

Infusioonravi lahused.
Kristalloidid

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 Anestesioloogia ja intensiivravi kliinik
 Tartu Ülikool
 Tartu Ülikooli Kliinikum



 21.05. 2015, Eesti Siseastide Ühenduse seminar Vihulas

MALIGNANT CHOLERA.
 DOCUMENTS
 COMMUNICATED BY THE
CENTRAL BOARD OF HEALTH,
 LONDON.
 RELATIVE TO THE TREATMENT OF CHOLERA
 BY THE COPIOUS INJECTION OF AQUOUS
 AND SALINE FLUIDS INTO THE VEINS.
 ———
 No. 1.
Letter from Dr. Latta, to the Secretary
 of the Central Board of Health, London,
 offering a Plan of the Remedies and
 Results of his Practice in the Treatment of
 Cholera by Aquous and Saline Injections.*
 ———
 Latta, May 25, 1832.
*Sir—My friend Dr. Levine has been
 successful in one year with a decided
 success of one method of re-establis-
 hing by saline injection into the veins, with
 which I now mean willingly comply. My
 scope for observation, since I commenced
 this treatment, has been too limited to
 allow me to be very opinion on the subject,
 but I think I can adduce sufficient proof to
 the unprejudiced, not only of its safety,
 but of its unquestionable efficacy. I have
 never yet seen one had symptoms attribu-
 table to it, and I have no doubt that it will be
 found, when judiciously applied, to be one
 of the most powerful, and one of the most
 remedial, yet used in the second stage of
 cholera, or that hopeless state of collapse
 to which the system is reduced.*
 * Dr. Latta having stipulated his wish that the
 communication should be published in The Lan-
 cet, the Central Board of Health have accordingly
 forwarded it to his journal.—E. S.

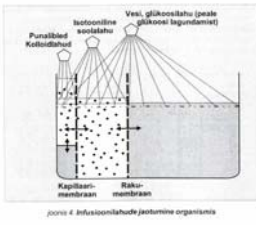
- 26. Okt. 1831, Sunderland, Inglismaa – **pandeemilise koolera** ohvrite arv Inglismaal jõuab 23 000-ni. Ravimeetodiks on „blood-letting with or without emetics“ [1]
- **William O’Shaughnessy**, Edinburgh – koolera lõpptulemuseks on ‘The universal stagnation of the venous system, and rapid cessation of the arterialisation of the blood, are the earliest, as well as the most characteristic effects. Hence the skin becomes blue...’ [2].
- Koolerahaigete veri: „... **had lost a large proportion of its water and ‘neutral saline ingredients’**“ [3]
- **Mai 1832. Thomas Latta**, Edinburghi perearst – „... attempted to restore the blood to its natural state, by injecting copiously into the larger intestine warm water holding in its solution the requisite salts, and also administered quantities from time to time by the mouth.“ [4].

1) Baskett TF. The Resuscitation Greats: William O’Shaughnessy, Thomas Latta and the origins of intravenous Saline. Resuscitation 2002; 55: 231-234.
 2) O’Shaughnessy WB. Proposal of a new method of treating the blue epidemic cholera by the injection of highly-oxygenised salts into the venous system. Lancet 1831;1366/1.
 3) O’Shaughnessy WB. Experiments on the blood in cholera. Lancet 1831;1:400.
 4) Latta TA. Relative to the treatment of cholera by the copious injection of aqueous and saline fluids into the veins. Lancet 1832;2:274-7.

Loengu sisu

- Osmolaarsus ja toonilisus
- Kristalloidlahuse mõiste
- Glükoosilahused
- Infusioonravi ajalugu
- Soolalahused
- Kristalloidlahuste füsioloogilised efektid ja omavaheline võrdlus
- Füsioloogiline vee ja elektrolüütide vajadus
- Patoloogiliste kadude elektrolüütikoostis

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Infusioonravi lahused

- elektrolüütide sisaldus
- kolloidosakeste sisaldus
- **Kristalloidlahused**
- **Kolloidlahused**

4

Osmolaarsus

- Osmootse rõhu tekitab osmootselt aktiivsete osakeste lahustumine vees
- Organismis tagavad osmootse rõhu 95 % ulatuses kehavedelike elektrolüütide sisaldus
- Kehavedelike osmootne rõhk on 280...295 (300) mosm/kg H₂O
- **Isotoonilised e. isoosmolaarsed lahused** – lahused, mille osmootne rõhk on võrdne
- Vereplasma suhtes **hüpotoonilised, isotoonilised ja hüpertoonilised** kristalloidlahuseid
- Osmolaalsus - mosm/kg H₂O; osmolaarsus - mosm/l H₂O

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Kristalloidlahused

- Koosnevad reeglina veest ja elektrolüütidest
- Vereplasma suhtes **hüpotoonilised, isotoonilised ja hüpertoonilised** kristalloidlahuseid.
- Lahuse osmolaalsuse arvutamiseks liidetakse kõikide osmootselt aktiivsete osakeste kontsentratsioonid.
- Sellise arvutuse kohaselt on 0,9% NaCl osmolaalsus ≈308 mosm/kg.
- Lahuse tegelik, st mõõdetud osmolaalsus, on aga väiksem, ≈285 mosm/kg, sest osakeste dissotsiatsioon lahustes ei ole kunagi täielik.
- Manustatavate infusioonilahuste püsimise rakuvälises ruumis määrab nende **Na+ sisaldus**.

6

Glükoosilahused

- Sisaldavad ainet (glükoosi), mis on võimeline kristalliseeruma ⇒ **kristalloidlahused**
- 5% glükoosilahus: 278 mosm/l ⇒ **isoosmolaarne**
- 10%, 20% ja 40% glükoosilahused ⇒ hüperosmolaarsed
- Viia organismi Na⁺-vaba vett
- Jaotub kõigis organismi vedelikuruumides
- Glükolüütiliste kudede vajadus - **100...200 g glükoosi ööpäevas**

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0.9 % NaCl

- **Normal saline** is the commonly used phrase
- about 300 mosm/L or 9.0 g NaCl per liter

Less commonly:

- **Physiological saline**
 - **Isotonic saline**
- neither of which is technically accurate

Awad S, Allison SP, Lobo DN. The history of 0.9% saline. *Clinical Nutrition* (2008), 179-188

Infusioonravi ajalugu

- **Thomas Latta** (1796 – 1833)
- **Sydney Ringer** (1835 – 1910)
- **Alexis Hartmann** (1898 – 1964)

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Clinical Nutrition (2008) 27, 179-188



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REVIEW

The history of 0.9% saline

Sherif Awad, Simon P. Allison, Dileep N. Lobo*



Professor of gastrointestinal surgery
University of Nottingham, UK

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MALIGNANT CHOLERA.

DOCUMENTS
COMMUNICATED BY THE
CENTRAL BOARD OF HEALTH,
LONDON,

RELATIVE TO THE TREATMENT OF CHOLERA
BY THE COPIOUS INJECTION OF SALINE
AND BAKING SODA INTO THE VEINS.

No. 1.

Letter from Dr. Latta* to the Secretary
of the Central Board of Health, London,
offering a Treatise of the Principles and
Results of his Practice in the Treatment of
Cholera by Saline and Soda Injections.

Leith, May 26, 1832.

Sir,—My friend Dr. Lewis has communicated to me your wish for a detailed account of my method of treating cholera by saline injections into the veins, with which I am more willingly comply. My scope for observation, since I commenced this treatment, has been too limited to allow me to be very copious on the subject, but I think I can adduce sufficient proof to the unprejudiced, and only of its safety, but of its unquestionable utility. I have never yet seen one had symptoms attributable to it, and I have no doubt that it will be found, when judiciously applied, to be one of the most powerful, and one of the safest remedies yet used in the second stage of cholera, or that impetuous stage of colic to which the system is reduced.

* Dr. Latta having stipulated his wish that his communication should be published in *The Lancet*, the Central Board of Health have accordingly forwarded it to this Journal.—*Ed. L.*

- Na⁺ 48 – 68 mmol/l
- Cl⁻ 39 – 59 mmol/l
- HCO₃⁻ 9 mmol/l
- Kolm patsienti neljast surid
- Latta arvates olid surma põhjusteks „liiga vähene kogus“, haigus ise ja „late application of the remedy“


Lancet, May 26th, 1832

Latta kolmas ja neljas lahus

- Half drachm muriate of soda, 8 grains subcarbonate of soda, 1 pound of water saturated with protoxide of azote
- „...the solution I used contained a third more saline matter...“
- Na⁺ 107 mmol/l
- Cl⁻ 91 mmol/l
- HCO₃⁻ 16 mmol/L
- Na⁺ 134 mmol/l
- Cl⁻ 118 mmol/l
- HCO₃⁻ 16 mmol/L

Clinical Nutrition (2008), 179-188


- **Sydney Ringer 1883**
- University College of London
- Isoleeritud südamelihaskas lakkas 20 minutiga töötamast, kui perfusioonilahus oli tehtud destilleeritud veest ja NaCl-st. Kui lahus kogemata tehti destilleerimata veest, lihase kontraktsioon jätkus
- Ca, K, HCO₃



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None of the intravenous saline solutions described between 1832 and 1895 bear any resemblance to 0.9% saline (Table 3). The first reference to a solution similar to 0.9% saline appeared in 1896.⁶⁰ In his article W.S. Lazarus-Barlow cites Hamburger as the main authority for suggesting that a concentration of 0.92% saline was 'normal' for mammalian blood.⁶⁰

- **Hartog Jacob Hamburger (1859 – 1924)**
- Hollandi keemik ja füsioloog
- 0,92 % NaCl
- Ex vivo katsed erütrotsüütidega



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Ringeri lahus	Hartmanni lahus
<ul style="list-style-type: none"> • Na⁺ 130 mmol/l • K⁺ 4 mmol/l • Ca⁺ 1.5 mmol/l • Cl⁻ 109 mmol/l • Lactate 28 mmol/L 	<ul style="list-style-type: none"> • Na⁺ 131 mmol/l • K⁺ 5 mmol/l • Ca⁺ 2 mmol/l • Cl⁻ 111 mmol/l • Lactate 29 mmol/L
1883	1932



0.9 % NaCl

- „It remains a mystery how it came into general use as an intravenous fluid in vivo.
- Perhaps it was due to the ease, convenience and low costs of mixing common salt with water.“
- Igal aastal kasutatakse Ühendkuningriikides u. **10 milj liitrit 0,9 % NaCl** intravenoosseks manustamiseks

Awad S, Allison SP, Lobo DN. The history of 0.9% saline. Clinical Nutrition (2008), 179-188

Balansseeritud ja mittebalanseeritud lahused

	Plasma	0,9 % NaCl	Ringeri lahus	Plasma-Lyte	Stero-fundin ISO
Na	135-145	154	130	140	145
K	3.5-5.3	-	5	5	4
Ca	2.2-2.6	-	2	0	2.5
Mg	0.7-1.2	-	0	1.5	1.0
Cl	95-105	154	111	98	127
Bikarbonaat/eellane	24-32	-	Laktaat 27	Atsetaat 27 Glükonaat 23	Atsetaat 24 Malaat 5
Na:Cl suhe	1.28-1.45:1	1:1	1.18:1	1.43:1	1.14:1
Mosm/l	275-295	308	276	294	309

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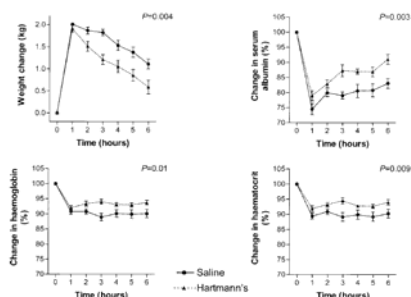
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Vabatahtlikele 2 liitrit lahust 60 min jooksul



⇒ Vee retensioon 0,9 % NaCl puhul

Reid F et al. Clinical Science (2003) 104, 17-24

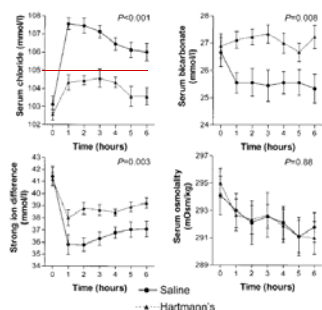
Vabatahtlikele 2 liitrit lahust 60 min jooksul

Parameter	Saline	Hartmann's solution	P
Time to first micturition (min)	165 (135-280)	70 (45-165)	0.008
Number of micturitions over 6 h	2 (1-3)	3 (2-4)	0.02
Total post-infusion urine volume over 6 h (ml)	450 (355-710)	1000 (410-1500)	0.049
Total post-infusion urinary sodium over 6 h (mmol)	73 (54-118)	322 (79-175)	0.049
Sodium excretion (% of sodium infused)	23.5 (20.7-35.9)	46.9 (30.4-67.2)	0.02
Total post-infusion urinary potassium over 6 h (mmol)	34 (24-49)	33 (31-49)	0.48
Osmolality of pre-infusion urine (mOsm/kg)	894 (831-972)	841 (771-1015)	0.86
Osmolality of pooled post-infusion urine (mOsm/kg)	670 (450-808)	432 (332-609)	0.48

⇒ Vee ja Na retensioon 0,9 % NaCl puhul

Reid F et al. Clinical Science (2003) 104, 17-24

Vabatahtlikele 2 liitrit lahust 60 min jooksul

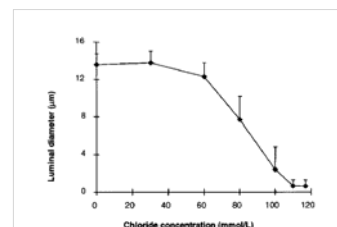


⇒ Hüperkloreemia 0,9 % NaCl puhul

Reid F et al. Clinical Science (2003) 104, 17-24

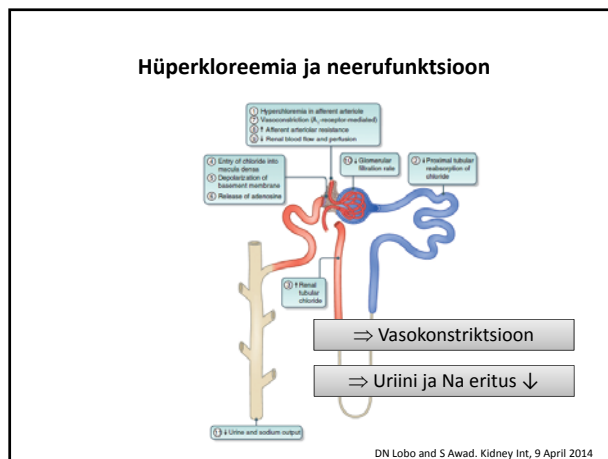
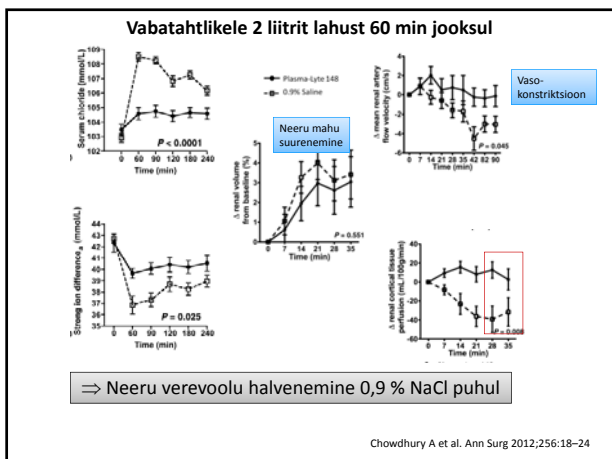
Kloriid-sõltuv vasokonstriktsioon neeruarterites

- Füsioloogilise Cl⁻ vahemikus 80-110 mmol/l toimub neeru aferentsetes veresoontes vasokonstriktsioon
- Cl⁻ vähesel tõusul on vasokonstriktsioon juba maksimaalselt tugev



Küüliku neeru aferentsed arterioolid

Hansen P et al. Hypertension. 1998;32:1066-1070



Neerusiirdamine

	0.9 % NaCl (n=26)	Ringer-Lactate (n=25)
4-h urine output, L	1.6±1.6	2.1±1.5
24-h Crea clearance, ml/min	81±41	94±30
Postop day 3 serum Crea, mg/dL	2.3±1.8	2.1±1.7
Metabolic acidosis, n (%)	8 (31)	0
Hyperkalemia, n (%)	5 (19)	0
1-wk serum Crea, mg/dL	1.9±1.2	1.6±1.3
6-mo serum Crea, mg/dL	1.5±0.6	1.5±0.4
Pt requiring dialysis, no (%)	2 (8)	1 (4)

Randomiseeritud, topelt-pime uuring

O'Malley C et al. Anesth Analg 2005;100:1518-24

Aordi aneurüsmi kirurgia

	0.9% NaCl (n=35)	Ringer-lactate (n=33)
Bicarbonate therapy, ml	30±62	4±16
Platelet transfusions, ml	478± 302	223 ± 24

- Haiged 0.9 % NaCl rühmas said rohkem veretoodete ülekandeid (P0.02)
- Ei olnud erinevust aparaadiringamise, intensiivravi või haiglaravi kestuses ega tüsistuste esinemissageduses

Randomiseeritud, topelt-pime uuring

Waters J et al. Anesth Analg 2001;93:817-22

- Paistab, et 0.9 % NaCl kasutamisel esineb mitmeid kõrvaltoimeid
 - Uuringute tase ei ole eriti hea
- Awad S, Allison SP, Lobo DN. The history of 0.9% saline. Clinical Nutrition (2008), 179-188

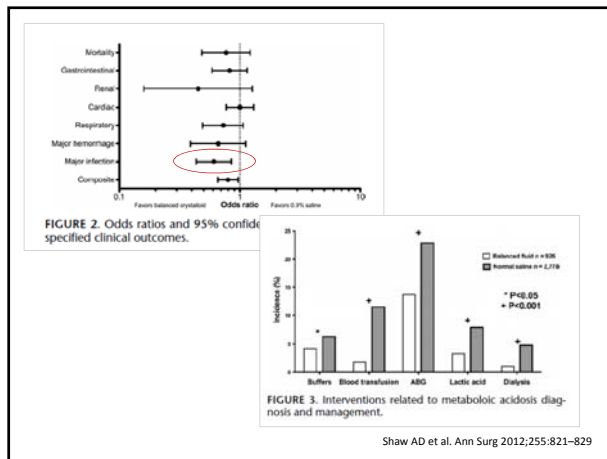
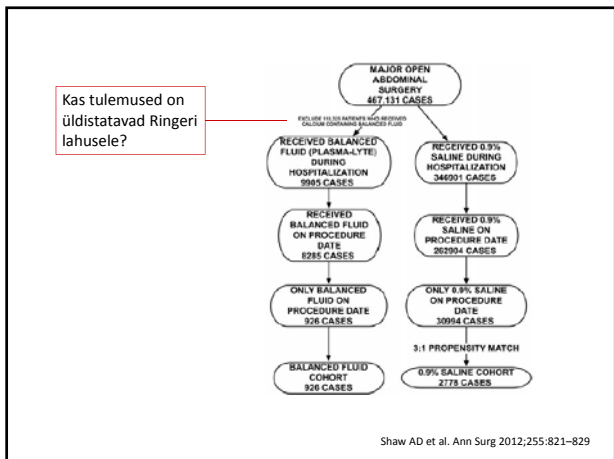
FEATURE

Major Complications, Mortality, and Resource Utilization After Open Abdominal Surgery

0.9% Saline Compared to Plasma-Lyte

Andrew D. Shaw, MB, FRCA, FCCM,* Sean M. Bagshaw, MD,† Stuart L. Goldstein, MD,‡ Lynette A. Scherer, MD,§ Michael Duan, MS,|| Carol R. Schermer, MD,¶ and John A. Kellum, MD||

Shaw AD et al. Ann Surg 2012;255:821-829



In conclusion, our analysis of hospital administrative data for patients undergoing major open abdominal surgery, involving more than 30,000 saline recipients in comparison with nearly 1000 balanced crystalloid recipients supports the hypothesis that there is an increased risk of major morbidity and resource utilization among recipients of 0.9% saline. Whether the increased risk is due to hyperchloremic acidosis alone or to other effects of saline administration is unclear but it does not appear to be due to chance or to patient or hospital characteristics. Perhaps the most concerning findings were the dramatic differences in postoperative infection and renal dysfunction, both suggested previously by in vitro and animal studies. Further research is needed to determine if these risks are extended to patients receiving saline along with balanced fluids and to better understand the mechanisms underlying these risks.

Shaw AD et al. Ann Surg 2012;255:821-829

Hüperkloreemia ja postoperatiivne suremus

• 22,851 kirurgilist haiget normaalse preoperatiivse seerumi kloriiditaseme ja neerufunktsiooniga

• Äge postoperatiivne hüperkloreemia (seerumi kloriid >110 mmol/L) on sage, esines 22 % uuritud haigetest

Hüperkloreemiaga haigetel oli

• Kõrgem suremus (3.0% vs 1.9%; OR = 1.58; 95% CI 1.25-1.98)

• Pikem haiglasviibimine (7.0 [4.1-12.3] vs 6.3 [4.0-11.3] päeva)

McCluskey SA et al. Anesth Analg 2013;117:412-121

0.9 % NaCl vs balanseeritud kristalloidlahused

Metaboolsed kõrvaltoimed	<ul style="list-style-type: none"> Hüperkloreemiline atsidoos Suurenenud vajadus eksogeensete puhvritega atsidoosi korrigeerimiseks 	The evidence has been collected from animal studies, healthy volunteer studies, small randomized clinical trials, and large patient cohort studies, and cannot be presently regarded as Grade A.
Keha vedelikruumid	<ul style="list-style-type: none"> Endoteeli glükokaalüksi võimalik kahjustus Intestinaalne vedeliku ↑, tursed 	
Neerud	<ul style="list-style-type: none"> Neerude turse, kapsli venitus Renaalne vasokonstriksioon, renaalse verevoolu ↓ Glomerulaarfiltratsiooni, diureesi ja Na erituse vähenemine 	
Seedetrakt	<ul style="list-style-type: none"> Sooleselina turse Illeus, anastomooside paranemine 	
Hematoloogia	<ul style="list-style-type: none"> Verekaotus ↑ Vereülekanne vajadus 	
Ravitulemused	<ul style="list-style-type: none"> Postoperatiivsed komplikatsioonid ↑ Suremus ↑ Neerupuudulikkus, dialüüsravi ↑ 	

DN Lobo and S Awad. Kidney Int, 9 April 2014

Puhverkomponendid?

- Laktaat mittetoksiline, energeetiline substraat
- Atsetaat kardiotoksilisus, hüpotensioon?
- Malaat andmed puuduvad
- Glükonaat eksperimendis kaitseb I/R kahjustuse eest

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Füsioloogiline vee ja elektrolüütide vajadus

- Vee tarbimine (1,5...) 2,0...2,5 (...8) L ööpäevas
- Soola tarbimine
 - Soovitus on alla 5 g päevas s.o. **90 mmol Na**
 - Soomlased u. 10 g päevas s.o. 180 mmol Na
- Infusioonravi
 - H₂O 20...40 ml/kg ööpäevas (2 liitrit/ööp.)
 - Na 1..2 mmol/kg ööpäevas (**85 mmol/ööp.**)
 - K 1 ...1.5 mmol/kg/ööpäevas (50 mmol/ööp.)

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Seedenõrede hulgad ja koostised

Sekret	Sülg	Maomahl	Sapp	Pankrease-nõre	Peen-sool	Feetses
Hulk ööpäevas ml H ₂ O	1500 (500...2000)	500... 2000	1000... 2000	1000... 2000	3000	100
Na ⁺ mmol/l	25 (10...60)	60 (40...100)	145 (130...160)	150 (130...160)	140 (80...150)	40
K ⁺ mmol/l	25 (20...30)	4...12	4...7	4...7	3...8	100
Cl ⁻ mmol/l	15 (10...20)	50...150	80...110	55...95	80... 125	20
HCO ₃ ⁻ mmol/l	40 (25...50)	HCl sisaldav 0; antatsiidne kuni 20	30..50	25...120	20...30	30
pH	7,0	1.0...4.0	7.4...7.6 (6.0...8.8)	7.0...8.7	7.4... 7.6	

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„Peidetud“ NaCl allikad intensiivraavis

- Kolloidlahused (=0.9 % NaCl)
- Veretooted
- Ravimite lahustamine (500...1500 ml 0.9 % NaCl ööpäevas)
- Parenteraalne toitmine
- Enteraalne toitmine

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Kokkuvõte

- ⇒ 0.9 % NaCl ei ole füsioloogiline lahus
- ⇒ Korrektseid randomiseeritud uuringuid on vähe
- ⇒ Võrreldes balanseeritud kristalloidlahustega esineb **0.9 % NaCl kasutamisel rohkem neerupuudulikkust**
- ⇒ **Hüperkloremia** on seotud atsoidoosi ning suurema suremusega kõhukoopa kirurgias

Koju kaasa

- ⇒ Vali kristalloidlahus vastavalt kliinilisele olukorrale
 - ⇒ Neerusiirdamine, suur kõhukoopakirurgia – balanseeritud kristalloid
- ⇒ Ööpäevas manustatav NaCl kogus! Ravimite lahustamine?
- ⇒ Jälgi Cl kontsentratsiooni intensiivravi haigetel

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Tänan tähelepanu eest!

