

Title: Palmar crease classification and relationship to Fetal Alcohol Spectrum Disorders (FASD).

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ABSTRACT

A normal human palm contains 3 major creases: the distal transverse crease; the proximal transverse crease and the thenar crease. Because permanent crease patterns are thought to be laid down during the first trimester, researchers have speculated that deviations in crease patterns could be indicative of insults during fetal development. The purpose of this study was twofold: 1) to compare the efficacy and reliability of two coding methods, the first (M1) classifying both “simian” and Sydney line variants and the second (M2) counting the total number of crease points of origin on the radial border of the hand; and 2) to ascertain the relationship between palmar crease patterns and fetal alcohol spectrum disorders (FASD).

Bilateral palm prints were taken using the carbon paper and tape method from 237 individuals diagnosed with FASD and 190 unexposed controls. All prints were coded for crease variants under M1 and M2. Additionally a random sample of 98 matched (right and left) prints was selected from the controls to determine the reliabilities of M1 and M2. For this analysis, each palm was read twice, at different times, by two readers. Intra-observer Kappa coefficients were similar under both methods, ranging from 0.804-0.910. Inter-observer Kappa coefficients ranged from 0.582–0.623 under M1 and from 0.647–0.757 under M2. Using data from the entire sample of 427 prints and controlling for sex and race, no relationship was found between palmar crease variants and FASD. Our results suggest that palmar creases can be classified reliably, but that they may not be useful in predicting fetal trauma due to *in utero* exposure to alcohol in most clinical settings.

A normal human palm contains three major creases. The thenar or vertical crease “begins at or slightly below the proximal transverse crease at the radial border of the palm” (Johnson and Opitz 1971). The proximal transverse crease “begins at the radial side of the palm... curves proximally, and ends at the medial border of the hypothenar eminence.” Finally, the distal horizontal crease, is found closest to the fingers, beginning at the “interdigital space between the index and middle fingers,” curving “gently wristward toward the ulnar side of the palm” and ending before the proximal crease of the fifth finger (Johnson and Opitz 1971). Several variations to the normal crease pattern exist, including the simian or single transverse palmar crease (STPC), which joins the proximal and distal creases to produce a single horizontal crease across the width of the palm, and the Sydney crease, which represents an extension of the proximal transverse crease to near the ulnar border of the palm.

Palmar creases are laid down during the first or second trimester of fetal life (Johnson and Opitz 1971, Dar *et al.* 1971, Cannon *et al.* 1994) and remain unchanged thereafter (Tay 1979). A fetus exposed to trauma during early development could show increased prevalence of abnormal palmar crease patterns (Purvis-Smith *et al.* 1972), for example, by changing the pattern of locomotion *in utero* (Jones *et al.* 1973). Previous studies classifying STPC and/or Sydney line variants have suggested that aberrant palmar crease patterns are associated with a variety of disorders, most commonly Down Syndrome, but also low birthweight (Dar *et al.* 1971; Davies 1966), congenital anomalies, deafness (Dar and Winter 1970), childhood leukemia (Wertelecki 1979), intrauterine methadone exposure (Dar *et al.* 1977) and even hyperactivity (Lerer 1977).

Alcohol is a wide-acting teratogen that causes abnormal fetal growth and development, impaired performance on intelligence and motor tests, and possibly abnormal palmar crease patterns

(Jones *et al.* 1973). Fetal alcohol spectrum disorders (FASD) are any of a variety of neurological or morphological abnormalities associated with *in utero* exposure to alcohol. These include fetal alcohol syndrome (FAS) and fetal alcohol effects (FAE) (see Streissguth and Connor, 2001, for definitions). In this study we sought to confirm whether FASD is associated with abnormal palmar creases in a relatively large, contemporary sample consisting of subjects diagnosed with FASD and normal controls.

While it is clear that the presence of STPC and Sydney creases are associated with certain fetal insults and genetic disorders, less is known about the relationship of other abnormal crease patterns to these disorders (Chaube 1977). Moreover, because researchers often use different classification schemes, it is sometimes difficult to compare results across studies. This study sought to compare two methods of palmar crease classification in which STPC, Sydney creases and other variants were included in the classification scheme. The first method (M1) includes classifications for both STPC and Sydney lines and their variants and the second (M2) counts the total number of crease points of origin on the radial border of the hand. While M1 represents the most traditional classification method, M2 has the potential to avoid a number of difficulties inherent in traditional classification schemes, including over-reliance on STPC and misclassification resulting from unclear prints (see Chaube 1977). In this paper, we present the inter- and intra-observer reliability of each method and compare the effectiveness of each method in predicting FASD.

MATERIALS AND METHODS

Data were collected from 237 individuals diagnosed with FAS or FAE. These individuals had been referred to the Fetal Alcohol Syndrome Diagnostic Clinic at the University of Washington for

evaluation and enrolled in a follow-up study in 1994-95. At the time of recruitment, age ranged from 6-51 years of age; 43% of subjects were age 6-11, 36% 12-20 and 21% 21-51. Additionally, 190 individuals were recruited as unexposed controls from undergraduates and staff at the University of Washington between 1996 and 2002. Only individuals who reported that their mother did not drink were included in the control sample.

All participants had palm prints taken using the carbon paper and tape method described by Aase and Lyons (1971). Prints were then digitally scanned at a resolution of 400 dots per inch and later read using Adobe Photoshop (version 8.0, Adobe Systems, Inc., San Jose, CA).

A sub-sample of 98 bilateral prints was randomly selected from the control group. This sub-sample was read twice by two independent readers to determine the inter- and intra-reliabilities of M1 and M2. After establishing relatively high inter- and intra-reader reliabilities, one reader then read the entire sample of 427 bilateral prints using M1 and M2, as described below.

Method 1 (crease patterns) - Based on the methods of Dar *et al.* (1977), prints were classified as normal, STPC-normal, STPC-aberrant, Sydney-normal and Sydney-aberrant (Figure 1). A palm print was considered normal if all three creases – proximal, distal and thenar – were present. If distal and proximal creases formed one solid line across the palm, the print was considered to be STPC-normal. STPC-aberrant palmar prints were those in which the proximal crease was rudimentary, where the STPC was formed by a connection of the distal and proximal creases running in the same direction, or where a STPC was generally present, but with some interruptions and often a rudimentary proximal crease. Sydney variants were considered normal if the proximal crease abutted at no greater than 2 epidermal ridges away from the ulnar border of the palm (cf. Dar *et al.* 1977). Sydney creases

were considered aberrant if the Sydney crease was branched, interrupted or broken, or if it extended to, but not beyond, the medial line of the fifth finger. To distinguish between strong palmar creases and weak palmar ridges, we employed a 2-ridge rule, in which a crease was defined by having a thickness at least as great as 2 ridges. We tended towards conservative estimates, classifying palmar prints as normal in cases where hands were highly wrinkled or the classification was otherwise rendered difficult.

Method 2 (*points of origin*) - Palm prints were further classified by the number of crease points of origin on the radial border of the palm (Chaube, 1977). Points of origin ranged from no fewer than 1 point (1 crease present) to no greater than 3 points (Figure 2). A third point of origin was only indicated in cases where a clear third point originated from the thenar crease and where the proximal and distal lines originated at the radial border of the palm.

Reliability Analysis

The sample of 98 paired prints (left and right) was randomly selected and read by two observers to determine intra- and inter-observer reliability for both methods used in this study. Each print was read twice by Reader A and twice by Reader B. To increase the independence of successive measurements of prints, each set of readings was made at different times, weeks or months apart. Prints were read in a random order; and right and left prints from the same individual were not read at the same time.

Results from both readers were compared using the simple Kappa coefficient (Cohen 1960). Kappa coefficients range from -1 to +1, where 1 indicates complete agreement between the raters, positive coefficients indicate better agreement than expected by chance, and negative coefficients

indicate lower agreement than expected by chance. Because Kappa coefficients control for chance agreement, values exceeding 0.5 generally indicate good agreement between observers.

FASD Analysis

In addition to the reliability analysis, the entire sample ($N=427$) was coded by Reader B using both M1 and M2 in order to determine the association between FASD and palmar crease patterns. Multinomial logistic regression and simple binary logistic regression models using robust standard errors were built to examine the relationship between crease pattern and FASD and between points of origin and FASD. Crease patterns and points of origin were examined as outcome variables in separate models. In each case, FASD was the primary independent variable of interest. We controlled for the subject's sex and race in all analyses. We further tested for an interaction between sex and race, but as the interaction term did not achieve statistical significance, it was dropped from all analyses. Covariates of interest were re-coded into categorical variables as follows: FASD diagnosis was coded as either affected or control; crease pattern was either normal or aberrant; and race was coded as white or non-white. All statistical analyses were performed using Stata, version 9.0 (College Station, Texas); p -values of 0.05 or less were considered significant.

RESULTS

Summary statistics of the sample are found in Table 1. The sample was composed of approximately equal numbers of males and females; however, there were more white than non-white individuals (binary test, two-sided, $p < 0.001$). Although over half the sample was diagnosed with a fetal alcohol spectrum disorder, most palmar prints were classified as normal.

Reliability Analysis

Kappa coefficients were very high for both intra- and inter-observer reliability. Intra-observer Kappa coefficients were 0.814 and 0.910 for Readers A and B under M1 and 0.804 and 0.885 under M2. Inter-observer Kappa coefficients ranged from 0.582–0.623 under M1 and from 0.647–0.757 under M2. Method 2 produced slightly higher inter-observer reliability estimates, but slightly lower intra-observer reliability estimates compared to M1.

There was a high degree of correspondence between the points-of-origins measure (M2) and the standard classification scheme (M1) (right: $X^2 = 101.0$, $p << 0.001$; left: $X^2 = 96.8$, $p << 0.001$; Table 2). In both palms, where palmar creases were classified as normal, in no instances were there fewer than 2 points of origin. We can thus conclude that a single point-of-origin is indicative of an aberrant crease pattern. Two points of origin were more prevalent than three points of origin in hands classified as “normal” under the standard classification scheme (M1), but this pattern was also found in palms classified as “aberrant” under the same scheme. Thus, the distinction between two and three points of origin may not be useful for determining whether palms are normal or aberrant.

FASD Analysis

Table 3 shows the prevalence of crease patterns and points-of-origin in relation to FASD diagnosis for both the right and left hands. Our models never yielded a significant association between palmar crease pattern and FASD, even when sex and race were included as controls in the models. Because the degree to which palmar creases are expected to deviate from normal changes with the timing and degree of fetal trauma, we also analyzed the relationship between Fetal Alcohol Syndrome (FAS), the most severe form of FASD, and crease patterns. Even in this analysis, we were unable to

detect a significant association between FAS and crease pattern. Similarly, we could not detect a significant association between points of origin and FAS. A possible explanation for our findings is that abnormal palmar creases were rare in our sample compared to normal palmar creases. This suggests that a larger sample size may be required to detect a relationship between crease patterns and FASD.

DISCUSSION

Classification, Methods and Reliability

During the late 1960s and early 1970s, a flurry of papers attempted to explain the significance of palmar creases in detecting fetal trauma. Much of this research focused on the relationship of the so-called “simian” crease (STPC) to various disorders, but less attention was paid to other abnormal variants such as the Sydney line and other transitional forms of STPC and the Sydney line. Furthermore, because researchers employed multiple classification methods, comparability across studies was limited. In this study, we performed a direct comparison of two prominent palmar crease classification methods and found that they were similar in reliability and comparable in terms of associating aberrant patterns with *in utero* alcohol exposure.

Studies of palmar creases differ not only in the scheme employed to classify palms, but also in the method of inspection. The most common method is direct visual inspection of the palm (e.g. Dar and Winter 1970, Dar *et al.* 1971, Dar *et al.* 1977, and by ultrasound Jeanty 1990). However, this method may introduce a bias in that other morphological traits characteristic of certain disorders may influence how palmar creases are classified. The standard ink and inkless methods of examining palmar crease patterns (e.g. Wertelecki 1979, Cannon *et al.* 1994, Dar and Jaffe 1983) remove any bias resulting from direct observation of the individual, but may be problematic with respect to the clarity and

quality of the print. We used the carbon paper and tape method (analogous to ink methods) to remove bias from direct interaction with subjects and classified palms conservatively if prints were unclear. This may have led to an overestimation of normal palm prints, which may have limited our ability to detect an association between aberrant prints and FASD.

Palmar Creases and the Relationship to FASD

Dermatoglyphics and palmar crease patterns have long been of interest to physicians because of associations with abnormal development and genetic disorders. Indeed, it has been suggested that palmar crease patterns may provide a reliable cue to physicians of impending dysfunction (e.g. Johnson and Opitz 1971). Alcohol is a known teratogen during prenatal life, and the long-term effects on morphology and neurobehavior are well documented (Streissguth *et al.* 1994; Streissguth and Connor 2001). Though we expected to find increased prevalence of aberrant palmar creases in individuals with FASD, we were unable to detect such an association.

There are many factors that may have limited our ability to detect an association between FASD and abnormal crease patterns. By categorizing palmar crease classifications into a binary “normal” versus “abnormal” categories, we may have missed a specific association between a given class of abnormal variant and FASD. It is known, however, that both transitional and complete forms of abnormal creases are associated with high levels of exposure to alcohol *in utero* (Jones *et al.* 1973). Furthermore, binning various forms of aberrant palmar creases seems warranted as heterogeneous manifestations of the same basic crease pattern are known to occur among relatives (Dar and Winter 1970, Dar *et al.* 1971).

It is possible that we were unable to capture an existing association because we did not control for disease severity. It has been suggested that timing and severity of fetal trauma may affect the degree to which palmar creases deviate from normal (Purvis Smith *et al.* 1972). Jones *et al.* (1973) found aberrant palmar creases in infants born to chronically alcoholic mothers. It may be that our subjects were all exposed to a sub-threshold level of alcohol, in which case palmar creases would not be expected to deviate substantially from normal patterns. We attempted to address this possibility by examining the relationship of severe cases of FAS to aberrant palmar creases, but were unable to detect an association. Nonetheless, further studies examining the timing and degree of trauma with respect to production of aberrant morphologies are warranted.

Palmar creases are known to differ by sex and among races, independently of their association with a given disorder (cf. Dar and Winter 1970, Wertelecki 1971, Boroffice 1981, Dar *et al.* 1977). Indeed, Tsai *et al.* (1999) have recently argued that simian creases could be considered normal in Chinese newborns, as they occur at frequencies of higher than 4%. Even controlling for sex and race, we were unable to detect an association between FASD and aberrant crease patterns.

CONCLUSION

Based on the results of this research, we suggest that palmar crease variants can be measured reliably. Kappa coefficients for both M1 and M2 were greater than 0.5, suggesting good agreement within and between readers. Using data from the entire sample of 427 prints and controlling for sex and race, we found no relationship between palmar crease variants and FASD. Various limitations, including small sample size for a rare event, may have hindered our ability to detect such a relationship.

These results suggest that while palmar creases can be classified reliably, they may not be useful in predicting fetal trauma due to *in utero* exposure to alcohol in the absence of very large samples.

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Table 1. Sample summary statistics (N=427).

Sex	Race	FASD Diagnosis*	Palmar Crease Classifications†		Points of Origin						
			right	left	right	left					
male	206	white	298	control	190	normal	352	344	one	19	19
female	200	non-white	90	FAS	77	STPC	5	10	two	319	340
unknown	21	unknown	39	FAE	143	STPC ab	19	11	three	87	65
				unknown	17	Sydney	8	11	undetermined	2	3
						Sydney ab	38	39			
						undetermined	5	12			

* FAS = fetal alcohol syndrome, FAE = fetal alcohol exposure

† STPC ab = aberrant single transverse palmar crease; Sydney ab = aberrant Sydney crease

Table 2. Comparison of crease classification and points of origin.

	right points of origin				left points of origin			
	1	2	3	total	1	2	3	total
normal	6	140	44	190	7	150	31	188
aberrant*	11	169	39	219	12	177	30	219
total	17	309	83	409	19	327	61	407

*Includes STPC, STPC aberrant, Sydney and Sydney aberrant prints

Table 3. FASD prevalence given crease patterns and points of origin.

	right		left	
	control	FASD	control	FASD
normal	163	176	153	176
STPC	1	4	4	6
STPC ab	8	9	6	5
Sydney	3	5	2	8
Sydney ab	13	24	15	23
1 PO	6	11	7	12
2 PO	140	169	150	177
3 PO	44	39	31	30

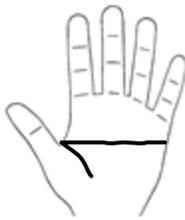
FIGURE CAPTIONS

Figure 1. Examples of palmar crease variants (Method 1) based on the classification system of Dar *et al.* (1977).

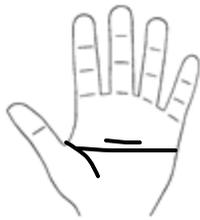
Figure 2. Points of origin (Method 2) based on the classification scheme of Chaube (1977).



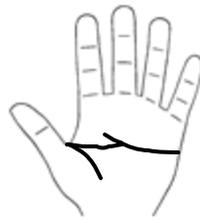
Normal



STPC



**Aberrant
STPC**



**Aberrant
STPC**



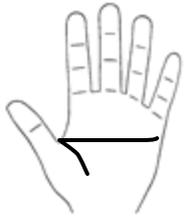
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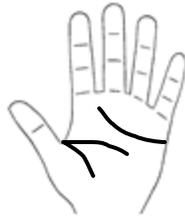
**Aberrant
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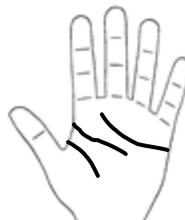
**Aberrant
Sydney**



1 origin



2 origins



3 origins