Sponsors: Swiss Society of Paediatrics (SSP) and Federal Office of Public Health (FOPH)

Invasive Infections caused by Group A Streptococci (iGAS)

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Summary:

Beside mostly mild infections like pharyngitis/tonsillitis or impetigo, group A beta-haemolytic streptococci are also causing severe invasive infections (iGAS). Until now, there is no data on incidence, epidemiology, clinical course, possible risk factors and characteristics of causing GAS-isolates in children in Switzerland. This study will provide data on these parameters by analysing a questionnaire sent to treating physicians in *SPSU*-participating hospitals. Furthermore, the study is going to be the basis for further molecular analysis (emm-types) of the causing GAS-isolates.

Begin of the study:

1st of December 2017

Duration of the study:

Four years

Aims of the study:

Collecting and analysing data on iGAS in Swiss children ≤ 16 years regarding

- Incidence
- Seasonality
- Age distribution
- Clinical manifestations and complications
- Treatment
- Risk factors (underlying disease, varicella, drugs (i.e. ibuprofen, paracetamol))
- Rate of recurrence
- Morbidity and mortality

In addition, it is planned to collect the iGAS strains in a first step for storage only but deferred emm-typing in a second step. This will be done in a separate project.

Background:

GAS infections in children are typically mild and self-limiting infections, such as tonsillitis. They rarely cause local suppurative complications and exceptionally result in severe rheumatic complications (e.g. rheumatic fever). During the last years, in the clinical perception of PIGS members (Pediatric Infectious Disease Group of Switzerland), the frequency and severity of iGAS has increased. Several studies have shown seasonal and geographic differences in the incidence of iGAS with a relatively stable local incidence over time. (1,2). Reasons for this are widely unknown. An important risk factor for iGAS is varicella primary infection, but also other skin lesions such as excoriations or after surgery, as well as close contact to patients with GAS infection have been described as risk factors in iGAS patients (2). Virulence factors of the bacteria or molecular characteristics, such as the emm-type, are also important in iGAS epidemiology (3).
Until now, we have no epidemiological data on frequency, age distribution, clinical presentation or risk factors for iGAS in children in Switzerland. Furthermore, molecular characteristics (factors of pathogenicity) and emm types of causing GAS are largely unknown.

Methodology:

Observational, multicentric study of iGAS in children to collect information on epidemiology, severity, treatment, risk factors and to provide the basis for further molecular characterisation of GAS causing invasive infections in Switzerland. Registration of all children and adolescents ≤ 16 years hospitalized in one of the participating hospitals because of iGAS, as defined in the case definition (see below). After notification by monthly sent *SPSU*-notification-card, an anonymized questionnaire is sent to the notifying physician. This questionnaire contains information on

- demographics (date of birth, sex, origin)
- clinical course and severity (localisation, onset and duration of symptoms, vital signs)
- treatment and course of symptoms during hospitalisation (ICU, antibiotics, surgery),
- risk factors (varicella infection, skin damage, underlying disease, drugs, possible GAS exposure)

as well as

- outcome (exitus, sequelae, complete recovery).
- If culture grown, pathogens are stored locally.

Case definition:

Confirmed case
Isolation of group A streptococci = GAS = *Streptococcus pyogenes* from a normally sterile site (culture, antigen or PCR) such as

Blood
Cerebrospinal fluid
Sterile site aspirate (pleura, joint, pericardial fluid)
Muscle-/bone tissue (deep tissue, surgical sampling)

Probable case
Severe clinical presentation* **without** alternative diagnosis **AND** GAS isolation from a non-sterile site (culture, antigen or PCR)

* Severe clinical presentation:

1) Toxic shock syndrome
   Arterial hypotension (systolic blood pressure < 5th Percentile for age, see Table below)
   PLUS ≥ 2 of the following criteria
   a) renal impairment (creatinine > 2 x the upper limit of normal for age)
   b) coagulopathy (Thrombocytes < 100 G/L or clinical signs of disseminated intravasal coagulation = DIC)
   c) liver impairment (ALAT, ASAT or bilirubin > 2 x the upper limit of normal for age)
   d) generalized erythema with/without subsequent desquamation
   e) ARDS (acute respiratory distress syndrome)

2) Necrotizing fasciitis

Table: Systolic blood pressure, 5th Percentile for age (5)

Age group	Systolic blood pressure in mmHg
0 days to 1 week	65
1 week to 1 month	75
1 month to 1 year	100
2–5 years	94
6–12 years	105
13 to < 18 years	117

Questionnaire:

The questions are formulated and should be answered directly on the 2 page questionnaire. **See annexe.**

Reporting instructions:

All cases of hospitalized patients with confirmed or probable diagnosis of iGAS in children ≤ 16 years (see Case definition) should be notified by the monthly sent *SPSU*-notification-card. The questionnaire will then be sent to the notifying physician for completion (see Questionnaire / annexe).

References:

1. Nelson GE, Pondo T, Toews K-A, Farley MM, Lindegren ML, Lynfield R, u. a. Epidemiology of Invasive Group A Streptococcal Infections in the United States, 2005-2012. Clin Infect Dis Off Publ Infect Dis Soc Am. 15. August 2016;63(4):478–86.
2. Tapiainen T, Launonen S, Renko M, Saxen H, Salo E, Korppi M, u. a. Invasive Group A Streptococcal Infections in Children: A Nationwide Survey in Finland. Pediatr Infect Dis J. 2016;35(2):123–128.
3. Watanabe S, Takemoto N, Ogura K, Miyoshi-Akiyama T. Severe invasive streptococcal infection by Streptococcus pyogenes and Streptococcus dysgalactiae subsp. equisimilis. Microbiol Immunol. Januar 2016;60(1):1–9.
4. Invasive Group A Streptococcal Disease - igas.pdf [Internet]. [zitiert 1. Mai 2017]. Verfügbar unter: https://www.gov.mb.ca/health/publichealth/cdc/protocol/igas.pdf
5. Goldstein B, Giroir B, Randolph A. International pediatric sepsis consensus conference: Definitions for sepsis and organ dysfunction in pediatrics*: Pediatr Crit Care Med. Januar 2005;6(1):2–8.

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