



## Letter to the Editor

## Conceptualising skin development diagrammatically from foetal and neonatal scientific evidence



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## 1. Background

Skin injury is a problem for at least 40% of the neonatal population, with increasing risk for neonates of decreased gestational age and those who require devices to support medical care (August et al., 2018a). Importantly, changes to skin integrity can affect a neonates' sensory perception (pain), hydration (trans-epidermal water-loss) and morbidity (length of stay) among other considerations (Brandon et al., 2018). Clinicians' understanding of the skin's physiology, structure, and development informs clinical decisions and is traditionally learned through text sources, accompanied by occasional figures or diagrams. However, the importance of visual models for knowledge acquisition continues to grow, supporting a shift away from text as the primary source of information (Butcher, 2006; Whitley, 2013). Examples of visual diagrams that regularly inform clinical practice are the three-dimensional cubes depicting degree of skin damage presented by the National Pressure Ulcer Advisory Panel (NPUAP) (Edsberg et al., 2016).

Visual representations of foetal and neonatal skin development from peer-reviewed sources have previously been published as electron/light micrographs, diagrams, figures and illustrations. Ersch and Stallmach (1999) represented skin development through schematic histological slides and illustrations, while contemporary models have demonstrated development of the skin through cross-sectional figures (Fox, 2011). Histological images are biological evidence and therefore a gold standard for identifying cell and tissue development. However, present day ethical and fiscal constraints reduce the possibility of large-scale histological investigations. Of the existing visual examples many were found to have limitations such as: the need for interpretation of electron micrographs and images of histological slides (Ersch and Stallmach, 1999; Holbrook and Odland, 1975; Lund et al., 1999), the absence of structures such as periderm and vernix (Fox, 2011; Lund et al., 1999) and missing gestational ages within figures (Fox, 2011). Using foetal

and neonatal scientific evidence we have developed a diagram for skin development from 0 to 40 weeks gestation.

## 2. Diagram development

During PhD research, the opportunity arose for collaboration between a neonatal nurse with a wound specialty, and a medical student with a background in communication design. It was identified there was a need for a diagram that would help clinicians conceptualise skin development from early genesis to term gestation, to improve understanding of the function limitations of underdeveloped skin. Like many organs, the skin has structural and functional weakness at term gestation with further deficiencies noted when born premature. The model proposed in Fox (2011) displays development of the organ from four weeks to 28 weeks (Fox, 2011). While the extremely premature time-frame presents increased skin challenges, all neonates requiring care in neonatal units are at increased risk of skin damage because of mechanical forces from securement of medical devices. Hence, using the lateral markers (time brackets for weeks of development) from Fox's work, we proposed an extended diagram to span from 0 to 40 weeks gestation and detailed developmental illustration of essential skin structures and elements.

The literature was reviewed for evidence of the development for each of the following elements and structures: ectoderm, periderm, basal cells, stratum (s.) (basale, spinosum, granulosum, corneum), dermal cells (papillary and reticular layers), dermoepidermal junction (rete ridges), hair follicle, sweat gland, adipose tissue, blood vessels, desmosomes, and vernix. Next gestational periods were populated with skin development milestones from multiple sources such as expert opinion statements, data (tables), diagrams, illustrations, figures, histology, and electron/light micrographs (photomicrographs) (August et al., 2018b; Hoath and Mauro, 2014; Ersch and Stallmach, 1999;

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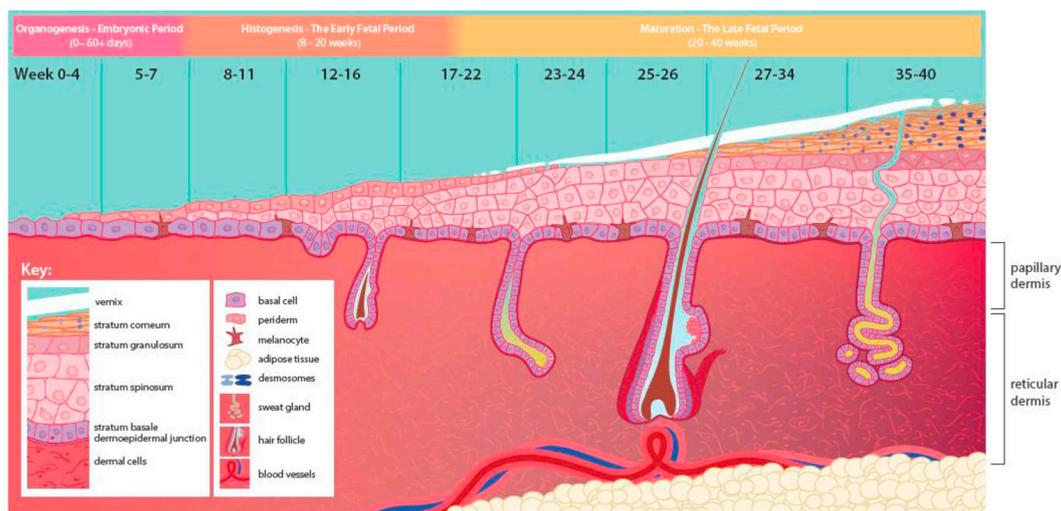


Table 1: Key development features and considerations by weeks

Week	0-4	5-7	8-11	12-16	17-22	23-24	25-26	27-34	35-40
Single layer of ectoderm. Periderm and basal layer emerges.	Melanocytes emerge.	Spinosus cell layer emerges.	Periderm, basal cells, desmosomes, hair follicles emerge. Two layers of spinosum.	Four-five layers of epidermis. Vernix begins to form	Epidermal layer begins to proliferate. Periderm deteriorates (finished by 24 weeks), adds to vernix.	Epidermis keratinised (cornified). Multiple layers of stratum corneum.	Vernix and stratum corneum thicken.	Thick vernix covers the skin and then by 40 weeks remains only in creases.	

(August et al., 2018b; Hoath, S. and Mauro, T., 2014; Holbrook and Odland, 1975; Visscher and Narendran, 2014a; Visscher and Narendran, 2014b). This diagram excludes the stratum lucidum.

Fig. 1. –Skin development from 0 to 40 weeks.

Evans and Rutter, 1986; Fluhr et al., 2014; Fox, 2011; Hoeger and Enzmann, 2002; Holbrook and Odland, 1975; Lund et al., 1999; Nikolovski et al., 2008; Stamatas et al., 2011; Visscher and Narendran, 2014a, 2014b). The genesis and development of each element within the diagram (for example: basal layer) was crosschecked against all sources. If there was disagreement between sources, as occurred with the genesis of adipose tissue, the decision was made based on most recent and majority consensus within the literature. The diagram was also designed inline with the stages of organ development: (i) organogenesis- embryonic period (0– 60-plus days) before 8 weeks, (ii) histogenesis - the early foetal period 8–20 weeks, and (iii) maturation - the late foetal period (5–9 months) 20 weeks onwards (Hoath and Mauro, 2014). Adobe Illustrator software was used to produce the diagram.

**3. An evidence-based visualisation for skin development from 0 to 40 weeks**

There is now an expectation that to enhance learning and memory processing, materials, where possible, should be presented in text and graphical formats (Whitley, 2013), giving more focus to the visual than the textual learning style alone. Thus, this skin diagram (Fig. 1), is presented with a table (Table 1) which outlines key development aspects for each lateral marker time period. This style of educational resource is likely to inform students, neonatal clinicians, clinicians for whom English is a second language and those whom infrequently care for neonates.

Additionally, Table 2 provides details on depth and sub-skin layers

for preterm and term infants comparative to adult measurements. These details facilitate contextualising the scale of skin depth demonstrated within the diagram.

**4. Limitations of sources to inform diagram**

This diagram is derived from the available evidence; combining foetal and neonatal skin evidence and therefore makes some assumptions about development after preterm birth. Half of the content originated from foetal skin literature (< 22 weeks gestation), while the remaining weeks of skin development are from a combination of foetal and neonatal sources. This combination of sources has been synthesised to resolve skin development post 22 weeks, with some discrepancies and gaps in the literature. Specifically, this diagram was unable to accurately depict i) the exact number of cell layers in the stratum spinosum after 17 weeks, ii) the variation in skin depth and structure across different anatomical locations as well as iii) when the stratum lucidum development was differentiable from other epidermal layers. Additionally, the stratum lucidum is only present in the soles and palms (Hoath and Mauro, 2014), thus it has not been presented in this diagram. Furthermore, the diagram's lateral markers were divided based on available evidence which has resulted in non-linear segments with some segments representing 2 weeks while others represent 5 weeks. Despite these challenges the authors believe this is the closest representation of overall skin structure and development based on currently available data.

**Table 1**  
Key development features and considerations by weeks.

0-4	Single layer of ectoderm. Periderm and basal layer emerges.
5-7	Melanocytes emerge.
8-11	Spinous cell layer emerges.
12-16	Periderm, basal cells, desmosomes, hair follicles emerge. Two layers of spinosum.
17-22	Four-five layers of epidermis. Vernix begins to form
23-24	Epidermal layer begins to proliferate. Periderm deteriorates (finished by 24 weeks), adds to vernix.
25-26	Epidermis keratinised (cornified). Multiple layers of stratum corneum.
27-34	Vernix and stratum corneum thicken.
35-40	Thick vernix covers the skin and then by 40 weeks remains only in creases.

(August et al., 2018b; Hoath and Mauro, 2014; Holbrook and Odland, 1975; Visscher and Narendran, 2014a, 2014b). This diagram excludes the stratum lucidum.

**Table 2**

Depth of skin and sub-layers for preterm and term neonate's comparative to adults.

Structure	Preterm <sup>a</sup>	Term	Adult
Skin	0.9mm (900µm)	1.2 mm (1200µm)	2.1 mm (2100 µm)
Epidermis	20-40 um	36-50 um	> 50 um
Stratum corneum	4-5 um (5-6 cells)	9-10 um (> 15 cells)	9-15 um (> 15 cells)

mm- millimetre, um- micrometre.

<sup>a</sup> (exact gestation not available); data from (Hoath and Mauro, 2014; Ersch and Stallmach, 1999).

**5. Future research**

While histological images are a gold standard; ethical constraints are likely to restrict future large-scale histological studies necessitating other visual representation of scientific knowledge. We acknowledge it will be difficult to research the development of the dermis, comprising of the dermo-epidermal junction (specifically rete ridges (Farage et al., 2008), as well as the papillary and reticular dermis. However, there is a specific need to enhance understanding of the junction's role in skin connectivity, to inform the prevention of neonatal medical adhesive related injuries (August et al., 2018a). Lastly, continued research regarding pre and post natal skin development will likely require non-invasive measurements applied to graphic illustrations to enhance clinician's knowledge of skin development and inform strategies to reduce majority of neonatal skin injuries.

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