Referrals and incidental findings for newborn screening for SCID in the Netherlands

First results of the SONNET-study

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Introduction

- Newborn screening for sev combined immunodeficiency (SCID) is ed on the detection of *T-cell receptor sion circles* (TREC) by PCR.
- Newborn screening for SCID is companied by incidental findings, raising ical issues concerned with screening fo untreatable diseases.
- Starting April 1 2018, 70,000 n orns in the Netherlands will be screened fo CID as part of a one-year prospective i ementation pilot (SONNET-study).

Material and methods

With the SCREEN-ID kit (Immu VD), TRECs and internal control beta-actin a detected in dried blood spots by quantitative l-time PCR. Dried blood spots with TREC-levels below cut-off (≤6 copies/µl) require repeated analysis in duplicate. Newborns with repeated low TREC-values are referred according to a pre-set follow-up protocol (Figure 1).

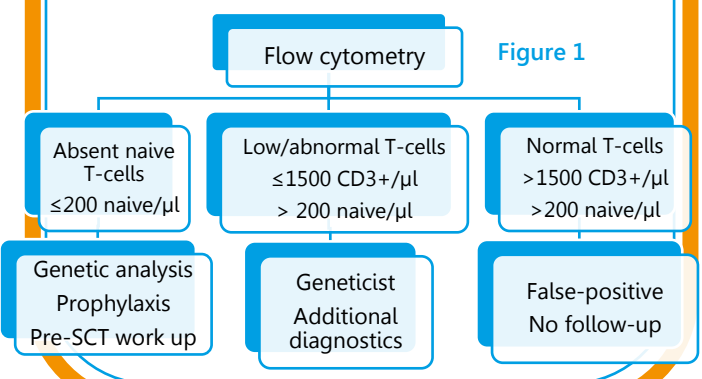

Figure 1

Results

From April to September 2018, 37,500 heel prick cards were analyzed from of which 39 required a repeated analysis (Table 1). Ten newborns required a second heel prick (n=5 preterms and n=5 poor quality). There were 5 referrals.

Table 1

Total number of heel prick cards analyzed	37500
Number of heel prick cards TREC ≤6 initial analysis	39
Number of heel prick cards normal after repeated analysis	26
Number of second heel pricks (insufficient quality/low ACTB)	5
Number of second heel pricks at 36.1 weeks (preterms)	5
Number of referrals	5

Results

No SCID patients were detected. Low TREC-values were due to various conditions at the time of the heel prick, or to findings observed previously in newborn screening for SCID (Figure 2).

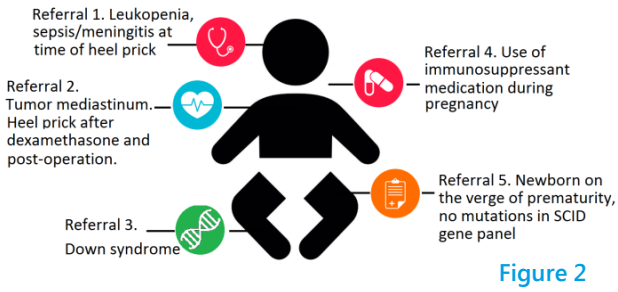

Figure 2

The number of repeated analyses and therefore the number of referrals, and incidental findings are dependent on the chosen cut-off value (Table 2).

Table 2

Cut-off	Number of heel prick cards below cut-off	Retest rate
TREC ≤ 6	39	0.10 %
TREC ≤ 10	71	0.19 %
TREC ≤ 15	180	0.48 %
TREC ≤ 20	330	0.88 %

Discussion

- Screening strictly for SCID or screening for T-lymphocytopenia has a direct impact on the TREC cut-off value.
- The variety of incidental findings indicates the importance of a pre-set follow-up protocol.
- Ataxia telangiectasia (AT) is a untreatable incidental finding, raising ethical issues. Inclusion of the *ATM*-gene in the genetic follow-up should be discussed prior to the implementation of newborn screening for SCID (Figure 3).
- To address ethical implications, (ELSI-) questionnaires will be developed in the final stage of our pilot study to query parents and health care providers.

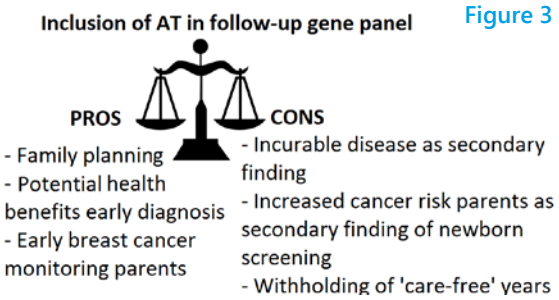

Figure 3

Conclusion

- Newborn screening for SCID is accompanied by a number of incidental findings.
- The TREC cut-off value greatly influences the number of incidental findings.
- A follow-up protocol with regard to ataxia telangiectasia should be established.

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