HHS Public Access

Author manuscript

Dev Psychobiol. Author manuscript; available in PMC 2019 July 15.

Published in final edited form as:

Dev Psychobiol. 2019 April ; 61(3): 465–476. doi:10.1002/dev.21830.

Innovations in biological assessments of chronic stress through hair and nail cortisol: Conceptual, developmental, and methodological issues

Cindy H. Liu[1] and **Stacey N. Doan**[2]

[1]Brigham and Women's Hospital, Harvard Medical School, Boston, MA

[2]Department of Psychology, Claremont McKenna College, Claremont, CA

Abstract

Much of the existing research on biological mechanisms underlying the stress experience has focused largely on moment-to-moment stress, rather than on *chronic stress*, an arguably more powerful predictor of long-term outcomes. Recent methodological innovations have paved the way for new lines of research on chronic stress, with promising implications for developmental researchers and for those who study health and adversity. In particular, there are increasing studies that have focused on chronic stress assessments by relying on cortisol derived from hair and nails as a biomarker for chronic stress. In this paper, we provide an overview of their use, describe how hair and nail cortisol ought to be conceptualized differently across the lifespan, how developmental factors may impact its interpretation, and the circumstances under which its use may be more methodologically sensible. The purpose of this review is to provoke further discussion and encourage careful research designs that utilize hair and nail cortisol for understanding the effects of chronic stress exposure from the early developmental period, across adverse contexts, and in association with psychological and physical health outcomes.

Keywords

chronic stress; development; hair cortisol; nail cortisol

1 | INTRODUCTION

Understanding the basic processes that underlie the effects of stress across development has major implications for addressing real world problems such as poverty and trauma. It is understood that childhood is a vulnerable period within development, by which the effects of stress may take hold, producing adverse outcomes later in life (National Scientific Council on the Developing Child, 2014). Yet, among researchers, there lacks a consensus regarding the definition and operationalization of stress. The distinction made between stress reactivity and *chronic* stress is a promising direction in assessing and understanding the effects of stress across development.

Correspondence: Cindy H. Liu, Brigham and Women's, Hospital, Harvard Medical School, Boston MA. chliu@bwh.harvard.edu.

Stress reactivity focuses on *moment-to-moment* responses to the exposure of acute stressors, characterized by uncontrollability and social-evaluative threat (Dickerson & Kemeny, 2004). On the other hand, chronic stress refers to the exposure to a stimulus or threat that takes place for an extended period of time. Methodological approaches to measuring chronic stress include documenting the presence of stressors, including major life events, daily events, and chronic strains; the psychological subjective reports of individuals' own affective responses; and related biological responses (Vanaelst, De Vriendt, Huybrechts, Rinaldi, & De Henauw, 2012). It is important to note that the distinction between chronic and acute stressors is not always clear (Gottlieb, 1997). For example, a situation where the acute stressor is associated with the loss of a spouse can in turn be both foreshadowed and followed by a series of stressful events that altogether are prolonged in nature.

As such, an ongoing challenge is determining whether chronic stress can be measured. Substantial efforts have been made to obtain measurements within and across systems. Much of the psychobiological research on physiological dysregulation in both children and adults have focused extensively on the hypothalamic–pituitary–adrenal (HPA) axis and the autonomic nervous system (Chida & Hamer, 2008), with cortisol, the end product of the HPA axis, being perhaps the most extensively studied biological stress variable in developmental science. Cortisol concentrations from saliva or urine inform a relatively short time frame (at most a few days), can be invasive (when collected via blood), and require repeated measurements across 24 hr over several days to obtain average chronic concentrations (Wosu, Valdimarsdóttir, Shields, Williams, & Williams, 2013). With respect to capturing chronic stress, diurnal cortisol rhythms and the total amount of cortisol released during a stressor (e.g., AUC, area under the curve) has been used to make assumptions about cumulative cortisol exposure. Specifically, chronic stress has been associated with a flattening of the diurnal slope (Suglia et al., 2010) and a lower cortisol awakening response (CAR; Heim, Ehlert, & Hellhammer, 2000). Research with children who have faced adversity, including children living in Romanian orphanages or foster care, have shown such stressful circumstances to be associated with higher levels of cortisol over the daytime hours (Gunnar, Morison, Chisholm, & Schuder, 2001), or blunted early morning cortisol levels and no decrease over the day (Bruce, Fisher, Pears, & Levine, 2009). Overall, much has been written regarding salivary cortisol (including the diurnal slope and CAR) as a biological marker of chronic stress and we refer the reader to recent reviews on this area (An et al., 2016; Smyth, Hucklebridge, Thorn, Evans, & Clow, 2013; Stalder et al., 2016). Vanaelst, De Vriendt, et al. (2012) also provide an overview on epidemiological approaches in the measurement of stress among children between the ages of 6–12 years, covering the use of questionnaires and interviews as well as the cortisol from serum, urine, saliva, and hair.

This paper critically evaluates the use of hair and nail cortisol as biological markers of chronic stress (Dettenborn, Muhtz et al., 2012; Russell, Koren, Rieder, & Uum, 2012; Yamada et al., 2007). We do so for the following reasons. First, hair and nail cortisol are believed to represent an accumulation of cortisol output over a time frame of months and thus may be a potential means for characterizing chronic stress. Second, there is ease in the sampling and storage of hair and nail cortisol, which may facilitate its use in children and other populations. For example, accumulated cortisol as an outcome among children may be less vulnerable to fluctuations (e.g., naptime, breastfeeding) relative to salivary cortisol

values (Russell et al., 2012); therefore, hair and nail cortisol may be an attractive potential biomarker for chronic stress in younger samples (Egliston, Mcmahon, & Austin, 2007; Gunnar & White, 2001; de Weerth & van Geert, 2002). Third, there is a rising interest in understanding the biological mechanisms of chronic stress, since capturing perceived or specific life stress through subjective report is not always feasible in very young children (Miller, Chen, & Parker, 2011). Overall, while stress responses in the moment can promote adaptation, prolonged stress over time can lead to biological dysregulation, producing vulnerabilities for illness and disease (McEwen, 2015). The accumulation of cortisol captured in early development may be a key mechanism underlying this link.

There are several reviews on the use of hair cortisol (Gow et al., 2010; Meyer & Novak, 2012; Mustonen et al., 2018; Russell et al., 2012; Stalder & Kirschbaum, 2012; Stalder et al., 2017; Staufenbiel, Penninx, Spijker, Elzinga, & van Rossum, 2013; Wosu et al., 2013), and our paper is by no means meant to be an exhaustive review. Instead we provide a brief overview of what is understood about hair cortisol as a purported measure of chronic stress and provide a review of the small number of studies that have been conducted with nail cortisol, a similar but newer potential measure of chronic stress. In our paper, we also cover conceptual, developmental, and methodological considerations for the use of these measures with children. Our purpose is to provoke further discussion and encourage thoughtful research designs that utilize hair and nail cortisol within developmental research.

1.1 | Hair cortisol

With the rapid evaluation and popularity of hair cortisol in human research over the course of the past decade, much more is known about hair cortisol concentration in contrast to nail cortisol. Cortisol production from the hair has been reliably measured. Assuming a growth rate of approximately 1-cm length of hair per month, a 6-cm length of hair represents the retrospective cortisol concentration over the previous 6 months (Meyer & Novak, 2012). Low to high intraindividual stability (within a 12-month interval) has been documented in adults (van Ockenburg et al., 2016; Short et al., 2016; Stalder, Steudte, Alexander et al., 2012), in infants with samples at or before 12 months (Liu, Fink, Brentani, & Brentani, 2017; Liu, Snidman, Leonard, Meyer, & Tronick, 2016), and in children at age 4 years (Groeneveld et al., 2013).

An important question for developmental researchers is the validity of hair cortisol in humans. Studies that have directly examined the relationship between hair cortisol and cortisol obtained from saliva, blood, or urine (e.g., D'Anna-Hernandez, Ross, Natvig, & Laudenslager, 2011; Davenport, Tiefenbacher, Lutz, Novak, & Meyer, 2006; Short et al., 2016; Stalder, Steudte, Alexander et al., 2012) show weak to moderate relationships. One recent validation study by Short et al. (2016) addressed the limitation of previous studies by assessing cortisol levels from adult hair, saliva, and urine over the same time span of 1-month, which included daily assessments of waking, postwakening, and bedtime samples of saliva. While the sample size was small with 17 participants, their findings showed that hair cortisol concentration was most strongly associated with salivary cortisol area under the curve (AUC) over the month ($r = 0.61$, $p = 0.01$) relative to calculations based on averages of salivary AUC in 1-, 2-, 3-, and 4-week durations ($r = 0.38–0.56$). This study also revealed

hair cortisol concentration to be a potentially more accurate reflection of overall cortisol output relative to other metrics of salivary cortisol (CAR or levels based on the diurnal rhythm), which showed no association with hair cortisol concentration. No association was obtained with cortisol concentrations from urine, with the authors proposing that cortisol conversion, which can affect the levels in the urine, as a reason for the lack of an association.

With regard to hair cortisol concentration and salivary cortisol in children, hair cortisol obtained among 7-year-old girls was associated with AUCg calculated from salivary cortisol collected post stressor (i.e., matching game) at 10, 20, 30, 40, and 50 min when the children were 3 years old (Ouellette et al., 2015). In a recent study by Kao, Doan, St. John, Meyer, and Tarullo (2018), hair cortisol was positively correlated with AUCg and AUCi, calculated from salivary cortisol responses at baseline, 20, and 40 min post stressor in preschool children. Hair cortisol was also associated with salivary cortisol AUC calculated from samples obtained at over the day in 5–11-year-old girls (Vanaelst, Huybrechts et al., 2012). Although a wider range of hair concentration values has been observed in younger children (1 year vs. 3, 5, and 8 years) perhaps due to the development of the HPA axis (e.g., Karlén, Frostell, Theodorsson, Faresjö, & Ludvigsson, 2013), these studies on children, to date, still suggest that there may be some association between hair cortisol and salivary cortisol, with chronic stress reflecting repeated measures of stress reactivity.

Aside from the validity of newer measures such as hair cortisol against previously established biological measures such as salivary cortisol, a critical question is whether the measures reflect psychosocial stress constructs, that is, whether hair cortisol is associated with either demographic or individual characteristics that reflect stress experiences, or self-reported stress. In focusing on the former, studies have examined hair cortisol in relation to categories of individuals exposed to chronic stress, either through stress-related conditions or contexts. These have included athletes (Skoluda, Dettenborn, Stalder, & Kirschbaum, 2012), those experiencing trauma from a natural disaster (Gao et al., 2014), and hospitalized infants (Yamada et al., 2007), to name a few. Despite the large variations in these conditions and contexts, and different analytical techniques for cortisol extraction, hair cortisol has generally been associated with those experiencing ongoing stress (for a review, see Herane-Vives, DeAngel et al., 2015). Indeed, a recent meta-analysis determined that groups exposed to chronic stress as a whole were estimated to have 22% elevated hair cortisol concentration, with those still currently experiencing the stress at the time of the study showing 43% increased hair cortisol concentration.

However, research examining hair cortisol and subjective reports of stress tend to report no association (Stalder et al., 2017). Despite the inconsistency in findings, it is hardly different from those found among salivary cortisol; in a review of the literature, Hjortskov, Garde Ørbæk, and Hansen (2004) reported that there was insufficient evidence for an association between subjective reports of psychological stress and the cortisol response in field studies (Hjortskov et al., 2004). Whether these findings generalize specifically in the hair cortisol from children cannot be concluded given the need to better define the experience of stress in children, the duration and timing of stress, and the developmental stages in which the exposures take place (Gray et al., 2018).

Relatedly, much work has focused on the evaluation of hair cortisol among individuals characterized by clinical concerns, including those experiencing high levels of chronic stress, such as those with major depressive disorder, bipolar disorder, generalized anxiety disorder, and post-traumatic stress disorder (PTSD). The findings involving such comparisons have been mixed and have been attributed to the complexities of participant characteristics such as psychiatric and physical comorbidities (Herane-Vives, Papadopoulos et al., 2015). Notably, meta-analysis by Stalder et al. (2017) covering an overwhelming number of adult studies showed a 17% *lower* hair cortisol concentration in those with anxiety disorders including PTSD. These findings align with the hypocortisolism documented in people who experience repeated traumatic events, such as those with PTSD. We discuss later on why hypocortisolism may also be observed in such chronically stressed groups.

A handful of studies have examined the relation between hair cortisol and clinical characteristics in children showing no association between hair cortisol concentration with anxiety and depression (Milam, Slaughter, Verma, & Mcconnell, 2014; Ouellette et al., 2015; Simmons et al., 2016; Ursache, Merz, Melvin, Meyer, & Noble, 2017). Higher hair cortisol levels were observed after school entry among children first entering elementary school at a mean age of 4.2 years, especially for fearful children (Groeneveld et al., 2013). Furthermore, higher hair cortisol levels were also associated with hospitalized infants compared to healthy term infants (Yamada et al., 2007). Notably, among children aged 5–11 years, AUC calculated from salivary cortisol obtained across the morning and evening was associated with child-reported stressful events in the recent past (3 months). On the other hand, hair cortisol from the past 6 months was associated with stressful events from beyond 3 months, altogether suggesting some link between reported stress and hair cortisol from periods further in history (Vanaelst, Huybrechts et al., 2012).

1.2 | Nail cortisol

Cortisol obtained through fingernails is an emerging chronic stress biomarker with features that may overcome some of the limitations involved in using hair cortisol. For example, nails may be more easily obtained from the majority of individuals, including infants and children who often lack sufficient hair and arguably more resistant to decomposition and disintegration. As with hair, nail clippings have been used previously to detect toxin and substance levels (Jenkins, 1979). The quantification of cortisol through nails has been demonstrated through liquid chromatography/electrospray ionization-tandem mass spectrometry (Higashi et al., 2016; Khelil et al., 2011) and enzyme immunoassay (Izawa et al., 2015). With the compound incorporated into the nail matrix, cortisol does not become metabolized given that nails consist of dead keratinous cells. As with hair, determining the average growth rate for nails is imperative for determining the duration of cortisol exposure. Fingernails grow at a rate of 1.0 mm/10 days on average. Unlike hair, it may take several months for the nails to extend from the nail matrix to the point where sampling is possible (Gupta et al., 2005; Warnock et al., 2010).

The validation of nail is less developed than in hair, although nail cortisol has been shown to have similar concentration levels and variance with hair cortisol concentration (Hubmann et

al., 2016), with moderate associations in hair cortisol concentration from facial hair (Nejad et al., 2016). Nail cortisol in humans has also been associated with salivary cortisol across the day, as calculated by AUC (Izawa et al., 2015). Interestingly, nail cortisol was also not found to be associated with hair cortisol in a recent study (Binz et al., 2018).

As with hair cortisol, the major question is whether the concentration of cortisol obtained from nail reflects psychosocial experience and whether it can be used as a reliable marker for chronic stress. Only a handful of studies have begun to examine this. Recently, Wu et al. (2018) showed an association between present perceived stress and increased nail cortisol among 51 medical students from China. In a small study of 19 university students, nail cortisol was higher during exam periods (Nejad et al., 2016). Nail cortisol was also positively correlated with stressful life events but not job stress or perceived stress in middle aged men and women (Izawa, Matsudaira, Miki, Arisaka, & Tsuchiya, 2017). Nail cortisol concentrations did not differ between healthy controls and individuals with bipolar disorder, nor was it associated with cognitive impairment (Herane-Vives, Papadopoulos et al., 2015). However, nail cortisol was higher in a sample of 26 depressed individuals than in 45 healthy controls matched by age and gender, and concentrations were positively associated with depression severity and particular symptomatology, although negatively associated with fatigue (Herane-Vives et al., 2018).

To our knowledge, a few studies have been conducted to examine nail cortisol in children. In a study we conducted with 46 mostly low-income minority adolescents, nail cortisol was not associated with perceived stress but instead was positively associated with selfregulation as assessed by effortful control (Doan, Deyoung, Fuller-Rowell, Liu, & Meyer, 2018).

An unpublished study presented in 2016 assessed nail cortisol in 124 at-risk children at 24 and 36 months but showed stability across time points in only a third of the children (Nejad et al., 2016). In a recent study, nail cortisol was also not found to be associated with diurnal measures of salivary cortisol among 324 children between 2 and 6 years of age (Messerli-Bürgy et al., 2018).

Compared to cortisol, dehydroepiandrosterone (DHEA) is a less researched adrenal steroid in its response to stress, although it is considered to be a cortisol antagonist that may serve to protect against the effects of cortisol. Although they did not assess nail cortisol, Tegethoff et al. (2011) observed that nail DHEA was higher for infants of mothers with greater life stress during pregnancy in a study of 80 infants (<3 weeks old). Among infants, nail DHEA was positively associated with prenatal stress in the first trimester, with nail DHEA positively associated with infant irritability (Mikoteit et al., 2018). Nail DHEA in the previously mentioned study on low-income minority adolescents was also shown to be positively associated with stressful events, sleep disturbance, and waking (Doan et al., 2018). In another study with 33 university students, an increase in the ratio between nail cortisol and nail DHEA was observed during a stressful period in the semester. This increase in ratio was attributed to a decrease in nail DHEA (Warnock et al., 2010), suggesting that chronic low levels of DHEA may be implicated as a result of repeated stress exposure. In light of these initial and intriguing findings, future work involving the analysis of cortisol and DHEA from nail may be promising for developmental research. Although steroid hormone extraction

from nail has been established, the reliance of steroids from nail as a biomarker of chronic stress should be considered with caution at this point in time, given the correlational nature of findings and the limited number of studies involving the steroid concentrations within nail.

2 | CONCEPTUAL, DEVELOPMENTAL, AND METHODOLOGICAL ISSUES

While both hair and nail cortisol offer exciting and new directions for understanding the biological role of chronic stress in children's development, several important conceptual, developmental, and methodological limitations must be raised when implementing these approaches as part of a study design.

2.1 | Conceptual issues

Do hair and nail cortisol represent stress? We put forth that the cumulative cortisol exposure from hair and nail cannot be readily assumed to represent "stress" of the psychosocial nature that is often the interest of developmental researchers. This is due in part to the different methods for defining and operationalizing stress, as discussed. Furthermore, given the months-long time frame of the sampling of hair and nail cortisol, disentangling the source for cortisol concentration levels is a challenge, relative to the salivary sampling obtained from acute paradigms.

Adding to the difficulty in definition is that the relations between cortisol and negative outcomes are not linear (Miller, Chen, & Zhou, 2007). Higher levels of cortisol are not always associated with negative outcomes, and alternative models explaining the mechanism by which stress affects health have argued that stress may negatively impact cortisol signaling and lead to stress-induced *declines* in cortisol (Heim et al., 2000). Treatment may involve the increase in cortisol (Papadopoulos & Cleare, 2012). Cortisol deviations—either too low or too high—can be detrimental, suggesting the importance of understanding the specific context or condition in order to determine the extent to which these levels are pathogenic (Marklund, Peltonent, Nilsson, & Olsson, 2004; Miller et al., 2007). At the same time, there is not a sufficiently large enough body of research to determine definitively the specific contexts in which high or low levels signal dysfunction. Thus, findings related to risk are framed post hoc, as a function of the results.

With respect to hair and nail cortisol, regulatory responses including increases in cortisol output from within positive or negative conditions altogether are embedded in the total concentration (McEwen & Seeman, 1999; Smith & Cidlowski, 2010). However, increases due to acute challenges, with some adaptive in the moment, likely produce wear-and-tear on the system over time. The extent to which hair and nail cortisol capture wear-and-tear make them ideal chronic stress indices that predict negative health outcomes. Interestingly, the onset of chronic stressors may initially lead to *hyper*cortisolism, but with advancing chronicity result in *hypo*cortisolism (Miller et al., 2007). That is, and analogously to subjective reports, in the context of chronic or repeated stress exposures, the HPA axis will habituate (Schommer, Hellhammer, & Kirschbaum, 2003). Moreover, the extent to which the stressor is still ongoing or in the past is likely to matter (Stalder et al., 2017). On balance, it is important to consider that hair and nail cortisol do not necessarily indicate stress but

reflect the accumulation of repeated and ongoing HPA axis responses from a variety of sources that altogether could reflect psychosocial stress. Furthermore, hair and nail cortisol occur within a dynamic regulatory system that may or may not have habituated.

One approach to determining the extent to which hair and nail cortisol represent psychosocial stress is by examining its association with additional measures. Studies that have examined the association of hair cortisol and perceived stress have been largely mixed, with positive (Kalra, Einarson, Karaskov, Uum, & Koren, 2007), negative (Gerber et al., 2013; Karlén, Ludvigsson, Frostell, Theodorsson, & Faresjö, 2011), or no associations documented. One explanation is that the studies including perceived stress measures have primarily been of populations experiencing lower intensity of stress (Stalder et al., 2017). Another possibility may be the discrepancies in time frame; for example, the commonly used Perceived Stress Scale indexes stress from the last month, in contrast to most studies of hair cortisol, which capture concentrations from over the past 3 months (Frodl & Keane, 2013). Beyond this, individuals may not be very good at reporting stress experiences over a long period of time either due to memory failures or social desirability (Stalder, Steudte, Alexander et al., 2012), or even simple habituation. Herane-Vives, DeAngel et al. (2015) argue that perceived stress may actually be less sensitive of a measure, given differences in hair cortisol concentration but no differences in perceived stress scores in comparison and control subjects across different populations of participants categorized based on exposures to chronic stress conditions (Herane-Vives, DeAngel et al., 2015). Indeed, greater associations between hair cortisol concentration and negative life events are observed compared to hair cortisol concentration and perceived stress (Karlén et al., 2011).

2.2 | Developmental issues

Various developmental factors can have an effect on cortisol concentrations in either hair or nail, including age-related changes of the HPA axis, developmental periods of sensitivity to stress (e.g., instability, rapid change), and genetic and contextual influences.

First, the HPA axis is not a static system but one that develops and changes over time (Gunnar, Wewerka, Frenn, Long, & Griggs, 2009). Specific time periods in development may be tied to normative fluctuations in cortisol, thus caution is required in the interpretation of hair cortisol across age groups in a cross-sectional design. For example, the HPA axis is relatively quiescent during childhood (Netherton, Goodyer, Tamplin, & Herbert, 2004) but reactivates during adolescence (Hankin, Badanes, Abela, & Watamura, 2010; Marceau, Ruttle, Shirtcliff, Essex, & Susman, 2015). Basal levels of HPA activity increase due to developmental changes, which may lead to increased responsivity of the stress response (Romeo, 2013). In addition, sex hormones influence the regulation of the HPA axis beginning in mid-adolescence (McCormick & Mathews, 2007), and chronic HPA activation can suppress gonadal function (Stratakis & Chrousos, 2007).

Second, the HPA axis may be also be more vulnerable during specific developmental periods. In animal models, there is evidence that glucocorticoids cross the placenta affect fetal HPA development, potentially resulting in long term and widespread changes to the organism (Kapoor, Petropoulos, & Matthews, 2008). Relatedly, prenatal stress is thought to influence the developing HPA axis; however, the effects are likely to vary based on a host of

factors including the nature of stress, stage of gestation, and sex (Glover, Connor, & O'Donnell, 2010). In humans, prenatal anxiety and stress have been shown to predict variability in children (Gutteling, Weerth, & Buitelaar, 2004; O'Connor et al., 2005). At the same time, the direction of the association between maternal stress and child cortisol is not consistent. Prenatal anxiety has been correlated with infant cortisol in the first year of life, but the association varied as a function of infant age and the nature of the stressor (Tollenaar, Beijers, Jansen, Riksen-Walraven, & De Weerth, 2011).

Cortisol is also influenced by particular developmental time periods. As such, standard interpretations in using cortisol as a measure of a stress response may require re-interpretation. For instance, in pregnancy, a multitude of altered physiological parameters affect adrenocortical activity leading to an increase in total cortisol levels, with varying changes across each trimester. Based on salivary cortisol, unstimulated cortisol levels increase at around the 25th week of gestation, returning to normal levels around 5–7 days after parturition (Allolio et al., 1990; Meulenberg & Hofman, 1990; de Weerth & Buitelaar, 2005). Hair cortisol levels across pregnancy appear to similarly reflect the rise of cortisol across trimesters until birth and its return to normal levels by the postpartum **(**D'Anna-Hernandez et al., 2011). It is possible that cortisol, like allostatic load, may not be an appropriate measure of stress during pregnancy because normal physiological changes related to pregnancy may affect these measures (Morrison, Shenassa, Mendola, Wu, & Schoendorf, 2013). Relatedly, biological and social changes associated with puberty, including higher overall hormonal activity of the adrenal gland during puberty (Kiess et al., 1995), may also have an effect on early life stress that is reflected through HPA activity (Netherton et al., 2004). However, puberty was not associated with hair cortisol levels in a recent study examining children up to age 14 years (Noppe et al., 2014).

For these reasons, the relationships between hair cortisol concentration and age require greater clarification (Gray et al., 2018). The hair cortisol concentrations of very young children have been reported to be particularly high, with decreases across early development (1–9 years of age; Dettenborn, Tietze, & Kirschbaum, Tietze, Kirschbaum & Stalder, 2012) and decreases by adolescence (Binz et al., 2018). On the other hand, others have not observed associations between age and hair cortisol (Manenschijn et al., 2011; Rippe et al., 2016). Overall, hair cortisol may be appropriate for capturing change in cortisol output when considering a time frame based on developmental phases that are conceptualized across months. This may not necessarily generalize to nail cortisol given its sampling timeframe.

Finally, beyond normative developmental changes associated with cortisol, contextual changes that take place across the lifespan must be taken into account. According to Bronfenbrenner's bioecological theory of development, the chronosystem is a fundamental level by which an individual and the larger context interact across development (Bronfenbrenner & Ceci, 1994). As such, adverse events or prolonged stress experiences following an exposure may vary in its impact based on both the child's developmental stage and the particular context at that given time (Charmandari, Kino, Souvatzoglou, & Chrousos, 2003). A characterization of the context and its change would provide meaningful information that would inform the interpretation of hair or nail cortisol.

Contextual considerations across development have been investigated in salivary cortisol studies, demonstrating its sensitivity to new experiences and encounters within the environment involving school, family, and the community (Gunnar, Kryzer, Van Ryzin, & Phillips, 2010). In contrast, there has been very little direct assessment of the enduring conditions in hair cortisol studies, and even more, in nail cortisol studies involving children. Animal studies have relied on experimental conditions (e.g., relocation of Rhesus monkeys) to detect change in hair cortisol **(**Dettmer, Novak, Suomi, & Meyer, 2012**)**. As we have previously described, chronic stress studies have often relied on natural experiment approaches, comparing groups of individuals in exposed and unexposed conditions, which may be valuable for looking at different populations of children.

Parent education and income have been examined in relation to child hair cortisol, which shed some light on context, although the findings remain mixed. The association between parent education or income with hair cortisol concentration has shown a negative relationship (Rippe et al., 2016; Ursache et al., 2017; Vaghri et al., 2013), positive relationship (White et al., 2017), or no relationship at all (Gerber et al., 2017; Groeneveld et al., 2013; Karlén et al., 2013, 2015; Liu et al., 2016; Maurer et al., 2016; Ursache et al., 2017). In one study of 26 children between the ages of 5–7 years, hair cortisol concentration was higher with lower parent education, but no association was observed between hair cortisol concentration and income (Ursache et al., 2017). Based on a review of the literature focusing on associations between socioeconomic status and hair cortisol concentration in children, most of the existing studies have been conducted on populations with little variation in wealth. It is possible that the lack of association with adversity may be due to methodological constraints. Beyond simple measures of parent education and income, however, lifetime history of trauma in mothers obtained during pregnancy was recently found to be associated hair cortisol in their children at age 3 and 4 years (Slopen et al., 2018). A crucial next step for research is to determine whether one's status in society and/or concurrent impoverished conditions can be biologically captured through chronic measures such as hair or nail cortisol within early development.

Given this, there is ample opportunity to carefully assess the specific stress experiences that occur, the experiences that appear to be elicited by "low level" exposures, and the extent to which consequences to exposures are psychologically, emotionally, and physically enduring. Doing so may help to determine what is involved in the change in cortisol output as assessed by hair or nail cortisol. While self-reported measures of stress are not ideal for use with children, other approaches such as comprehensive behavioral (e.g., observational) and physiological monitoring (e.g., cardiac response) over the target period may further contribute to this assessment.

2.3 | Methodological issues

Hair and nail assessments of cortisol may be more sensible for some groups than others. A question often asked by developmental researchers is whether hair can be obtained in children. Hair sampling may not be permissible for certain populations, who object to providing hair samples for cultural or religious reasons, or as a personal preference. Furthermore, some children, including infants and children with short hairstyles (often

boys), will not have sufficient hair. Even when hair is available, a certain amount is required. The minimum weight of a required hair sample depends on the type of analysis; immunoassay analyses require approximately 5–50 mg (Karlén et al., 2011; Kirschbaum, Tietze, Skoluda, & Dettenborn, 2009). For high-performance liquid chromatography tandem mass spectrometry (LC–MS/MS), 20 mg of hair is required (Xie et al., 2011). In general, LC-MS methods are more difficult and costly as compared to immunoassays; however, they show high sensitivity, reproducibility, and little cross reactivity (Gao et al., 2013).

Assumptions regarding hair and nail growth rates are made when using hair and nail cortisol, introducing some probability of error in the time frame that is being studied. As of now, there is no easy method to assess individual hair growth rate (however, see Hayashi, Miyamoto, & Takeda, 1991 for a method using optical microscopy and image analysis). To date, the minimum length of hair reported in the hair cortisol concentration literature has been 1 cm of hair taken from the scalp, indexing an approximate 1-month retrospective period (Kirschbaum et al., 2009). There are individual variations in hair growth rate (LeBeau, Montgomery, & Brewer, 2011), seasonal effects (Randall & Ebling, 1991), and demographic differences (Loussouarn, 2001) to be considered.

Additionally, although analysis of cortisol in less than 1 cm is theoretically possible, the exact details and timing of cortisol incorporation into the scalp and hair root, and time for the hair to grow out is not fully understood (Pragst & Balikova, 2006), thus limiting interpretation of the timing of stress exposure. The activity of hair follicles consists of an active phase (anagen), transitional (catagen), and resting phase (telogen), and it is unclear the extent to which these stages affect cortisol levels (Sauvé et al., 2007). Relatedly, once grown, cortisol levels in hair are likely not static. Currently, the idea that a 1-cm length of hair reflects a 1-month period may not be generalizable across individuals, although improved time estimation is possible by relying on anagen hair, the individual growth rate, and methodologically consistent sampling (Pragst, Rothe, Spioegel, & Sporkert, 1998). There is some evidence to suggest the occurrence of degradation in cortisol obtained from the hair, which may render it unreliable for a 6-month period (Kirschbaum et al., 2009), although Manenschijn and colleagues found stable mean cortisol levels in women across 18 months through the analysis of six 3-cm segments (Manenschijn, Koper, Lamberts, & van Rossum, 2011).

Nails may be a promising alternative to hair given its availability, although issues remain in obtaining a sufficient amount, especially in very young children (e.g., newborns). Methods for surveying nail growth rate, including the marking of nails close to the proximal nail fold with a nail file, followed by measuring the distance of the mark from the nail fold at a later date have been reported in the literature (Yaemsiri, Hou, Slining, & He, 2010). With this approach, there seems to be variation in nail growth across fingers with the little finger growing more slowly (Yaemsiri et al., 2010). The growth rate of nails is also variable, which may affect the assessment of cumulative exposure. While fingernails grow from the nail matrix about 0.1 mm per day, the rate of growth is faster during pregnancy and adolescence and slower among older adults (Shearn, 1978). As such, it appears that the growth rate slows down across the lifespan (Orentreich, Markofsky, & Vogelman, 1979). Race, disease status (Geyer, Onumah, Uyttendaele, & Scher, 2004), handedness, geographical location

(Geoghegan, Roberts, & Sampford, 1958), but not seasons (Bean, 1974), influence fingernail growth rates (Griffiths & Reshad, 1983). Toenails seem to grow slower and may potentially reflect a longer window of time (Bean, 1980).

An understanding of nail growth rate is needed given nail sampling requirements. While hair cut from the root indexes the recent past (depending on how much hair is cut), nails that are available to be cut are actually indexing several months past the time the nail emerges from the matrix. Thus, it may make more sense to collect data on potential causes of cortisol (e.g., stressful events) and wait a few months before collecting nail samples (Doan et al., 2018). Overall, there may be some imprecision in the time frame of the cortisol output being assessed when using hair and nail cortisol; accordingly, the measures would not be well suited for studies that aiming to detect change by the day.

Finally, important confounds affecting cortisol in hair need to be considered (Greff et al., 2018). In addition to age and sex (Dettenborn, Tietze et al., 2012), physical activity, adiposity, substance abuse (Wosu et al., 2013), and light exposure have been shown to influence cortisol levels in hair (Grass et al., 2016). In pregnant women, BMI, smoking, single motherhood, season, and mode of delivery has been associated with maternal hair cortisol in the last trimester (Braig et al., 2015). Certain medical conditions including diabetes mellitus (Staufenbiel, Penninx, de Rijke, van den Akker, & van Rossum, 2015) and use of cardiovascular medications (Abell et al., 2016) also influence hair cortisol levels. In a sample of 3,507 participants aged 59–60 years, seasonal variation, length of sample storage, and demographics (higher in Black as compared to other ethnic groups) had an impact on hair cortisol levels (Abell et al., 2016). Some of these relations (e.g., ethnic differences) may be mediated by stress exposure, but other factors (e.g., physical characteristics of hair) still need to be ruled out. For example, hair color, which overlaps with ethnicity, has been shown to be associated with hair cortisol concentration (Binz et al., 2018; Rippe et al., 2016). Because sweat on the scalp affects hair cortisol concentrations, frequency of hair washes should be considered (Greff et al., 2018). However, the effect of chemical treatment of hairs (e.g., dyes, shampoos) on hair cortisol has been inconclusive and thus should be documented (Hoffman, Karban, Benitez, Goodteacher, & Laudenslager, 2014; Kristensen, Larsen, Olsen, Fahrenkrug, & Heitmann, 2017). Relatedly, nail polish on nails seems to lead to implausibly high levels of cortisol and thus should be considered as a confound (Frugé et al., 2018).

3 | CONCLUSION

Advances in methodology have improved the ease by which cortisol is assessed, leading to a substantial increase in studies using cortisol as a proxy for biological assessments of stress. For developmental researchers there is tremendous opportunity at the moment in evaluating and using hair and nail cortisol in the study of chronic stress across development, and in contributing to our understanding of concerns, such as poverty and trauma.

The ease of collection, storage, and analysis of hair cortisol, in particular, has led to its increased use. In light of this, we raise several important considerations for its use in future developmental research. Major conceptual considerations are needed to understand whether hair and nail cortisol are useful in relation to other constructs being studied and the

particular study context being used before assuming its use as a measure of stress. We urge researchers to avoid simply assuming cortisol to be “the stress hormone,” and to consider the complexity of human behavior and physiology, which account for the cortisol concentration. Measures such as hair and nail cortisol reflect a cumulative response to a series of nonspecific exposures. There is a need to better capture the duration and timing of stress exposures on the developing HPA system before determining the extent to which it confers long-term outcomes. As it stands, our ability to capture these exposures alongside the collection of hair and nail cortisol has been limited, with much reliance on demographic or clinical characteristics and other self-reported stress.

The HPA axis is impacted by particular developmental periods and related contextual changes; as such, the interpretation of hair and nail cortisol must take this into account. As noted, there has been very little characterization of the contexts among studies using hair or nail cortisol, with studies mostly relying on simple measures of socioeconomic status. For instance, only a few hair cortisol studies have made minority and low-income children and families a focus of study (Doan et al., 2018; Liu et al., 2017; Rippe et al., 2016; Vaghri et al., 2013). Given the very little variation in context among most studies, there remains a limited understanding regarding the influence of context on hair and nail cortisol across development. Hair and nail cortisol may be particularly promising for the study of stress among vulnerable populations for children and families, and an important key construct toward addressing health disparities within underserved communities.

Finally, methodological considerations such as hair and nail growth rates, and confounds and factors related to both growth rates and the cortisol output (e.g., timing) from these samples should be considered in the use of hair and nail cortisol. Methodological studies that contribute to resolving these concerns would help to improve the utility of these biomarkers across different populations.

While the overall literature is definitive in suggesting that numerous social and demographic factors shape the HPA axis and hence cortisol levels, their relative contributions, the direction of association between the factors and cortisol levels, and importantly, the consequences of high or low cortisol levels remain to be seen. Future studies that capitalize on the existing literature while carefully considering these conceptual, developmental, and methodological concerns may provide meaningful information that addresses stress-based health outcomes, especially for vulnerable populations of children.

ACKNOWLEDGEMENTS

We are grateful for support from the National Institutes of Health (K23 MH 107714–01 A1) and the Tynan Faculty Research Fellowship awarded to Cindy Liu and for the assistance by Sylvie Wong and Emily Zhang on the manuscript preparation.

Funding information Tynan Research Faculty Fellowship; National Institutes of Health, Grant/Award Number: K23 MH 107714–01 A1

REFERENCES

Abell JG, Stalder T, Ferrie JE, Shipley MJ, Kirschbaum C, Kivimäki M, & Kumari M (2016). Assessing cortisol from hair samples in a large observational cohort: The Whitehall II study. Psychoneuroendocrinology, 73, 148–156. 10.1016/j.psyneuen.2016.07.214 [PubMed: 27498290]

Allolio B, Hoffmann J, Linton EA, Winkleman W, Kusche M, & Schulte HM (1990). Diurnal salivary cortisol patterns during pregnancy and after delivery: Relationship to plasma corticotrophin-releasing-hormone. Clinical Endocrinology, 33(2), 279–289. 10.1111/j.1365-2265.1990.tb00492.x [PubMed: 2225483]

An K, Salyer J, Brown RE, Kao H-F-S, Starkweather A, & Shim I (2016). Salivary biomarkers of chronic psychosocial stress and CVD risks: A systematic review. Biological Research for Nursing, 18(3), 241–263. 10.1177/1099800415604437 [PubMed: 26349905]

Bean WB (1974). Nail growth: 30 years of observation. Archives of Internal Medicine, 134, 497–502. 10.1001/archinte.134.3.497 [PubMed: 4137073]

Bean WB (1980). Nail growth: Thirty-five years of observation. Archives of Internal Medicine, 140(1), 73–76. 10.1001/archinte.140.1.73. [PubMed: 7352807]

Binz TM, Rietschel L, Streit F, Hofmann M, Gehrke J, Herdener M, … Baumgartner MR (2018). Endogenous cortisol in keratinized matrices: Systematic determination of baseline cortisol levels in hair and the influence of sex, age and hair color. Forensic Science International, 284, 33–38. 10.1016/j.forsciint.2017.12.032 [PubMed: 29331681]

Braig S, Grabher F, Ntomchukwu C, Reister F, Stalder T, Kirschbaum C, … Rothenbacher D (2015). Determinants of maternal hair cortisol concentrations at delivery reflecting the last trimester of pregnancy. Psychoneuroendocrinology, 52, 289–296. 10.1016/j.psyneuen.2014.12.006 [PubMed: 25553388]

Bronfenbrenner U, & Ceci SJ (1994). Nature-nuture reconceptualized in developmental perspective: A bioecological model. Psychological Review, 101(4), 568–586. 10.1037/0033-295X.101.4.568 [PubMed: 7984707]

Bruce J, Fisher PA, Pears KC, & Levine S (2009). Morning cortisol Levels in preschool-aged foster children: Differential effects of maltreatment type. Developmental Psychobiology, 51(1), 14–23. 10.1002/dev.20333 [PubMed: 18720365]

Charmandari E, Kino T, Souvatzoglou E, & Chrousos GP (2003). Pediatric stress: Hormonal mediators and human development. Hormone Research in Paediatrics, 59(4), 161–179. 10.1159/000069325

Chida Y, & Hamer M (2008). Chronic psychosocial factors and acute physiological responses to laboratory-induced stress in healthy populations: A quantitative review of 30 years of investigations. Psychological Bulletin, 134(6), 829 10.1037/a0013342 [PubMed: 18954159]

D'Anna-Hernandez KL, Ross RG, Natvig CL, & Laudenslager ML (2011). Hair cortisol levels as a retrospective marker of hypothalamic–pituitary axis activity throughout pregnancy: Comparison to salivary cortisol. Physiology and Behavior, 104(2), 348–353. 10.1016/j.physbeh.2011.02.041 [PubMed: 21397617]

Davenport MD, Tiefenbacher S, Lutz CK, Novak MA, & Meyer JS (2006). Analysis of endogenous cortisol concentrations in the hair of rhesus macaques. General and Comparative Endocrinology, 147(3), 255–261. 10.1016/j.ygcen.2006.01.005 [PubMed: 16483573]

de Weerth C, & Buitelaar JK (2005). Cortisol awakening response in pregnant women. Psychoneuroendocrinology, 30(9), 902–907. 10.1016/j.psyneuen.2005.05.003 [PubMed: 15970390]

de Weerth C, & van Geert P (2002). A longitudinal study of basal cortisol in infants: Intra-individual variability, circadian rhythm and developmental trends. Infant Behavior and Development, 25(4), 375–398. 10.1016/S0163-6383(02)00141-8

Dettenborn L, Tietze A, Kirschbaum C, & Stalder T (2012). The assessment of cortisol in human hair: Associations with sociodemographic variables and potential confounders. Stress, 15(6), 578–588. 10.3109/10253890.2012.654479 [PubMed: 22356099]

Dettenborn L, Muhtz C, Skoluda N, Stalder T, Steudte S, Hinkelmann K, … Otte C (2012). Introducing a novel method to assess cumulative steroid concentrations: Increased hair cortisol

concentrations over 6 months in medicated patients with depression. Stress, 15(3), 348–353. 10.3109/10253890.2011.619239 [PubMed: 22043813]

Dettmer AM, Novak MA, Suomi SJ, & Meyer JS (2012). Physiological and behavioral adaptation to relocation stress in differentially reared rhesus monkeys: Hair cortisol as a biomarker for anxiety-related responses. Psychoneuroendocrinology, 37(2), 191–199. 10.1016/j.psyneuen.2011.06.003 [PubMed: 21715101]

Dickerson SS, & Kemeny ME (2004). Acute stressors and cortisol responses: A theoretical integration and synthesis of laboratory research. Psychological Bulletin, 130(3), 355–391. 10.1037/0033-2909.130.3.355 [PubMed: 15122924]

Doan SN, Deyoung G, Fuller-Rowell TE, Liu C, & Meyer JS (2018). Investigating relations among stress, sleep and nail cortisol and DHEA. Stress, 21(2), 188–193. 10.1080/10253890.2018.1429398 [PubMed: 29373934]

Egliston K-A, Mcmahon C, & Austin M-P (2007). Stress in pregnancy and infant HPA axis function: Conceptual and methodological issues relating to the use of salivary cortisol as an outcome measure. Psychoneuroendocrinology, 32(1), 1–13. 10.1016/j.psyneuen.2006.10.003 [PubMed: 17123741]

Frodl T, & O'Keane V (2013). How does the brain deal with cumulative stress? A review with focus on developmental stress, HPA axis function and hippocampal structure in humans. Neurobiology of Disease, 52, 24–37. 10.1016/j.nbd.2012.03.012 [PubMed: 22426398]

Frugé AD, Cases MG, Howell CR, Tsuruta Y, Smith-Johnston K, Moellering DR, & Demark-Wahnefried W (2018). Fingernail and toenail clippings as a non-invasive measure of chronic cortisol levels in adult cancer survivors. Cancer Causes & Control, 29(1), 185–191. 10.1007/s10552-017-0989-5 [PubMed: 29170880]

Gao W, Stalder T, Foley P, Rauh M, Deng H, & Kirschbaum C (2013). Quantitative analysis of steroid hormones in human hair using a column-switching LC–APCI–MS/MS assay. Journal of Chromatography B, 928, 1–8.

Gao W, Zhong P, Xie Q, Wang H, Jin J, Deng H, & Lu Z (2014). Temporal features of elevated hair cortisol among earthquake survivors. Psychophysiology, 51(4), 319–326. 10.1111/psyp.12179 [PubMed: 24611842]

Geoghegan B, Roberts DF, & Sampford MR (1958). A possible climatic effect on nail growth. Journal of Applied Physiology, 13(1), 135–138. [PubMed: 13563356]

Gerber M, Kalak N, Elliot C, Holsboer-Trachsler E, Pühse U, & Brand S (2013). Both hair cortisol levels and perceived stress predict increased symptoms of depression: An exploratory study in young adults. Neuropsychobiology, 68(2), 100–109. 10.1159/000351735 [PubMed: 23881183]

Gerber M, Endes K, Brand S, Herrmann C, Colledge F, Donath L, … Zahner L (2017). In 6-to 8-year-old children, hair cortisol is associated with body mass index and somatic complaints, but not with stress, health-related quality of life, blood pressure, retinal vessel diameters, and cardiorespiratory fitness. Psychoneuroendocrinology, 76, 1–10. 10.1016/j.psyneuen.2016.11.008 [PubMed: 27865992]

Geyer AS, Onumah N, Uyttendaele H, & Scher RK (2004). Modulation of linear nail growth to treat diseases of the nail. Journal of the American Academy of Dermatology, 50, 229–234. 10.1016/j.jaad.2003.07.011 [PubMed: 14726877]

Glover V, O'Connor TG, & O'Donnell K (2010). Prenatal stress and the programming of the HPA axis. *Neuroscience &* Biobehavioral Reviews, 35(1), 17–22. 10.1016/j.neubiorev.2009.11.008

Gottlieb BH (1997). Conceptual and measurement issues in the study of coping with chronic stress In Gottlieb BH (Ed.), Coping with chronic stress (pp. 3–40). Boston, MA: Springer.

Gow R, Thomson S, Rieder M, Van Uum S, & Koren G (2010). An assessment of cortisol analysis in hair and its clinical applications. Forensic Science International, 196(1–3), 32–37. 10.1016/j.forsciint.2009.12.040 [PubMed: 20096513]

Grass J, Miller R, Carlitz EH, Patrovsky F, Gao W, Kirschbaum C, & Stalder T (2016). In vitro influence of light radiation on hair steroid concentrations. Psychoneuroendocrinology, 73, 109–116. 10.1016/j.psyneuen.2016.07.221 [PubMed: 27494069]

Gray NA, Dhana A, Van Der Vyver L, Van Wyk J, Khumalo NP, & Stein DJ (2018). Determinants of hair cortisol concentration in children: A systematic review. Psychoneuroendocrinology, 87, 204–214. 10.1016/j.psyneuen.2017.10.022 [PubMed: 29112905]

Greff MJ, Levine JM, Abuzgaia AM, Elzagallaai AA, Rieder MJ, & van Uum SH (2018). Hair cortisol analysis: An update on methodological considerations and clinical applications. Clinical Biochemistry.

Griffiths WAD, & Reshad H (1983). Hair and nail growth: An investigation of the role of left-and right-handedness. Clinical and Experimental Dermatology, 8(2), 129–133. 10.1111/j.1365-2230.1983.tb01756.x [PubMed: 6851234]

Groeneveld MG, Vermeer HJ, Linting M, Noppe G, Van Rossum EFC, & Van Ijzendoorn MH (2013). Children's hair cortisol as a biomarker of stress at school entry. Stress, 16(6), 711–715. 10.3109/10253890.2013.817553 [PubMed: 23786528]

Gunnar MR, Kryzer E, Van Ryzin MJ, & Phillips DA (2010). The rise in cortisol in family day care: Associations with aspects of care quality, child behavior, and child sex. Child Development, 81(3), 851–869. 10.1111/j.1467-8624.2010.01438.x [PubMed: 20573109]

Gunnar MR, Morison SJ, Chisholm K, & Schuder M (2001). Salivary cortisol levels in children adopted from Romanian orphanages. Development and Psychopathology, 13(3), 611–628. 10.1017/S095457940100311X [PubMed: 11523851]

Gunnar MR, Wewerka S, Frenn K, Long JD, & Griggs C (2009). Developmental changes in hypothalamus–pituitary–adrenal activity over the transition to adolescence: Normative changes and associations with puberty. Development and Psychopathology, 21(1), 69–85. 10.1017/S0954579409000054 [PubMed: 19144223]

Gunnar MR, & White BP (2001). Salivary cortisol measures in infant and child assessment In Singer LT & Zeskind PS (Eds.),Biobehavioral assessment of the infant (pp. 167–189). New York: Guilford Press.

Gupta GR, Dhruw VK, Athawal BK, Siddiqui P, Agrawal HK, & Chandra H (2005). Human nail growth pattern and medicolegal aspect. Journal of Indian Academy of Forensic Medicine, 27(2), 87–91.

Gutteling BM, de Weerth C, & Buitelaar JK (2004). Short Communication Maternal Prenatal Stress and 4–6 Year Old Children's Salivary Cortisol Concentrations Pre-and Post-vaccination. Stress, 7(4), 257–260. 10.1080/10253890500044521 [PubMed: 16019591]

Hankin BL, Badanes LS, Abela JRZ, & Watamura SE (2010). Hypothalamic-pituitary-adrenal axis dysregulation in dysphoric children and adolescents: Cortisol reactivity to psychosocial stress from preschool through middle adolescence. Biological Psychology, 68(5), 484–490. 10.1016/j.biopsych.2010.04.004

Hayashi S, Miyamoto I, & Takeda K (1991). Measurement of human hair growth by optical microscopy and image analysis. British Journal of Dermatology, 125(2), 123–129. 10.1111/j.1365-2133.1991.tb06058.x [PubMed: 1911294]

Heim C, Ehlert U, & Hellhammer DH (2000). Potential role of hypocortisolism in the pathophysiology of stress-related bodily disorders. Psychoneuroendocrinology, 25(1), 1–35. 10.1016/S0306-4530(99)00035-9 [PubMed: 10633533]

Herane-Vives A, De Angel V, Papadopoulos A, Strawbridge R, Wise T, Young AH, … Cleare AJ (2015). The relationship between cortisol, stress and psychiatric illness: New insights using hair analysis. Journal of Psychiatric Research, 70, 38–49. 10.1016/j.jpsychires.2015.08.007 [PubMed: 26424422]

Herane-Vives A, Fischer S, de Angel V, Wise T, Cheung E, Chua K-C, … Cleare AJ (2018). Elevated fingernail cortisol levels in major depressive episodes. Psychoneuroendocrinology, 88, 17–23. 10.1016/j.psyneuen.2017.10.026 [PubMed: 29153629]

Herane-Vives A, Papadopoulos A, Chang C-K, Cheung EYW, Halari R, De Angel V, … Young AH (2015). Cortisol levels in fingernails and neurocognitive performance in euthymic bipolar I patients and healthy controls. Psychoneuroendocrinology, 61, 70 10.1016/j.psyneuen.2015.07.583

Higashi T, Yamagata K, Kato Y, Ogawa Y, Takano K, Nakaaze Y, … Ogawa S (2016). Methods for determination of fingernail steroids by LC/MS/MS and differences in their contents between right and left hands. Steroids, 109, 60–65. 10.1016/j.steroids.2016.02.013 [PubMed: 26898540]

Hjortskov N, Garde AH, Ørbæk P, & Hansen ÅM (2004). Evaluation of salivary cortisol as a biomarker of self-reported mental stress in field studies. Stress and Health: Journal of the International Society for the Investigation of Stress, 20(2), 91–98. 10.1002/smi.1000

Hoffman MC, Karban LV, Benitez P, Goodteacher A, & Laudenslager ML (2014). Chemical processing and shampooing impact cortisol measured in human hair. Clinical and Investigative Medicine. Medecine Clinique Et Experimentale, 37(4), E252 10.25011/cim.v37i4.21731 [PubMed: 25090265]

Hubmann P, Neuhauser A, Schaub S, Burkhardt SCA, Lanfranchi A, & Ehlert U (2016). A longitudinal view on nail cortisol: Stability and changes over one year in early childhood. Psychoneuroendocrinology, 71, 75 10.1016/j.psyneuen.2016.07.194

Izawa S, Matsudaira K, Miki K, Arisaka M, & Tsuchiya M (2017). Psychosocial correlates of cortisol levels in fingernails among middle-aged workers. Stress, 20(4), 386–389. 10.1080/10253890.2017.1342808 [PubMed: 28612641]

Izawa S, Miki K, Tsuchiya M, Mitani T, Midorikawa T, Fuchu T, … Togo F (2015). Cortisol level measurements in fingernails as a retrospective index of hormone production. Psychoneuroendocrinology, 54, 24–30. 10.1016/j.psyneuen.2015.01.015 [PubMed: 25662340]

Jenkins DW (1979). Toxic trace metals in mammalian hair and nails. Las Vegas, NV: Environmental Monitoring and Support Laboratory, Office of Research and Development, United States Environmental Protection Agency.

Kalra S, Einarson A, Karaskov T, Van Uum S, & Koren G (2007). The relationship between stress and hair cortisol in healthy pregnant women. Clinical and Investigative Medicine, 30(2), 103–107. 10.25011/cim.v30i2.986

Kao K, Doan SN, St. John AM, Meyer JS, & Tarullo AR (2018). Salivary cortisol reactivity in preschoolers is associated with hair cortisol and behavioral problems. Stress, 21(1), 28–35. 10.1080/10253890.2017.1391210 [PubMed: 29065770]

Kapoor A, Petropoulos S, & Matthews SG (2008). Fetal programming of hypothalamic–pituitary–adrenal (HPA) axis function and behavior by synthetic glucocorticoids. Brain Research Reviews, 57(2), 586–595. 10.1016/j.brainresrev.2007.06.013 [PubMed: 17716742]

Karlén J, Frostell A, Theodorsson E, Faresjö T, & Ludvigsson J (2013). Maternal influence on child HPA axis: A prospective study of cortisol levels in hair. Pediatrics, 132(5), 1333–1340. 10.1542/peds.2013-1178

Karlén J, Ludvigsson J, Frostell A, Theodorsson E, & Faresjö T (2011). Cortisol in hair measured in young adults - a biomarker of major life stressors? BMC Clinical Pathology, 11(1), 12 10.1186/1472-6890-11-12 [PubMed: 22026917]

Karlén J, Ludvigsson J, Hedmark M, Faresjö Å, Theodorsson E, & Faresjö T (2015). Early psychosocial exposures, hair cortisol levels, and disease risk. Pediatrics, 135, e1450–e1457. 10.1542/peds.2014-2561 [PubMed: 25941311]

Khelil MB, Tegethoff M, Meinlschmidt G, Jamey C, Ludes B, & Raul J-S (2011). Simultaneous measurement of endogenous cortisol, cortisone, dehydroepiandrosterone, and dehydroepiandrosterone sulfate in nails by use of UPLC–MS–MS. Analytical and Bioanalytical Chemistry, 401(4), 1153–1162. 10.1007/s00216-011-5172-3 [PubMed: 21720737]

Kiess W, Meidert A, Dressendörfer RA, Schriever K, Kessler U, Köunig A, … Strasburger CJ (1995). Salivary Cortisol levels throughout childhood and adolescence: Relation with age, pubertal stage, and weight. Pediatric Research, 37(4), 502–506. 10.1203/00006450-199504000-00020 [PubMed: 7596692]

Kirschbaum C, Tietze A, Skoluda N, & Dettenborn L (2009). Hair as a retrospective calendar of cortisol production—increased cortisol incorporation into hair in the third trimester of pregnancy. Psychoneuroendocrinology, 34(1), 32–37. 10.1016/j.psyneuen.2008.08.024 [PubMed: 18947933]

Kristensen SK, Larsen SC, Olsen NJ, Fahrenkrug J, & Heitmann BL (2017). Hair dyeing, hair washing and hair cortisol concentrations among women from the healthy start study. Psychoneuroendocrinology, 77, 182–185. 10.1016/j.psyneuen.2016.12.016 [PubMed: 28073090]

LeBeau MA, Montgomery MA, & Brewer JD (2011). The role of variations in growth rate and sample collection on interpreting results of segmental analyses of hair. Forensic Science International, 210(1–3), 110–116. 10.1016/j.forsciint.2011.02.015 [PubMed: 21382678]

Liu CH, Fink G, Brentani H, & Brentani A (2017). An assessment of hair cortisol among postpartum Brazilian mothers and infants from a high-risk community in São Paulo: Intra-individual stability and association in mother–infant dyads. Developmental Psychobiology, 59(7), 916–926. 10.1002/dev.21557 [PubMed: 28834537]

Liu CH, Snidman N, Leonard A, Meyer J, & Tronick E (2016). Intraindividual stability and developmental change in hair cortisol among postpartum mothers and infants: Implications for understanding chronic stress. Developmental Psychobiology, 58(4), 509–518. 10.1002/dev.21394 [PubMed: 26806857]

Loussouarn G (2001). African hair growth parameters. British Journal of Dermatology, 145(2), 294–297. 10.1046/j.1365-2133.2001.04350.x [PubMed: 11531795]

Manenschijn L, Koper JW, Lamberts SWJ, & van Rossum EFC (2011). Evaluation of a method to measure long term cortisol levels. Steroids, 76(10), 1032–1036. 10.1016/j.steroids.2011.04.005 [PubMed: 21515299]

Manenschijn L, van Kruysbergen RGPM, de Jong FH, Koper JW, & Van Rossum EFC (2011). Shift work at young age Is associated with elevated long-term cortisol levels and body mass index. The Journal of Clinical Endocrinology & Metabolism, 96(11), E1862–E1865. 10.1210/jc.2011-1551 [PubMed: 21880805]

Marceau K, Ruttle PL, Shirtcliff EA, Essex MJ, & Susman EJ (2015). Developmental and contextual considerations for adrenal and gonadal hormone functioning during adolescence: Implications for adolescent mental health. Developmental Psychobiology, 57(6), 742–768. 10.1002/dev.21214 [PubMed: 24729154]

Marklund N, Peltonen M, Nilsson TK, & Olsson T (2004). Low and high circulating cortisol levels predict mortality and cognitive dysfunction early after stroke. Journal of Internal Medicine, 256(1), 15–21. 10.1111/j.1365-2796.2004.01334.x [PubMed: 15189361]

Maurer N, Perkinson-Gloor N, Stalder T, Hagmann-von Arx P, Brand S, Holsboer-Trachsler E, … Sakari L (2016). very preterm children show more behavioral and emotional problems and decreased cortisol and cortisone in saliva and hair: p2273. International Journal of Psychology, 51, 933.

McCormick CM, & Mathews IZ (2007). HPA function in adolescence: Role of sex hormones in its regulation and the enduring consequences of exposure to stressors. Pharmacology, Biochemistry and Behavior, 86(2), 220–233. 10.1016/j.pbb.2006.07.012

McEwen BS (2015). Biomarkers for assessing population and individual health and disease related to stress and adaptation. Metabolism, 64(3, Supplement, 1), S2–S10. 10.1016/j.metabol.2014.10.029 [PubMed: 25496803]

McEwen BS, & Seeman T (1999). Protective and damaging effects of mediators of stress: Elaborating and testing the concepts of allostasis and allostatic load. Annals of the New York Academy of Sciences, 896(1), 30–47. 10.1111/j.1749-6632.1999.tb08103.x [PubMed: 10681886]

Messerli-Bürgy N, Arhab A, Stülb K, Kakebeeke TH, Zysset AE, Leeger-Aschmann CS, … Munsch S (2018). Physiological stress measures in preschool children and their relationship with body composition and behavioral problems. Developmental Psychobiology, 60:1009–1022. 10.1002/dev.21782 [PubMed: 30270564]

Meulenberg PM, & Hofman JA (1990). Differences between concentrations of salivary cortisol and cortisone and of free cortisol and cortisone in plasma during pregnancy and postpartum. Clinical Chemistry, 36(1), 70–75. [PubMed: 2297937]

Meyer JS, & Novak MA (2012). Minireview: Hair cortisol: A novel biomarker of hypothalamic-pituitary-adrenocortical activity. Endocrinology, 153(9), 4120–4127. 10.1210/en.2012-1226 [PubMed: 22778226]

Mikoteit T, Kurath J, Meinlschmidt G, Tegethoff M, Brand S, Hatzinger M, … Holsboer-Trachsler E (2018). S143. Steroid hormone analysis of retrospective maternal hair and newborn nail samples indicate effects of prenatal stress on postpartum well-being of mother and offspring. Biological Psychiatry, 83(9), S403–S404. 10.1016/j.biopsych.2018.02.1035

Milam J, Slaughter R, Verma G, & Mcconnell R (2014). Hair cortisol, perceived stress and dispositional optimism: A pilot study among adolescents. Journal of Traumatic Stress Disorders & Treatment, 3(3), 1000126 10.4172/2324-8947.1000126 [PubMed: 25426491]

Miller GE, Chen E, & Parker KJ (2011). Psychological stress in childhood and susceptibility to the chronic diseases of aging: Moving toward a model of behavioral and biological mechanisms. Psychological Bulletin, 137(6), 959 10.1037/a0024768 [PubMed: 21787044]

Miller GE, Chen E, & Zhou ES (2007). If it goes up, must it come down? Chronic stress and the hypothalamic-pituitary-adrenocortical axis in humans. Psychological Bulletin, 133(1), 25–45. 10.1037/0033-2909.133.1.25 [PubMed: 17201569]

Morrison S, Shenassa ED, Mendola P, Wu T, & Schoendorf K (2013). Allostatic load may not be associated with chronic stress in pregnant women, NHANES 1999–2006. Annals of Epidemiology, 23(5), 294–297. 10.1016/j.annepidem.2013.03.006 [PubMed: 23621995]

Mustonen P, Karlsson L, Scheinin NM, Kortesluoma S, Coimbra B, Rodrigues AJ, & Karlsson H (2018). Hair cortisol concentration (HCC) as a measure for prenatal psychological distress—A systematic review. Psychoneuroendocrinology, 92, 21–28. 10.1016/j.psyneuen.2018.03.019 [PubMed: 29609112]

National Scientific Council on the Developing Child. (2014). Excessive Stress Disrupts the Architecture of the Developing Brain: Working Paper 3. Updated Edition. Retrieved from http://www.developingchild.harvard.edu

Nejad JG, Ghaseminezhad M, Snug K-I, Hoseinzadeh F, Cabibi JBA, & Lee J (2016). A cortisol study; Facial hair and nails. Journal of Steroids Hormone Science, 7(2), 177 10.4172/2157-7536.1000177

Netherton C, Goodyer I, Tamplin A, & Herbert J (2004). Salivary cortisol and dehydroepiandrosterone in relation to puberty and gender. Psychoneuroendocrinology, 29(2), 125–140. 10.1016/S0306-4530(02)00150-6 [PubMed: 14604596]

Noppe G, Rossum EFCV, Koper JW, Manenschijn L, Bruining GJ, de Rijke YB, & van den Akker ELT (2014). Validation and reference ranges of hair cortisol measurement in healthy children. Hormone Research in Paediatrics, 82(2), 97–102. 10.1159/000362519 [PubMed: 25115629]

O'Connor TG, Ben-Shlomo Y, Heron J, Golding J, Adams D, & Glover V (2005). Prenatal anxiety predicts individual differences in cortisol in pre-adolescent children. Biological Psychiatry, 58(3), 211–217. 10.1016/j.biopsych.2005.03.032 [PubMed: 16084841]

Orentreich N, Markofsky J, & Vogelman JH (1979). The effect of aging on the rate of linear nail growth. Journal of Investigative Dermatology, 73(1).

Ouellette SJ, Russell E, Kryski KR, Sheikh HI, Singh SM, Koren G, & Hayden EP (2015). Hair cortisol concentrations in higherand lower-stress mother–daughter dyads: A pilot study of associations and moderators. Developmental Psychobiology, 57(5), 519–534. 10.1002/dev.21302 [PubMed: 25820649]

Papadopoulos AS, & Cleare AJ (2012). Hypothalamic–pituitary–adrenal axis dysfunction in chronic fatigue syndrome. Nature Reviews Endocrinology, 8(1), 22 10.1038/nrendo.2011.153

Pragst F, & Balikova MA (2006). State of the art in hair analysis for detection of drug and alcohol abuse. Clinica Chimica Acta, 370(1–2), 17–49. 10.1016/j.cca.2006.02.019

Pragst F, Rothe M, Spiegel K, & Sporkert F (1998). Illegal and therapeutic drug concentrations in hair segments-a timetable of drug exposure? Forensic Science Review, 10(2), 81–111. [PubMed: 26255716]

Randall VA, & Ebling FJG (1991). Seasonal changes in human hair growth. British Journal of Dermatology, 124(2), 146–151. 10.1111/j.1365-2133.1991.tb00423.x [PubMed: 2003996]

Rippe RCA, Noppe G, Windhorst DA, Tiemeier H, Van Rossum EFC, Jaddoe VWV, … van Den Akker ELT (2016). Splitting hair for cortisol? Associations of socio-economic status, ethnicity, hair color, gender and other child characteristics with hair cortisol and cortisone. Psychoneuroendocrinology, 66, 56–64. 10.1016/j.psyneuen.2015.12.016 [PubMed: 26773401]

Romeo RD (2013). The teenage brain: The stress response and the adolescent brain. Current Directions in Psychological Science, 22(2), 140–145. 10.1177/0963721413475445 [PubMed: 25541572]

Russell E, Koren G, Rieder M, & Van Uum S (2012). Hair cortisol as a biological marker of chronic stress: Current status, future directions and unanswered questions. Psychoneuroendocrinology, 37(5), 589–601. 10.1016/j.psyneuen.2011.09.009 [PubMed: 21974976]

Sauvé B, Koren G, Walsh G, Tokmakejian S, & Van Uum SH (2007). Measurement of cortisol in human hair as a biomarker of systemic exposure. Clinical & Investigative Medicine, 30(5), 183–191. 10.25011/cim.v30i5.2894

Schommer NC, Hellhammer DH, & Kirschbaum C (2003). Dissociation between reactivity of the hypothalamus-pituitary-adrenal axis and the sympathetic-adrenal-medullary system to repeated psychosocial stress. Psychosomatic Medicine, 65(3), 450–460. 10.1097/01.PSY.0000035721.12441.17 [PubMed: 12764219]

Shearn MA (1978). Nails and systemic disease. Western Journal of Medicine, 129(4), 358. [PubMed: 716393]

Short SJ, Stalder T, Marceau K, Entringer S, Moog NK, Shirtcliff EA, … Buss C (2016). Correspondence between hair cortisol concentrations and 30-day integrated daily salivary and weekly urinary cortisol measures. Psychoneuroendocrinology, 71, 12–18. 10.1016/j.psyneuen.2016.05.007 [PubMed: 27235635]

Simmons JG, Badcock PB, Whittle SL, Byrne ML, Mundy L, Patton GC, … Allen NB (2016). The lifetime experience of traumatic events is associated with hair cortisol concentrations in community-based children. Psychoneuroendocrinology, 63, 276–281. 10.1016/j.psyneuen.2015.10.004 [PubMed: 26529051]

Skoluda N, Dettenborn L, Stalder T, & Kirschbaum C (2012). Elevated hair cortisol concentrations in endurance athletes. Psychoneuroendocrinology, 37(5), 611–617. 10.1016/j.psyneuen.2011.09.001 [PubMed: 21944954]

Slopen N, Roberts AL, LeWinn KZ, Bush NR, Rovnaghi CR, Tylavsky F, & Anand KJ (2018). Maternal experiences of trauma and hair cortisol in early childhood in a prospective cohort. Psychoneuroendocrinology, 98, 168–176. 10.1016/j.psyneuen.2018.08.027 [PubMed: 30170311]

Smith LK, & Cidlowski JA (2010). Glucocorticoid-induced apoptosis of healthy and malignant lymphocytes In Martini L (Ed.), Progress in brain research (Vol. 182, pp. 1–30). Amsterdam, Netherlands: Elsevier. [PubMed: 20541659]

Smyth N, Hucklebridge F, Thorn L, Evans P, & Clow A (2013). Salivary cortisol as a biomarker in social science research. Social and Personality Psychology Compass, 7(9), 605–625. 10.1111/spc3.12057

Stalder T, & Kirschbaum C (2012). Analysis of cortisol in hair–state of the art and future directions. Brain, Behavior, and Immunity, 26(7), 1019–1029. 10.1016/j.bbi.2012.02.002

Stalder T, Steudte S, Alexander N, Miller R, Gao W, Dettenborn L, & Kirschbaum C (2012). Cortisol in hair, body mass index and stressrelated measures. Biological Psychology, 90(3), 218–223. 10.1016/j.biopsycho.2012.03.010 [PubMed: 22476032]

Stalder T, Kirschbaum C, Kudielka BM, Adam EK, Pruessner JC, Wüst S, … Clow A (2016). Assessment of the cortisol awakening response: Expert consensus guidelines. Psychoneuroendocrinology, 63, 414–432. 10.1016/j.psyneuen.2015.10.010 [PubMed: 26563991]

Stalder T, Steudte-Schmiedgen S, Alexander N, Klucken T, Vater A, Wichmann S, … Miller R (2017). Stress-related and basic determinants of hair cortisol in humans: A meta-analysis. Psychoneuroendocrinology, 77, 261–274. 10.1016/j.psyneuen.2016.12.017 [PubMed: 28135674]

Staufenbiel SM, Penninx BW, de Rijke YB, van den Akker EL, & van Rossum EF (2015). Determinants of hair cortisol and hair cortisone concentrations in adults. Psychoneuroendocrinology, 60, 182–194. [PubMed: 26176863]

Staufenbiel SM, Penninx BW, Spijker AT, Elzinga BM, & van Rossum EF (2013). Hair cortisol, stress exposure, and mental health in humans: A systematic review. Psychoneuroendocrinology, 38(8), 1220–1235. 10.1016/j.psyneuen.2012.11.015 [PubMed: 23253896]

Stratakis CA, & Chrousos GP (2007). Neuroendocrinology and pathophysiology of the stress system. Annals of the New York Academy of Sciences, 771(1), 1–18.

Suglia SF, Staudenmayer J, Cohen S, Enlow MB, Rich-Edwards JW, & Wright RJ (2010). Cumulative stress and cortisol disruption among Black and Hispanic pregnant women in an urban cohort. Psychological Trauma: Theory, Research, Practice, and Policy, 2(4), 326 10.1037/a0018953

Tegethoff M, Raul J-S, Jamey C, Khelil MB, Ludes B, & Meinlschmidt G (2011). Dehydroepiandrosterone in nails of infants: A potential biomarker of intrauterine responses to maternal stress. Biological Psychology, 87(3), 414–420. 10.1016/j.biopsycho.2011.05.007 [PubMed: 21645584]

Tollenaar MS, Beijers R, Jansen J, Riksen-Walraven JMA, & De Weerth C (2011). Maternal prenatal stress and cortisol reactivity to stressors in human infants. Stress, 14(1), 53–65. 10.3109/10253890.2010.499485 [PubMed: 20666659]

Ursache A, Merz EC, Melvin S, Meyer J, & Noble KG (2017). Socioeconomic status, hair cortisol and internalizing symptoms in parents and children. Psychoneuroendocrinology, 78, 142–150. 10.1016/j.psyneuen.2017.01.020 [PubMed: 28199857]

Vaghri Z, Guhn M, Weinberg J, Grunau RE, Yu W, & Hertzman C (2013). Hair cortisol reflects socio-economic factors and hair zinc in preschoolers. Psychoneuroendocrinology, 38(3), 331–340. 10.1016/j.psyneuen.2012.06.009 [PubMed: 22809790]

van Ockenburg SL, Schenk HM, van Der Veen A, Kema IP, & Rosmalen JGM (2016). The relationship between 63 days of 24-h urinary free cortisol and hair cortisol levels in 10 healthy individuals. Psychoneuroendocrinology, 73, 142–147. 10.1016/j.psyneuen.2016.07.220 [PubMed: 27497154]

Vanaelst B, De Vriendt T, Huybrechts I, Rinaldi S, & De Henauw S (2012). Epidemiological approaches to measure childhood stress. Paediatric and Perinatal Epidemiology, 26(3), 280–297. 10.1111/j.1365-3016.2012.01258.x [PubMed: 22471688]

Vanaelst B, Huybrechts I, Bammann K, Michels N, Vriendt T, Vyncke K, … Henauw S (2012). Intercorrelations between serum, salivary, and hair cortisol and child-reported estimates of stress in elementary school girls. Psychophysiology, 49(8), 1072–1081. 10.1111/j.1469-8986.2012.01396.x [PubMed: 22725679]

Warnock F, Mcelwee K, Seo RJ, Mcisaac S, Seim D, Ramirez-Aponte T, … Young AH (2010). Measuring cortisol and DHEA in fingernails: A pilot study. Neuropsychiatric Disease and Treatment, 6, 1–7. [PubMed: 20169040]

White LO, Ising M, von Klitzing K, Sierau S, Michel A, Klein AM, … Stalder T (2017). Reduced hair cortisol after maltreatment mediates externalizing symptoms in middle childhood and adolescence. Journal of Child Psychology and Psychiatry, 58(9), 998–1007. 10.1111/jcpp.12700 [PubMed: 28244601]

Wosu AC, Valdimarsdóttir U, Shields AE, Williams DR, & Williams MA (2013). Correlates of cortisol in human hair: Implications for epidemiologic studies on health effects of chronic stress. Annals of Epidemiology, 23(12), 797–811. 10.1016/j.annepidem.2013.09.006 [PubMed: 24184029]

Wu H, Zhou K, Xu P, Xue J, Xu X, & Liu L (2018). Associations of perceived stress with the present and subsequent cortisol levels in fingernails among medical students: A prospective pilot study. Psychology Research and Behavior Management, 11, 439. [PubMed: 30349410]

Xie Q, Gao W, Li J, Qiao T, Jin J, Deng H, & Lu Z (2011). Correlation of cortisol in 1-cm hair segment with salivary cortisol in human: Hair cortisol as an endogenous biomarker. Clinical Chemistry and Laboratory Medicine (CCLM), 49(12), 2013–2019. 10.1515/CCLM.2011.706 [PubMed: 21902574]

Yaemsiri S, Hou N, Slining MM, & He K (2010). Growth rate of human fingernails and toenails in healthy American young adults. Journal of the European Academy of Dermatology and Venereology, 24(4), 420–423. 10.1111/j.1468-3083.2009.03426.x [PubMed: 19744178]

Yamada J, Stevens B, de Silva N, Gibbins S, Beyene J, Taddio A, … Koren G (2007). Hair cortisol as a potential biologic marker of chronic stress in hospitalized neonates. Neonatology, 92(1), 42–49. 10.1159/000100085 [PubMed: 17356304]