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**Introduction & Objectives:** In hypospadias, also penile skin has shown to be involved and is considered "dysplastic". Nevertheless, little is known on the implications of this finding on skin immunology, despite the penis being a site of entry for a number of relevant pathogens. Langerhans cells (LCs), the dendritic cells of the epidermis, play a pivotal role in specific immune responses as for instance to HPV or HIV. The presence or morphology of LCs has not been investigated before in the skin of hypospadias patients.

**Materials & Methods:** 28 patients were prospectively included. Epidermal sheets and full-thickness skin sections were prepared from foreskin samples of 18 patients with hypospadias (13 distal, 6 proximal) and compared to samples from 10 patients without a penile malformation. Sheets were stained with anti-HLA-DR/FITC and anti-CD207/Langerin/A594, sections were stained with a 929F3.01-anti-CD207/Langerin/Biot/DABMAP (Ventana Roche®). HLA-DR/CD207 double positive cells were considered LCs. The phenotype of epidermal LCs and their frequency was assessed by immunofluorescence microscopy in 12 high-power-fields of at least one representative sheet per patient. On the sections, LCs were counted and evaluated by bright-field microscopy.

**Results:** The mean frequency of epidermal HLA-DR/CD207 positive cells accounted to  $860,5 \pm 66,74/\text{mm}^2$  (n=19) in patients with hypospadias as compared to  $888,3 \pm 92,59/\text{mm}^2$  (n=10) in patients with normal penile development (p=0.8089, t-test). There was no significant difference in Langerhans cell frequency between distal and proximal hypospadias ( $856,5 \pm 82,26/\text{mm}^2$ , n=13, distal vs.  $869,1 \pm 124,8/\text{mm}^2$ , n=6 proximal, p=0.9331). In the dermis only few HLA-DR/CD207 cells ( $<10/\text{mm}^2$ ) were detected. The morphology of the cells was normal in both groups.

**Conclusions:** There is no difference in frequency or morphology of epidermal LCs in the foreskin of hypospadias patients as compared to patients without penile malformations. This suggests that patients with hypospadias are not different from patients with normal penile development considering their specific skin immunity.