luzerner kantonsspital
LUZERN SURSEE WOLHUSEN

ESIM Winter School Riga

06.02. – 11.02.2017

Prof. Verena Briner, FRCP

Woman 32 years

History:

since 4 years, up to 2/month syncope without prodromal signs, thereafter slightly weak, never loss of urine, no convulsion, starts while standing

Past history:

chronic abdominal discomfort (IBS since ca. 2010)
depression after pregnancy (2011)
‘psychiatric problems’ such as syncope (2015)

Family history:

mother depression, father diabetes

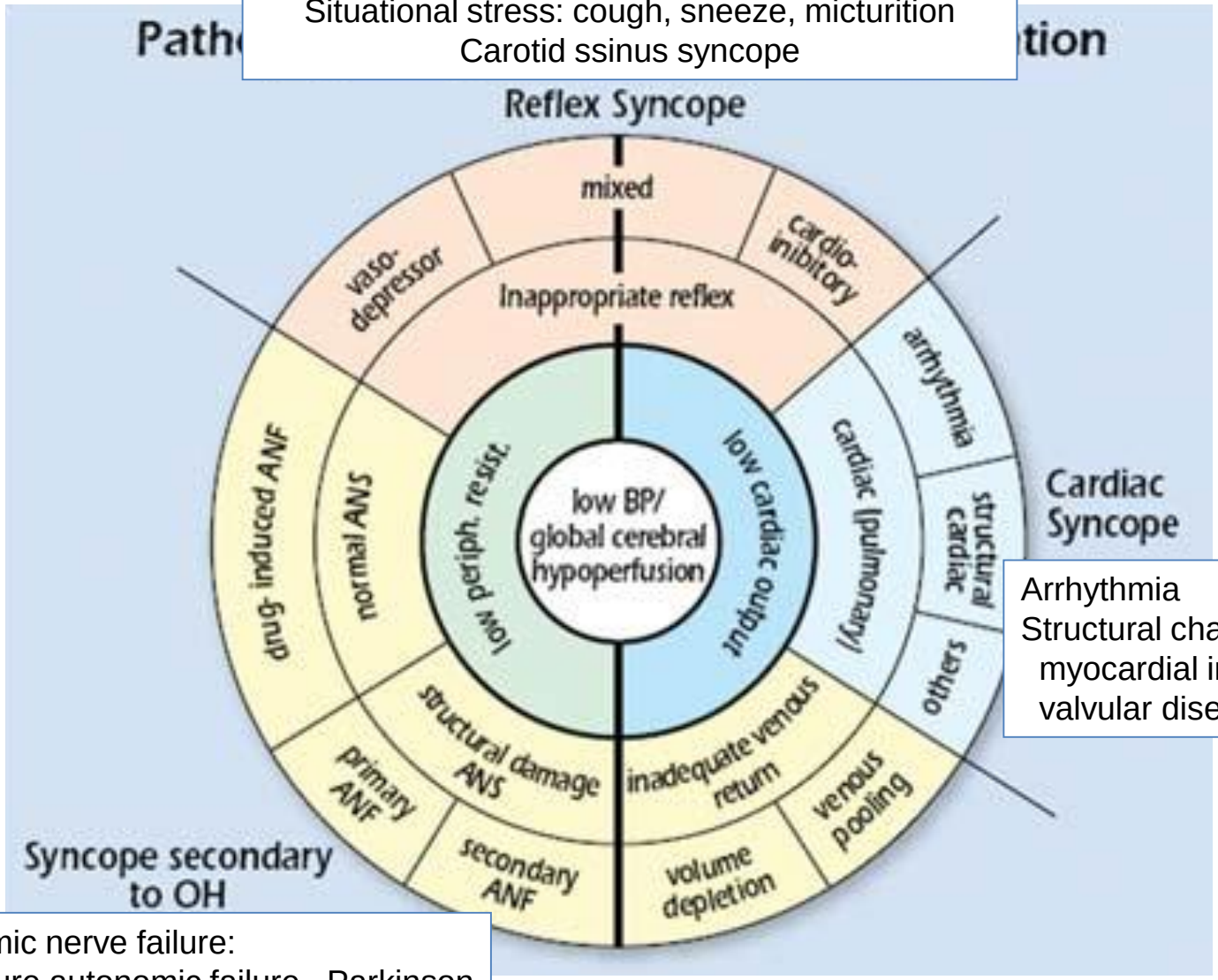
Woman 32 years

Clinical findings:	normal BP 108/77mmHg, pulse rate 70/min.
Schellongtest:	no orthostatic hypotension
24h ECG:	sinus rhythm
ECHO:	normal
CT & MRI head:	normal
EEG:	normal
Carotic artery duplexsono:	no stenosis, no p laque
Carotis sinus massage:	no asystoly
Blood tests:	normal

Woman 32 years

what is our hypothesis ?

Vasovagal syncope: mediated by emotion, pain, orthostatic
Situational stress: cough, sneeze, micturition
Carotid ssinus syncope

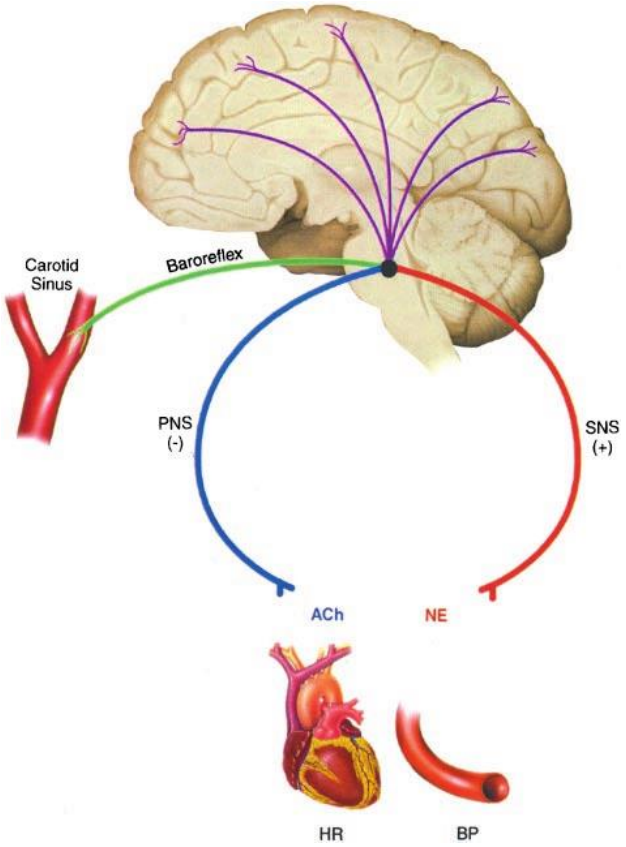


Arrhythmia
Structural changes:
myocardial infarction, valvular disease, HOCM

Prim. autonomic nerve failure:
pure autonomic failure, Parkinson
Sec. autonomic nerve failure:
diabetes, drugs (alcohol,vasodilators, etc.)
Volume depletion: haemorrhage, diarrhea

European Heart J 30:2631-2671;2009

Baroreflex



Tractus solitarii

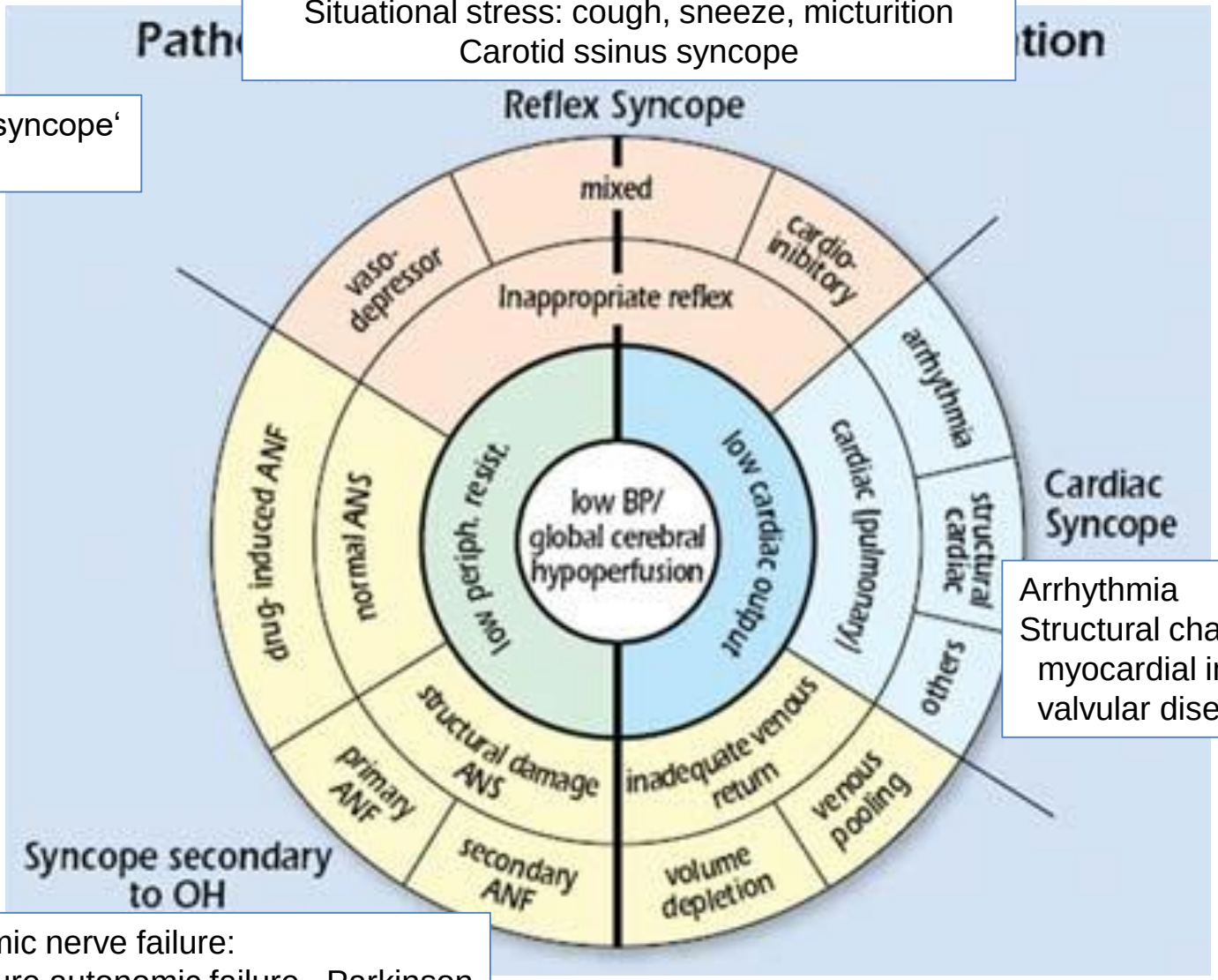
N. Glossopharyngeus

sympathetic and parasympathetic efference to the heart and blood vessel

Circulation 105:2518-2523,2002

Vasovagal syncope: mediated by emotion, pain, orthostatic
Situational stress: cough, sneeze, micturition
Carotid ssinus syncope

‚Psychiatric syncope‘
factitious



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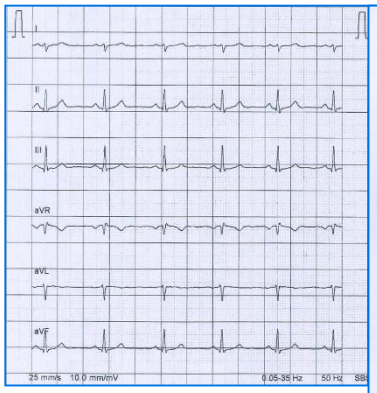
What next ?

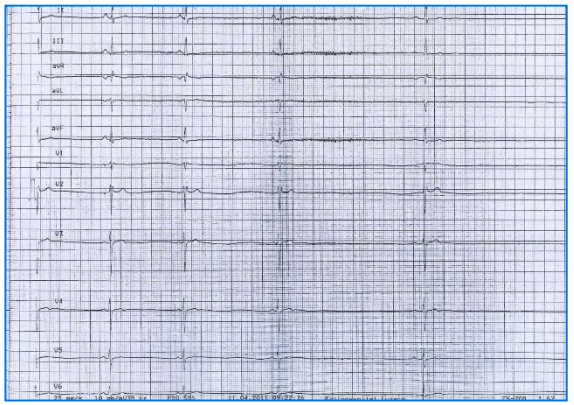
Woman 32 years

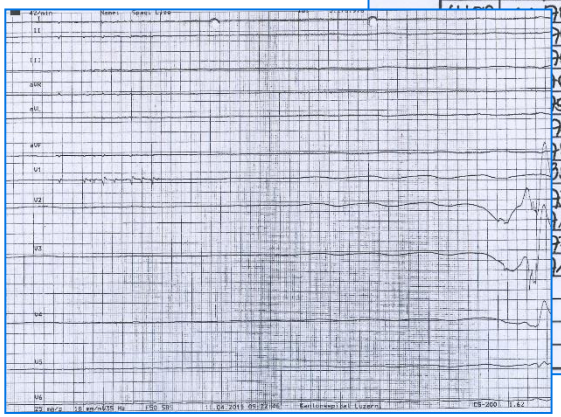
Tilt table test

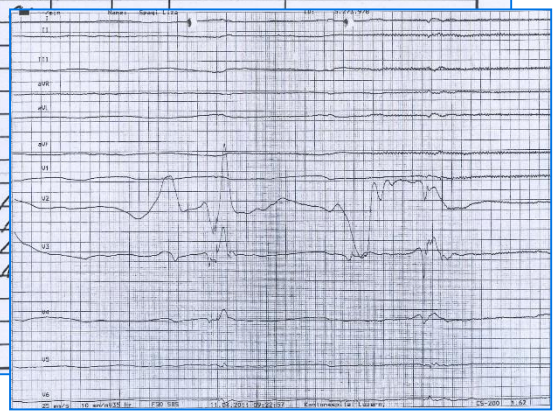
Tilt table test



	Zeit	BD	Puls	SaO2	O2	Infusion Medikament	Bemerkungen
	re.	108/77	70				Carotismassage li
	re.	118/76	70				"
	li.	105/77	68				Carotismassage re.
	li.	118/74	68				"
Skife 1	1:00	107/71	78				
	2:00	116/75	78				
	3:00	104/69	76				
	4:00	114/75	84				
	5:00	114/75	85				
	1:00	113/75	81				
Skife 2	2:00	111/73	79				
	3:00	115/77	89				
	4:00	109/70	81				
	5:00	116/77	82				
	1:00	112/71	78				
Skife 3	2:00	111/74	80				
	3:00	106/70	82				

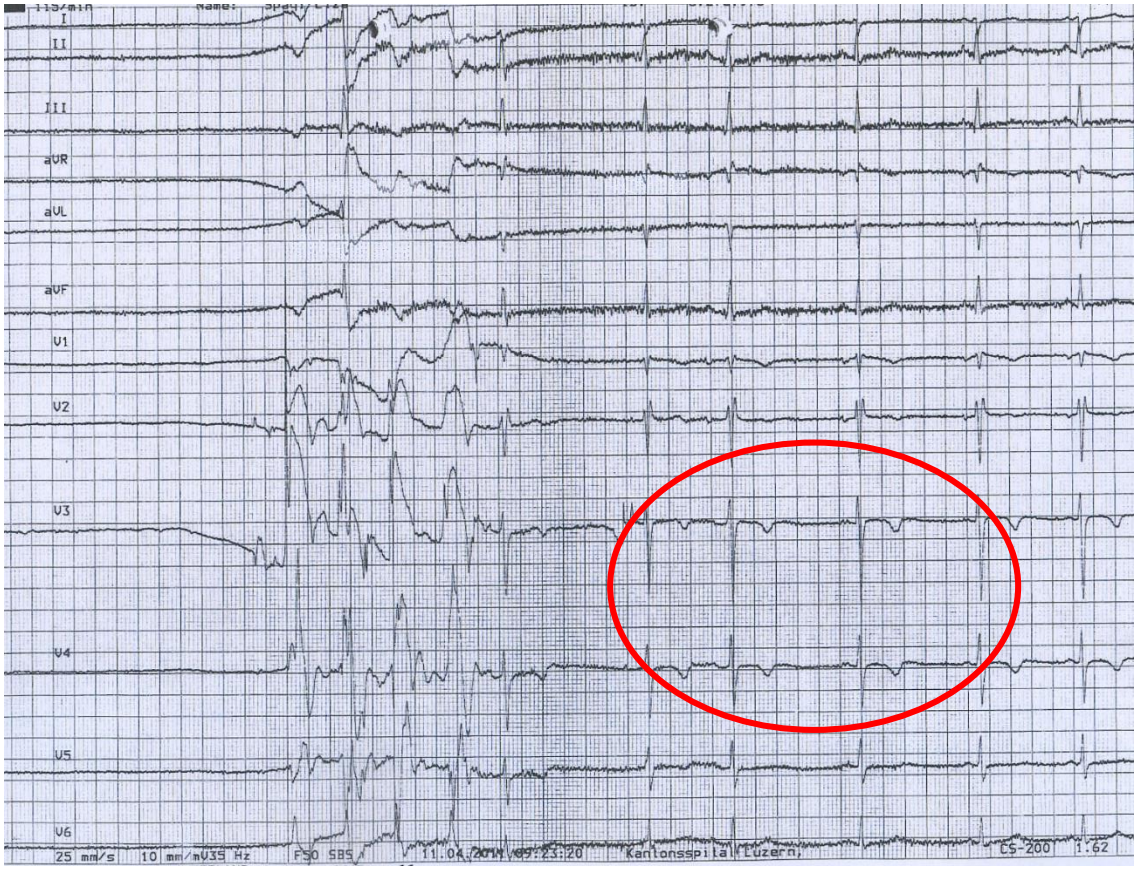






45 seconds asystole !

Woman 32 years

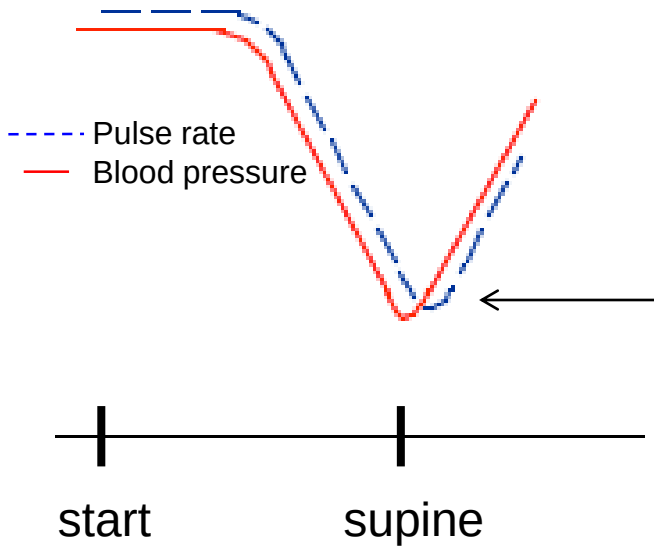


ECG after
the tilt table test

ischemia after
the 45 sec of
asystole

Woman 32 years - Tilt table test

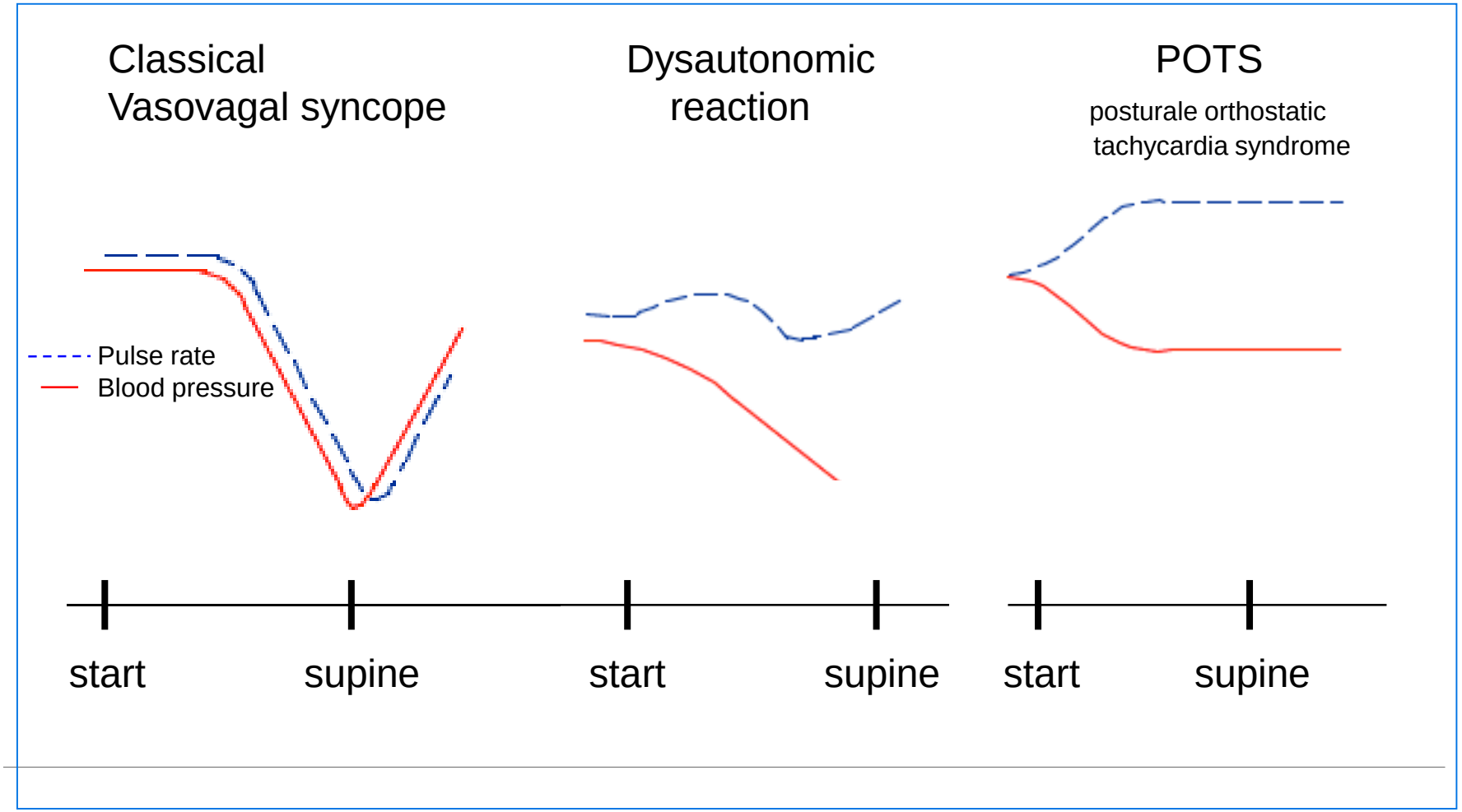
Classical
Vasovagal syncope



Interpretation

reflex syncope (vasovagal)
prolonged asystole
and coronary
ischemia

Tilt table test



Woman 32 years

Treatment: compressive stockings
NaCl and water

Pace maker implantation
since 1 y free of syncope
no malaise, no weakness

Woman 32 years

Pace maker implantation

504 patients: age >4y, syncope and severe asystole

162 patients had cardio-inhibitory etiology

	syncope recurrence in 27 months
60 with PM	10 (17 %)
86 without PM	40 (46 %)

Sutton et al. Europace 16: 595, 2014

Syncope scores

				cohort)
S. Francisco Syncope Rule[44]	-Abnormal ECG -Congestive heart failure -Shortness of breath -Haematocrit <30% -Systolic blood pressure <90 mmHg	No risk = 0 item Risk = ≥1 item	Serious events at 7 days	98% sensitive and 56% specific
Martin *et al.* [40]	-Abnormal ECG -History of ventricular arrhythmia -History of congestive heart failure -Age >45 years	0 to 4 (1 point each item)	1-year severe arrhythmias or arrhythmic death	0% score 0 5% score 1 16% score 2 27% score 3 or 4
OESIL score[41]	-Abnormal ECG -History of cardiovascular disease -Lack of prodrome -Age >65 years	0 to 4 (1 point each item)	1-year total mortality	0% score 0 0.6% score 1 14% score 2 29% score 3 53% score 4
EGSYS score[42]	-Palpitations before syncope (+4) -Abnormal ECG and/or heart disease (+3) -Syncope during effort (+3) -Syncope while supine (+2) -Autonomic prodrome[a] (−1) -Predisposing and/or precipitating factors[b] (−1)	Sum of + and − points	2-year total mortality ..... Cardiac syncope probability	2% score <3 21% score ≥3 ..... 2% score <3 13% score 3 33% score 4 77% score >4

This table shows several different studies that have analysed the impact of different clinical data on the follow-up of patients presenting with syncope. Overall, the

European Heart J 30:2631-2671;2009

Take home message

It‘s easy to miss something you are not looking for (https://www.youtube.com/watch?v=1D07neiB7HI)

It’s easy to copy a former diagnosis / draw premature conclusions and thus pretend to have solved the patients problem


LABBÉ

Woman 19 years, secretary in a bank

History:	mother of patient tells: 1 week diarrhea, for 1d rather strange behaviour, confusion. Stress in office, maybe needs psychiatrist because she is ‘very sensitive girl’
Medication:	over the counter: various vitamins and nutritional supplements vegetarian
Past history:	GP: patient has psychosomatic symptoms
Family history:	unremarkable

Woman 19 years

Clinical findings:	normal, BP 97/70mmHg, PR 88/min slow in following orders, fidget with cloth
CT head:	normal
Lumbar puncture:	normal neurotropic viruses negative
Drug screening:	negative
Blood tests:	normal (Hb 123g/l, leuco 4G/L, neutrophils 72%, Na 133mmol/l, K 3.5mmol/l, creatinine 68µmol/l, normal liver function: ASAT, ALAT, alk. phos., bili-rubin, CRP 10mg/l (normal <5mg/l)

What's your hypothesis ?

Hypothesis: Intoxication
with unknown substance

Woman 19 years

Intermediate care unit:	NaCl and glucose No drugs
Past history	malaise, nausea and vomiting, little diarrhea, did not eat for 2 days. Similar mild episode 2 y ago and as teenager: it was meant to be ‘psychological’
Diagnosis	Maybe some kind of psychological stupor ?

Woman 19 years

Intermediate care unit:	no focal neurologic sign, still slow in following orders
MRI head:	normal
EEG:	normal

Are all blood tests normal?

Acid-base analysis:	pH 7.51, pCO_2 4.01kPa (normal 5.1-6.0), pO_2 13.1kPa (normal 12-13.39) = respiratory alkalosis

Woman 19 years

Intermediate care unit: no focal neurologic sign, still slow in following orders, fidget with cloth

MRI head: normal

EEG: normal

Acid-base analysis: pH 7.51, pCO_2 4.01kPa (normal 5.1-6.0), pO_2 13.1kPa (normal 12-13.39)
= respiratory alkalosis

what might cause respiratory alkalosis ?

Ammonia: 88µmol/l (normal <40µmol/l)

Where comes ammonia from ?

- **90% liver cirrhosis**
- **10% non-hepatic**
  - **reduced elimination**
  - **increased production**

Where comes ammonia from ?

- **90% liver cirrhosis**
- **10% non-hepatic**
  - **reduced elimination**
  - **increased production**

- Bacterial metabolism of proteins and urea in the gut
- Shunting of the hepatic metabolism
- Ureteral-sigmoidotomy
- Increased production: hemato-oncologic diseases, infection, increased catabolism, protein load
- Glucocorticoids increases protein turnover
- Valproatic acid inhibits urea production
- Total parenteral nutrition

Where comes ammonia from ?

- **90% liver cirrhosis**
- **10% non-hepatic**

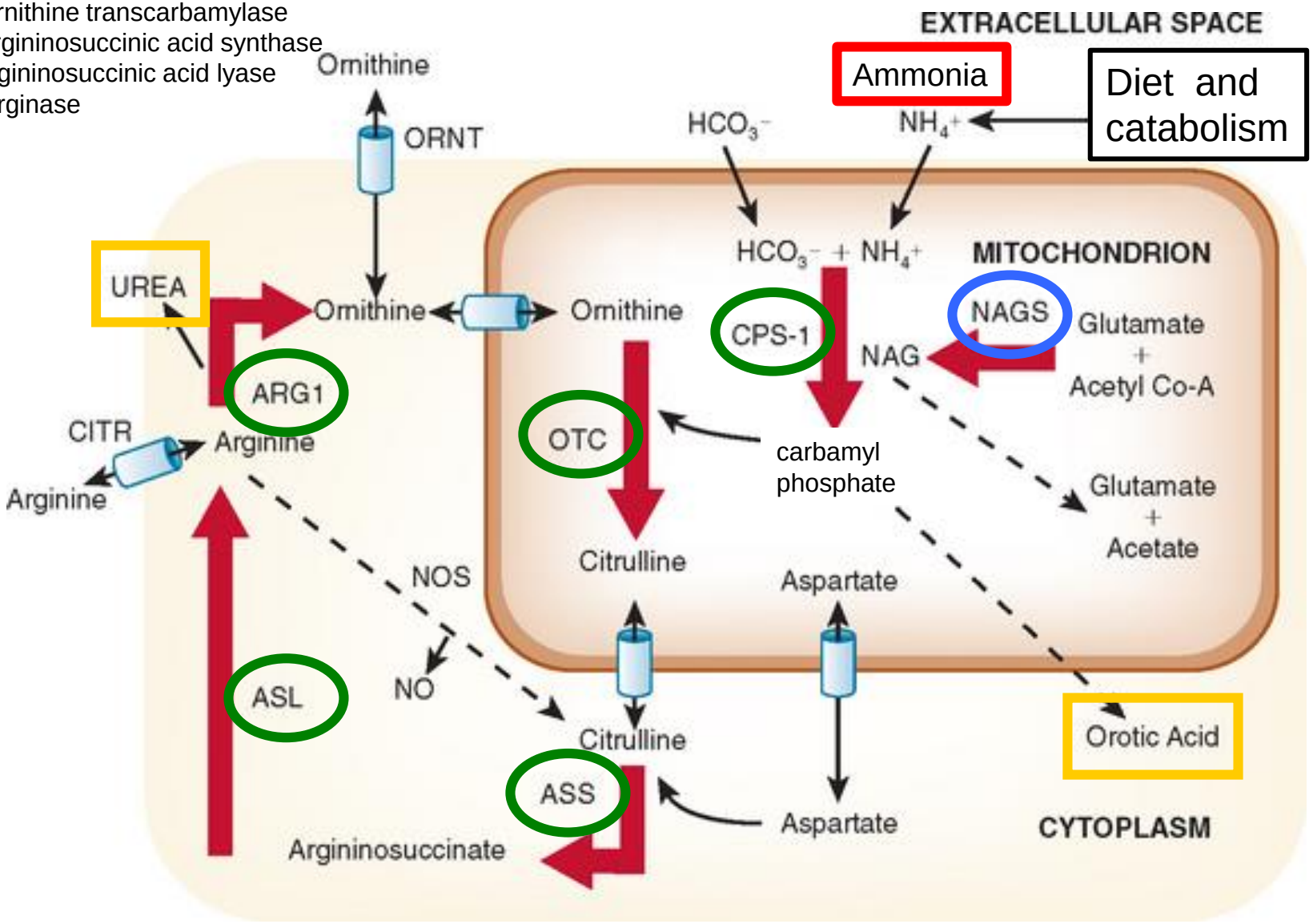
Ammonia

is metabolized in the liver
and when this process is defect

muscle take up ammonia to synthesis glutamin
brain to forming glutamin from glutamate
kidney excretion of ammonia rises from 30% to 70%

➔still ammonia level may increase and cause brain edema

NAGS N-acetylglutamat-synthetase
CPS-1 carbamyl phosphate synthetase
OTC ornithine transcarbamylase
ASS argininosuccinic acid synthase
ASL argininosuccinic acid lyase
ARG arginase



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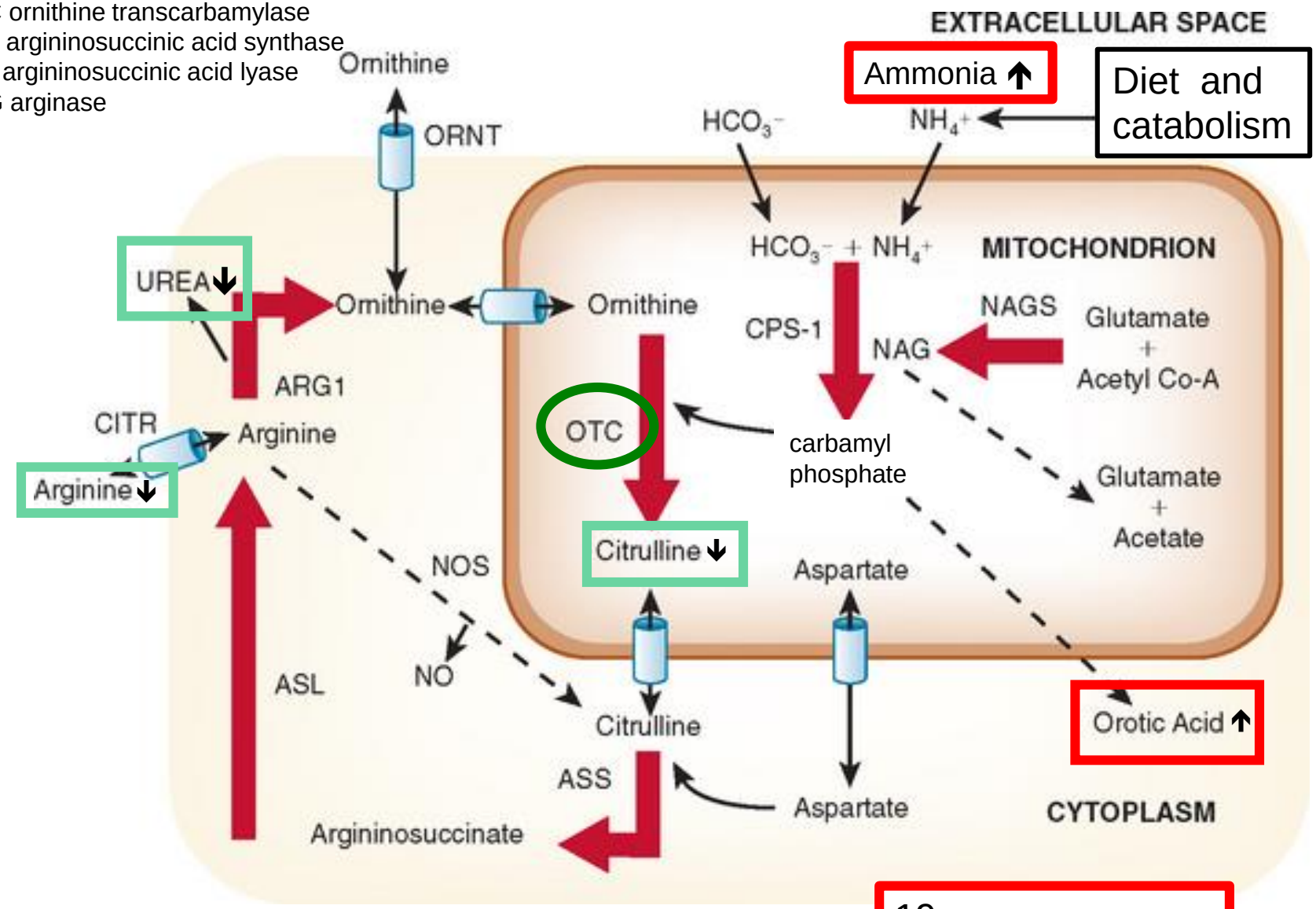


19y woman
Urine orotic acid ↑

Big variation of phenotype in women due to
various proportion of active X chromosme with mutant allele

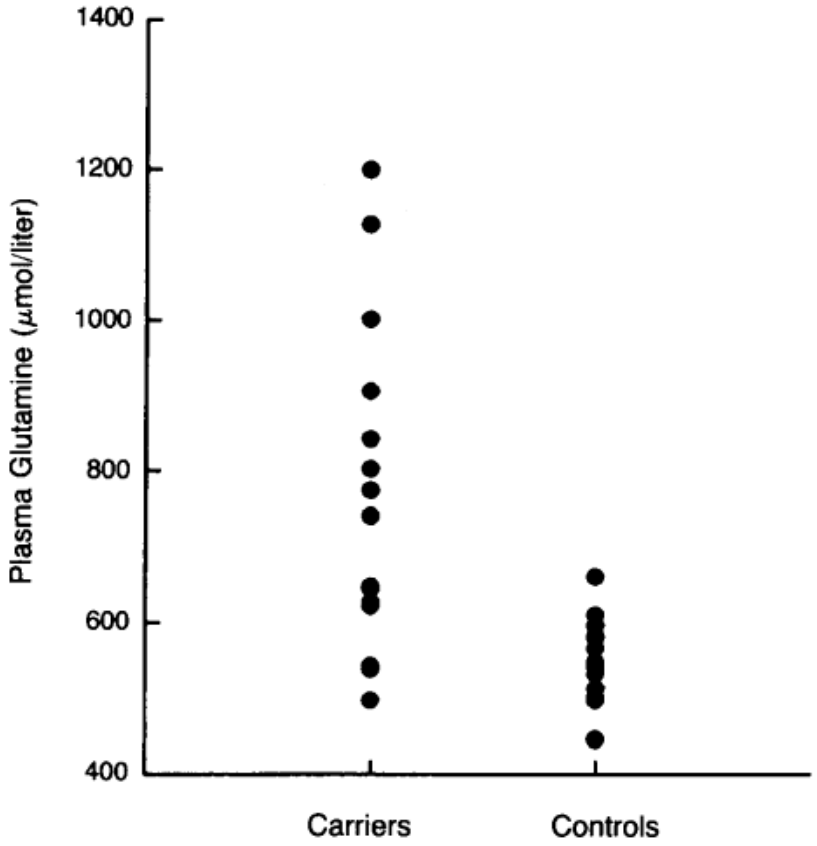


Figure 2. Plasma Glutamine Levels in 16 Controls and in 16 Women with a Mutation at the Ornithine Carbamoyltransferase Locus.

Trigger of hyperammonemia in urea cycle disorders

- catabolic events
- protein overload
- drugs

infections, fever
gastro-intestinal or internal bleeding
reduced energy intake (fasting, pre surgery, trauma)
postpartal uterus involution
valproic acid, carbamazepine, glucocorticooids
phenobarbitone, primidone, hydrochlorthiazide
‘chemotherapy’ (myeloma, leukemia)

Treatment of patients with OTC deficiency

Emergency

no protein
glucose 10% or 20%
lipids 2g/kg/d
Nitrogen scavengers: Na-benzoate,
Na-phenylacetate
arginine hydrochloride

Ammonia

>400µmol/l
>200 µmol/l with treatment
brain edema ?

} hemofiltration
hemodialysis

Steady state

protein 0.8-1g/kg/d
? arginine, Fe, Cu, Ca, Zn, cobalamin

Diagnostic clues

Family history: childhood death unclear
Vegeterian (high carbohydrates, low protein)
Recurrent ‘psychiatric behaviour’ with ‘routine illnesses’
Episodes of vomiting and ‘lethargia’ and headache

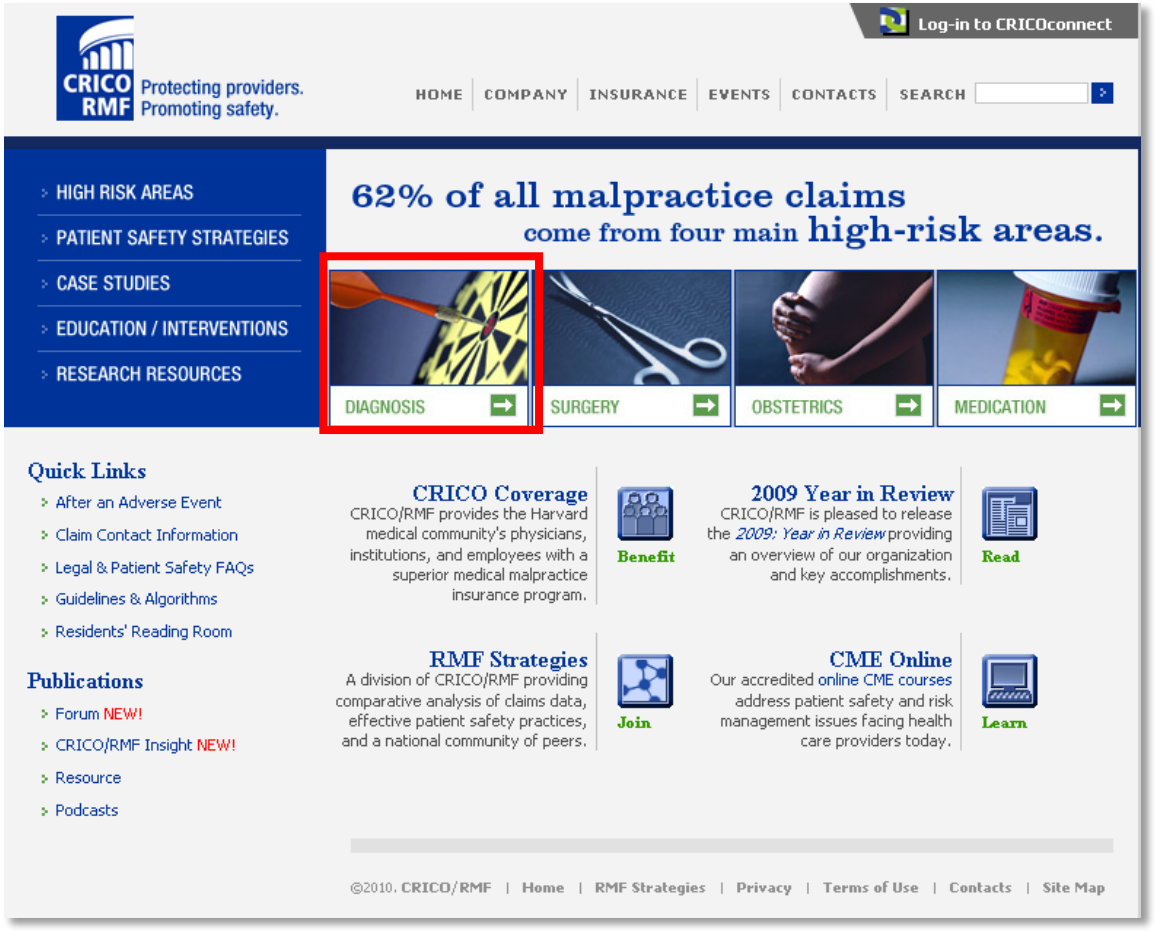
Take home message

think of inborn error of metabolism

when intoxication seems likely but isn’t !

Pitfalls in medicine

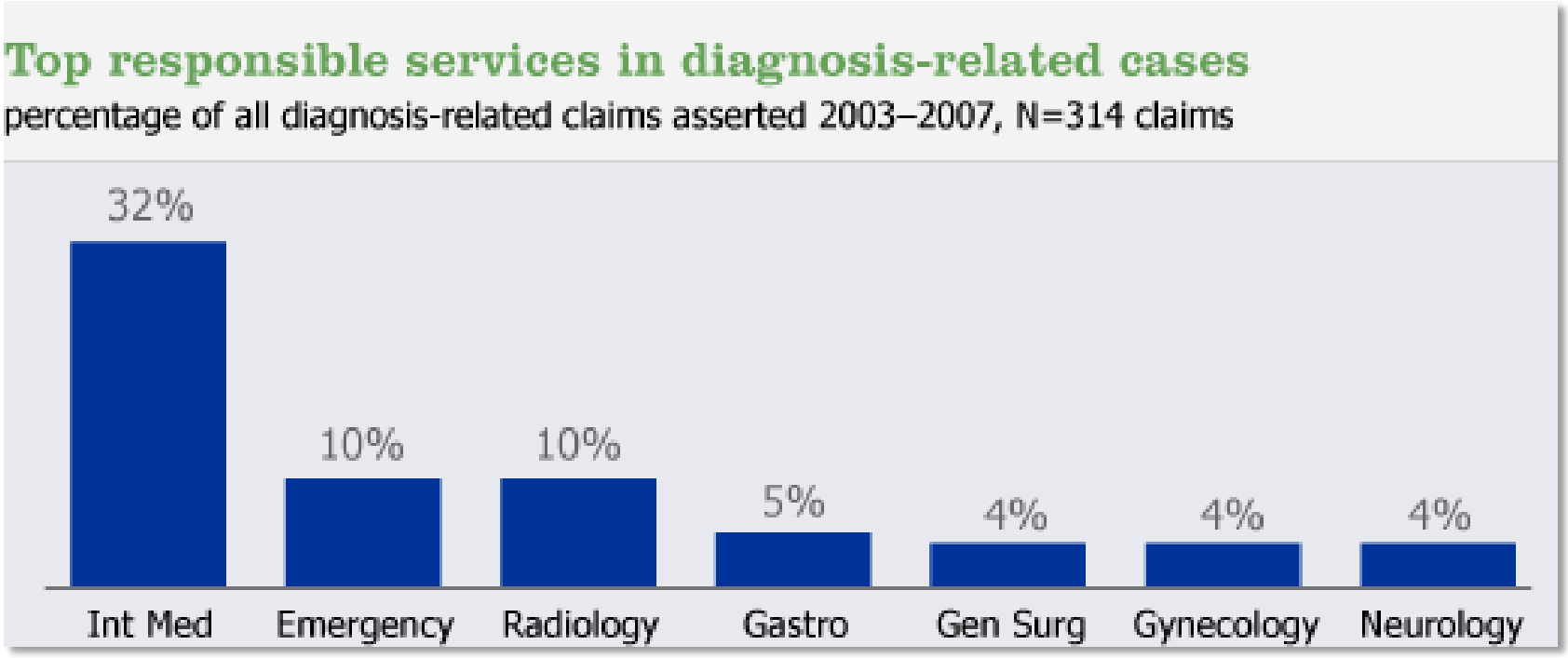
Diagnostic errors are frequent: in malpractice claims



Cited in Schiff GD & Bates DW. N Engl J Med. 2010;362:1066-9.

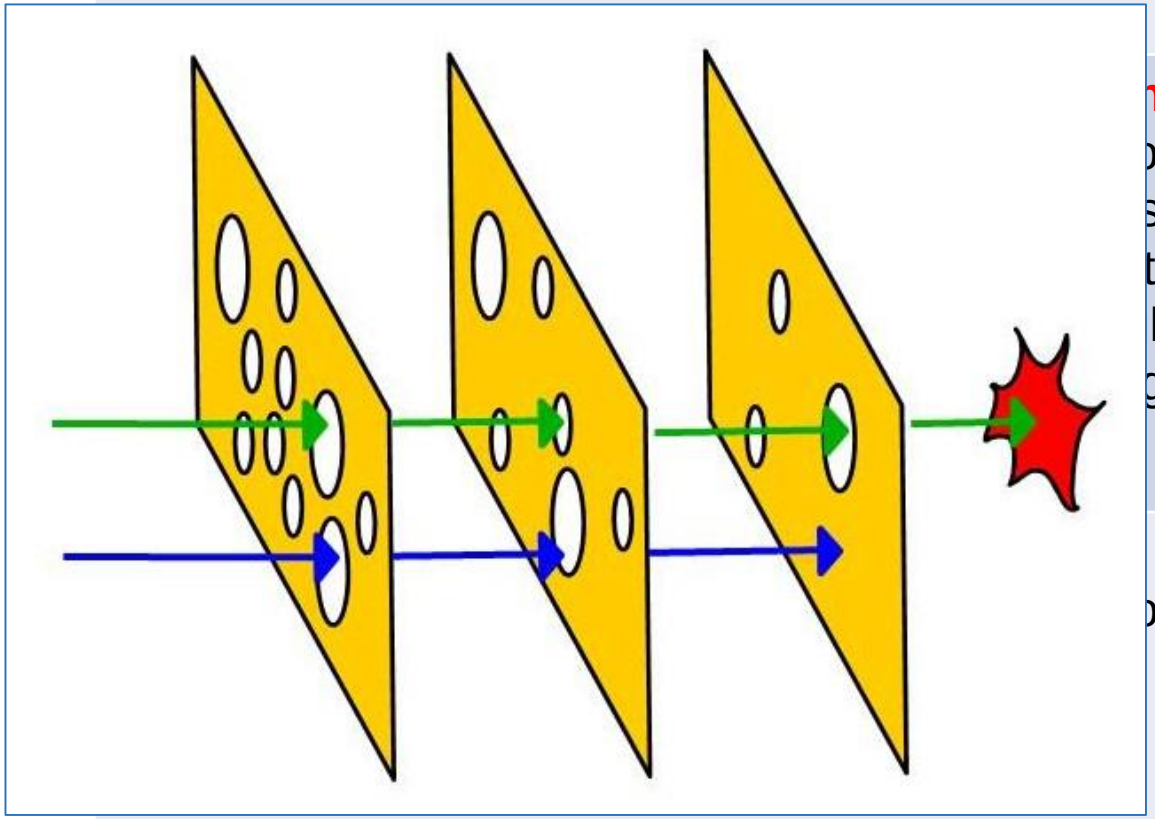
Can electronic clinical documentation help prevent diagnostic errors?

Diagnostic errors are frequent in internal medicine!



Diagnostic error is typically multifactorial in origin – 100 patients in 5 tertiary care hospitals in Australia

Cognitive factor contributing to error	N
Faulty knowledge (missread ECG with complete heart block)	11
Faulty data-gathering - Failure to collect **appropriate information** from the initial interview and examination	45
ng **r** salience of a syndrome) thorax in X-ray) lmonary embolism) gnosis of	159
    ssibilities once an	106



Arch Intern Med. 2005;165:1493-1499

Problem solving in clinical medicine: Mental short cuts = heuristics to arrive at a diagnosis *Klein JG. Five pitfalls in decisions about diagnosis and prescribing. BMJ 2005;330:781–4*

- **Representativeness heuristic** something looks similar to other things in a category, thus it has to be a member of that category
- **Availability heuristic** examples that come to mind easily because they are easily remembered
- **Overconfidence** most of us tend to overestimate both, how much we know and how reliably we know it
- **Confirmatory bias** tendency to look for information that fits our pre-existing expectations
- **Illusory correlation** tendency to perceive two events causally related when there is coincidental or non-existing

Problem solving in clinical medicine

Klein JG. Five pitfalls in decisions about diagnosis and prescribing. BMJ 2005;330:781–4

- **Representativeness heuristic** something looks similar to other things in a category, thus it has to be a member of that category

Doctor trained in the US in an area with a very high prevalence of histoplasmosis

He moves to Riga

Patient with pulmonary infiltrates: he continues to evoke histoplasmosis systematically despite a very low prevalence !

Problem solving in clinical medicine

Klein JG. Five pitfalls in decisions about diagnosis and prescribing. BMJ 2005;330:781–4

- **Representativeness heuristic** something looks similar to other things in a category, thus it has to be a member of that category
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Doctor recently admitted a patient for severe hypertension
Diagnosis: Hyperaldosteronism
Since then he thinks of hyperaldosteronism in every hypertensive patient

Frequent is frequent and rare is rare…

if you hear hoof beats, don't think zebra

however,

zebras exist - you might see one sometime

Problem solving in clinical medicine

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Heuristics in medical reasoning

Klein JG. Five pitfalls in decisions about diagnosis and prescribing. BMJ 2005;330:781–4

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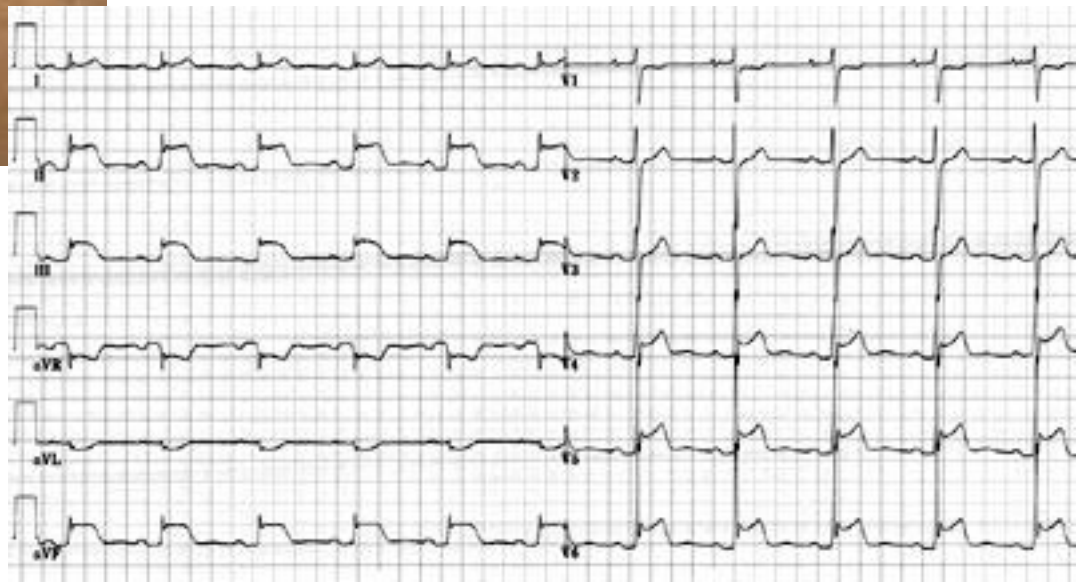
Immediate recognition of the diagnosis



But be careful !
Look for a single diagnosis
that can explain all the findings

If it looks like a duck, sound like a duck, and walks like a duck, it is a duck.

Problem solving in clinical medicine

Klein JG. Five pitfalls in decisions about diagnosis and prescribing. BMJ 2005;330:781–4

- **Representativeness heuristic** something looks similar to

Patients had twice myocardial infarction last year and now chest pain and dyspnoea

Diagnosis: coronary ischemia an heart failure and sending him to the catheter lab

He had pulmonary embolism after long distance flight

- **Illusory correlation** tendency to perceive two events causally related when there is coincidental or non-existing

Take home message

- Diagnostic errors are frequent, potentially harmful
- Diagnostic errors are more often due to cognitive errors than insufficient knowledge

Prevention of diagnostic errors

- Good training, ongoing professional development
- Seeking second opinions / ask colleagues
- Clinical decision support system
- Robust handover
- Feedback from mortality and morbidity review
- Clinical reasoning: it is complex and involves a mix of immediate recognition and systematic hypothetico-deductive reasoning


Thank you