

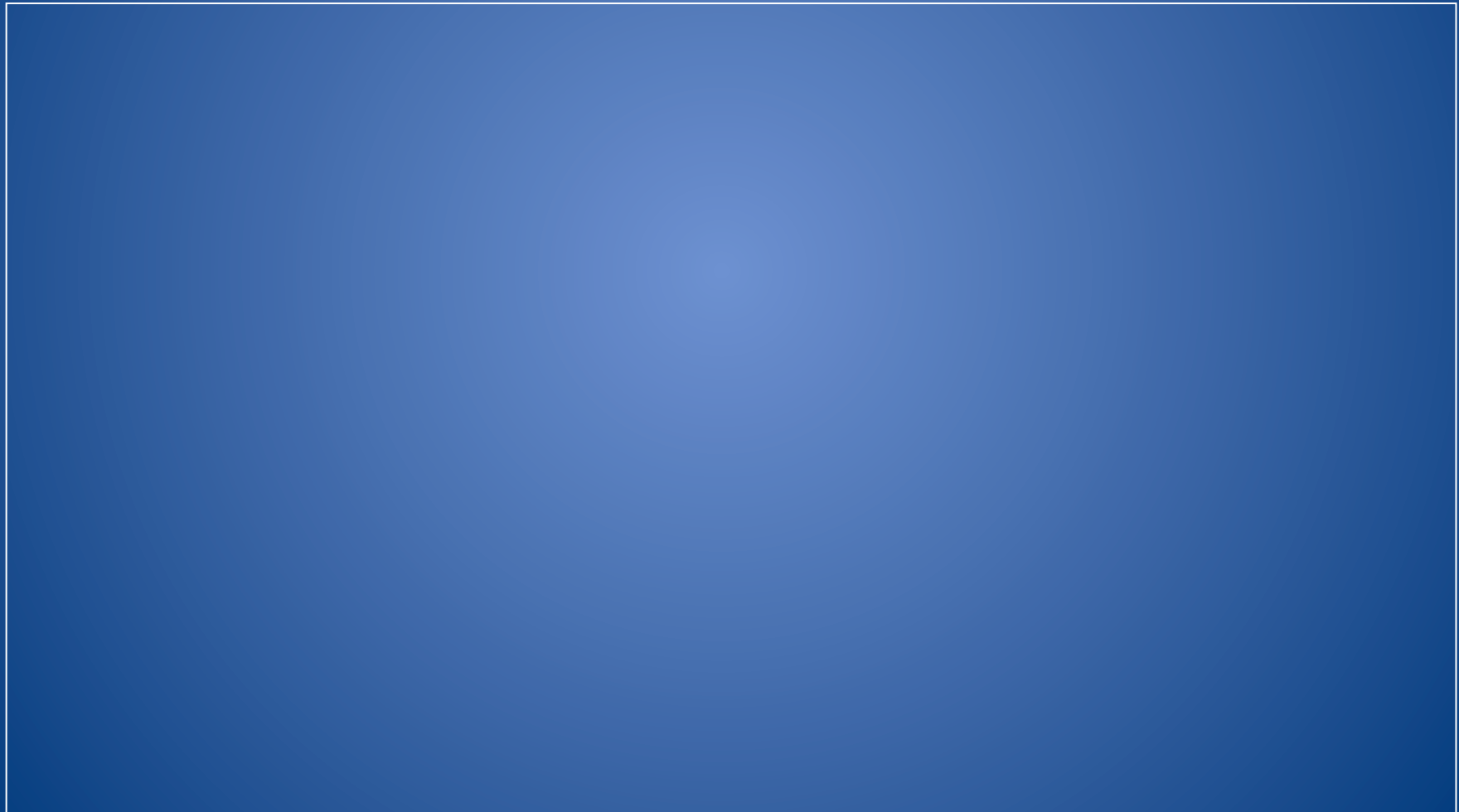
ESIM Winter School 2014

Cases seen in Internal Medicine

13 January 2014



Three Topics



46 y Secretary of the hospital

While passing my office she mentioned to have a strange sensation since 2 days on the left side of her neck

Past history

Tonsillectomy

Appendectomy

No smoking, little wine, no drugs

46 y Secretary of the hospital

Clinical findings

slight ptosis on left side
miosis and endophthalmus
No other findings
BP 130/75mmHg, P 80/min

Blood analysis

1 month earlier (insurance issue)
normal





67y Businessman

Reason for consultation

Patient changed his town of living and wanted a check up

Personal history

Diabetes mellitus since 5 y (OAD)

Cigarette smoking ca. 30 py

67y Businessman

Check up at the University Hospital Austria
1 month earlier

Thorax Rx	normal
CT abdomen	normal
Coloscopy	normal
Endoscopy	normal
Biopsy of prostate	normal
Blood analysis	normal, HbA1c 7.1 %

67y Businessman

Clinical findings

141/84mmHg, HR 67/min
heart, lungs and abdomen normal

Feet without vibration sensitivity }
No Achilles tendon reflex }

DD
diabetic
Neuropathy





39 y Secretary in town

History

Sudden onset of vertigo, she hardly could walk, felt pins and needles in the right hand. One day earlier she had a headache but not now. When arriving in the emergency room, the symptoms had improved very much.

Past history

Adhesive ileus 2 y earlier

39 y Secretary in town

Clinical

BP 150/83mmHg, P 77/min, heart normal
sensibility of the left face reduced
left eye with ptosis, endophthalmus,
miosis, cold discrimination normal ?
other neurological findings normal, GCS 15

Blood

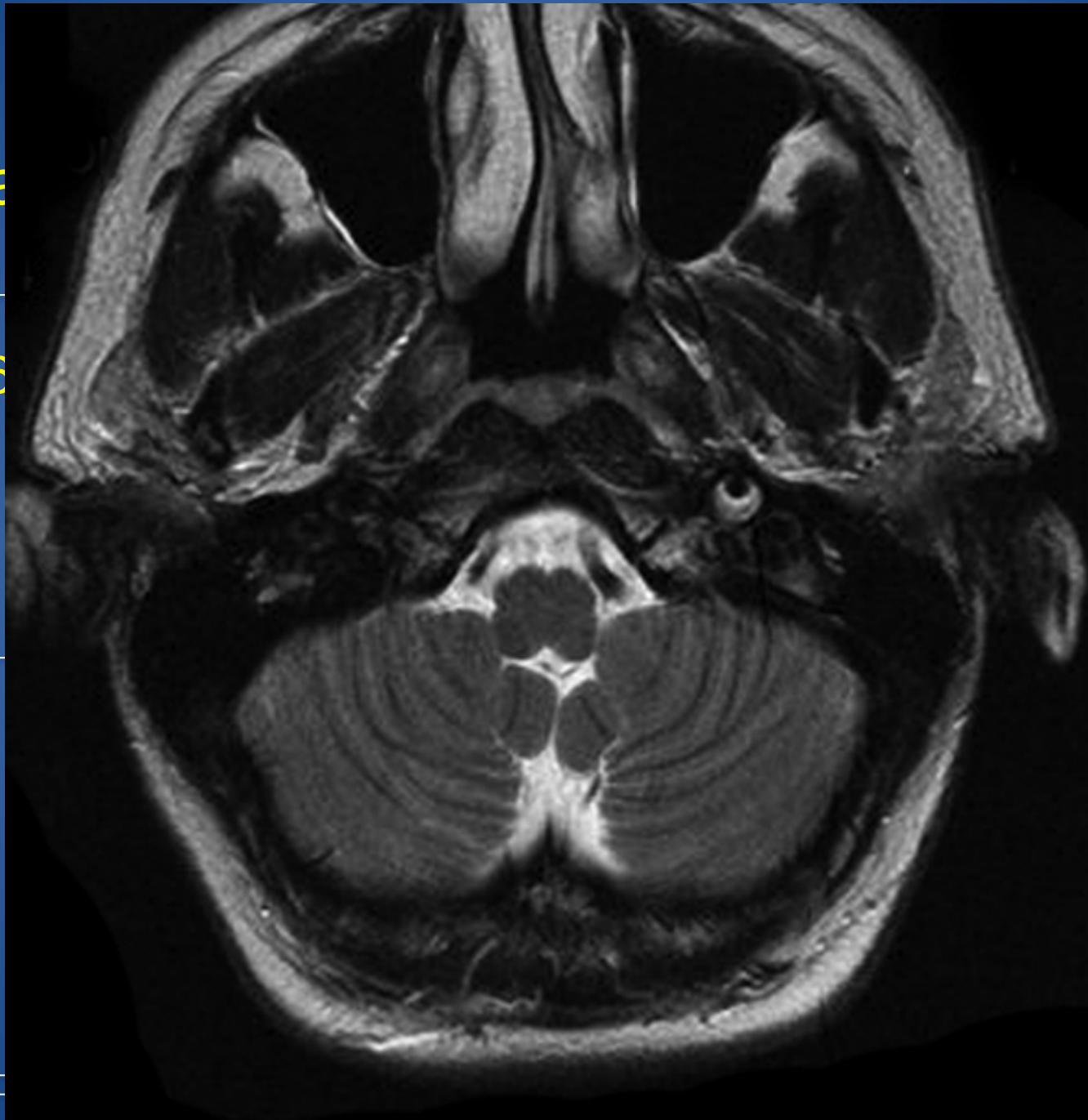
Hb 128/l, Leuc 9.9G/l, Tc 314G/l, BSR 9mm
Na 138, K 4.1mmol/l, Creat 81 μ mol/l, CRP <7mg/l
LDH 261U/l, liver enzyme normal, glucose 6.8mmol/l



What do the 3 cases have in common ?

3 Pa

46



next ?

y

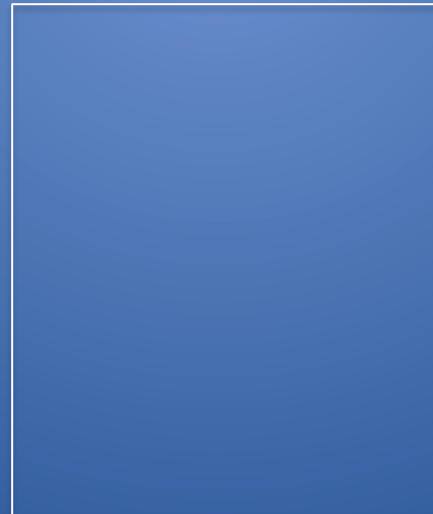
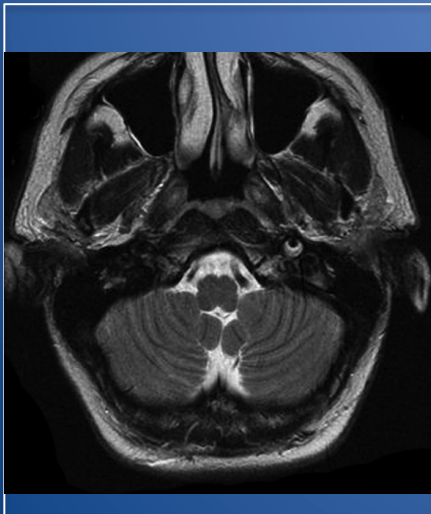
3 Patients with Horner Syndrom: What next ?

46j Secretary

67j Businessman

39j Secretary

MRI T2 Blood
in wall of artery



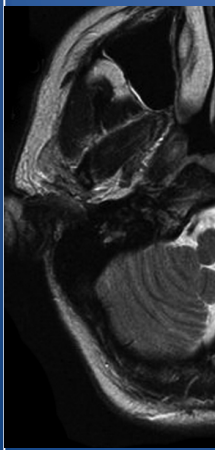
3 Patients

What next ?

46j Secre

Secretary

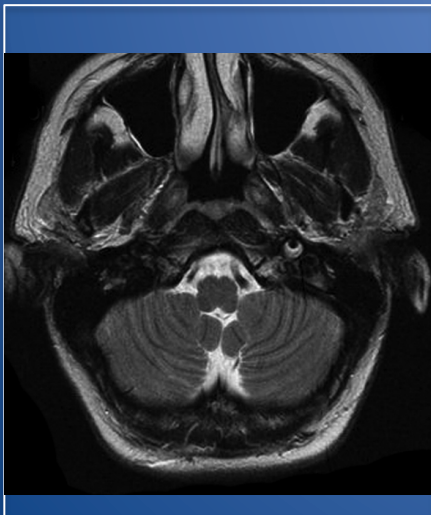
MRI T2 Blo
in wall o



3 Patients with Horner Syndrom: What next ?

46j Secretary

MRI T2 Blood
in wall of artery



67j Businessman

MRI and CT
Pancoast tumor



39j Secretary

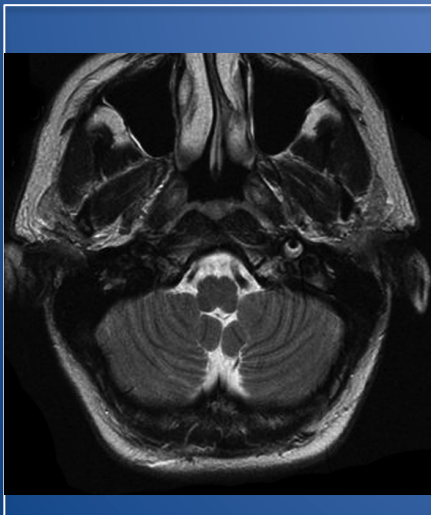




3 Patients with Horner Syndrom: What next ?

46j Secretary

MRI T2 Blood
in wall of artery



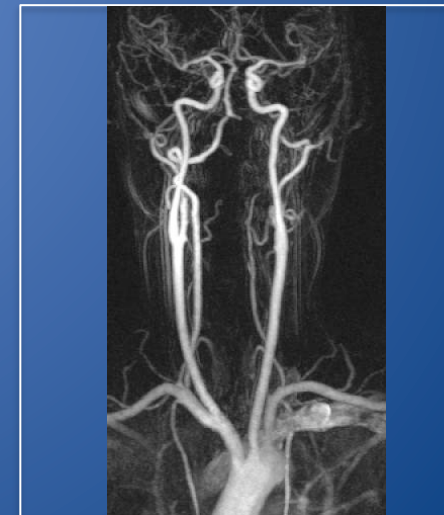
67j Businessman

MRI and CT
Pancoast tumor



39j Secretary

MRI A. verte-
bralis missing
dissection ?

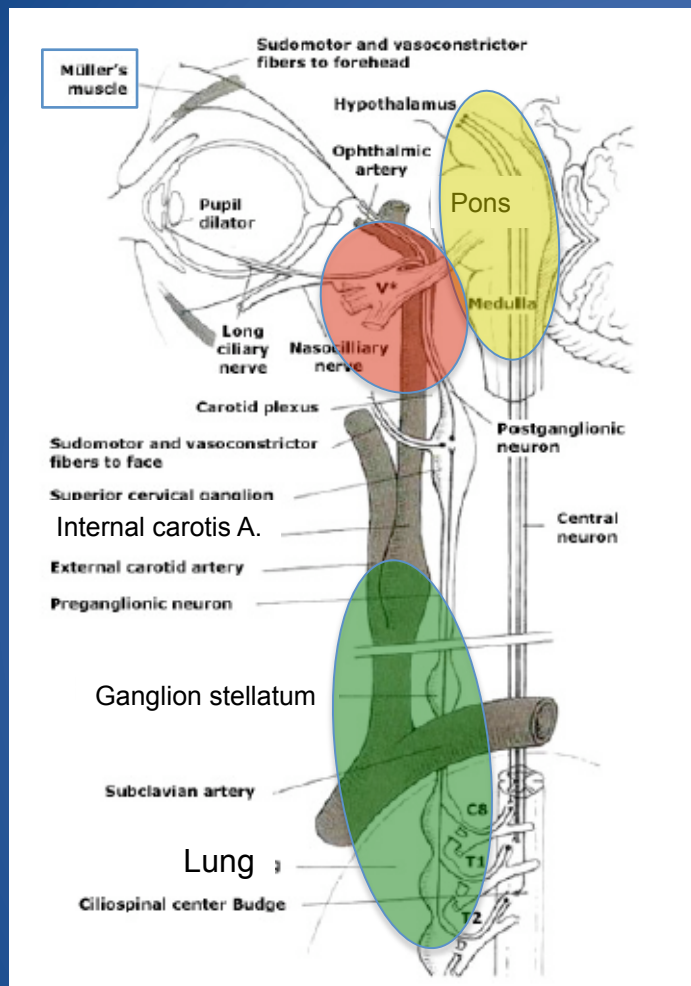


Horner's Syndrom



Prof. Johann Friedrich Horner
Swiss ophthalmologist Zurich

He wrote in 1869: A particular form of ptosis



Site of the lesion

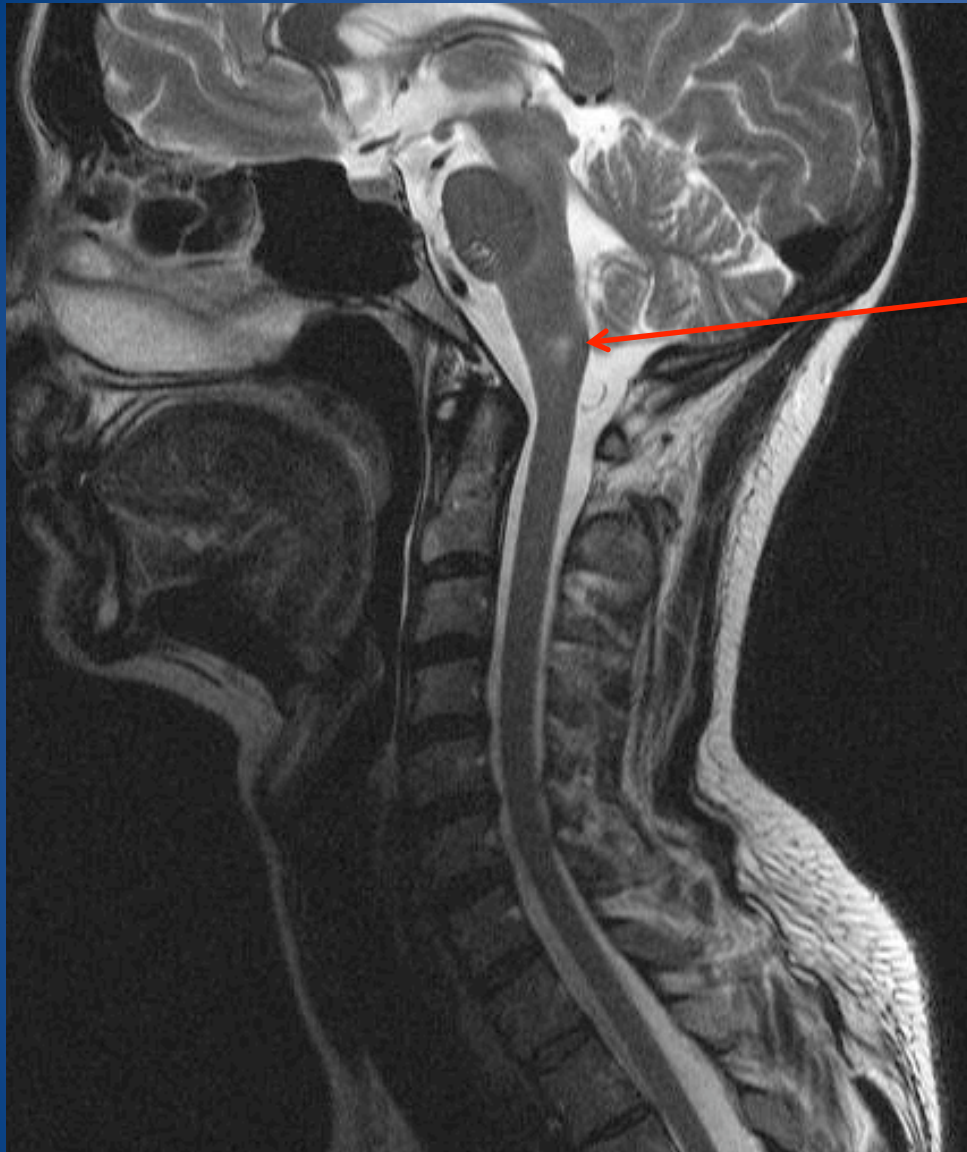
1. central
2. Preganglionic
3. Postganglionic

Periarterial plexus of internal carotid A.

↑
Sympathetic chain

↑
Sympathetic nerves
C8 – Th 2 effect: dilates the pupil

Sudosecretory fibres
Th 3 – Th 7 face, neck, arm



Central site Horner's Syndrom

Medulla oblongata
Infarction dorso-lateral

Wallenbergs Syndrom

Horner, hypoesthesia of the face, nystagmus, impaired nerves: vagus N, glossopharyngeal N, dizziness, cerebellar ataxia ipsilateral, hypoesthesia for pain & temperature contralateral site

Infarct reaching ventral site:
also hemiparesis contralateral
site of the body

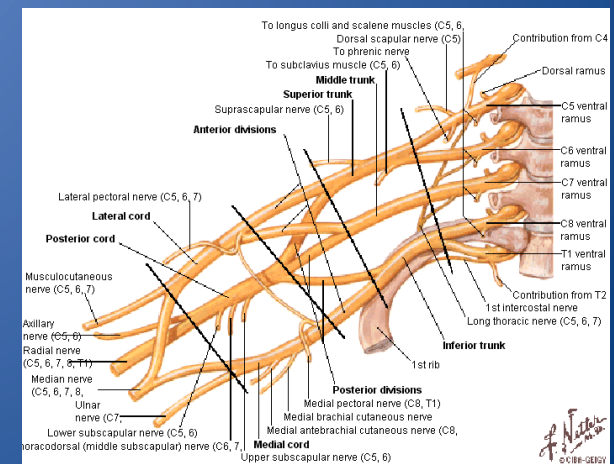
Preganglionic Horner's Syndrom

Pancoast tumor or infection
Fracture of the first rib
Carcinoma of the thyroid gland
or esophagus

Struma

Trauma or infection of the neck

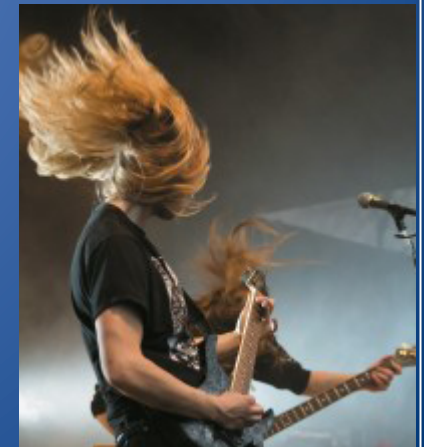
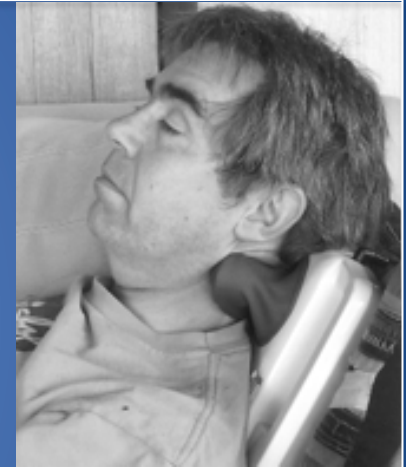
Dissection arteries of the neck



Postganglionic causes of Horner's Syndrom

neck trauma and dissection of internal carotid A.

Connective tissue diseases
Spinal manipulation therapy (chiropractor)
Shiatsu massage machine
Sports (boxing, surfing, wrestling etc.)
Jumping with head turned to the side
Cervical distension
Tickling
Musician
Coughing fit
Turning the head while car driving
Flue-like infection ?

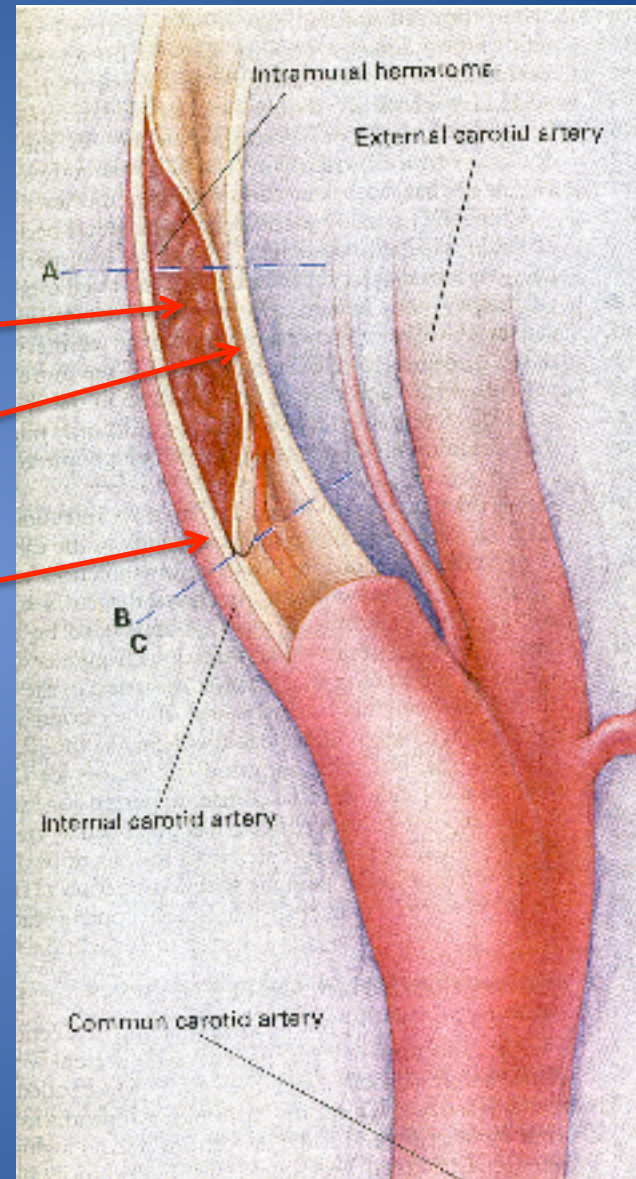


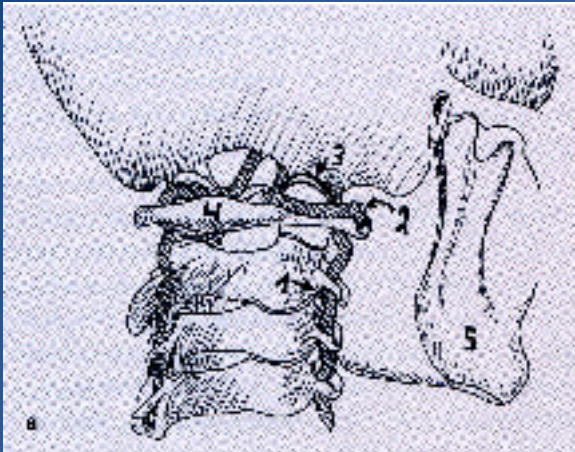
Dissection Internal carotid artery

Intramural hematoma

Lumen of the artery

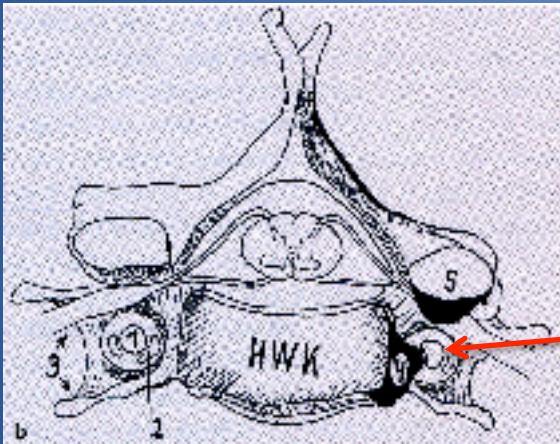
Dissection starts





Dissection of the vertebral artery

- 1 Intervertebral joint
- 2 Vertebral artery
- 3 Atlanto-occipital joint
- 4 Atlas



Vertebral artery



Rotation of the head to the right stretches the left vertebral artery between C1 and C2

Chiropractor Manipulation

582 patients with ischemia in the vertebral artery run off
(2328 matched controls)

<45 y age: 5.5x more often chiropractor treatment

>45 y age: no correlation

Stroke 32:1054-1060;2001

Prognosis: 165 patients with chiropractic manipulation
induced dissection of the vertebral artery

		other study
Complete recovery	27%	
Partial recovery	52%	75%
Death	18%	<5%

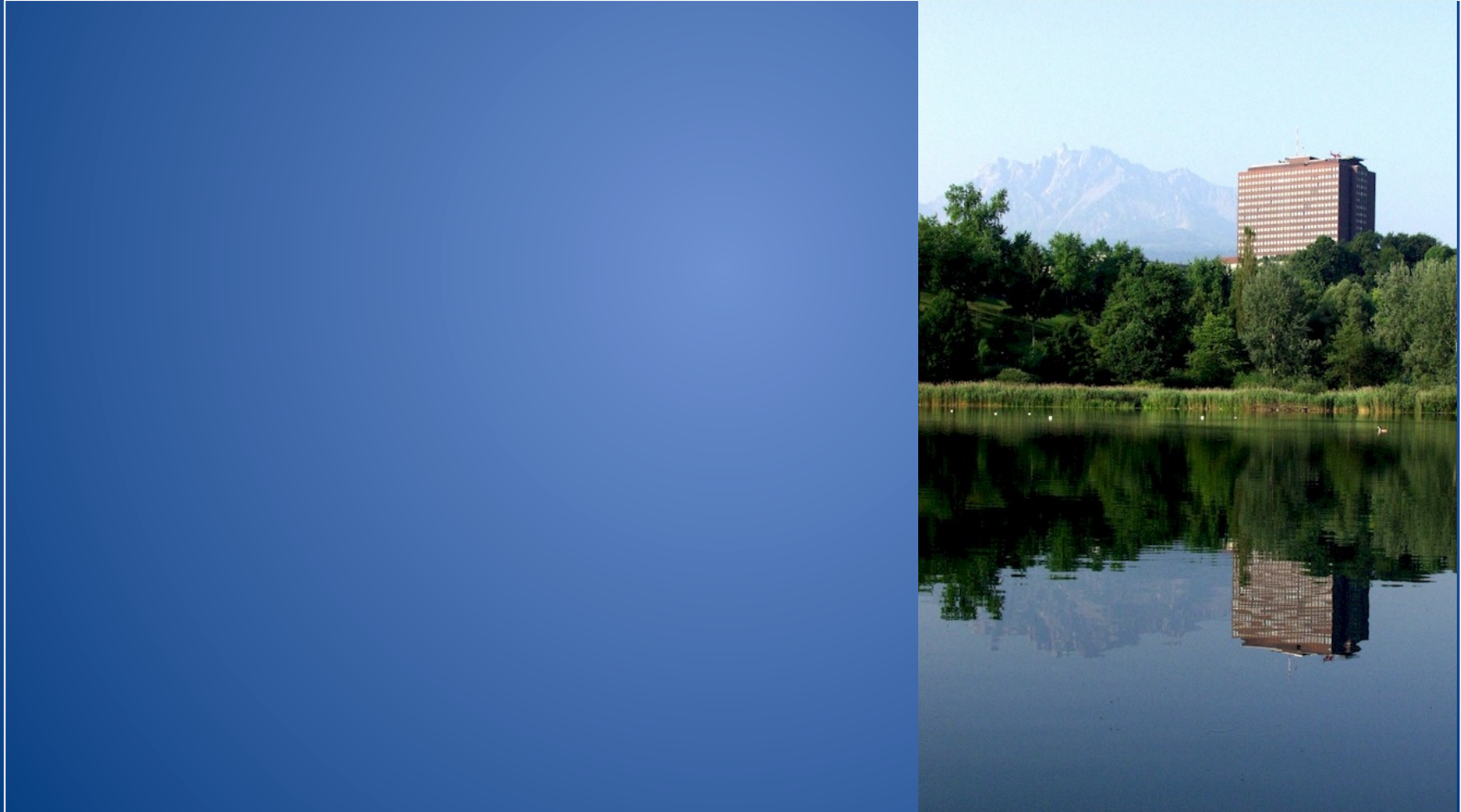
Headache 34:187-193;1994

Take home message

It is worth looking in the eyes of your patients !

>30% of Horner's Syndrome are idiopathic
and of no significance !

However it may be a sign of potential danger.



32 y house wife frequently running long distances

Current symptoms

Collapse during the race
Feels unwell

Past history

No serious disease

Clinical findings

BP 110/60 mmHg, P 98/min.
heart and lung normal



32 y house wife frequently running long distances

P_{Na} mmol/l	121
Osm mosm/kgH ₂ O	261
P_K mmol/l	3.9
Albumine g/l	32
Hb g/l	118
Tc g/l	125
Quick %	78
Urine Spec. weight	1005





32 y house wife
frequently running long distances

Blood- and Urine-Osmolality are low

Blood_{Osm.} 261 mOsm/kg > Urine_{Osm.} 97 mOsm/kg

Diagnosis: Water intoxication

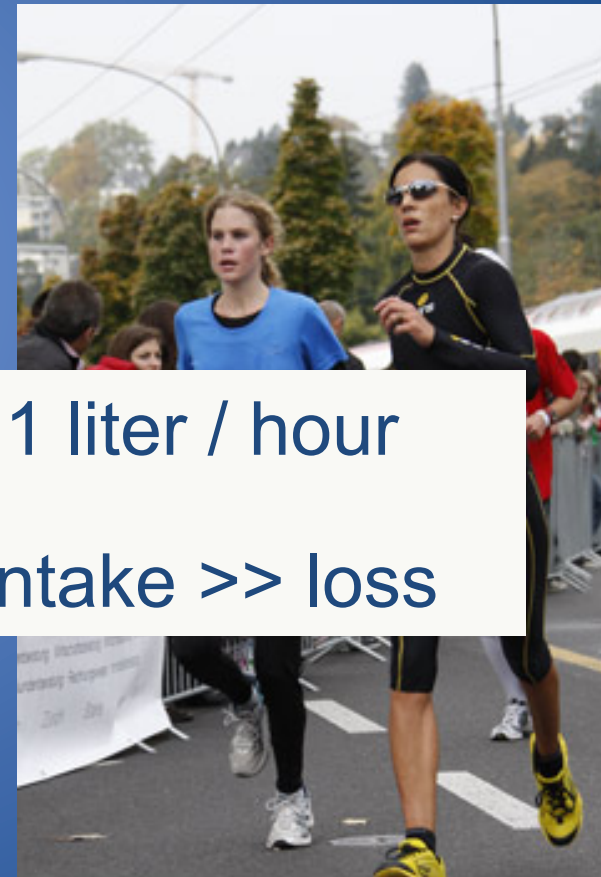
32 y house wife frequently running long distances

P_{Na} mmol/l	121
Osm mosm/kgH ₂ O	261
P_K mmol/l	3.9
Albumine g/l	32

Inappropriate water intake 1 liter / hour

→ water intoxication when intake >> loss

Quick %	78
Urine Spec. weight	1005



Complications in Marathon runners

	New Zealand Ironman	Boston Marathon
Collapse (6-30% <i>hyponatremia!</i>)	27 %	
Water intoxication		
Na <135 mmol/l	18 %	13 %
Na <120 mmol/l	3.4 %	0.6 %
Dehydration	12 %	
Runner's anemia		
hemolysis, iron deficiency		
Seizure		

Complications in Marathon runners

Water intoxication
started in 1981 when
recommendations
changed from drinking
little to drinking a lot
→ 1200 ml/h !

Schwere Hyponatriämie mit Lungen- und Hirnödemen bei einer Ironman-Triathletin

Severe hyponatremia, pulmonary and cerebral edema in an ironman triathlete

Autoren

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Institut

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Anamnese und klinischer Befund: Eine 45-jährige Frau wurde nach Beendigung ihres ersten Ironman-Triathlon mit einer Vigilanzminderung und einem zerebralen Krampfanfall stationär aufgenommen. Neben der Somnolenz waren Gesicht- und Knöchelödeme sowie grobblasige Rasselgeräusche über der Lunge auffällig. Vorer-

und war katecholaminpflichtig. Nach Behandlung mit Furosemid besserte sich die Situation zusehends, die Patientin konnte extubiert und eine Woche nach Aufnahme ohne neurologisches Defizit in ein heimatnahes Krankenhaus verlegt werden. Ein Jahr später nahm die Patientin erneut am Ironman-Triathlon teil. Nach er-

Nephrologie

Schlüsselwörter
• Hyponatriämie
• Hirnödem
• Lungenödem
• Ausdauersport

DMW 132:1892;2007

NLZ

Risk factors for hyponatremia

Risk factors

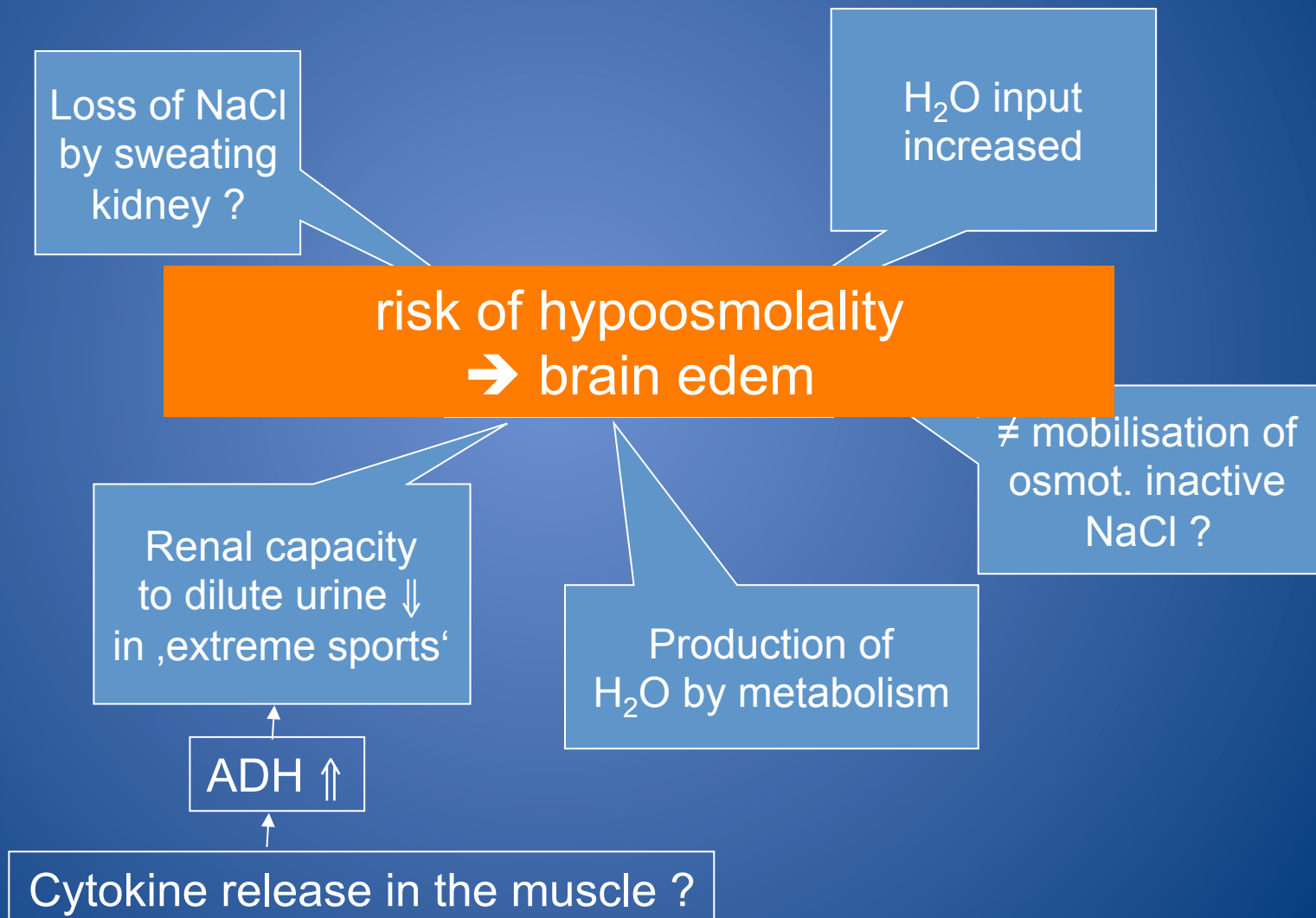
women

>4 h heavy exercise

>1.5 l/h liquid intake (no prevention when 10-20mmol/l NaCl)

NSAID ??

Causes of water intoxication in marathon runner



Prevention of hyponatremia in long distance runner

Risk factors

women

>4 h heavy exercise

>1.5 l/h liquid intake (no prevention when 10-20mmol/l NaCl)

NSAID ??

Ironman Marathon and Triathlon New Zealand

number of food stations
restriction of liquid intake
measuring body weight



400-800ml/h
during training



58 y Office employee

History

He did not arrive at work.
His neighbours did not know him well.

Letter box was very full !
They called the police



58 y Office employee - tiredness, somnolence

Heart and lung	normal
Pulse rate	72/min
BP	145/85 mmHg

Blood

Na	120 mmol/l
Osm.	252 mOsm/kg

Urine

Osm.	74 mOsm/kg
Volume	4.8 l/day



58 y Office employee

Blood and urine osmolality are low !

Blood_{Osm.} 252 mOsm/kg > Urine_{Osm.} 74 mOsm/kg

Diagnosis: Water intoxication



Discussion point: free water clearance

Food

10g protein = 60mOsm

150mmol Na⁺ salt

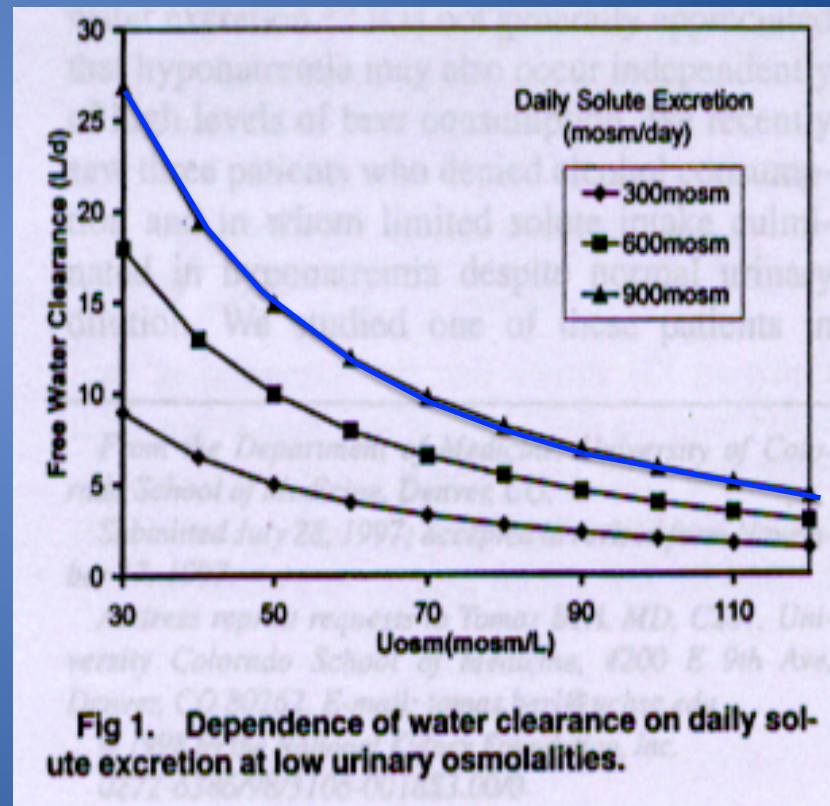
50mmol K⁺ salt

Catabolism

100-150 mOsm

Creatinine, urea

Total: 700-900 mOsm



58 y Office employee - tiredness, somnolence

Very little food, lots of beer !

Beer blocks

endogenous protein catabolism

„Hunger catabolism“

⇒ ca. 300 mOsm/day

Dilution capacity

minimal: 74 mOsmol/kg

⇒ water intoxication when he
drinks >4.05 L/day beer (300:74=4.05)



Discussion point

reduced production of osmolytes

Man, 58 y,
water intoxication

Liquid restriction/day ↓↓
Regular food intake ↑

Osmolyte production ↑↑
→ urinary solutes ↑
→ urine volume ↑

(900mOsm solutes: 74mOsm min.
renal dilution capacity = 12.1 L)



Patients with reduced production of osmolytes

Old age patients

Acute geriatrics USA:

30-50 % malnutrition

Kantonsspital Basel:

19 % malnutrition

Schweiz Med Wochenschr 126Suppl.79:9S-24S;1996

Anorexia nervosa

Ovo-Lacto-Vegetarien

Cancer

Alcoholics

Neurologic disease

Lost sailor

Ann Intern Med 35:69;1951

Patients with reduced production of osmolytes

Old age patients

Acute geriatrics USA:

Kantonsspital Basel:

Schweiz Med Wochenschr 126Suppl.79:9S-24S;1996

Anorexia nervosa

Ovo-Lacto-Vegetarien

Cancer

Alcoholics

Neurologic disease

Lost sailor

Japanese prisoner of war 1945

Ann Intern Med 35:69;1951

Malnutrition, anorexia

Cave:

**Iatrogenic water intoxication
when 'normal' daily supply !**

Cave

Fluid shift in interstitium and
Refeeding syndrome

Calories intake 25 – (50%)

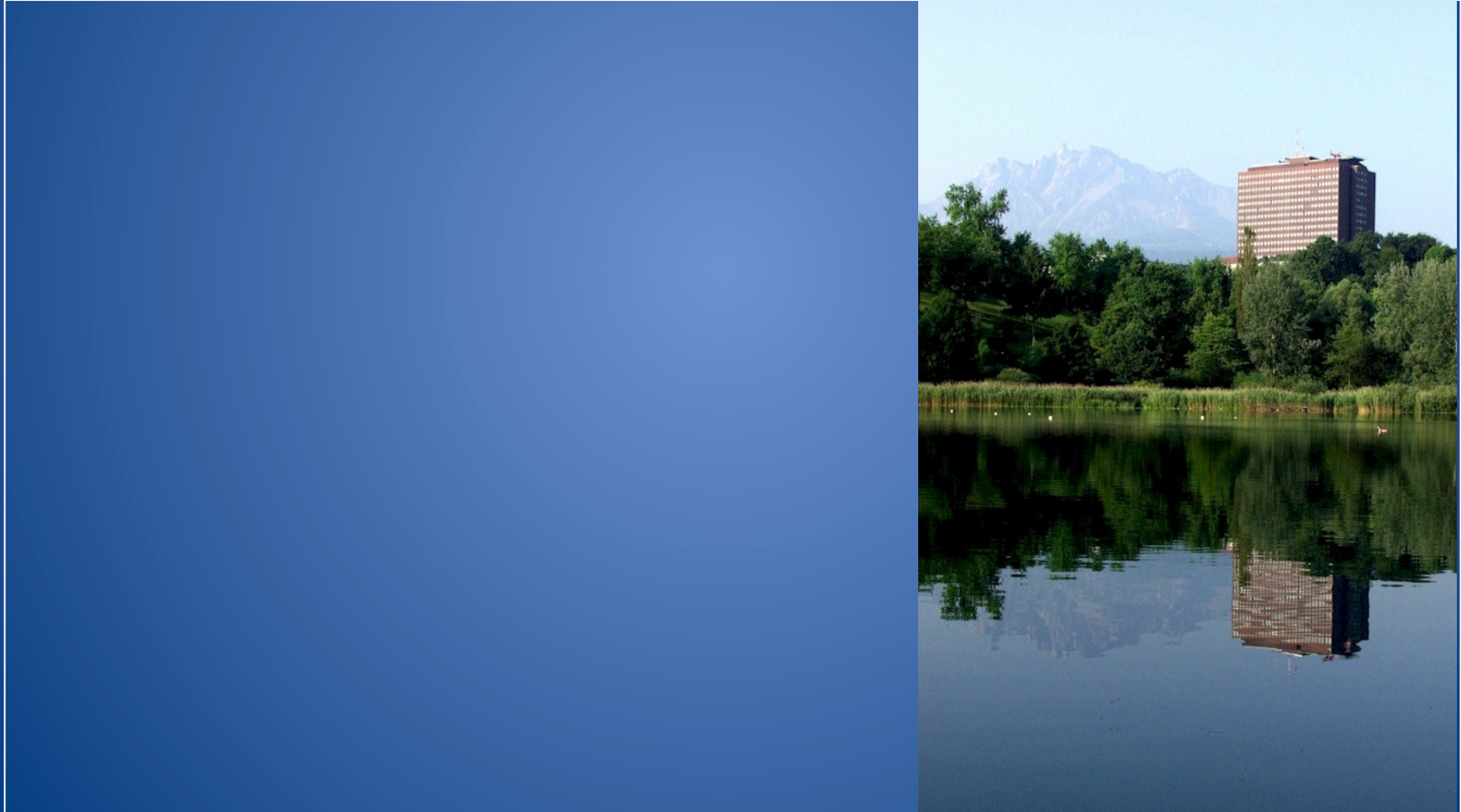
Phosphate 50mmol/d

Take home message

Hyponatremia may be due to

To much water or to little osmolytes

→ inappropriate water balance !



79 y Women

History

Oct. 2012 pneumonia, spotted infiltrates right>left
general condition ↓ despite of antibiotics
Jan. 2013 sent to the hospital

Past history

2006	CLL
2009	2 bronchitis
2010	long lasting bronchitis
2011	pneumonia and bronchitis



Blood

Leuc 36 7

Hb 10

T

WBC

CRP

ESR

Procalcitonin

IL-6

IL-8

IL-10

IL-12

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In school several respiratory infections

Since 1995 Bronchitis in winter

2000 pneumonia of left lower lobe

2001 chronic coughing in winter

12/2001 bilateral pneumonia (st. pneumoniae)

Respiratory failure, mechanical ventilation

**Does this patient have an
impaired immune system ?**

27 y student

Childhood	normal
since 1991	Flue like illnesses 3-4x/year Allergy ?
1999	Maxillary sinusitis Twice antibiotics
2001	Operation of maxillary sinus Recurrent flue like illness, hyposmia
2005	Bronchitis and maxillary sinusitis

27 y student

Laboratory results before discharge

Leucocytes	6.5 G/l (fractions normal)
Platelet	125 G/l
Hemoglobine	139 g/l, MCV 89 fl
CRP	17 mg/l
Electrolytes	normal
Auto-antibodies	negative
Complement	normal
Total IgG	normal

CT Scan	Maxillary chronic sinusitis
---------	-----------------------------

Ultrasound	no pathology
------------	--------------



**For >15 years infections
is there some 'immune deficiency' ?**

ults before dis

Leucocytes	6.5	(normal)
Platelet		
Hemoglobin		
CRP		
ESR		
	normal	
	negative	
	normal	
gG	normal	

CT Scan

Maxillary chronic sinusitis

Ultrasound

no pathology



What shall we do next ?

Protective mechanisms against infections

Skin and mucous membrane
Stasis

Bacterial infections

Neutrophils

Opportunistic infections
Mycobacteria, brucellae, listeria
nocardia, candida, CMV, EBV
herpes, v. zoster, toxoplasma
giardia, leishmania

Cellular immune response

Bacterial infections
neutrophils normal

Humoral immune response

Complement

Bacterial infections
meningitis (recurrent)
screening: CH50 complement

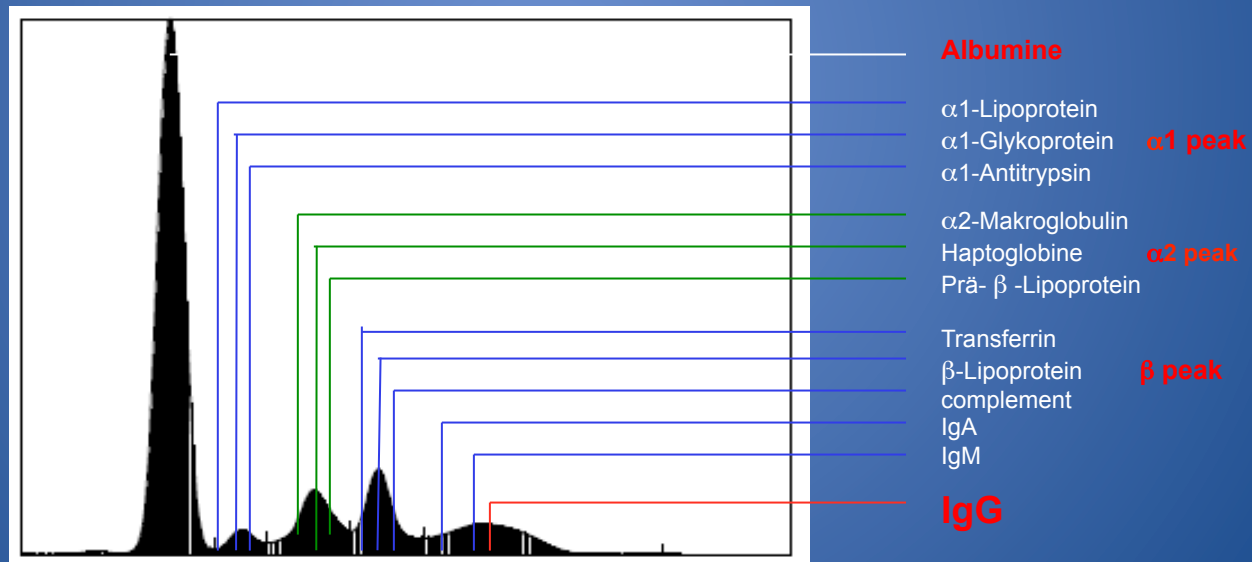
79 y Women with CLL and recurrent bronchitis

Leucocytes	36.7 G/l
Granulo	3.2 G/l

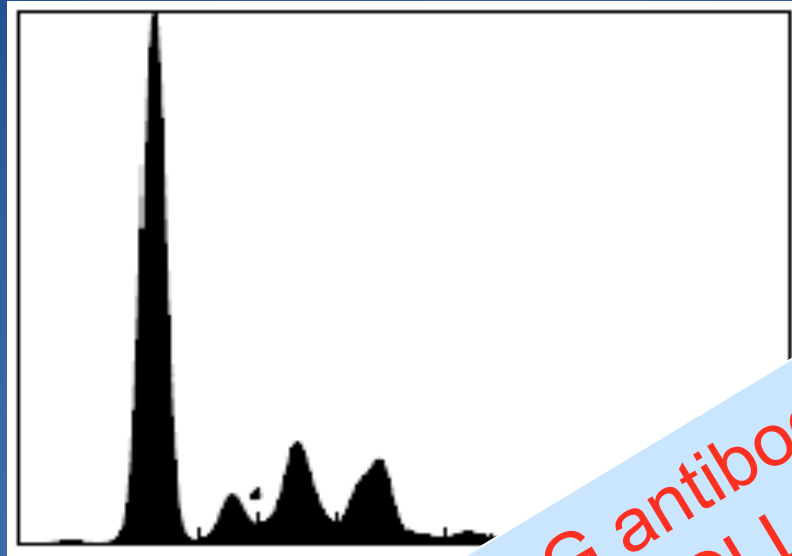
Lymphocyte	>30 G/l
Function ?	

Humoral immune response ?

Protein electrophoresis



normal peaks of the various protein fractions



**This patient has an IgG antibody deficiency
due to her CLL**
Course: 1x25g IgG substitution
fast recovery !

Protein electrophoresis

α1-Lipoprotein
 α1-Glykoprotein
 α1-Antitrypsin
 α2-Makroglobulin
 Haptoglobine
 Prä- β -Lipoprotein
 Transferrin
 β-Lipoprotein
 complement
 IgA
 IgM
IgG

α1 peak

α2 peak

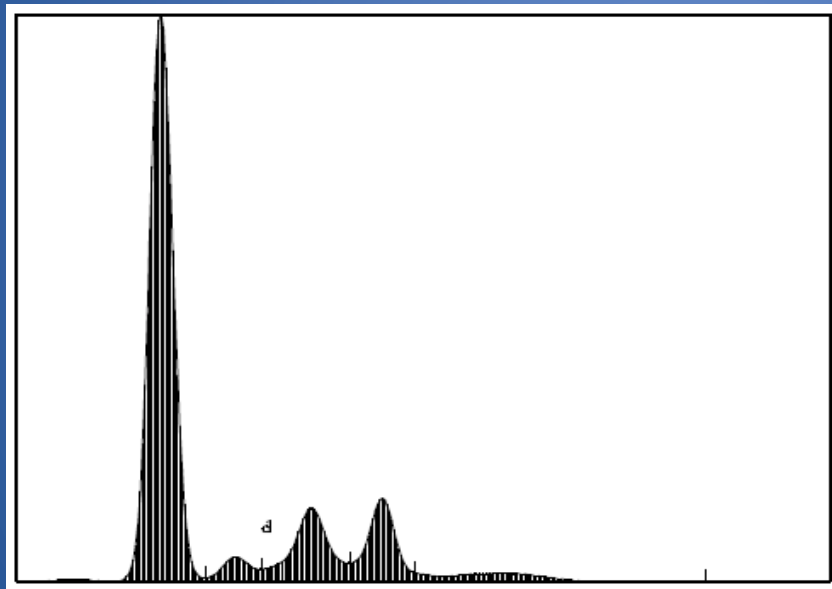
β peak

above: electrophoresis of the patient – IgG total 2.5 g/l
(normal >10g/l)

below: normal peaks of the various protein fractions



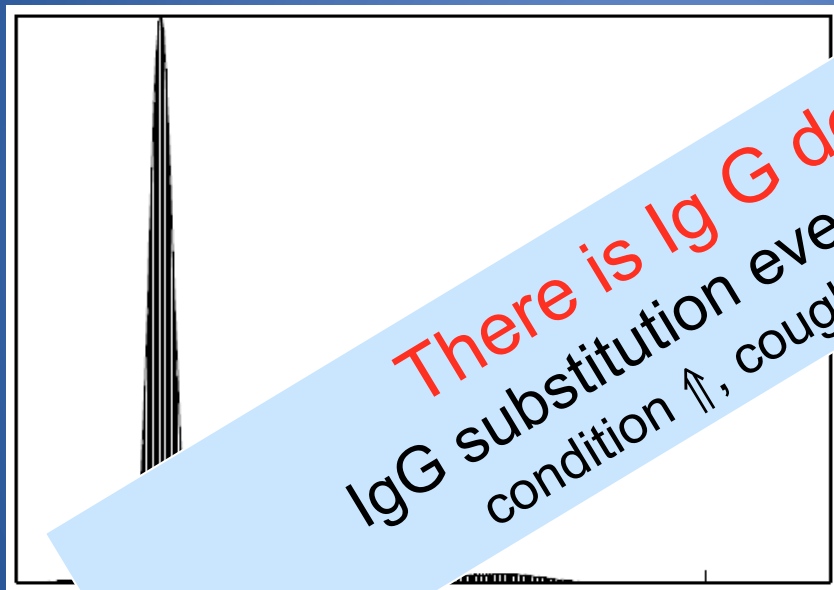
30 y Teacher with bronchitis and severe pneumonia



Total protein	normal
Total IgG (normal: 7-16g/l)	2.5 - 3.2 g/l
IgA (normal: 0.7-4 g/l)	0.27 g/l



30 y Teacher with bronchitis and severe pneumonia



There is Ig G deficiency
IgG substitution every ca. 2 months
condition ↑, cough and sputum ↓



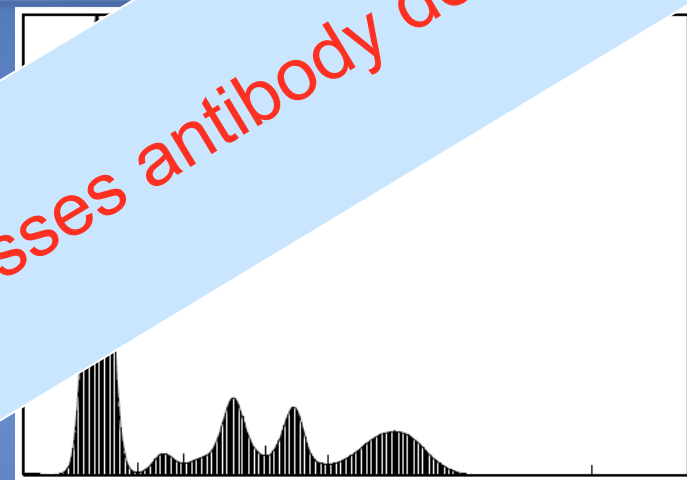
Total protein	normal
Total IgG (normal: 7-16g/l)	2.5 - 3.2 g/l
IgA (normal: 0.7-4 g/l)	0.27 g/l



27 y student



Ig G2 and Ig G4 subclasses antibody defect



5.1.2006

8.4g/l



<0.25

normal

IgA
IgM

0.8g/l



<0.25

normal

Patients with antibody deficiency syndrome

Hereditary

Common variable Immunodeficiency
Deficiency of IgG subclass
X-Chrom. hypogammaglobulinemia
IgA Mangel
Hyper-IgM-Immundefizit

Acquired

Malignancies

Myeloma, CLL, lymphom, M. Waldenström

Infection

EBV, HIV, Parvovirus B19, CMV
congenital: Toxoplasmosis, rubella

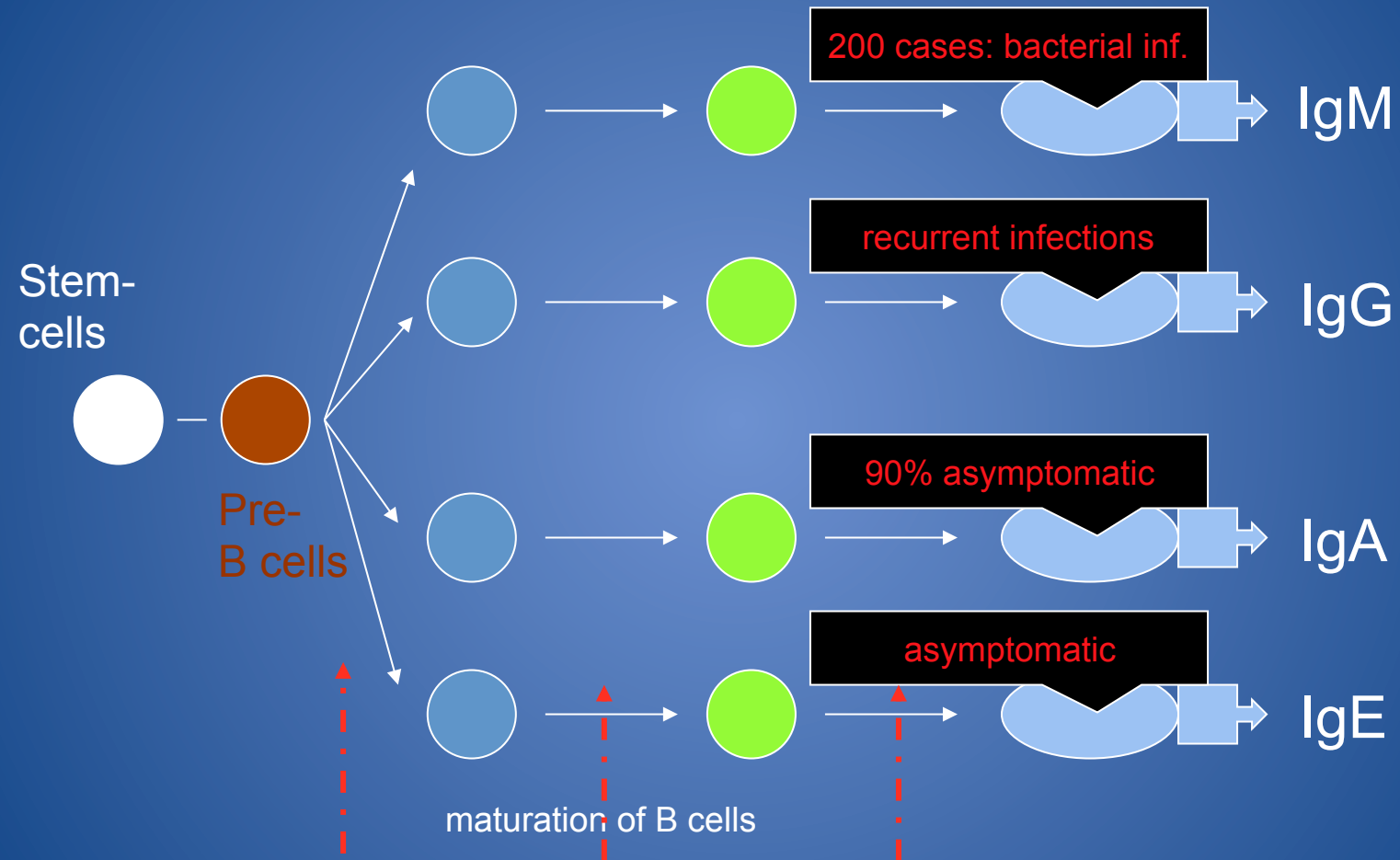
Drugs

IS, sulfasalacine, antiepileptics, gold
malaria treatment, etc.

Protein loss

Nephrotic syndrom, protein losing
enteropathy

Development of B cells



no development

hereditary agammaglobulinemia

Common variable immunodeficiency syndrome

Most frequent & ,classic' form of antibody deficiency syndrome (IgG <4g/l and low IgA and IgM; lymphocyte count normal) Prevalenz 1:10'000

heterogeneous patient group = variable deficiency of Ig

major symptom

recurrent infection

Bronchitis	98 %
Pneumonia	77 %
Viral hepatitis	6.5 %

1. Manifestation

Age 25 to 40 y

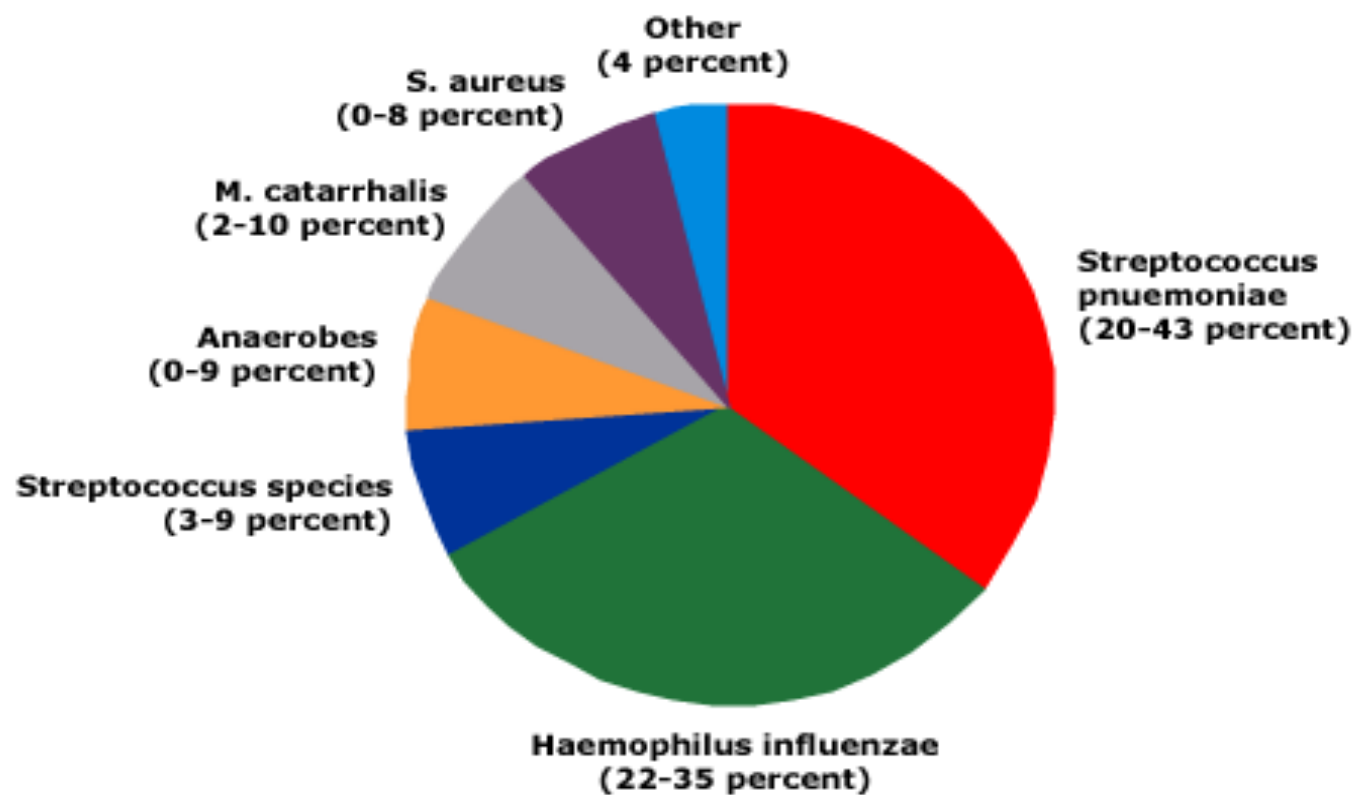
Complications

Bronchiektasis 27 %

Subpopulation with CVID

Noncaseating granuloma	20 %
Autoimmune diseases	20 %
Malignancy (lymphoma)	

Common variable immunodeficiency syndrome



Deficiency of Ig Subclass

Ig	Amount	IgG _{total}	Response polysacch.	Response protein	Normale g/l
Ig G1*	60-80%	↓	(↓)	↓	3.0-10.0
Ig G2	20-30%	(no-↓)	↓	normal	1.0-3.5
Ig G3	5-8 %	normal	normal	normal	0.3-1.0
Ig G4	1-4 %	normal	normal	normal	0.2-0.5
Total IgG					5.0-15.0

Combinations

Ig G1+3 or Ig G1+others

Ig G2+4 or Ig G2+Ig G4+Ig A (Pre-CVID?)

*Ig G1 = CVID: 3005 patients with recurrent, bacterial infections
119 patients had Ig G1 deficiency ! (2 tests without infection)

Clin Immunopath 84:194;1997

Treatment of patients with CVIDS with Ig ?

50 patients with CVID

before IgG substitution ≥ 1 pneumonia/y 42 patients

with IgG substitution ≥ 1 pneumonia/y 11 patients

rate of autoimmune diseases and malignancy not ↓

⇒ Incidence rate for pneumonia decreases ? All Clin Imm 109:1001;2002

⇒ Progression of lung destruction / bronchiectasis is diminished ?

since not all the patients improve, evaluation is required after 2y of therapy !

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Indication for immunglobuline substitution

< 2.5 g/l ,always‘

2.5-5 g/l increased rate of infection and no response to vaccine

Immunglobuline i.v. 0.4-0.6 g/kg body weight

Goal IgG total 5 g/l before next substitution

Treatment of patients with CVIDS

1. Treatment of acute infection with antibiotics

2. Evaluation of prophylaxis with antibiotics

Conjugated vaccine *St. pneumoniae* Prevnar, Wyeth-Ayerst

3. Ig G substitution when

1. no response to vaccine

(Tetanus, Diphtherie, Pneumovacc)

and

2. insufficient protection with antibiotic prophylaxis

do not forget

3. evaluation if infection rate is dropping with substitution of Ig G !

Take Home Message

1. Ig deficiency is easily overlooked !
2. Think of Ig deficiency when the patient has frequent pulmonary infections
3. Prophylaxis with antibiotics may reduce infection rate
4. Ig G substitution when antibiotics and antibiotic prophylaxis fail and no insufficient response to vaccine (Tetanus, Diphtherie, Pneumovacc)
5. Evaluation of the infection rate/year to continue IgG !





Thank you !