

Biological causes of variation of test results

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- **The discrimination between normal and abnormal results is affected by various physiological factors which must be considered when interpreting any given result.**
- **These include:**

- ***AGE***
- ***SEX OF THE PATIENT***
- ***PREGNANCY***
- ***MENSTRUAL CYCLE***
- ***RACE***
- ***EFFECTS OF ENVIRONMENTAL FACTORS***
- ***SEASONAL INFLUENCES***
- ***CIRCADIAN VARIATION***
- ***POSTURE OF THE PATIENT***
- ***EFFECTS OF EXERCISE***
- ***EFFECTS OF DIET***
- ***SMOKING***

AGE

- **different reference ranges for neonates, children, adults, and the elderly**
- **Newborn infant:**
- **the body fluids reflect:**
- **trauma of birth**
- **the changes related to adaptation to an independent existence**
- **maturity of the infant at birth (HbA - HbF)**
- **The serum activities of several enzymes (CK, AST, GMT) are high.**
- **The concentration of bilirubin rises following birth and peaks about the 3rd to 5th day of life = physiological jaundice of the newborn.**

Examples

- ***total body water***: newborn 80% of body weight, the elderly 50%
- most important ***enzyme activities*** (ALT, AST, ALP, GMT, LD, HBD, CK) higher in childhood (growth and development)
- ***ALP***

< 1 m.	0.6 – 5.3 $\mu\text{kat/l}$
1 m. – 15 y.	1.0 – 4.8 $\mu\text{kat/l}$
adults	0.5 – 2.4 $\mu\text{kat/l}$
- examples of successive increase during life: ***LDL-chol, hcy***
- ***NH₃/P***

0-1 m.	$\leq 100 \mu\text{mol/l}$	> 1 m.	$\leq 55 \mu\text{mol/l}$
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- ***K/S***

0-1 m.	4.0-7.7 mmol/l	adults	3.8 – 5.5 mmol/l
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Examples

- ***Fe /S*** **0-1 m. 9 - 36 $\mu\text{mol/l}$** **adults 10 -25 $\mu\text{mol/l}$**
- ***ferritin /S***

< 18 y.	15 – 120 $\mu\text{g/l}$	
18 – 45 y.	♂ 30 – 220 $\mu\text{g/l}$	♀ 10 – 70 $\mu\text{g/l}$
45 – 55 y.	♂ 30 – 350 $\mu\text{g/l}$	♀ 20 – 110 $\mu\text{g/l}$
> 55 y.	♂ 30 – 400 $\mu\text{g/l}$	♀ 30 – 120 $\mu\text{g/l}$
- ***total bil /S*** **1st weeeek ≤ 150 (300) $\mu\text{mol/l}$** **adults ≤ 20 $\mu\text{mol/l}$**
- ***creatinin***

0-2 d.	20-140 $\mu\text{mol/l}$	2-7 d.	17-100 $\mu\text{mol/l}$
7-14 d.	15-80 $\mu\text{mol/l}$	14-28 d.	10-70 $\mu\text{mol/l}$
< 1 y.	17-50 $\mu\text{mol/l}$	1-5 y.	17-60 $\mu\text{mol/l}$
5-10 y.	26-90 $\mu\text{mol/l}$	> 10 y.	35-110 $\mu\text{mol/l}$
- **The same values in both children and adults: pH and osmolality**

SEX OF THE PATIENT

- **Different values since pubescence occurs**
- sex hormones and their metabolites
- Fe/S, ferritin
- hemoglobin
- lipoproteins
- urea, creatinin
- uric acid
- homocysteine
- ALT, AST, ALP, GMT, LD, CK
- CRP
- generally higher values in males

PREGNANCY

- **Change of the values:**
- **Estradiol**
- **FSH**
- **LH**
- **Progesterone**
- **Prolactin**
- **hCG**

PREGNANCY

- **Increased plasma volume → hemodilution**
- **↑ in glomerular filtration rate (↑ creatinine clearance)**
- **↑ in total urine volume, mainly during the 3rd trimester (25%)**
- **↑ in serum apolipoproteins, TG and chol**
- **↑ in ALP activity**
- **↑ in ceruloplasmin, T₄, acute phase proteins (CRP) synthesis**
- **relative deficiency of Fe, ferritin**
- **↓ hcy**

MENSTRUAL CYCLE

- **Influents mainly:**
- **Estradiol**
- **FSH**
- **LH**
- **Progesterone**

- **Hcy, chol, Fe**

RACE

Examples:

- **Afroamericans ↓ glucose tolerance than Caucasians**
- **Afroamericans ↑ total CK and LD than Caucasians**
- **Hispanics and Afroamericans ↑ AFP and hCG**
- **Afroamericans ↑ Cu /S**
- **Far-east Asians ↑ salivary AMS**

EFFECT OF ENVIRONMENTAL FACTORS

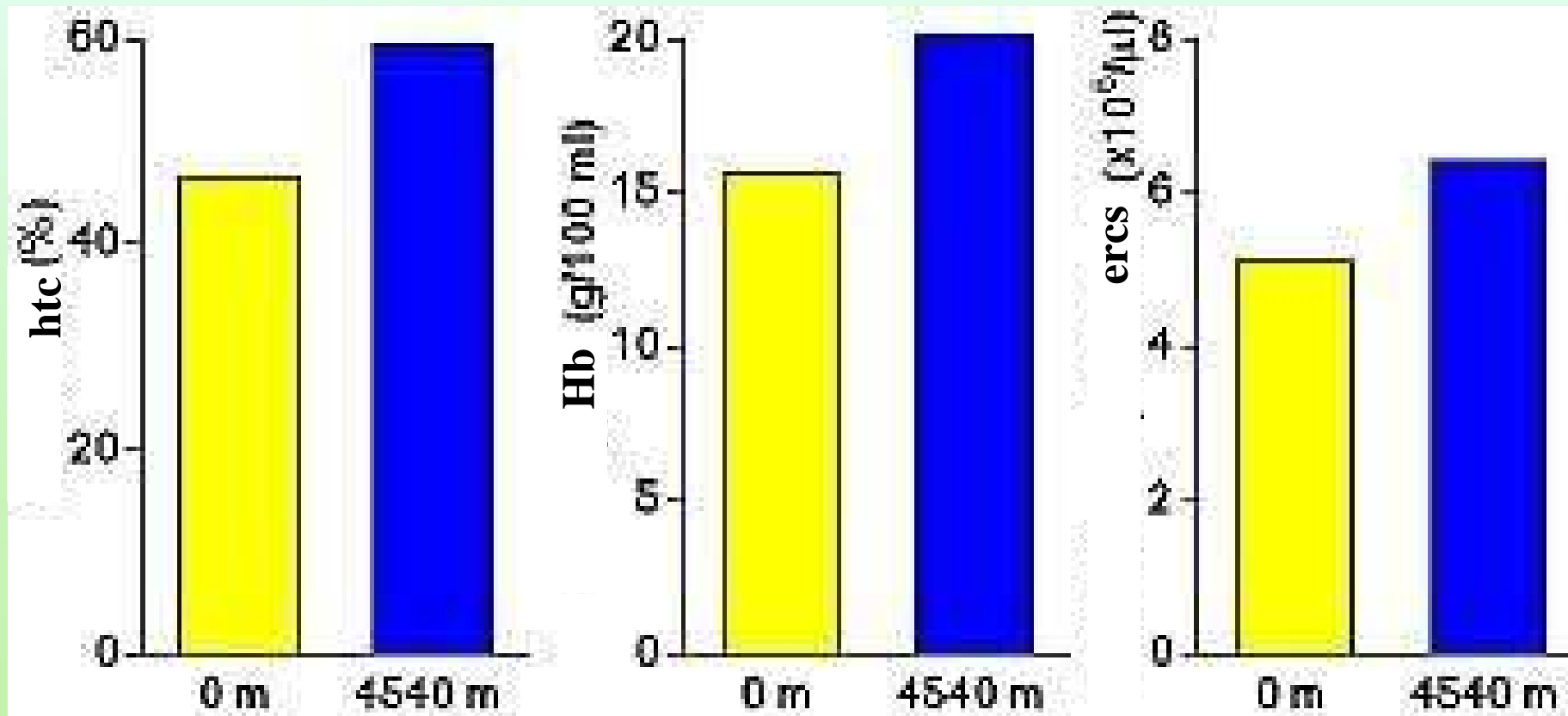
- **geographical location** (drinking water composition, pollution)
- **altitude**

Effects of altitude

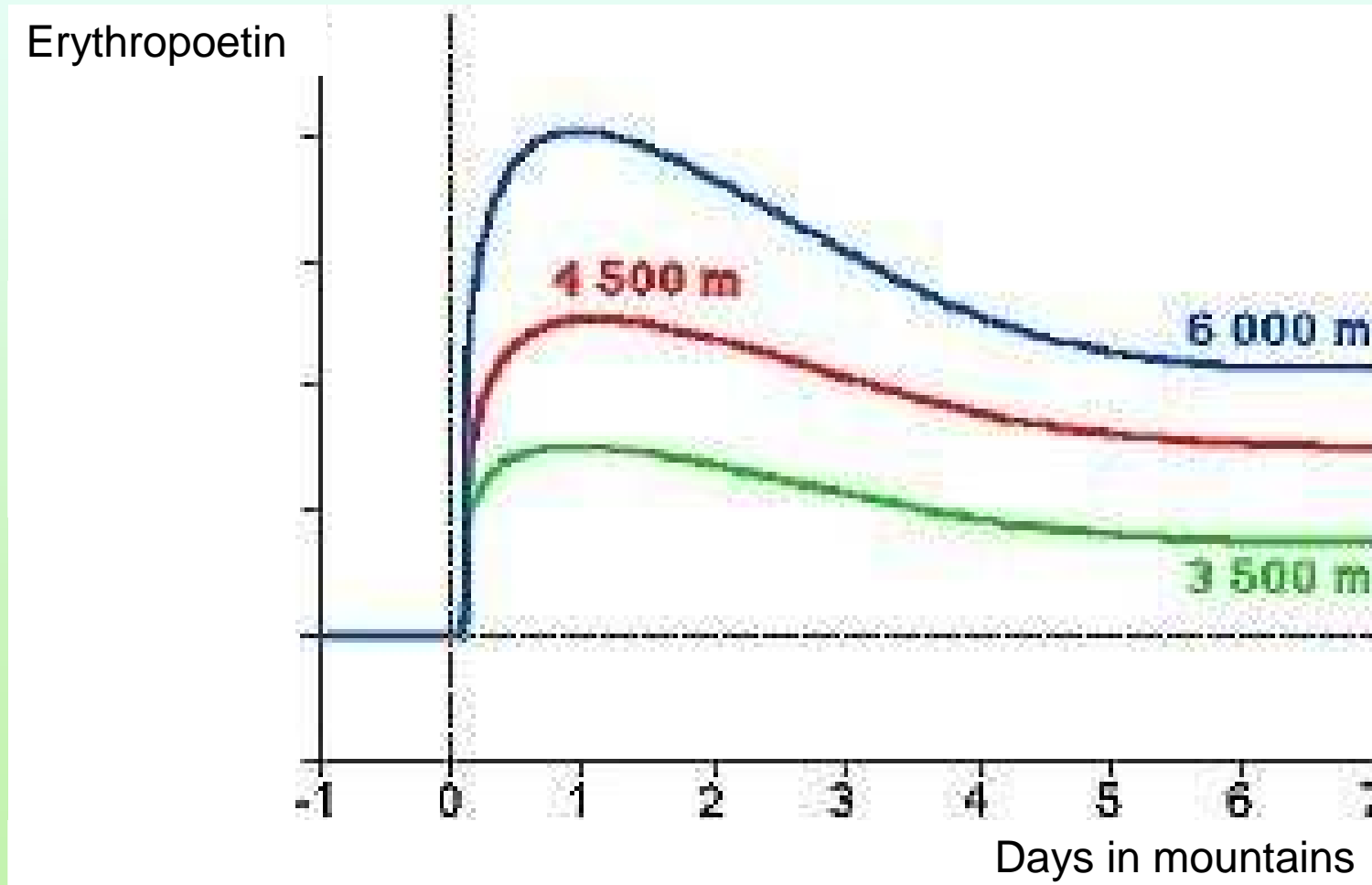
- **↑in:**
- **Haematocrit**
 - » (difference sea level – 1 400 m.a.s.l. = 8%)
- **Haemoglobin**
- **Erythropoetin**
- **CRP** (difference sea level – 3 600 m.a.s.l. = 65%)

Increase in htc, Hb, ercs

Initially, Hb increases as a result of plasma volume decline caused by *dehydration* (trend not to drink + water lost by hyperventilation + lower humidity), subsequently increased production of ercs (\leftarrow erythropoetin) gives in.



Erythropoietin synthesis and erythrocytogenesis starts to increase in 2 hours after hypoxia occurs.



SEASONAL INFLUENCES

on the composition of body fluids are small.

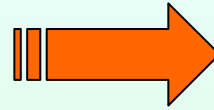
- **Evaluations of seasonal variation are difficult, since they depend on the definition of a season and on the magnitude of temperature change from one season to another. Day-to-day variability in the composition of body fluids is greater in summer than in winter.**
- **Examples:**
- **D vitamin ↑ in summer (length of sun exposure)**
- **thyroid hormones ↓ in summer (20%)**

CIRCADIAN VARIATION

- = time when sample was taken
- examples:
- cortisol maximal value at 6 a.m.
 morning 250-650 nmol/l
 afternoon 50-280 nmol/l
- Fe 30% higher in the morning
- creatinine 10-20% higher in the afternoon
- STH secreted at midnight

POSTURE OF THE PATIENT

- **head pressure → redistribution of body fluids**
- **The blood volume of an adult in an upright position compared to an adult in a lying position is typically 600 - 700 ml less. Fluid reduction in plasma is associated with a comparable increase in the plasma protein concentration.**
- **adrenalin and noradrenalin values in an upright position almost 2times higher compared to a lying position**



blood drawing to the

sitting patient

EFFECTS OF EXERCISE

- **Exercise changes blood levels of all substances that participate in energy metabolism, e.g. glucose, lactate, FA, phosphate, creatinine.**
- **Strenuous exercise can release enzymes from tissues.**
- **Blood pH, oxygen saturation, and venous bicarbonate are decreased.**
- **Long-term exercise increases the concentrations of sex hormones.**

EFFECTS OF DIET

- **The sample may be inappropriate if taken when the patient is fasting or after a meal.**

Define the term fasting patient!

Fasting patient

- **didn't eat 10-12 h. during night**
 - **was all quiet (didn't ride a bicycle or walk a long time),**
 - **didn't smoke,**
 - **didn't drink coffee or alcohol or sweetened drinks**
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- **blood drawing between 6 – 9 a.m.**

EFFECTS OF DIET

- **food rich in fats :** ↑ TG, chol;
 ↓ nitrogen compounds (uric acid)
- **food rich in proteins:** ↑ urea, uric acid, phosphates
- **food rich in saccharides:** ↑ ALP, LD;
 ↓ TG, chol, total proteins
- **vegetarians:** ↓ uric acid, urea, ammonia, total and
 LDL-chol, TG;
 ↑ bil;
 alkalization of urine (phosphate stones!)

EFFECTS OF DIET

- *immediate food intake :*

↑ **glc, TG, uric acid, Fe, Na**

↓ **LD**

- *other examples of diet interferences:*
- **gFOBT test : violation of the blood- and Fe –less diet**
- **clearance determination: insufficient fluid intake**

EFFECTS OF DIET – LONG-TERM FASTING

= FASTING LONGER THAN 24 HOURS

- glycogenolysis in liver (→ glc - energy for CNS and ercs)
- proteolysis in muscles (→ AA for gluconeogenesis)
- TG degradation in adipose tissue → glycerol (→ gluconeogenesis) and FA (direct energy for myocardium, muscles and kidneys + in liver → keton bodies)

- **↑ TG, FA, glycerol**
- **↓ glc**
- **↑ bil**

EFFECTS OF DIET - CAFFEINE CONSUMPTION

- **phosphodiesterase inhibition** → ↑ cAMP →
↑ glycolysis → ↑ energy + alertness of an
organism
TG cleavage → ↑ glycerol and FA
- ↑ **renin and catecholamines** (within 3 h)

EFFECTS OF DIET - ALCOHOL CONSUMPTION

- **degradation velocity = 0.15 ‰ / h**
- **acute consumption:**
 - ↑ TG, aldosterone
 - ↓ prolactin, ADH, cortisol
- **chronic consumption:**
 - ↑ ALT, AST, GMT;
cortisol, adrenaline, estradiol,
uric acid, lactate (MAc)
 - ↓ glc; ketoacidosis
- **hepatotoxicity**

SMOKING

- **↑ HbCO (8%)**
 - **↓ vit. B₁₂ and Ig**
 - **↑ total chol and TG, ↓ HDL-chol**
 - **↑ cortisol, CEA, Pb, Cd**
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- **Beware smoking as a risk factor.**

*There is a maxim that doctors should always **'treat the patient, rather than the laboratory report'**.*

*Beware of overreacting to the **slightly abnormal result in the otherwise healthy individual.***