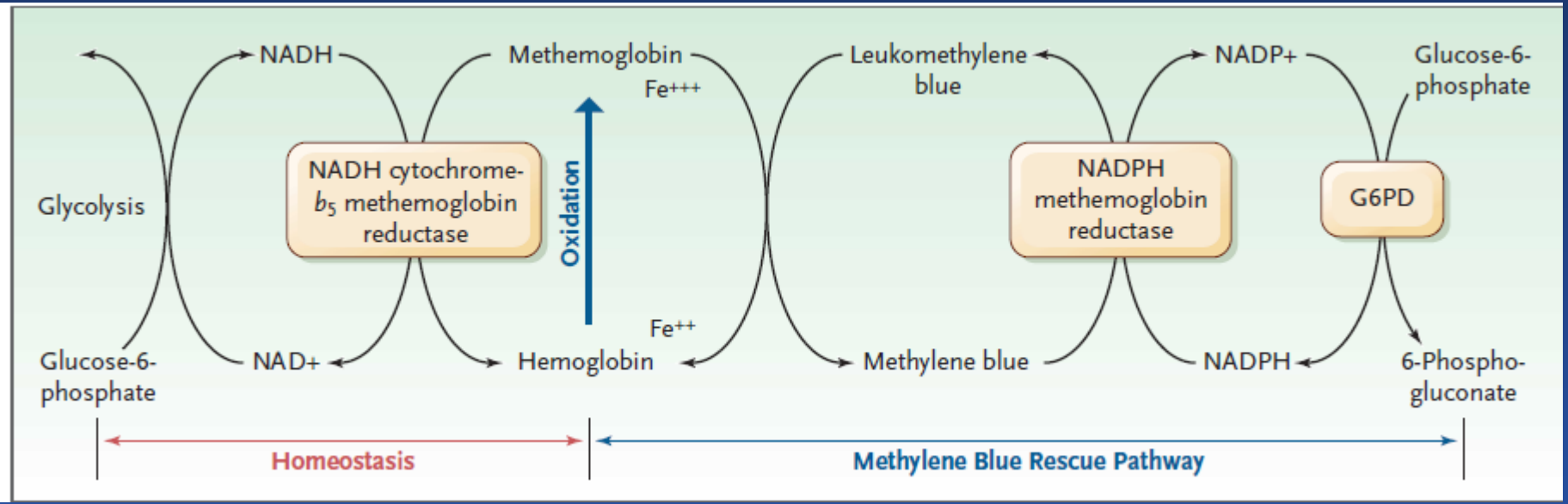


Methemoglobin is formed by oxidation of the iron moiety of hemoglobin

Fe3+ Heme is incapable of binding oxygen and impairs the release of oxygen

Cyanosis may be evident at a methemoglobin concentration of 1,5 gr per dl (10% of hemoglobin)

Normally an equilibrium exists between the proportions of hemoglobin and methemoglobin



Methemoglobin is present when

1. Increased production of methemoglobin (exposure to drugs such as topical anaesthetics)
2. Abnormal hemoglobin (methemoglobin becomes resistant to reduction)
3. Decreased activity of NADH-cytochrome b5 reductase (autosomal recessive disease)

Final diagnosis

- Methemoglobin level on a sample measured in a co-oximeter: 8.5%
- Cytochrome b5-reductase 6.9 IU per gram hemoglobin (normal value 10-19)
- Autosomal recessive inherited cytochrome b5-reductase deficiency

51-year old man

- Seen in the emergency room with a 3-day history of fever, fatigue, headache, coughing and sore throat
- Past medical history:
  - diabetes mellitus type 1
  - hypertension, hyperlipidemia
  - glaucoma
  - dermatitis herpetiformis
  - frequent episodes of headache, also a possible seizure
- Was on insulin, lisinopril, dapsone, metoprolol, atorvastatin, aspirin

Clinical examination

- BP 164/75
- Pulse 81 per minute
- Temp 37,7°C
- Respiratory rate 16/min
- Clear auscultation, no murmurs
- Oxygen saturation 85-90%

Lab results

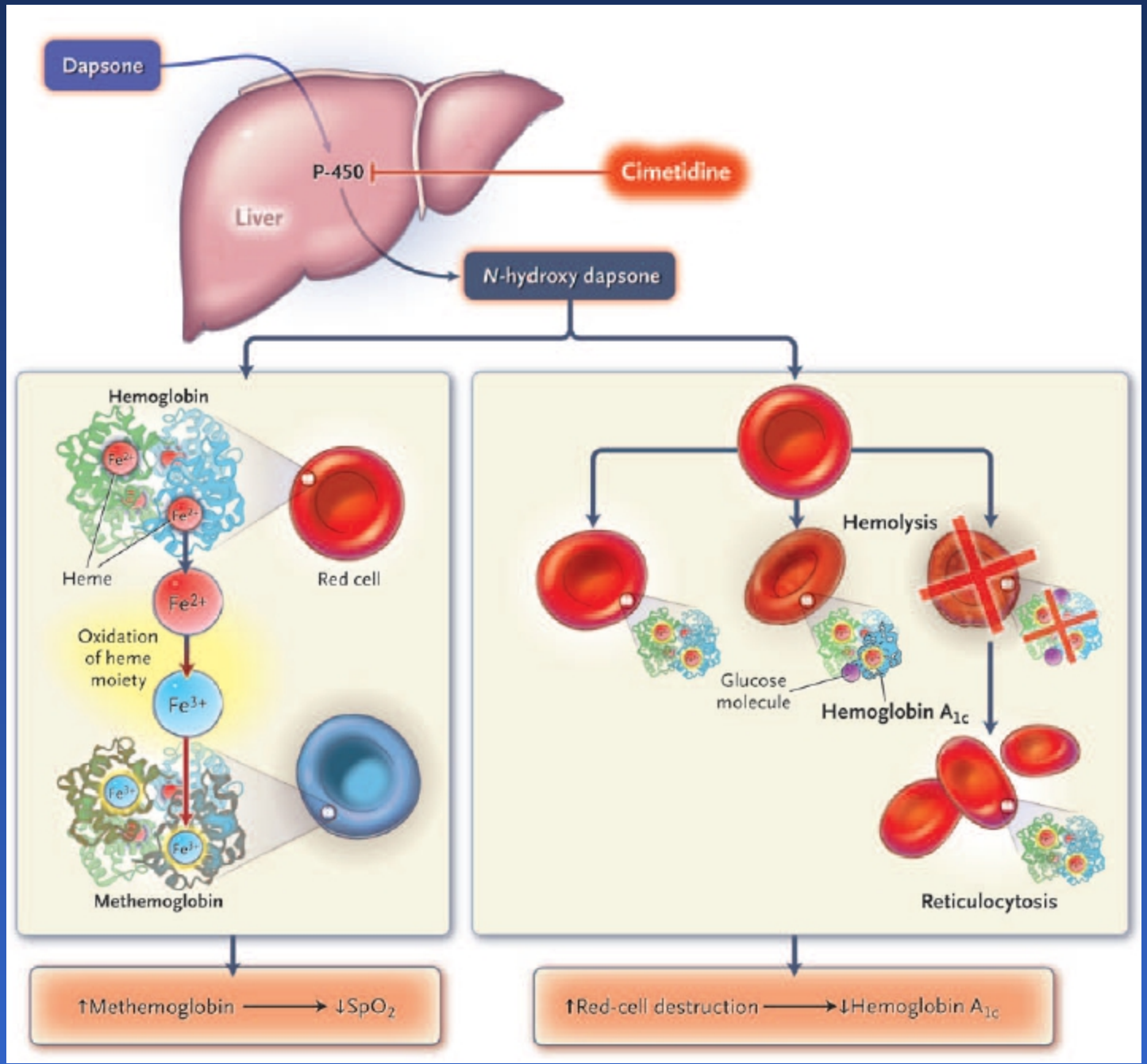
Variabele	1-7-2013	Normal values
Hemoglobin	13,8 g/dl	12-16
Reticulocyte count	6,6%	0.5-2.5
White cell count	13,600/mm^3	4000-10000
% neutrophils	63%	38-77
Hemoglobin A1c	4.7%	3.8-6.4
Glucose level	227 mg/dl	70-110
Total bilirubin	2.6 mg/dl	0.0-1.0
Direct bilirubin	0.8 mg/dl	0.0-0.4
AST	24 U/lit	< 32
LDH	405 U/lit	135-250
Alkaline phosphatase	70 U/lit	< 150
MCV	92	80-100
hematocrit	39%	41-53

Two striking elements:

- Low oxygen saturation
- Low hemoglobin A1c levels despite poor control of diabetes

Blood gas analysis with co-oximeter

- p_aO_2 83 mHg
- Oxygen saturation blood gas 96%
- Oxygen saturation pulse oximetry 87%
- Arterial blood methemoglobin level 16%


Dapsone
P-450
Cimetidine
Liver
N-hydroxy dapsone
Hemoglobin
Heme
Red cell
Oxidation of heme moiety
Methemoglobin
Hemolysis
Glucose molecule
Hemoglobin A1c
Reticulocytosis
↑Methemoglobin → ↓SpO2
↑Red-cell destruction → ↓Hemoglobin A1c