GLUT1 deficiency syndrome
into adulthood

Willemijn Leen
Nijmegen, the Netherlands

No conflicts of interest

Broad phenotypic spectrum

* Classical, complex phenotype:
  * Intellectual disabillity
  * Epilepsy
  * Movement disorder (spasticity, ataxia, dystonia)

* Other (often milder) phenotypes, such as:
  * Generalized epilepsy
  * Paroxysmal exertion-induced dystonia

Course of GLUT1DS

Initial assumption:

- Stabile neurological disorder
- Treatment with ketogenic diet:
  - Start as soon as possible
  - Continue into adolescence

But…:

- What do we actually know about the disease course?
- Disorder is now known for 2.5 decades

Systematic review (2013)

Pubmed search

- Inclusion: all GLUT1DS patients aged ≥18 years

56 articles:

- 194 GLUT1DS patients:
  - 91 adults

Classification into 3 phenotypes

* Classical, complex

  Intellectual disability + epilepsy *or* movement disorder

* Epilepsy - dominant

  Epilepsy (+ paroxysmal movement disorder)

* Movement disorder - dominant

  Isolated movement disorder

Results of systematic review

	Total *N=91*	Complex phenotype *N=33 (36%)*	Epilepsy-dominant *N=28 (31%)*	Movement disorder-dominant *N=27 (30%)*
Age (mean±SD)	37y±15	29y±10	39y±14	41y±14
CSF glucose (mmol/L)	1.4-2.8	1.4-2.3	2.1-2.8	2.3-2.7
Intellectual disability	36 %	100 %	-	-
Epilepsy (ever)	56 %			-
Epilepsy (current)	22 %	30 %	36 %	-
Epilepsy (onset)	2m – 35y	2m – 17y (58% <10y)	0 – 34 y (57% < 10y)	-
Movement disorder	79 %	82 %	64 %	100 %
Paroxysmal exertion induced dyskinesia (PED)	68 %	64 %	57 %	93 %
PED (onset)	1y-30y (44 % <10y; 34% 10-20y)	2y-20y (70 %<10y)	5y-30y (31% <10y; 38% 10-20y)	1y-19y

Reduction of epilepsy during life

High frequency of PED

Cohort study

- Nijmegen, the Netherlands
- Inclusion:
  - GLUT1DS patients aged ≥18 years
  - Classical, complex phenotype
  - Follow-up from childhood

Cohort study

* 7 patients
* Classical, complex phenotype
* *SLC2A1* mutation
* GLUT1DS CSF profile

Results of cohort study

	Total N=7
Age (range)	24-44 y
CSF glucose (mmol/L) CSF/blood glucose	1.9 - 2.1 0.3 - 0.58
Intellectual disability	Mild to severe
Epilepsy	6 out of 7
Epilepsy (onset)	3m - 4y
Seizures (current)	2 out of 7
Movement disorder	100 %
Paroxysmal exertion induced dyskinesia (PED)	4 out of 7 (all ambulatory pts)
PED (onset)	10-20y

Outcome

Patiënt	1	2	3	4	5	6	7
Sex; age	F; 23y	F; 24y	F; 26y	M; 27y	F; 31y	M; 33y	M; 44y
Intellectual disability	Mild	Mild	Mild	Moderate	Moderate	Moderate-severe	Mild
Language	Full sentence						Normal
Speech	Mild dysarthria			dysarthria	dysarthria	dysarthria	Normal
Education	Special needs	Vocational	Special	Special	Special	Special	Vocational school
Independence							endent
Mobility	Wheelchair for long distances	Unassisted	Unassisted wheelchiar during PED	Wheelchair	Wheelchair	Wheelchai	Unassisted walking

24-44 years

Mild to moderate-severe

Single words to normal

Severe dysarthria to normal

Special needs to vocational school

Assisted living with 24/7 care to totally independent

Wheelchairbound to unassisted walking

Current treatment

Ketogenic diet:
- n = 1/7 (since the age of 8 yrs)

Modified Atkins diet:
- n = 4/7 (since the age of 20-26 yrs)
  - Indication: epilepsy(1); movement disorder(3)

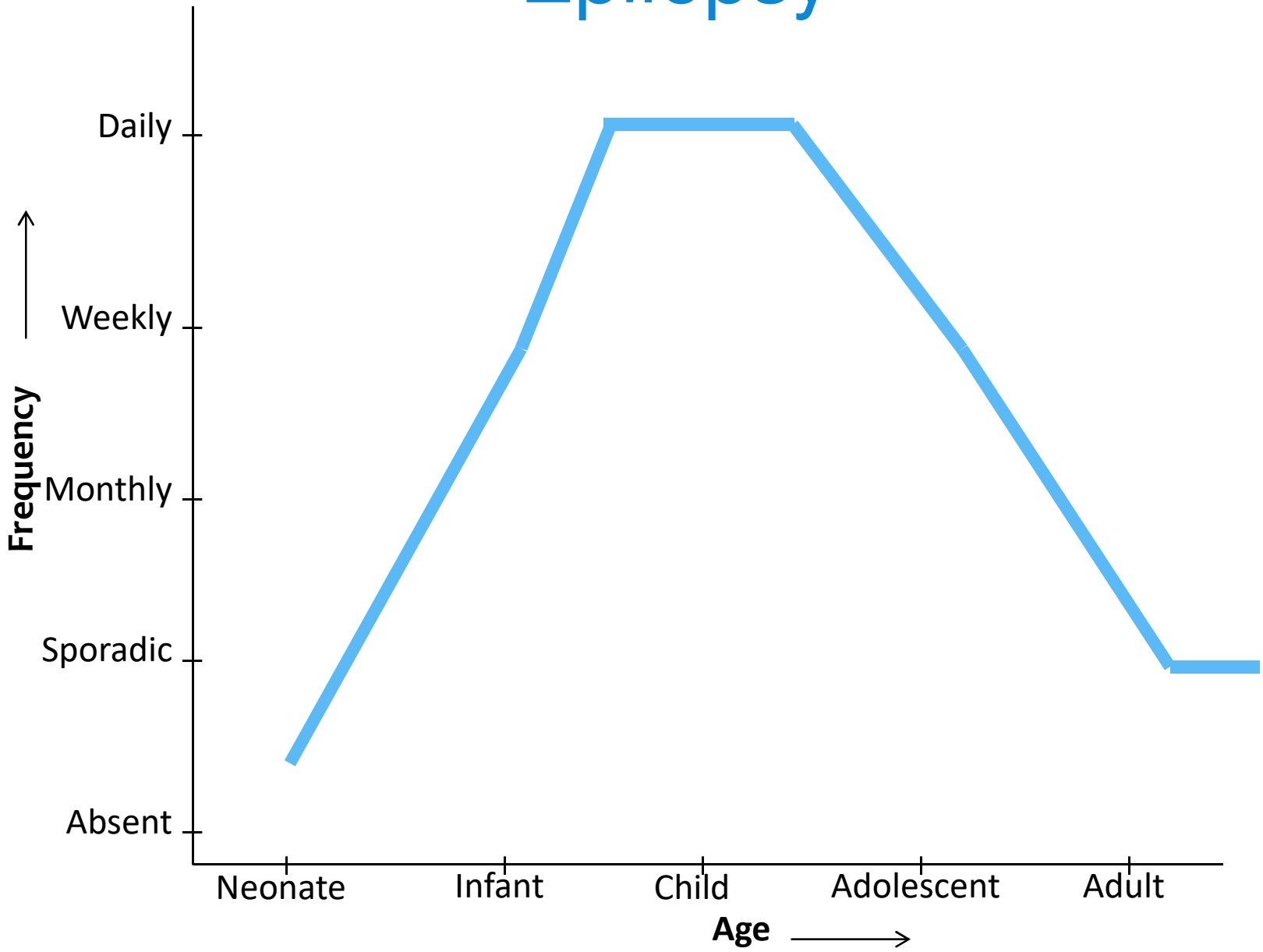
Anti-epileptic drugs:
- n= 3/7 (seizures after drug reduction in 2)

Other:
Oxcarbazepine for PED (n = 3)
Acetazolamide for PED (n = 2)

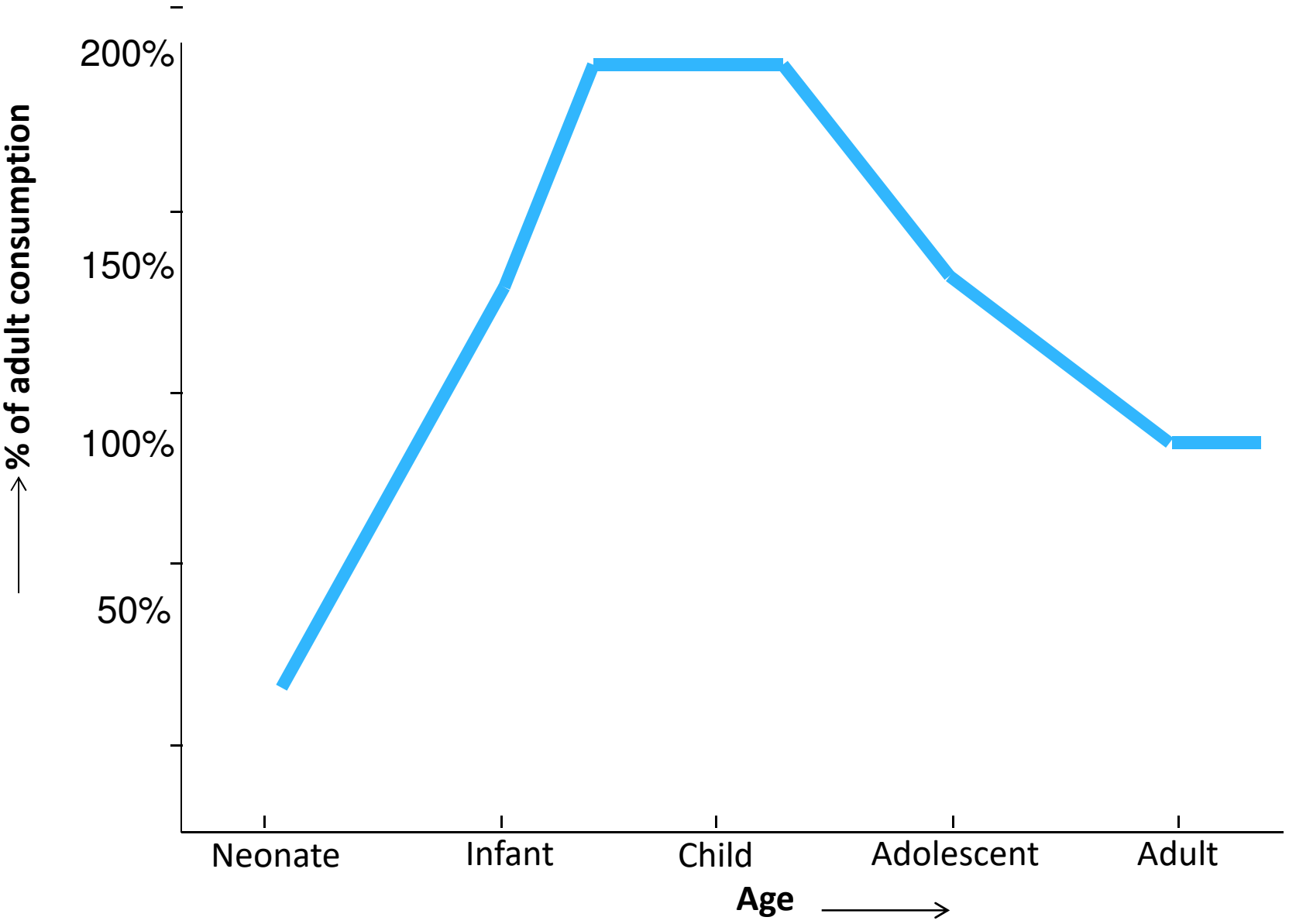
Conclusion (1)

Seizure frequency decreases during adolescence.

Epilepsy


Daily
Weekly
Monthly
Sporadic
Absent
Frequency
Neonate
Infant
Child
Adolescent
Adult
Age

Glucose consumption of cortex



Conclusion (2)

Onset / worsening of
paroxysmal exertion induced dyskinesia
during adolescence

Take home message (1)

Classical, complex GLUT1DS:

- Large individual differences
- Intellectual disability appears to be stabile
- Change of dominating symtom with age:
    - Epilepsy most disabling symptom during childhood
    - PED occurs or worsens during adolescence

Take home message (2)

Treatment of adolescents and adults with GLUT1DS:

- Modified Atkins diet is good alternative
- If possible, try to reduce anti-epileptic drugs
- Oxcarbazepine and acetazolamide can be effective for PED