# SIM – PHYSIOLOGY E-BOOK

## (SIM LAB GUIDE for 2nd YEAR MEDICAL STUDENTS)

**B1**

- Introduction to Simulation Medicine in Physiology Course
- Primary Investigation and Evaluation

**B2**

- Handover (SBAR)
- Circulation, Blood Pressure, Determinants of Blood Pressure

**B3**

- Respiration
- Relationship between Respiration and Circulation
- Oxygen Supply (DO2)
- Determinants of Oxygen Delivery (DO2)

**B4**

- CO2 elimination
- Capnometry
- etCO2 variables
- Monitoring of the Organism during General Anesthesia
- Reaction to a Change in Condition

**B5**

- Invasive Blood Pressure Measurement
- Determinants of Glomerular Filtration

**B6**

- Consciousness (determinants and evaluation)
- Intrinsic Environment

# B5

## INVASIVE BLOOD PRESSURE MEASUREMENT

### Blood Pressure Monitoring (NON/INVASIVE)

**Non-invasive** monitoring (long-term monitoring) of BP can be performed by repeated cuff measurements. Patient monitors can be programmed to take repeated measurements (inflation/deflation of the cuff) at regular intervals (typically minutes to hours). BP can also be monitored using a portable monitor (called Holter Monitor). However, frequent inflation of the cuff has its limits as it is very bothersome to the patients.

**Invasive** (direct) pressure measurement is a measurement directly from the vascular bed (possibly the heart).

**Importance:**

i. continuous measurement (important especially in case of circulation failure), the output is a continuous curve.

ii . Reliable measurement even at very low pressure (e.g. shock), when measurement with a cuff is difficult.

iii . For CVP, invasive measurement is the only accurate method.

**Principle:** percutaneous insertion of the catheter into the vessels. The sensor is usually outside the patient's body, at the level of the heart *Why?* . The sensor and the catheter are connected by a tube (similar to an infusion) filled with FR, which must be air-free *Why?* .

**A. Central venous pressure (CVP)**

**CVP is** the pressure in the large veins at the level of the heart.

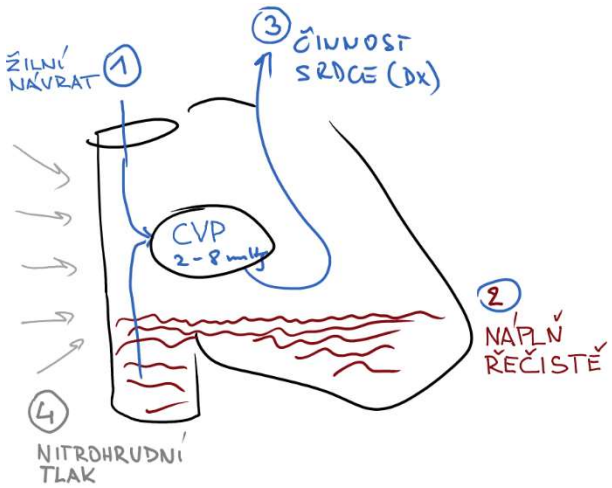
**CVP depends** mainly on i) venous return, ii) filling of the vascular bed with blood and iii) the pumping function of the right heart iv) venous tone /chest pressure (there is also an influence of breathing).

**Importance:** *Decreased* CVP values are seen in hypovolemia, reduced venous return. *Increased CVP values* in hypervolemia and conditions in which the pumping of blood is restricted by the right heart to the lungs.

**Normal** CVP values are around 2-8 mmHg .

**CVP - Execution** (see model in the classroom)

The distal end of the catheter is in the vena cava at the level of the heart. A typical approach is through the jugular or subclavian vein. Catheterization of central veins is quite common in a number of departments due to long-term




infusion therapy, parenteral nutrition, etc. (ICU, operating room, ARO). Catheterization of central veins carries certain risks (infection, thrombosis, pneumothorax during insertion). These risks must be lower than the expected benefit.**The output of** the invasive CVP measurement is a curve on the monitor labeled CVP and the mean pressure value is expressed numerically, typically in mmHg .

**B. Arterial blood pressure invasively (ABP, ART, RAD, FEM, Ao , …)**

**ART is the pressure** in the arterial bed (at the end of the catheter, but relative to the level of the heart)

**ART typically depends** on: i) cardiac output, ii ) peripheral vascular resistance, iii ) volume of circulating fluids

**Meaning:** assessment of hemodynamics ( perfusion ), control of vasopressor treatment management

**Indications for IBP:** Hemodynamically unstable patients (ICU, ARO, surgery), cardiac surgery

**Risks of IBP** . Arterial injury, watershed ischemia, air embolism, hemorrhage. The risks are greater than with CVP and must be weighed against the benefit. However, IBP is fully indicated for unstable hemodynamics.

**The output of** the invasive measurement of ART is a curve on the monitor marked as ABP or ART or according to the relevant artery, RAD, FEM, Ao, PAP, or heart chambers (LVP, RVP, RAP...) and numerically expressed values of SBP/DBP, typically in mmHg .

***Questions-assignments:***

- *View the direct pressure measurement model. Test the effect of changing the position of the sensor*
- *Draw the ART curve (from memory).*
- *Why is ART measurement more risky than CVP?*
- *Why does the IBP sensor have to be at heart level and the NIBP sphygmomanometer not necessarily?*
- *What is the difference between an IBP curve and an SpO2 curve (more precisely plethysmographic )?*
- *What is "Pressure Reset"? [calibration of the sensor against the atmosphere. Atmospheric pressure is set as 0 mmHg ]*
- *Is there a risk of coagulation/ thrombosis of the catheter, embolism/ thrombosis of vessels? [YES. To reduce the risk, the catheter is continuously flushed with FR with heparin. Very slowly.]*
- *Would you be free to change the value of your CVP?*

# EVALUATION OF BODY HYDRATION, FLUID BALANCE

## Body hydration

**Clinical manifestations:**

| Good hydration | Insufficient hydration |
|---|---|
| • Moist mucous membranes<br>• Good skin turgor, the formed skin fold quickly returns to its original form after release<br>• Light colored urine<br>• Soft stools | • Dry mucous membranes, chapped lips, dry tongue<br>• Reduced skin turgor, the formed skin fold persists even after release<br>• Dark urine<br>• Hard stools |

**Measured parameters: Balance fluids (positive / negative / balanced), CVP, concentration metabolites in blood and urine**

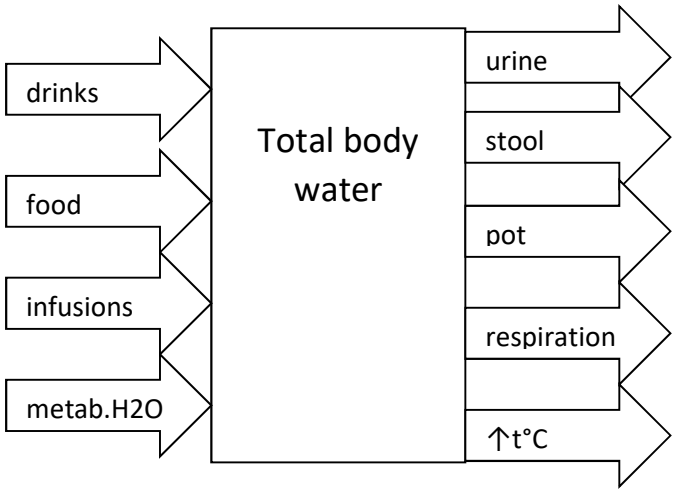
## Fluid balance

**Fluid Intake:**

a. Drinks
b. Food
c. Infusions
d. Metabolism (water 250 - 500 ml and more according to metabolism, depends on individual size)

**Fluid Losses:**

a. Urine: according to balance: 500ml – 20L
b. By stool according to composition and quantity, diet 60-80% by weight stool
c. Thermoregulatory needs / hydration / hormonal and nervous regulation: 250ml – 20l
d. Respiration according to size of individual and corporeal loads: 250-500 ml and more
e. If peripheral physical temperature is elevated, then we estimate: for every °C above 36.5°C, a loss of 200 ml $H_2O$/24 h




**Normal diuresis**

Amount of urine produced per 24 hours

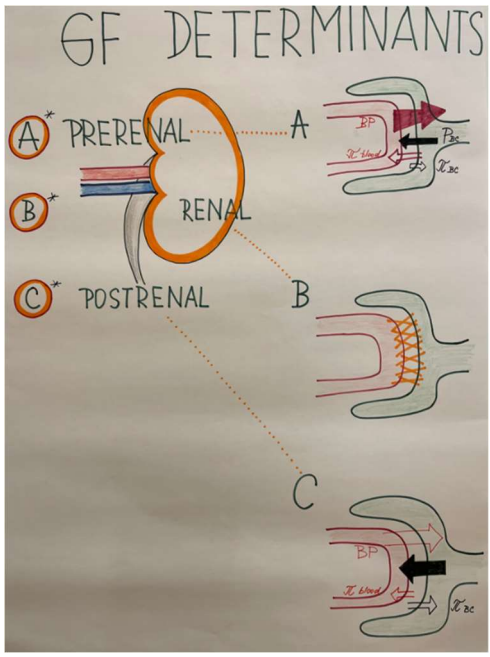
Standard values: physiological diuresis > 500 ml/d according to fluid and solute balance (theoretically approx. up to 20 l)

- Oliguria < 500 ml/ day
- Polyuria > 2500 ml/ day

We use these criteria to evaluate fluid balance and as one of the components of renal function evaluation in addition to blood analysis and determination of metabolites that are excreted in the urine, urinalysis or kidney function tests.

## DETERMINANTS OF GLOMERULAR FILTRATION

Glomerular filtration is the process by which the blood is cleaned of foreign substances and metabolic products. Its importance is enormous. The blood flow through the kidney is a quarter of the cardiac output, the filtration fraction is a fifth of the flowing plasma. Cessation of glomerular filtration would soon lead to death due to metabolic breakdown. That is why it is important to recognize its dysregulation in time.




If the limitation of glomerular filtration is significant and long-lasting, it will be clearly manifested by an increase in the substances that the kidneys excrete (urea, creatinine, potassium...) in the blood.

Physiological Blood Values:

urea: 2-8 mmol /l
creatinine: 50-100 µmol /l
potassium: 3.8-5.4 mmol /l

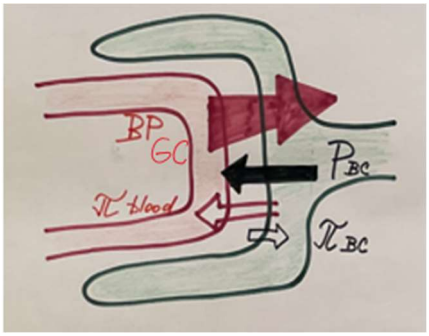
If the loss of glomerular filtration is gradual (over the course of years), urea and creatinine concentrations remain normal for a long time, and to detect a decrease in glomerular filtration, it is necessary to use other methods (kidney function tests, isotopic examination, see simulated tasks and further study).

**Physiological glomerular filtration is determined by three parameters:**

A. Prerenal : good circulatory function
B. Renal: physiological filtration membrane, functional renal parenchyma
C. Postrenal : through the free draining urinary tract

**Ad A: Prerenal conditions of glomerular filtration, principle of primary urine formation**

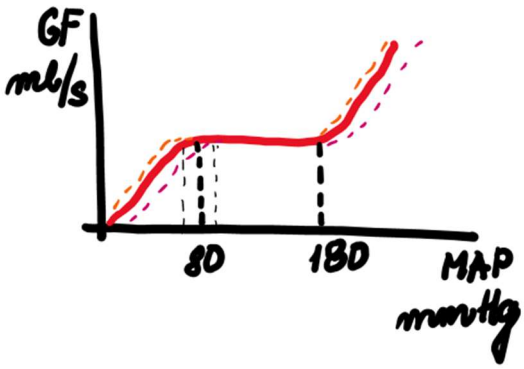
The formation of urine in the kidney is a consequence of the effective filtration pressure (GFP). The filtration pressure can be determined as the difference between the pressures that act in the capillaries of the glomeruli towards Bowman's capsule (can be simplified to blood pressure $BP_{GC}$ = 60 mmHg , the oncotic pressure of the glomerular filtrate $\pi_{BC}$ can be neglected due to the low protein content) and the pressures acting towards the lumen of the glomerular capillaries (oncotic pressure of plasma proteins $\pi_{blood}$ =29 mmHg + hydrostatic pressure in Bowman's capsule $P_{BC}$ = 15 mmHg ).




$GFP = BP_{GC} - P_{BC} + \pi_{BC} - \pi_{blood}$

GFP = 60 – 15 -29 = 16 mmHg

The pressure and flow of blood through the kidney is controlled mainly by local mechanisms so that filtration is approximately constant during fluctuations in systemic pressure.




This applies in the range of mean pressure in the arterial bed from 80 to 180 mmHg . For people with long-term lower pressure, the range is slightly shifted towards lower values and for people with higher pressure the range is shifted upwards.

If the blood pressure falls outside the regulation range, the filtration pressure falls and with it the formation of primary, and thus also definitive, urine.

**Hourly diuresis**

Since perfusion pressure in the kidney determines renal blood flow and glomerular filtration, and glomerular filtration therefore affects diuresis, hourly diuresis monitoring is a functional monitoring of renal perfusion .

Since the kidney is a relatively preserved organ in terms of the distribution of blood flow through the organism (only the brain and heart have a higher priority), monitoring the perfusion of the kidney is also an indicator of the blood flow of other less preferred areas. If current urine production decreases due to limited perfusion pressure in the kidney, flow through peripheral tissues is probably even worse.

**Thus, hourly diuresis is an indirect monitoring of circulation.**

If we use a collection bag with a fine scale and the possibility to collect separate portions of urine during the day, we can indirectly monitor the current perfusion conditions in the kidney after a therapeutic intervention (hydrating the patient, arteriolar sphincters toning, affecting cardiac output, reducing pathologically elevated CVP during poor pumping function of the heart....).

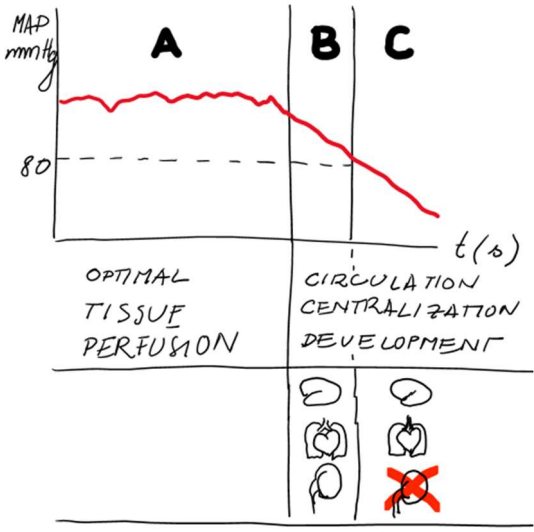
**Reference value hourly diuresis:**

oliguria: <0.5 ml/kg/h

Attention: Assessment of hourly diuresis does not coincide with that of full day diuresis. *Why?*

**Assessment of hourly diuresis is used for recognition of current changes in urine production corresponding to current changes of blood pressure, while both, hydration and solutes load remain unchanged.**

Graphically expressed, it serves as a functional check if the circulation status of the patient is still in the AB band of the image or is already outside this area in zone C. Additional knowledge of BP values is important for a few reasons. Firstly, there can be a complex pathological situation (eg: value of secondary arterial pressure is sufficient, but at the same time there are higher venous pressures



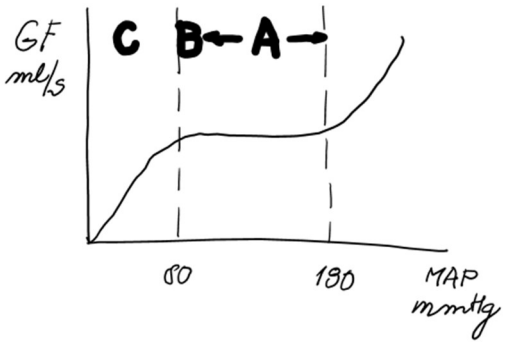




**Fig.: Centralization of circulation during a gradual decrease in blood pressure**

etc., see next study) and secondly, the scope of regulatory GF ranges varies between individuals as well.

In general, the exact amount of primary filtrate cannot be reliably deduced from the amount of definitive urine. We would neglect the facultative resorption processes, which are dependent on the hydration and osmotic load of the organism. In a situation of failing circulation, this simplification is allowed because we observe that diuresis decreases simultaneously with blood pressure drop without a simultaneous decrease in hydration or osmotic load.

**Illustrative examples:**

**Example 1:**

A: Final urine production in a person adapted to low fluid intake (their kidneys have a high concentration capacity) can be as little as 0.25 ml/kg/h. This can be physiological if the person has normal blood pressure and is able to eliminate the entire daily osmotic load.

B: On the contrary, it will be very unphysiological if it is a well-hydrated person with critically low blood pressure.

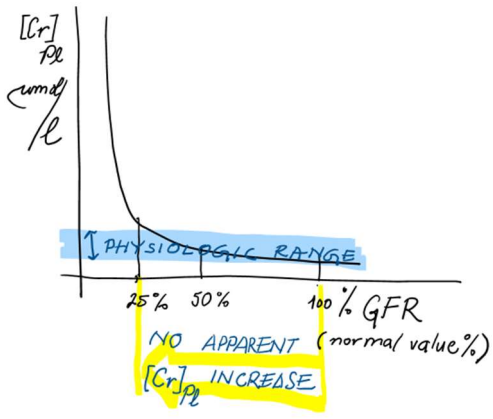
**Example 2:**

A: A healthy 20-year-old individual weighing 80 kg finds himself in need of water for a period of time. The osmotic load that he needs to eliminate per day is 600 mosmol and the concentration capacity of his kidneys reaches a value of 1200 mosmol /l. In what volume of definitive urine will the osmotic charge be eliminated? is it physiological?

B: The same healthy individual, this time in conditions of optimal hydration, suffers an injury with a large blood loss. His mean blood pressure value is 60 mmHg . Produces 20 ml of urine per hour. The osmolarity of this urine is between 350 and 600 mosmol /l. Compare the amount of urine produced with the normal for hourly diuresis? Is this a reduced value? If he passed the same volume of urine in each subsequent hour, how much would it be in 24 hours? Would it be physiological? Why?

**Ad B: Renal conditions of glomerular filtration (GF)**

There is a group of diseases that leads to impaired permeability of the glomerular-capillary membrane or gradual destruction of the renal parenchyma (see further study). As already stated above, at first the decrease in GF is not evident by the rise in plasma urea and creatinine. It only becomes apparent when the GF drops to 1/4 of the original value, and that is usually too late for treatment, see **Fig.** In the final stages of such diseases, the individual produces no urine and is fully dependent on dialysis. Therefore, when renal disease is suspected, it is necessary to determine the value of glomerular filtration (i.e. the volume of primary filtrate that is formed per unit of time) and start treatment in time.



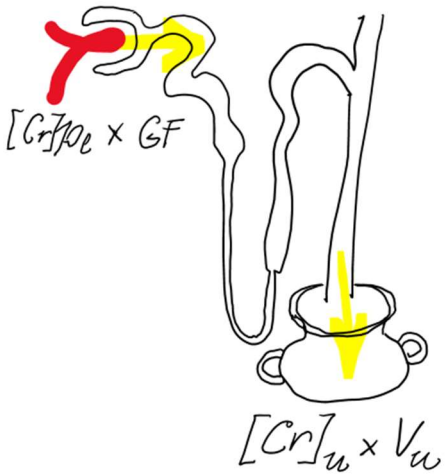

**Reference value of GFR ( glomerular filtration rate ):**

depends on gender, age and body constitution

Generally 180 l/24 hours, 1.5-2.2 ml/s

This value can be measured or estimated.

Measurement is necessary wherever the accuracy/reliability of the result matters a lot (see further study).




To measure GF, we want to use a substance that is freely filtered into the primary urine, not absorbed or secreted. For example, exogenous **inulin**, or endogenous **creatinine**.

Assume that all the creatinine that is filtered through the glomerular-capillary membrane appears in the urine. See picture:

$[Cr]_{Pl}$ concentration creatinine in plasma

GF volume of plasma filtered to Bowman capsule per day (= volume primary filtrate /d)

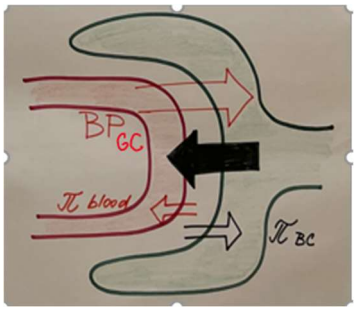
$[Cr]_{U}$ concentration creatinine in urine

$V_{U}$ volume urine throughout the day

$[Cr]_{Pl} \times GF = [Cr]_{U} \times V_{U}$

In clinical practice, we estimate glomerular filtration from the concentration of creatinine in plasma by substituting into the equation, which takes into account the gender, age and body type of the patient. The reason of difficulty in the measurement is the need to urine collection over 24 hours, which is often not successful. Furthermore, it is the fact that with decreasing filtration abilities, the kidney with creatinine excludes not only filtration, but also secretion, so the measured GF is overestimated. For exact measurement, it is necessary to give inulin in specific indications. Next options in the determination of glomerular filtration is isotopic examination (see next study).

**Ad C: Postrenal Conditions of Glomerular Filtration (GF)**




Urinary tract obstruction is very common in clinical practice.
The organism is threatened by two main problems:
**1: a local increase in tubular fluid pressure** above the obstruction

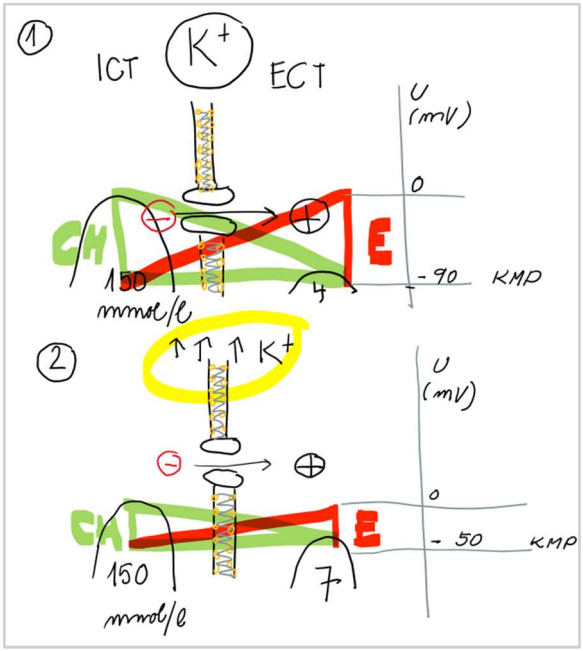
**2: by the accumulation of substances that cannot be removed from the blood**

**ad 1:** See fig: If the urine stops draining, glomerular filtration will continue until the sum of the oncotic pressure in the capillaries of the glomerulus $\pi_{blood}$ and the pressure in the Bowman's capsule $P_{BC}$ (tubular system of the nephron) equal the hydrostatic pressure in the glomerular capillaries $BP_{GC}$. A tubular system filled in this way will lead to oppression of the secondary capillary network of the kidney, where the pressure is physiologically low (below the oncotic pressure of the plasma, the function of secondary capillary network in kidney is resorptive). This condition threatens the renal parenchyma with ischemia and must be quickly addressed by urinary catheterization or suprapubic puncture.

**ad 2:** Complete obstruction of the urinary tract will lead to complete cessation of glomerular filtration. During the blood analysis, this is manifested by an increase in creatinine, urea, potassium, non-volatile acids and other substances excreted mainly in the urine. Water retention is also a problem.

**Hyperkalemia**

The kidneys are the main organ responsible for excreting dietary potassium. While the intracellular concentration of K+ is high, 150 mmol /l, the extracellular concentration is considerably lower, 3.8 – 5.4 mmol /l. The concentration gradient of potassium across the plasma membrane of cells is the basis of resting membrane potential. This is because the membrane of most cells is by far the most permeable to potassium compared to other ions.




Change in membrane potential when the concentration of K+ in the extracellular fluid increases. ICT/ECT: intra/extra-cellular fluid, CH: chemical gradient, E: electrical gradient, RMP: resting membrane potential

**Description of the picture:**

**ad1:** A concentration gradient leads to the flow of potassium ions out of the cell. When a positive particle leaves the IC space, a relative minus is left behind. This creates an electrical force that prevents the transfer of additional K+ to the ECT. This force is called an electrical gradient. The flow of K+ ions stops when the magnitude of the chemical and electrical gradients are equal. The size of the electric force is equal to the size of the membrane voltage, which we would measure on the membrane. If we take into account all the ions that can affect the resulting voltage on the membrane, we speak of the resting membrane potential

**ad2:** By increasing the concentration of K+ in the ECT, the chemical gradient for K+ will decrease, a smaller chemical force will be stopped by a smaller electrical force, therefore the resulting resting membrane potential will be closer to zero.

The consequences of this change can be significant, especially for cells whose function depends on the correct value of the membrane voltage. This especially applies to heart rhythm generators. During hyperkalemia, we can expect various rhythm disturbances, but typically bradycardia up to cardiac arrest, see further study.