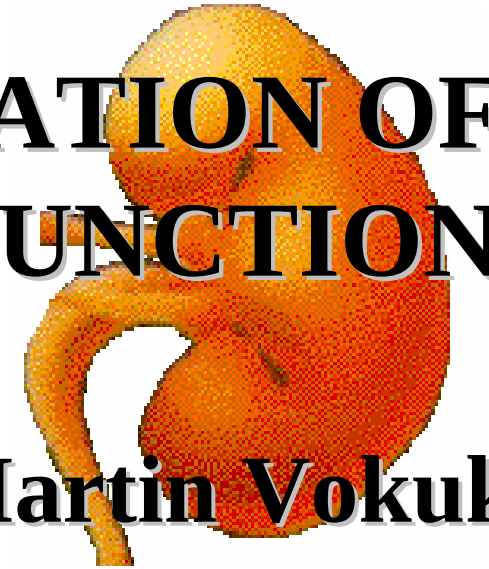
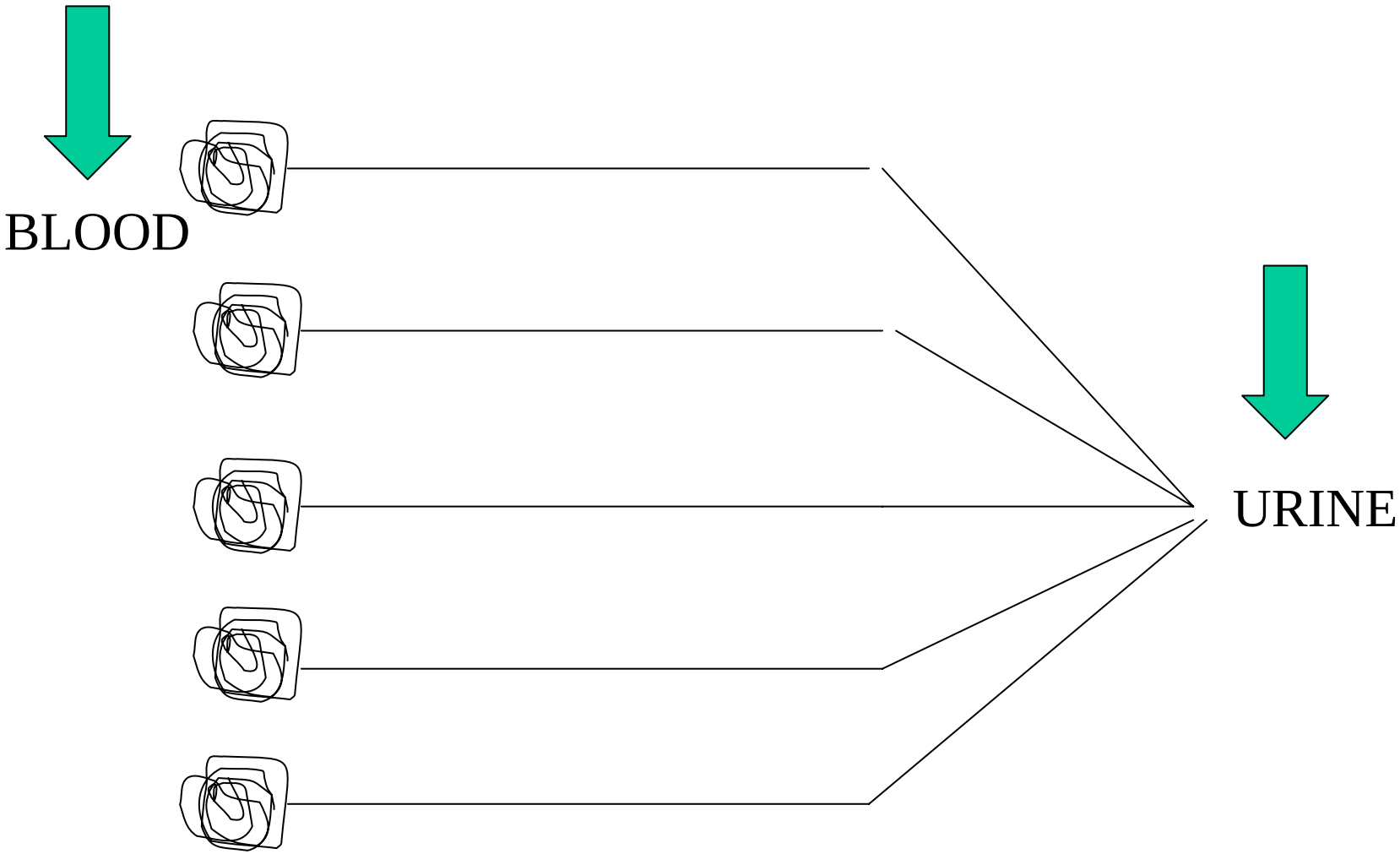
EXAMINATION OF KIDNEY FUNCTIONS



Martin Vokuka

Unofficial study material



The kidneys regulate the composition and volume of the plasma water. This, in turn, determines the composition and volume of the entire *extracellular* fluid compartment.

These functions are served by a variety of physiologic mechanism

The volume of excreted urine:

-ultrafiltration – ***glomerular filtration*** (GF)
-Reabsorption/secretion – ***tubular processes***

Glomerulus

Ultrafiltration (Glomerular filtration) – primary urine

- ***Volume***
- ***Composition***

Glomerulus

Ultrafiltration (glomerular filtration) – *primary urine*

- Volume (intensity of GF) – can be *determined*

- Composition (analogical to the plasma with the exception of proteins)

Tubuli

primary urine is further processed in quantity/quality (composition)with the result of *final urine* (amount, composition)

From the final urine the composition of primary urine and the tubular processes can be partially estimated

Final urine

- **kidneys**
- **whole organism**

1. **Blood composition (e.g. hyperglycemia, paraproteinemia, drugs, toxic substances…)**

2. **Glomerular filtration (quantity, permeability of glomer. membrane – morphology, charge…)**

3. **Tubular processes – resorption or secretion, hormonal regulation (e.g. aldosteron, ADH)**

4. **Urinary tract**

URINE ANALYSIS

Chemical
-PROTEINS (PROTEINURIA)
-BLOOD (HEMATURIA)
-pH
-GLUCOSE
-BILIRUBIN
-KETOBODIES
-LEUCOCYTES

Sediment

Microbiology

Special test

URINE ANALYSIS

pH 5 – 7

Specific mass 1010-1020 kg/m^3

- amount of all substances in urine

Proteins up to 0,3 g/L (300 mg/L)

- test specific for albumin (false negative in multiple myeloma)
- semiaquantitative sulfosalicyle test is sensitive also for globulines
- quantitative proteinuria (24 hours)

Glucose negative

- diabetes mellitus glycemia more than 10 mmol/L
- benign glykosuria (normal glycemia)

Ketone bodies negative

- fasting, diabetes mellitus (1. type)

Bilirubine negativní

- obstructive jaundice (conjugated)
- negative in hemolysis (unconjugated bilirubine does not enter the urine)

Urobilinogene 3,2 – 16 µmol/l

- increased in hemolytic icterus

Blood < 10/µl

- chemical test is not decisive, sediment analysis required

Leukocytes < 15/µl

- urinary infection

Nitrites negative

- positive in urinary infection by bacterias which reduces nitrates to nitrites (E. coli, Proteus, Klebsiella, Pseudomonas, Staphylococcus, Aerobacter)

PROTEINURIA

Size and charge of proteins

-Glomerular
-Tubular
-Overflow

Selectivity
Clearance ratio of IgG/albumine (transferrin)

PROTEINURIA

Size and charge of proteins

- Glomerular
- Tubular
- Overflow

Quantity

physiological: to 150 mg/day (Tamm-Horsfall protein)
to 1,5 g/day: **glomerular** damage or **tubular** damage
over 1,5 g/day: always **glomerular** damage
over 3 (3,5/5) g/day: nephrotic syndrome (**glomerular**)

Selectivity

Ratio of clearance IgG/albumin (transferrin)

Electrophoretical examination:

GLOMERULAR PROTEINURIA:

SELECTIVE – albumin (Mr 67 000), transferin (Mr 89 000)
– damage of podocytes and outer part of basal membrane

NONSELECTIVE – all proteins incl. immunoglobulines
– damage of mesangium and inner part of basal membrane

Index of selectivity (IS) = $\frac{\text{U-IgG}}{\text{S-IgG}} \times \frac{\text{S-transferrin}}{\text{U-transferrin}}$

IS $<$ 0,1 selective proteinuria
IS $>$ 0,2 nonselective proteinuria
IS = 0,1-0,2 middle selective proteinuria

MICROALBUMINURIA

Early damage of kidney in diabetic nephropathy and in hypertension.

Special RIA methods.

Normoalbuminuria: to 20 µg/min or to 30 mg/24 hours

Microalbuminuria: **20-200 µg/min** or **30-300 mg/24 hours**

URINARY SEDIMENT

SEMIQUANTITATIVE – MICROSCOPY

Arbitr. units	0	1	2	3	4
Amount of elements					
RBC	0.3	3.6	6.0	25	>25
WBC	0.5	2.5	5.0	15	>15
Casts	0.0	0.2	0.5	1.0	>1.0

FLOW CYTOMETRY

RBC	to 10 x 10^6/l
WBC	to 20 x 10^6/l
Epithelias flat	to 10 x 10^6/l
Epithelias rounded	to 3 x 10^6/l
Casts hyaline	to 2 x 10^6/l
Casts granulated	0
Bacterias	to 5000 x 10^6/l
Spermias	to 3 x 10^6/l
Cristalls	to 10 x 10^6/l

QUANTITATIVE ACC. TO **HAMBURGER**

Urine collection 3 hours – minute precision.

RBC to 2000/min.

WBC to 4000/min.

Casts to 60 - 70/min.

HEMATURIA

Exam in ***phase contrast*** under microskopy:

RENAL (GLOMERULAR) HEMATURIA

Deformated elements
(deformation during the crossing of glomerular membrane and tubuli)

Cause: ***glomerulonephritis*** with nephritic syndrome

POSTRENAL (NONGLOMERULAR) HEMATURIA

Non-deformated elements

Causes: bleeding from ***renal parenchyme***:
* tumors (Grawitz)
* cystosis
* TB

bleeding from ***urinary tract***:
* stones
* inflammation
* tumors
* injury
*self-injury, simulation

Glomerulonephritis, glomerulopathies

damage fo glomeruli – thickening of membranes, proliferation of mesangium…

glomeruli become permeable for proteins, RBC,
but GF gradually decreases

Causes: inflammatory, mainly autoimmune with immunocomplexes deposition, glycation of proteins in DM…

many types according to histology, clinical course…

<u>In urine</u>:
-erythrocytes and/or proteinuria + decline in GFR

Nephrotic syndrome

-albuminuria
-hypoalbuminemia
-edemas
-hyperlipoproteinemia
-hypercoagulation
-loss of substances bound to albumine by urine

Causes:
-some types of glomerulonefritis
-diabetic nephropathy
-NS with minimal changes
-paraneoplastic disease, drugs…

Examination of glomerular filtration

Amount of GF is identical with the clearance of substance, from which the blood can be completely cleared during the glomerular filtration without any further tubular processing

- is filtered freely
- is not processed by tubuli
- is nontoxic

1. **creatinine** (current – mild tubular secretion)
2. inulin (used more in experiments)

C = UV / P

U … concentration in urine
V … volume of urine
P … concentration in plasma

GFR (20-29 yrs: 122 ± 16 ml/min)

Normal values of creatinie clearance – GFR (ml/s/1,73 m^2):

Age	**W**	**M**
to 20 yr	1,8 ± 0,4	1,8 ± 0,4
20-40 yr	2 ± 0,28	2,17 ± 0,39
over 40 yr	1,5 ± 0,5	1,85 ± 0,6

Cardiac output	**5000 ml /min**
↓	
Kidney perfusion	**1000 ml/min** (20 %)
↓	
Plasma flow in kidneys	**600 ml/min**
↓	
GFR	**120 ml/min** (20%-filtr. fraction)
↓	
Final urine	2000 ml/24 hours, i.e. **1,4 ml/min** (cca 1%)

Glomerular filtration rate (GFR) depends on **glomerular** flow, ultrafiltration pressure and surface.

GFR of single nephron (SNGFR) = Kf ($\Delta P - \Delta\Pi$)

ΔP … mean transcapillary difference of ***hydrostatic*** pressures
$\Delta\Pi$ … mean transcapillary difference of ***oncotic*** pressures
Kf … filtration coefficient (permeability, surface)

Blood flow, ultrafiltration pressure and surface are regulated by changes in the tonus of *afferent* and *efferent* arterioles (blood flow and ultrafiltration pressure) and contractility of *mesangial* cells (**filtration** surface)

Total GFR = N x SNGFR

N … number of glomeruli

SNGFR might be different in different glomeruli

Decreased glomerular filtration rate

- **glomerular hydraulic pressure is reduced** (as in circulatory shock)

- **tubule** (hence Bowman's space) **hydraulic pressure is elevated**, as in urinary tract obstruction

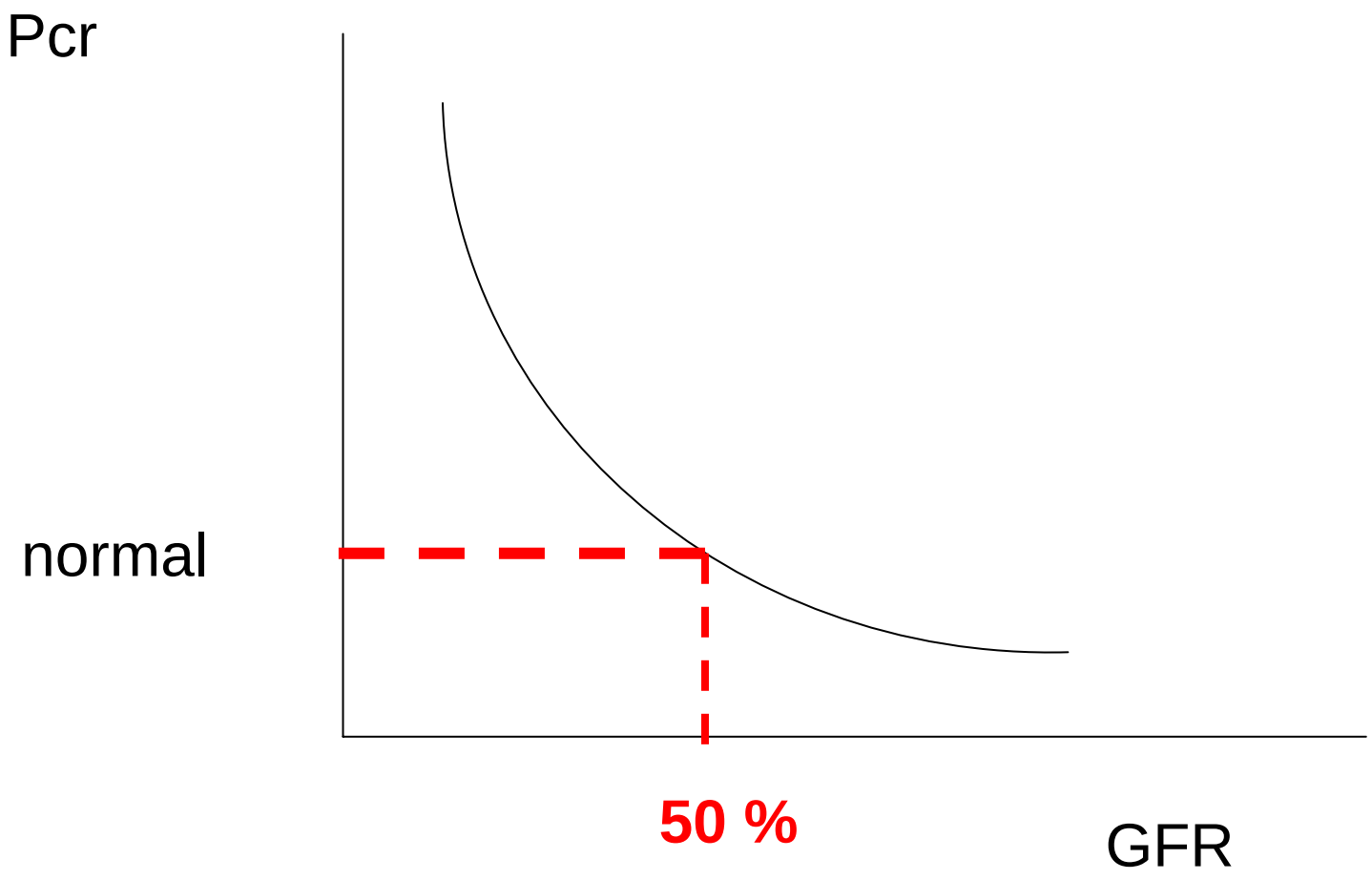
- **plasma colloid osmotic pressure rises** to high levels (hemoconcentration due to severe volume depletion, myeloma, or other dysproteinemias)

- renal, and hence glomerular, **blood flow is reduced** (severe hypovolemia, cardiac failure)

- **permeability is reduced** (diffuse glomerular disease)

- **filtration surface area is diminished**, through focal or diffuse nephron loss in progressive renal failure

GFR vs. plasma creatinine concentration



SERUM CREATININE CONCENTRATION

women **60 – 100 µmol/L**, men **70 – 110 µmol/L**

from muscles, the musculatury influences the concentration

increase with urea in ***decrease of glomerular filtration*** below 50%

increase without urea:
damage of muscles, muscles dystrophy, acromegaly

SERUM CONCENTRATION OF UREA

1,7 – 8,3 mmol/L

endproduct of protein metabolism, produced in the liver

increase without (or more than) creatinine:

- ***dehydratation***
- increased ***protein intake***
- increased of ***protein catabolism***: burns, bleeding to GIT, sepsis, after corticoid administration

decrease :

- ***hyperhydration***
- ***protein malnutrition***
- ***severe liver disease***

Cystacin C

small nuclear protein
its serum concentration is sometimes used for GFR evaluation

Glomerular Adaptations To Nephron Loss

remaining healthy (or least injured) nephrons tend to hypertrophy and take on an increased functional burden

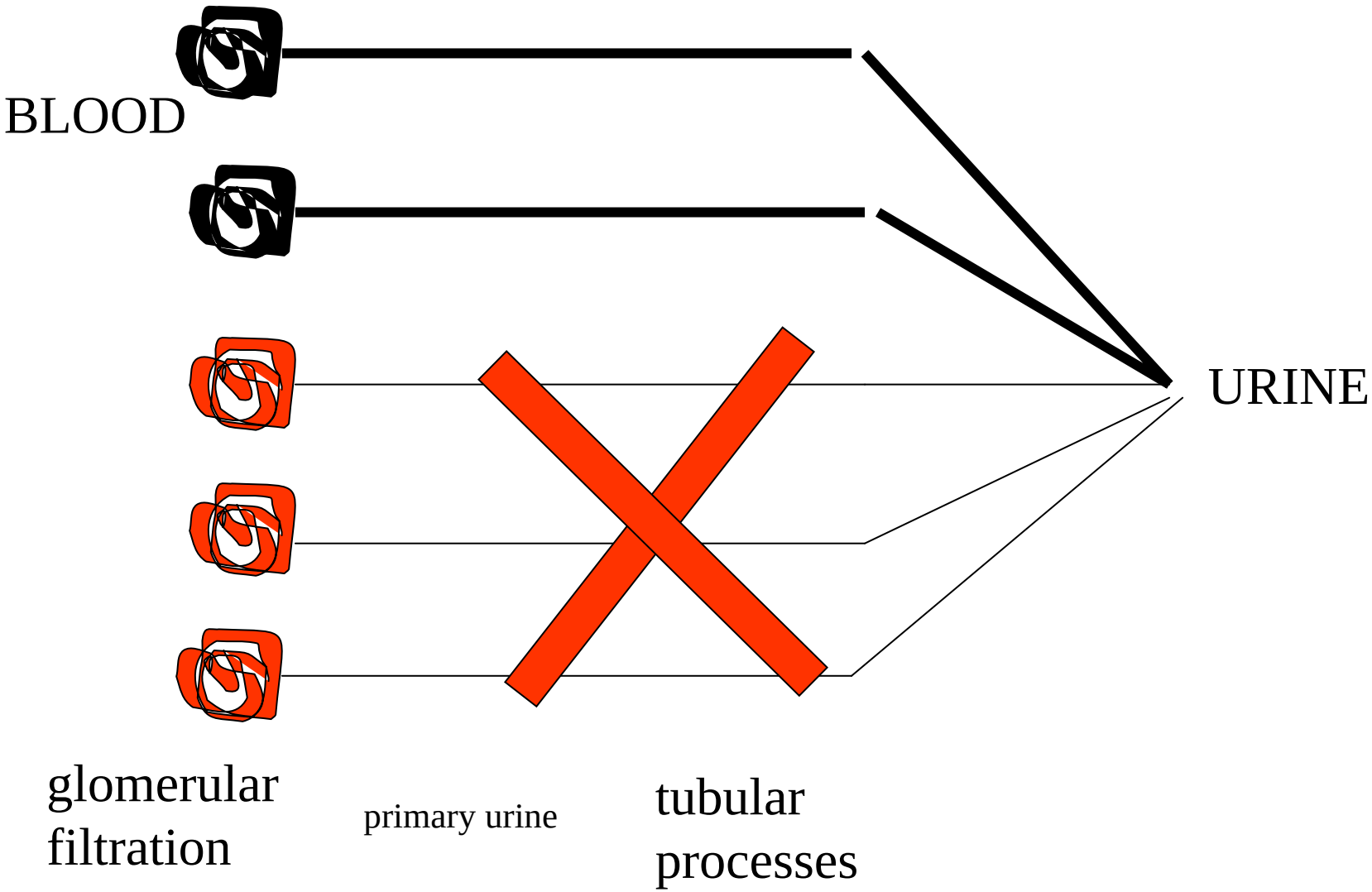
Increases in single-nephron GFR may be achieved by renal ***hemodynamic*** adjustments (increased glomerular plasma flow and increased glomerular capillary hydraulic pressure, and by glomerular ***hypertrophy***, which increases the maximum surface area available for filtration.

***Intact-nephron hypothesis*:**

as chronic renal failure (CRF) advances, kidney **function is supported by a diminishing pool of functioning (or hyperfunctioning) nephrons**, rather than relatively constant numbers of nephrons, each with diminishing function

single-nephron ***hyperfiltration***

Up to **50 %** loss of glomeruli the compensatory increase in GFR has no serious adverse consequences



COMPENSATION

- hyperfiltration in **glomeruli**
- changes in **tubular** processes

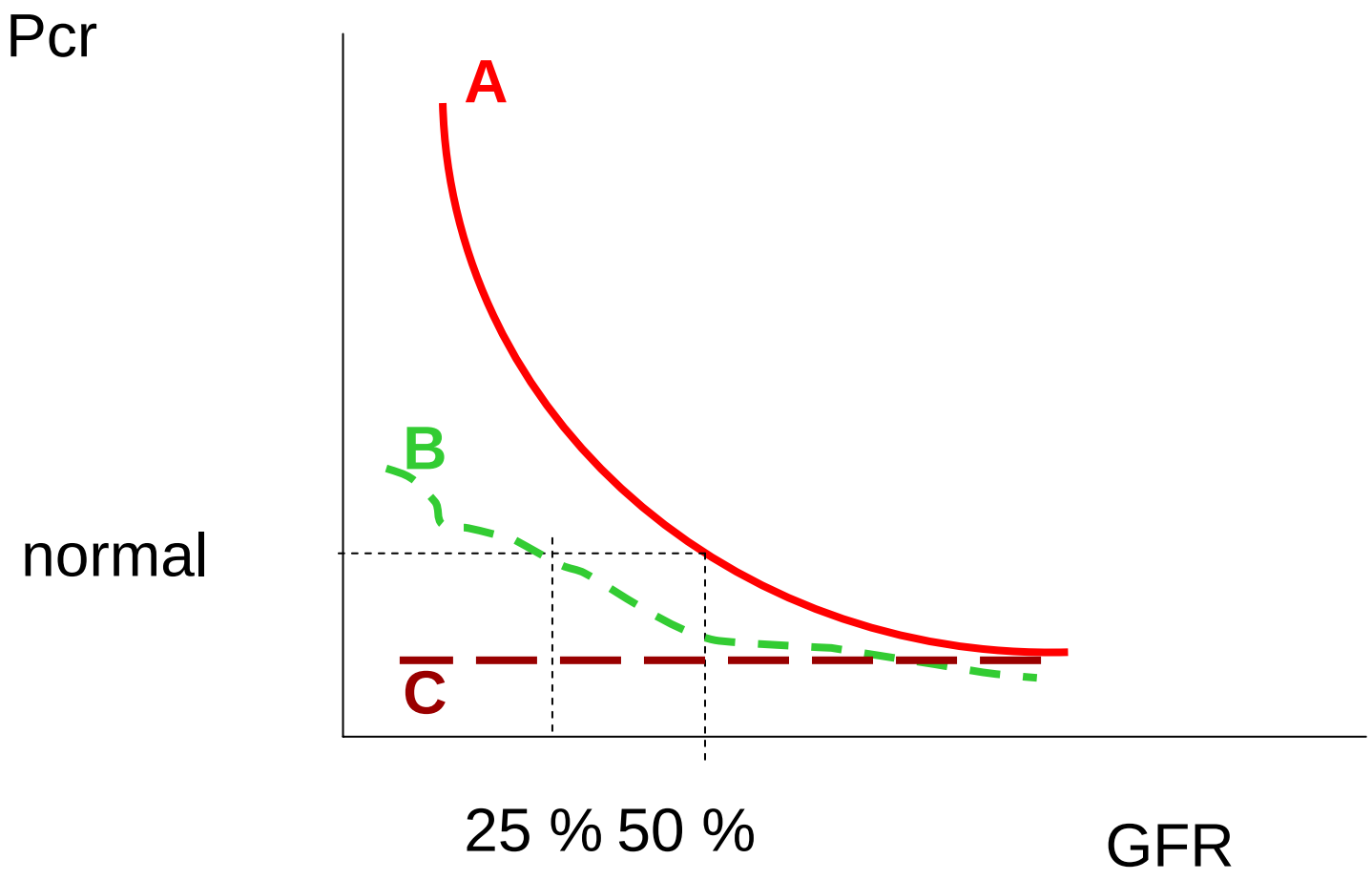
Remarkable short-term success at offsetting the tendency for GFR to fall, over time, ***proteinuria*** and focal and segmental ***glomerulosclerosis*** develop, the more so where greater amounts of nephrons are lost or removed.

As a result, a progressive decline in GFR ensues

the adverse long-term consequences of severe nephron deficits are invariably preceded by increases in glomerular capillary hydraulic pressure (***glomerular capillary hypertension), glomerular hyperperfusion, and hypertrophy***

More and more glomeruli cease to function through advancing glomerulosclerosis and disruption of tubule structure and function, leading eventually to total loss of GFR (i.e., end-stage renal disease)

Major types of response to impaired GFR
A – elimin. depends mainly on **glomerular filtration**
B – participation of tubule **transport mechanisms** in the excretion of these substances (potassium, phosphate, urate, protons…)
C – effective compensatory actions in **tubular reabsorption** – e.g. natrium



Tubuli

Tubular processes
- Secretion (excretory function)
- Reabsorption

Tubular function can compensate for changes in glomerular filtration

Glomerulotubular balance

High rate of solute excretion per surviving nephron (so-called ***osmotic diuresis*** due to urea and other retained solutes

If the *obligatory solute load* to be excreted by each is 600 mmol/d and the urine osmolality is 300 mmol/kg water, a urine volume of 2 L/d will be required to excrete the total solute.

GFR in normal subject is 180 L/d

In uremic individuals 4 L/d,

urinary volume excretion of 2 L/d represents

excretion of slightly more than **1 percent** of the total glomerular filtrate in the **normal** subject

and **50 percent** in the **uremic** patient.

Urine osmolalities that the **diseased** kidney can achieve [**250 to 350 mmol/kg**] is narrower than

in the **normal** kidney [**40 to 1200** mmol/kg],

the individual with **normal** function is able to excrete the obligatory daily solute load of 600 mmol in as little as **500 mL** urine per day or as much as **15 L/d**, compared

with the narrower range in **renal insufficiency**, from about **1.7 to 2.4** L/d.

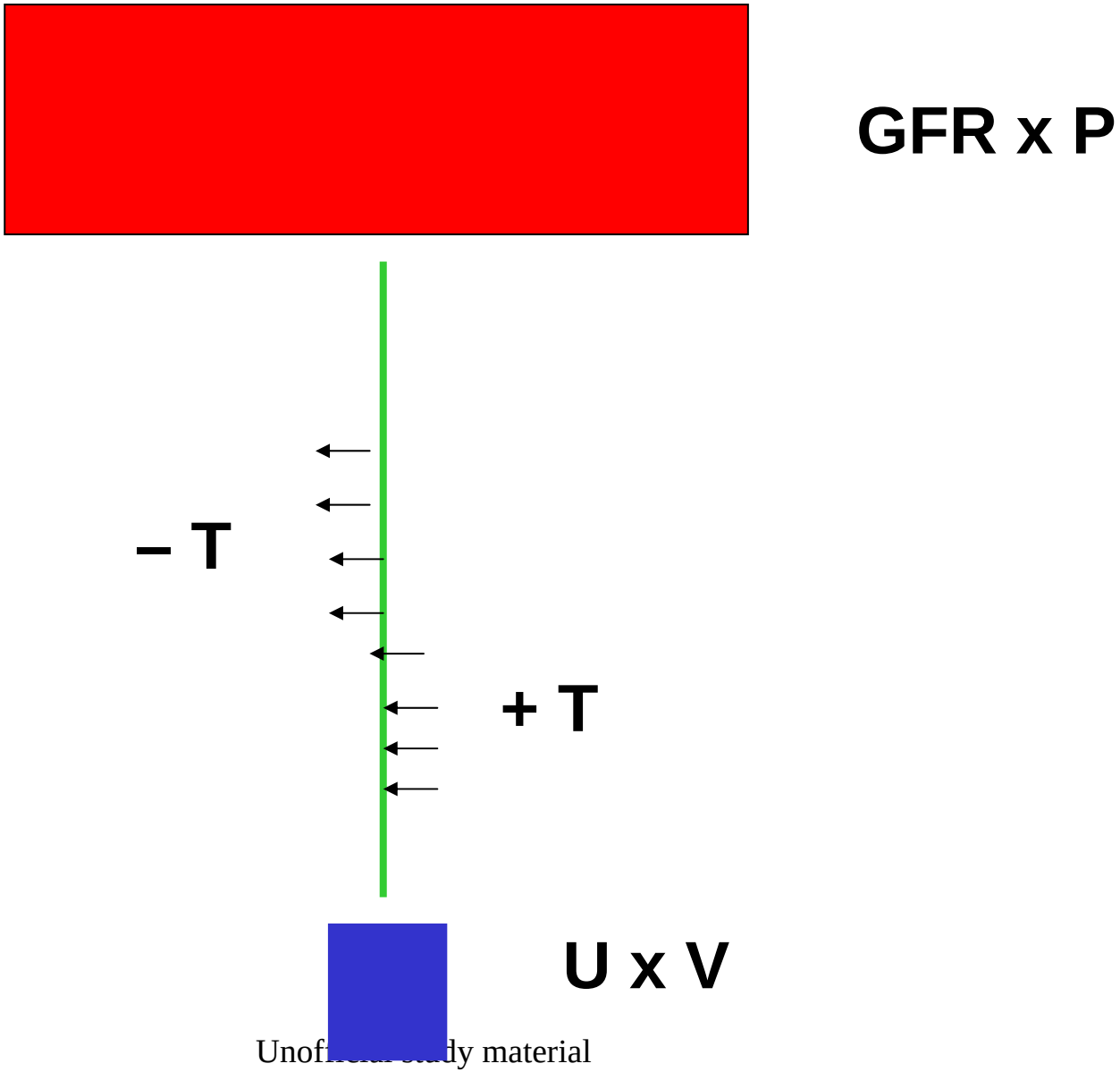
Fractional excretion / fractional reabsorption

Total excretion = U x V

U … concentration in urine
V … volume of urine

= GFR x P – T

P … plasma concentration
T … tubular process: + secretion; - reabsorption



Fraction excretion

FE = amount in the urine / amount in glomerular filtrate

$= \mathbf{U_y \times V_y / GFR \times P_y}$

$= GFR_y / GFR$

$= C_y / C_{cr}$

Fractional excretion

FE **sodium**: about 1 %

FE **potassium**: 5-20 % but can exceed 100 %

FE **osm.active** substances: about 1,5 – 3 %
Increase in FEosm is in *osmotic diuresis*

FE **water** = V / GFR = P_{cr} / U_{cr} ; about 1 % (0,4-2,0)

If Uosm equals Posm, FEwater and FEosm are practically identical (ISOSTENURIA)

Increase in net excretion

GFR x P – ***overflow osmotic diuresis***
-increase in plasma concentration
-Hyperfiltration in glomeruli (compensatory in renal failure)

T … tubular processes – ***tubular osmotic diuresis***
-reabsorptive capacity is saturated
-reabsorptive capacity is pathologically decreased

DIURESIS

Osmotic

Glucose, sodium etc.
Uosm > Posm
FEwater increased
FEosm increased

Water

Decrease in ADH
Uosm < Posm
FEwater increased
FEosm normal

Concentrating ability

Countercurrent mechanism – loop of Henle, transport mechanisms, intrarenal blood flow (vasa recta), antidiuretic hormone

Disturbances

-anatomical deformation of medulla
-Decrease of tubular transport
-Distribution of intrarenal blood flow
-ADH

FE water
FE osm
Urinary osmolality

Measurement

ADH (DDAVP) + urine osmolality
Age-dependent
15-50 yrs: at least 900 mosm/l

Early impairment of the concentrating ability is a characteristic feature of interstitial nephritis

Adiuretine test:
Supper without fluids, 12 hrs without drinking. In the morning 2 drops of (10 µg) of adiuretin (ADH). Then urine collection each hour, 4x. At least in one portion of urine the osmolality (mOsm/l) should be:

15-20 yr	970
21-50 yr	940
51-60 yr	830
61-70 yr	790
71-80 yr	780

Differential diagnosis of acute renal failure

PRERENAL

Dehydration

Kidney elaborates a small volume of urine of high osmolarity which exceeds 500 mOsm/l

U-sodium excretion is low (below 20 mmol), FE less than 1 %

RENAL

Tubular impairment

Urine osmolarity about 300 mOsm/l (isostenuria)

U-sodium excretion is higher (above 40 mmol), FE greater than 2 %

Urine sediment	0	casts, ery, leu
Na^+ in urine (mmol/L)	<20	>40
FE Na^+	<0.01	>0.01
Osmol. of urine mOsm/l	>500	<300
Specif. mass	>1020	<1020
U/P creatitine	>50	<50
	Prerenal	**Renal**