The Kidneys and Urinary Tract

Medicine for students in technology and science

MFEL 3010

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Overview

- 3 lectures covering
  - Anatomy / physiology / diagnostic tools
  - Diseases
  - Dialysis
Urinary tract

- 2 kidneys
- 2 ureters
- 1 bladder
- 1 urethra
Tasks

- Kidneys
  - Remove waist products from the blood
  - Remove water
  - Produce hormones

- The rest
  - Transport the urine produced in the kidney out of the body
Anatomy

The kidneys and its neighbour organs, seen from the front.
Anatomy

Position of the kidneys under the lower ribs and muscles, seen from behind
Anatomy

Cross section showing the kidneys, spleen, stomach and liver (seen from above)
Anatomy

Kidney with its capsule, artery, vein and ureter
Anatomi

Cortex vs marrow, pyramids, collection system, fat.
Anatomy

Arterial supply
Anatomy

Urinary bladder, prostate, uretra
Anatomy

2 nephrons:
arteriole, glomerulus, tubulus, collecting ducts
Anatomy

Drawing of the Glomerulus

Urine

Capillaries (small blood vessels)

Blood
Anatomy

Glomerulus

Scanning Electron Microscope, 1000 x
Anatomy

Glomerulus, vessels, tubulus

Seen with a light-microscope, 400 x
Anatomy

Normal Glomerular Capillary

- epithelial foot process
- basement membrane
- lumen
- endothelial cell
- mesangial cell
- mesangial matrix
Anatomy

The border between the blood and the urinary space.

Elektronmikroskop, 50000 x
Physiology

Water reabs.
Biochemical tests

- Autoanalyzers
  - Fully automatic
  - High throughput
  - Very precise results
  - Low price per test
Biochemical tests for the kidney

- Blood (hematology)
  - Hemoglobin (Hb)
  - Leucocytes (white)
  - Trombocytes (platelets)

- Electrolytes
  - Na
  - K
  - Ca
  - Phosphate

- Kidney function
  - Creatinine
  - Carbamide (urea)

- Other
  - Albumine
  - Bicarbonate

- Urine
  - Stix
  - Culture (bacterial)
Biochemical tests

- Hematology
  - Flowcytometer
  - Single cells are examined with
    - Laser
    - Current / resistance
    - Staining
  - 1000s of cells are characterised regarding
    - Size
    - Nuclear size
    - Granularity
    - Enzyme content
Biochemical tests

- Hematology
  - Microscopy
    - Red blood cells
    - 2 different white blood cells (leucoc.)
    - 1 platelet (trombocyte)
Imaging of renal disorders

- X-ray (± contrast medium)
- Ultrasound
- CT / MR
- Angiography
- Nuclear medicine
Imaging

**X-ray without contrast:**
Many big kidney stones
X-ray with iv contrast (urography): Normal
Ultrasound:

Kidney with dilated renal pelvis due to obstruction

Problems:
low picture quality, time consuming, highly operator dependent.
Ultrasound:

Kidney with 2 stones giving shadows
Imaging

**Computer Tomography**
(cross sections through the kidneys, seen from below):

Right: normal
Left: reduced contrast enhancement, increased size, hematoma under the capsule after car crash

Problems:
High radiation dose, contrast toxicity
Angiography:
Normal.
Catheter seen at top

Problems:
Expensive, high contrast dose, embolism (blood clots), radiation
Angiography:

No kidney on right side, very narrow lumen (stenosis) in left artery. Dilated during the same procedure.
Imaging

CT Angiography:

(non-invasive, computer-based reconstruction of vessels and organs containing contrast)
Common Diseases

- Urine infection
- Prostate
  - Benign enlargement
  - Cancer
- High blood pressure
- Kidney stone
- Chronic kidney failure
  - Dialysis
  - Transplantation
Urinary Tract Infection

- **Bacteria**
  - Gram neg. rods
  - E.Coli, Klebsiella, Proteus, etc

- **Natural inhabitants**
  - Gut
  - Skin

- **Defence mechanism**
  - Flowing fluids
  - Mechanical barriers
  - Cells
UTI - symptoms

- **Lower**
  - "Cystitis"
  - No fever
  - Burning, pain, smell, frequent voiding
  - Not dangerous

- **Upper**
  - "Pyelonephritis"
  - Fever
  - Pain in back, shivering, nausea,
  - Dangerous
  - Needs antibiotic, sometimes hospitalization
UTI- evaluation and treatment

- Urine
  - Dipstic (red and white cells, bacteria)
  - Culturing
    - Type
    - Effect of antibiotics

- Imaging
  - Obstruction
  - Reflux

- Antibiotics
  - Penicillins
    - Ampicillin
    - Selexid
  - Cefalosporins
  - Aminoglykocids
  - Trimetoprim, Sulfa

- Supportive treatment
  - IV fluids
  - BP-increasing drugs
  - Oxygen
  - etc
Prostate - enlargement

- Common
  - Frequency (%)= age
- Diffuse enlargement
  - Not cancer
  - Nodules (soft)
  - Increased outflow resistance from bladder
- Symptoms
  - Frequent voiding
  - Nocturia
  - Difficult to start or stop
  - Sometimes without symptoms

Normal 20 gr

Prostate - 300 Gms
Prostate - enlargement

- Complikations
  - UT infections
  - Kidney failure

- Treatment
  - Bladder catheter
    - Permanent
    - Intermittent
  - TURP
  - Other
    - Local heating
    - Drugs

Bladder: dilated and with increased muscle trabecles
Prostate - cancer

- Common
  - 20% of all men
  - Many dies with and not due to the cancer
  - Harde nodules

- Reasons
  - DNA damage
  - Testosteron-dependent

The tumor is composed of small glands that are lined by a single layer of hyperchromatic cells. In contrast to normal glands, which have two layers, these neoplastic glands have only one layer and abut directly onto the interstitial connective tissue. A normal prostatic duct appears at the far right.
Prostate - cancer

**Symptoms**
- Local
  - Obstruction
  - Blood in urine (seldom)
- Metastases
  - Bone pain

**Treatment**
- Curative
  - Prostate removal
  - Radiation of prostate
- Palliative
  - TURP
  - Castration (- testo)
    - Surgical
    - Drugs
  - Radiation of bone lesions
    - X-ray
    - Radioactive isotopes
High blood pressure

140 cm water / blood column

10 cm (100 mm) Mercury (Hg)

Left Brachial Artery
listen for sounds

Hypertension: “in the old days”

- US-president Roosevelt
  - 1938: 170/90, - sympt
  - 1941: 185/105
  - 1943: 200/110, heart + kidney failure
  - 1945: died of bleeding in brain

- Treatment:
  - rest, saltrestriction, sedativa

- Loss of years (untreated)

<table>
<thead>
<tr>
<th>Blood Pressure</th>
<th>M 35</th>
<th>M 45</th>
<th>M 55</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>42</td>
<td>32</td>
<td>23</td>
</tr>
<tr>
<td>130/90</td>
<td>-4</td>
<td>-3</td>
<td>-1</td>
</tr>
<tr>
<td>140/95</td>
<td>-9</td>
<td>-6</td>
<td>-4</td>
</tr>
<tr>
<td>150/100</td>
<td>-16.5</td>
<td>-11.5</td>
<td>-6</td>
</tr>
</tbody>
</table>
Hypertension: complications

...no critical border, but a continuum ...
<table>
<thead>
<tr>
<th>Modification</th>
<th>Recommendation</th>
<th>Approximate systolic BP reduction, range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight reduction</td>
<td>Maintain normal body weight (BMI, 18.5 to 24.9 kg/m²)</td>
<td>5-20 mmHg per 10-kg weight loss</td>
</tr>
<tr>
<td>Adopt DASH eating plan</td>
<td>Consume a diet rich in fruits, vegetables, and low-fat dairy products with a reduced content of saturated and total fat</td>
<td>8 to 14 mmHg</td>
</tr>
<tr>
<td>Dietary sodium reduction</td>
<td>Reduce dietary sodium intake to no more than 100 meq/day (2.4 g sodium or 6 g sodium chloride)</td>
<td>2 to 8 mmHg</td>
</tr>
<tr>
<td>Physical activity</td>
<td>Engage in regular aerobic physical activity such as brisk walking (at least 30 minutes per day, most days of the week)</td>
<td>4 to 9 mmHg</td>
</tr>
<tr>
<td>Moderation of alcohol</td>
<td>Limit consumption to no more than 2 drinks per day in most men and no more than 1 drink per day in women and lighter-weight persons</td>
<td>2 to 4 mmHg</td>
</tr>
</tbody>
</table>

BMI: body mass index; BP: blood pressure; DASH: Dietary Approaches to Stop Hypertension.
Hypertension: drug treatment

- **Reduction of pressure**
  - 8-15 mm Hg reduction for most drugs

- **Effect on clinical endpoints**
  - 30-40% reduction of stroke
  - 20% reduction of heart infarction
Kidney stones

- Frequent disease
- Causes
  - Super-saturation of urine
    - Calciumfosfat
    - Calciiumoxalat
    - Fosfat / infection
    - Urate
- Size
  - 1-80 mm.
  - < 6-7 mm will pass
# Kidney stones

- **Symptoms**
  - Very severe pain
  - Colic type, radiating to groin
  - Blood in urine

- **Examinations**
  - X-ray
    - Stone
    - Passage of urine

- **Complications**
  - Infection
  - Acute kidney failure
  - Chronic kidney failure
Kidney stones: treatment

- **Fragmentation**
  - Extracorporeal shock waves
  - Laser / US directly on stone

- **Removal**
  - Laparoscopy
  - Ureteroscopy
Chronic kidney disease

- **Frequency**
  - Mild: 5%
  - Serious: 0.5%
  - Dialysis: 0.1%

- **Progressive**

- **Lifelong**

- **Causes**
  - Kidney inflammation
  - Diabetes
  - High blood pressure
  - Atherosclerosis
  - Cystic diseases (genetic)
  - Infection / stone
  - Obstruction
  - other
    - Cancer
    - Drugs
    - Inflammation in vessels
Kidney failure (CKD stage 5)

- Symptoms
  - None at mild – moderate disease (stage 1,2,3 (4))
  - Fatigue, lethargy
  - Nausea, vomiting
  - Anorexia, loss of muscle mass
  - Itching

- Complications
  - Cardiovascular disease
    - Heart infarction, angina
    - Stroke
    - Heart failure
  - Anemia
  - Bone disease
  - Infections
  - Other
    - bleeding
    - Nerve damage
    - Red fertility and sex drive
Kidney failure

- **Evaluation**
  - **Blood tests**
    - Hb
    - Na, K, Ca, Fosfat
    - Creatinine
    - Blood sugar, cholesterol
  - **Urine**
    - Protein
  - **Ultrasound ex of kidney**
    - Size
    - Obstruction
    - Scarring

![Graph showing Glomerular Filtration Rate (ml/min/1.73m2)]
Kidney failure: treatment

- **Mild - moderate**
  - Reduce BP
  - Reduce u-protein
  - Strict blood sugar control
  - Correction of
    - Low hemoglobin (Epo)
    - High phosphate
    - High potassium
    - Acid retention
    - Low calcium

- **Serious**
  - Dialyse
  - Transplantation
Renal replacement therapy in Norway
Status by end of year - pats. pr mill. inhabitants

In dialysis
New in RRT
Tx performed
Waiting list

TL 05/03
Dialysis

Hemodialysis

Peritoneal dialysis
- Semipermeable membrane
- Diffusion of small molecules
- Convection of medium molecules
- Ultrafiltration of water
The hemodialysis machine

- Filter
- Dialysis fluid:
  - High/low potassium
  - High/low calcium
  - Bicarbonate
Hemodialysis

Anticoagulant

Used dialysis fluid

Dialyzer (Filter)

Fresh dialysis fluid

To the Patient

From the Patient

Blood pump

Hemodialysis
Dialysis water

- “Standard-HD-pas” is exposed to
  0.5 l/min x 4 h x 3 x 52 = 18 720 l/yr

In the early days of dialysis treatment problems with Al.

**Bacteria and endotoxins**: stimulation of inflammation, decreased response of erythropoietin and possibly aggravation of atherosclerosis.
Blood access

Two lumen large bore catheter in neck vein with subcutaneous tunnelation
Arterio-venous fistula («short-cut»)

Can be used 6-8 weeks after the operation
“Needles were the worst thing I could think about, so I never thought I could do this myself. But now, nobody else is allowed to get near my arm……..”
How much dialysis is enough?

\[
stdKt/V = \frac{10080 \cdot (1-e^{-eKt/V})}{1-e^{-eKt/V}} + \frac{10080}{N \cdot t} - 1
\]

\[
BUN_t = \text{pre BUN} \left[ \frac{V_{sp} + Quf \times t}{V_{sp}} \right]^{-\frac{G}{Kd + Kr UN + Quf}} + \frac{G}{Kd + Kr UN + Quf} \times \left[ 1 - \frac{V_{sp} + Quf \times t}{V_{sp}} \right]^{-\frac{G}{Kd + Kr UN + Quf}}
\]

\[
c(t, \Theta) = \frac{\dot{G}}{\dot{k} + \dot{\beta}} + \left( c(0) - \frac{\dot{G}}{\dot{k} + \dot{\beta}} \right) \cdot \left( \frac{V(0) + \dot{\beta} t}{V(0)} \right)^{-\frac{(k+\beta)}{\beta}}
\]

\[
Kt/V = \ln \left( \frac{1}{1 - URR} \right)
\]
Kidney transplantation
- Necro donation
  - Traffic accidents, cerebral bleedings
  - Waitinglist 1-2 years
- Living donation
  - Parents, siblings, children
  - Spouse, good friend
  - 40% of all Tx in Norway
  - Waitinglist 2-3 months
  - Better survival of the new kidney
First renal graft survival in patients below 60y.
By donor source and HLA match
Norway 1989-2002

LD (N=839) vs. CD (N=780): p = 0.0016
LD non-id. vs. CD 0 DR mm.: n.s. (p = 0.2157)
LD non-id. vs. CD 1-2 DR mm.: p < 0.001
CD 0 DR mm. vs. CD 1-2 DR mm.: p < 0.0001
Surgery
- “Medium operation”
- Low risk of death

Immunosuppression
- Prednisolone
- Cyclosporin
- Cytostaticum

Acute complications
- Acute rejection
- Urine leakage, bleeding, clotting of vessel
- Infection in wound, urine, lungs, sepsis (“blood poisoning”)
Benefits over dialysis
- Cheaper
- Much better quality of life
- Better survival
- Less cardiovascular complications

Complications
- Infections
- Loss of transplant function
- Cardiovascular disease
- Cancer
Prednisolon

- Antiinflammatory + immunosuppressiv effect
- Reduced the production of many cytokines

40 mg x1 reduced to 5 mg x 1
Calcineurin inhibitors
cyclosporin A
Imurel

- Interferes with DNA synthesis. Built into DNA- og reduces celleproliferation

- Nobel prize 1988
Figure 2. Individual Immunosuppressive Drugs and Sites of Action in the Three-Signal Model.

Anti-CD154 antibody has been withdrawn from clinical trials but remains of interest. FTY720 engagement of sphingosine-1-phosphate (S-1-P) receptors triggers and internalizes the receptors and alters lymphocyte recirculation, causing lymphopenia. Antagonists of chemokine receptors (not shown) are also being developed in preclinical models. MPA denotes mycophenolic acid.
Survival of first CD renal grafts

Graft Survival %

Months

0 12 24 36 48 60 72 84 96 108 120

1992-97
1987-91
1983-87
1978-82
Kidney and urinary tract diseases include:

- Very frequent and very seldom diseases
- Acute and chronic, harmless and deadly
- Strong dependence of technical solutions for evaluation and treatment
- Great challenges in the time to come