

## ESES

Dear colleagues,

Thank you for your consideration to participate in this comprehensive survey on steroid treatment in children with Electrical Status Epilepticus in Sleep (ESES) in Europe.

Replying the survey takes approximately 5 minutes. We are aiming for an overview of common practices per center, so we kindly ask you to answer the survey only once per center.

For the purpose of this study, we do not differ between the terms "ESES" and "CSWS" (continuous spike waves during sleep). Spike wave index during non-REM sleep is abbreviated as SWI.

During the active phase of the survey, data protection policies are strictly observed, IP addresses are not recorded. Data storage and evaluation is only done in an anonymous matter. Correlation of data to participants or to a center is not possible.

For further information please contact us at any time. We appreciate your time and consideration for contribution.

Kind regards,

Dr. Alexandra Klotz and Prof. Dr. Julia Jacobs (Freiburg/Germany) and Dr. Floor Jansen (Utrecht/Netherlands)

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## Part 1 General information

1. Please select all statements that apply for your person.

I am.....

- ☐ ... a general pediatrician
- ☐ ... a neuropediatrician
- ☐ ... a neurologist
- ☐ ... formally trained as a epileptologist
- ☐ ... head of the center
- ☐ ... a consultant in this center
- ☐ ... an epilepsy (research) nurse in this center
- ☐ ... other, please specify

2. I am working at ...

- ☐ ... a Neuropediatric/Neurology department of a university hospital
- ☐ ... Neuropediatric/Neurology department of a non-university hospital
- ☐ ... an Epilepsy Center
- ☐ ... other (please specify)

3. In which country is your Center located?

- |                                                  |                                   |
|--------------------------------------------------|-----------------------------------|
| <input type="radio"/> Austria                    | <input type="radio"/> Italy       |
| <input type="radio"/> Belgium                    | <input type="radio"/> Latvia      |
| <input type="radio"/> Croatia                    | <input type="radio"/> Lithuania   |
| <input type="radio"/> Czechoslovakia             | <input type="radio"/> Netherlands |
| <input type="radio"/> Denmark                    | <input type="radio"/> Norway      |
| <input type="radio"/> Estonia                    | <input type="radio"/> Poland      |
| <input type="radio"/> Finland                    | <input type="radio"/> Portugal    |
| <input type="radio"/> France                     | <input type="radio"/> Romania     |
| <input type="radio"/> Georgia                    | <input type="radio"/> Scotland    |
| <input type="radio"/> Germany                    | <input type="radio"/> Spain       |
| <input type="radio"/> Greek                      | <input type="radio"/> Sweden      |
| <input type="radio"/> Hungary                    | <input type="radio"/> Switzerland |
| <input type="radio"/> Ireland                    | <input type="radio"/> UK          |
| <input type="radio"/> ... other (please specify) |                                   |

4. How many patients with ESES (as per definition used in your center) are seen at your center per year?

- ☐ 1 or less
- ☐ 2-5
- ☐ 6-10
- ☐ 11-20
- ☐ >20

## ESES

### Part 2 - General aspects of ESES

5. Are there national guidelines for diagnostic criteria and treatment of ESES in your country?

- ☐ Yes
- ☐ No
- ☐ I am not sure

6. Does your center have a standardized departmental treatment protocol (SOP) for patients with ESES?

- ☐ Yes
- ☐ No

7. What definition(s) of ESES is/are used at your center? (SWI=spike wave index during non-REM sleep, all definitions mean bilateral SWI)

- ☐ SWI >85% REGARDLESS of cognition
- ☐ SWI >85% PLUS cognitive delay, arrest or regression
- ☐ SWI >50% REGARDLESS of cognition
- ☐ SWI >50% PLUS cognitive delay, arrest or regression
- ☐ Strong activation of interictal epileptiform activity in non-REM sleep without SWI threshold
- ☐ Other (please specify)

8. Please rate how often the following treatment options are prescribed for ESES at your center

|                                   | very often            | often                 | sometimes             | rarely or never       |
|-----------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Sultiame                          | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| Clobazam or other benzodiazepines | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| Steroids                          | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| Valproate                         | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| Ethosuximide                      | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| Acetazolamid                      | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| Ketogenic diet                    | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| Levetiracetam                     | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| Topiramate                        | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| Intravenous immunoglobulins       | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| Epilepsy surgery                  | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |

## ESES

9. Is treatment at your Center different for "idiopathic" (including atypical rolandic epilepsy and Landau Kleffner syndrome) versus "symptomatic" ESES?

- ☐ Yes
- ☐ No
- ☐ Please comment shortly what is different for symptomatic ESES

10. How are ESES-patients managed at your center? Please select all that apply.

- ☐ Always as outpatients
- ☐ Always as inpatients
- ☐ Mainly as outpatients, inhouse only for diagnostics
- ☐ Mainly as outpatients, inhouse only for steroid treatment

11. Please rate if ESES-patients at your center are repeatedly (at least 2 times) monitored for

|                                                                                     | always                | usually               | sometimes             | rarely                | never                 |
|-------------------------------------------------------------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Routine EEG                                                                         | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| Sleep EEG (up to 2 hrs)                                                             | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| Overnight sleep EEG or video-EEG                                                    | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| Neurocognitive testing                                                              | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| Behavioral or psychiatric problems (consultation of psychiatrist or questionnaires) | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |

## ESES

### Part 3 specific questions about steroids for ESES treatment

\* 12. Does your center have a standardized departmental treatment protocol (SOP) for steroid treatment in ESES (or a section about steroids in the general ESES-protocol)?

☐ Yes

☐ No

## ESES

13. How is steroid treatment performed in general at your Center?

- ☐ Steroid treatment is based on individual decision and varies from case to case
- ☐ Steroid treatment is basically based on one typical scheme that will be adapted for individual patients
- ☐ Even without a formal SOP, steroid treatment always follows the same scheme

14. What are the indications of steroids in ESES-patients at your center? (please select all that apply)

- ☐ Just ESES diagnosis (regardless of SWI and neurocognitive impairment)
- ☐ Only if SWI > 85% uni- or bilaterally
- ☐ Only if SWI >50% bilaterally or >85% unilaterally
- ☐ As soon as neurocognitive arrest is present
- ☐ Only if neurocognitive regression is present
- ☐ Only if seizures are present
- ☐ Failure of Clobazam
- ☐ Failure of any other antiseizure medication

15. What are the main treatment goals for steroids in ESES patients at your center?

- ☐ Reduction of SWI
- ☐ Improvement of sleep architecture in EEG
- ☐ Reduction of seizure frequency >50%
- ☐ Seizure freedom
- ☐ Neurocognitive improvement
- ☐ Improvement of behavioral problems and/or psychiatric comorbidities as ADHS

## ESES

16. Steroid treatment for ESES at your center is considered as ...

- ☐ ... always first line
- ☐ ... first line only if SWI is >85% bilaterally
- ☐ ... first line only if neurocognitive regression or arrest are present
- ☐ ... always second line
- ☐ ... not earlier than third line
- ☐ ... only in case of secondary relapse
- ☐ I can't answer the question, first or second line depends too much on individual constellations

17. Please rate how often the following steroids are used at your center for ESES

|                                 | always                | usually               | sometimes             | rarely                | never                 |
|---------------------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Prednison orally                | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| Prednison intravenously         | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| Prednisolon orally              | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| Prednisolon intravenously       | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| Methylprednisolon orally        | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| Methylprednisolon intravenously | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| ACTH intramuscularly            | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| Dexamethason orally             | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| Dexamethason intraveously       | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| Hydrocortisone orally           | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| Hydrocortisone intravenously    | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |

18. What is the preferred type of steroid therapy at your center

- ☐ Pulse therapy only
- ☐ Continuous therapy only
- ☐ Pulses first followed by daily doses
- ☐ I can't answer the question because it is an individual decision

19. What are the reasons for the above mentioned steroid type and frequency? Please select all that apply.

- ☐ Best short-term efficacy based on own experience
- ☐ Best long-term efficacy (prevention of relapses) based on own experiences
- ☐ Best tolerance (lowest adverse events) based on own experience
- ☐ Availability of different steroids
- ☐ National guidelines
- ☐ Scientific publication (if possible please enter author +/- year below)
- ☐ Not applicable, we use several different types of steroids

Publication:

20. Please state if steroid treatment is regarded as contraindicated at your center if one of the following comorbidities is present

|                             | absolute contraindication | relative contraindication | no contraindication   |
|-----------------------------|---------------------------|---------------------------|-----------------------|
| Obesity                     | <input type="radio"/>     | <input type="radio"/>     | <input type="radio"/> |
| Diabetes melitus            | <input type="radio"/>     | <input type="radio"/>     | <input type="radio"/> |
| Metabolic disorder          | <input type="radio"/>     | <input type="radio"/>     | <input type="radio"/> |
| High blood pressure         | <input type="radio"/>     | <input type="radio"/>     | <input type="radio"/> |
| History of cardiac disorder | <input type="radio"/>     | <input type="radio"/>     | <input type="radio"/> |

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21. How often are the following check-ups performed in case of steroid PULSE treatment? (either at your center or recommended by you to be done by general pediatrician)

|                   | always                | usually               | sometimes             | rarely                | never                 |
|-------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Blood pressure    | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| Urine glucose     | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| Blood glucose     | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| Echocardiography  | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| Body measurements | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |

22. How often are the following check-ups performed in case of CONTINUOUS steroid treatment? (either at your center or recommended by you to be done by general pediatrician)

|                   | always                | usually               | sometimes             | rarely                | never                 |
|-------------------|-----------------------|-----------------------|-----------------------|-----------------------|-----------------------|
| Blood pressure    | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| Urine glucose     | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| Blood glucose     | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| Echocardiography  | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| Body measurements | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |

23. How long is steroid treatment for ESES usually performed at your center (good tolerance provided)? Please select all that apply.

- ☐ At least one month (pulses or continuous treatment)
- ☐ At least 6 months (pulses or continuous treatment)
- ☐ At least until SWI <50% bilaterally
- ☐ At least until neurocognitive improvement is seen
- ☐ None of the above

24. What would be the reasons to end steroid therapy for ESES at your center? Please select all that apply.

- ☐ Predefined time per protocol or standards
- ☐ Occurrence of arterial hypertension
- ☐ Fasting blood glucose > 200mg/dl
- ☐ Weight gain resulting in obesity
- ☐ other (moderate to severe) adverse events
- ☐ SWI < 50%
- ☐ Normalization/remarkable improvement of language and or cognitive function
- ☐ No improvement of SWI and/or cognitive functioning after .... (please enter time below)
- ☐ Time

## ESES

25. Please look at the following steroid schemes that have been used in previous studies and select if one is similar to the one used at your center.

|                                                                                                                                | exactly the same      | similar               | not used              |
|--------------------------------------------------------------------------------------------------------------------------------|-----------------------|-----------------------|-----------------------|
| <b>Prednisone</b> 2mg/kg weekly for 6 weeks<br>(Hempel et al 2019)                                                             | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| <b>Prednisolone</b> 20mg/kg on 3 days per week, duration 4 weeks, then re-evaluation (modified Bast et al 2014)                | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| <b>Prednisone</b> 1mg/kg daily for 6 months<br>(Sinclair & Snyder 2006)                                                        | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| <b>ACTH</b> 0.01-1mg/kg/d daily in repetitive courses of for 6-15 days (Altunel et al 2017)                                    | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| <b>ACTH</b> 0.01-0.04mg/kg daily for 11-43 days (Inutsuka et al 2006)                                                          | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| <b>Dexamethasone</b> 0.15mg/kg daily for 4 weeks, slowly decreasing after (Chen et al 2016)                                    | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| <b>Methylprednisolone</b> 20mg/kg on 3 days every 4 weeks, duration 6 months<br>(Munckhof 2016)                                | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| <b>Methylprednisolone</b> 20mg/kg on 3 days per week, duration 4 weeks, then re-evaluation (Bast et al 2014)                   | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| <b>Methylprednisolone</b> 30mg/kg daily than weaning, followed by Prednisolon 2mg/kg daily for 6 months<br>(Okuzay et al 2005) | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| <b>Hydocortisone</b> 5mg/kg daily for 1 month, then reducing over 9 months total<br>(Buzatu 2009)                              | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |
| <b>Hydocortisone</b> 20mg/kg daily for                                                                                         | <input type="radio"/> | <input type="radio"/> | <input type="radio"/> |

several months  
(Verhelst *et al* 2005)

Please describe shortly "your" scheme if not listed above

A large, empty rectangular box with a thin black border, intended for a user to describe their scheme. The box is positioned below the instruction text and occupies a significant portion of the page's vertical space.

ESES

End of survey

**We thank you very much for participating in our survey and appreciate your time!**

**If there are any questions please do not hesitate to contact us at any time**

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