Development of human palmar and digital flexion creases

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To determine the timing of the development of the various palmar and digital creases, we examined the hands of 100 human fetuses obtained after therapeutic abortion. The fetuses ranged in age from 7 to 19 fetal weeks, with age being established by menstrual period dates and ultrasound examination before termination. Our observations show that palmar and digital creases develop between 8 and 13 fetal weeks. Digital creases are well defined by 10 weeks; palmar creases are consistently seen by 13 weeks of gestation. The volar pads are present from 8 to 14 fetal weeks. A hand malformation or specific insult that occurs before the time of crease development and that alters the form or function of the fetal hand can cause secondary alterations in crease patterns of the hand. (J Pediatr 1988;113:128-32)

Hand creases have been studied for thousands of years by palmists or chiromancers, but only in the last 50 years has medical science attempted to study these creases in relation to medical disorders. Recently we were involved in the case of a baby who was exposed to carbon monoxide at 13 postmenstrual weeks of gestation. The baby had multiple congenital anomalies, including absent flexion creases of the fingers. This case led us to review the literature regarding flexion crease development in the human hand. We were surprised to find that the information was very limited and that conventional wisdom is largely based on a 1970 paper by Popich and Smith,[1] which states that hand creases develop between 7 and 14 weeks gestation. We performed the following study to determine the specific timing of the development of the various palmar and digital creases. Additionally, we considered the evidence regarding the origin of these creases.

METHODS

We examined 132 hands from 100 human fetuses obtained in unselected fashion after therapeutic abortion. None of the terminations were performed for suspected abnormalities. The fetuses ranged in age from 7 to 19 fetal weeks; at least 11 fetuses were examined at each week during the critical period of 8 to 12 weeks. Gestational ages were determined by a combination of menstrual period dates and ultrasound examination before termination. The hands were fixed in 10% formalin and examined under a dissecting microscope. Staining with toluidine blue did not significantly improve crease examination. All hands were evaluated by the same investigator (C.A.S.).

The nomenclature of palmar and digital creases is illustrated in Fig. 1. We developed a scoring system for evaluating the hands. If a crease or pad was absent, a negative was recorded. If it was barely visible, a 1+ was given, and if the crease was well defined, a 2+ was scored. The information was then compiled for hands at each week of gestation.

RESULTS

The Table summarizes the development of the palmar and digital creases and the volar pads. The figures in each column indicate the number of fetuses in which the specific crease or pad was at least faintly visible (1+ on the scoring system) on two or more fingers at that particular gestational age. There were some minor variations among fetuses of the same age, between two hands in the same fetus, and

Submitted for publication Dec. 7, 1987; accepted Feb. 2, 1988.

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between fingers on a single hand. However, the overall pattern and sequence of development were consistent. Fig. 2 illustrates fetal hands from 7 to 18 weeks of gestation. Formation of the various palmar and digital creases is outlined in the following paragraphs:

7 weeks (Fig. 2, *a*), 6 hands, 4 fetuses: The fingers are separated, but the hand has a smooth, glovelike appearance without pads or creases. It is difficult to distinguish between the dorsal and volar surfaces of the hand, and the thumb is in the same plane as the fingers.

8 weeks (Fig. 2, *b*), 21 hands, 17 fetuses: The first creases, primarily the distal interphalangeal and metacarpophalangeal creases, are faintly visible. The digital (fingertip) and interdigital pads are also seen. The thumb is starting to rotate into a different plane.

9 weeks (Fig. 2, *c*), 32 hands, 23 fetuses: The distal interphalangeal and metacarpophalangeal creases are more distinct. Additionally, the proximal interphalangeal creases are faintly visible. The thenar crease originates at the radial side of the hand and extends proximally, encircling the thenar eminence. The thumb is now fully rotated, and the nail beds are beginning to form.

10 weeks (Fig. 2, *d*), 14 hands, 11 fetuses: All digital creases are well defined by 10 weeks of gestation. The interdigital pads are beginning to regress, and a central depression is seen in each digital pad. Many small papillary integumentary thickenings are present in the center of the palm. The nail beds are better defined.

11 weeks (Fig. 2, *e*), 19 hands, 13 fetuses: By 11 weeks the distal palmar crease is well defined. It extends from the area between the second and third metacarpophalangeal joints to the ulnar border of the palm. The proximal palmar crease is faintly seen, first visible at the radial edge of the palm and either fused with or just distal to the thenar crease.

12 weeks (Fig. 2, *f*), 17 hands, 12 fetuses: The proximal palmar crease is consistently seen extending from the radial edge of the palm to the medial border of the hypothenar eminence. The digital pads are well seen, but the interdigital pads are now gone.

13 weeks (Fig. 2, *g*), 7 hands, 5 fetuses: By 13 weeks of gestation, all palmar and digital creases are well defined. The digital pads are beginning to regress.

14 to 16 weeks (Fig. 2, *h*), 8 hands, 7 fetuses: There is little change in appearance of the fetal hand during this time. The digital pads are absent by 15 weeks.

17 to 19 weeks (Fig. 2, *i*), 8 hands, 8 fetuses: The proximal interphalangeal creases appear double. This extra crease, which appears distal to the proximal interphalangeal crease, is limited to the volar side of the digit, whereas the distal interphalangeal, proximal interphalangeal, and metacarpophalangeal creases all extend onto the lateral aspect of the digit.

DISCUSSION

There has been some disagreement regarding the origin of palmar and digital creases. In 1937, the German researcher Würth[2] found that hand creases develop during the second and third embryonic months of life. He concluded that the flexion creases develop independently of palmar and finger movement because he thought that the hand musculature was not sufficiently developed for flexion to occur. Kimura and Kitagawa[3] also proposed that hand creases develop independently of flexion movements. Those investigators based this conclusion largely on studies by Humphrey,[4] which show that spontaneous hand movements are not observed in the fetus of less than 11.5 weeks gestation. However, Humphrey actually stated that palmar sensitivity and finger flexion are observed by 10.5 weeks of menstrual age, which corresponds to 8.5 fetal weeks and is consistent with our observation of the earliest appearance of flexion creases on the fingers.

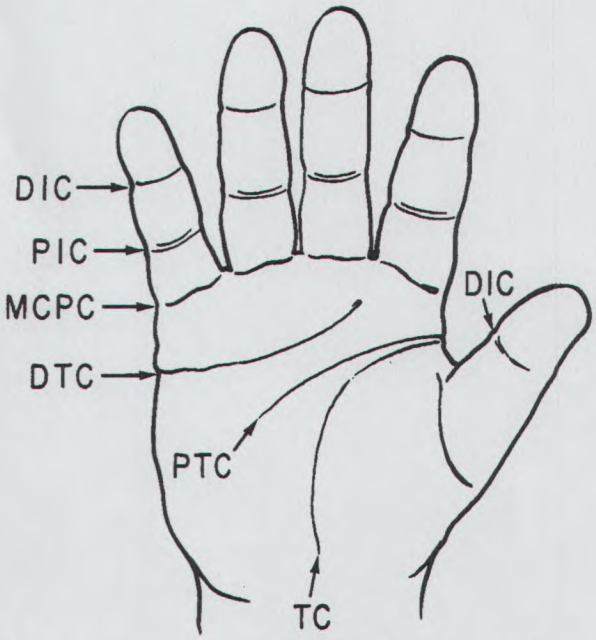

Fig. 1. Hand crease nomenclature. *DIC*, Distal interphalangeal crease; *PIC*, proximal interphalangeal crease; *MCPC*, metacarpophalangeal crease; *DTC*, distal transverse crease; *PTC*, proximal transverse crease; *TC*, thenar crease.

The second hypothesis is that hand creases are secondary features determined by the form and function of the developing hand. This view is supported by studies of creases in malformed hands performed by Popich and Smith.[1] Additional evidence includes the correspondence of the creases to the location of the underlying joints of the hand. Two crease variations have been observed that cannot be explained by this second hypothesis. An extra interphalangeal transverse crease between the metacarpophalangeal and proximal interphalangeal creases of the fifth finger was observed in 4 of 551 people by Komatz et al.[5] In none of the cases was this extra crease associated with an underlying bone or joint abnormality. The second observation is that of an extra transverse crease just distal

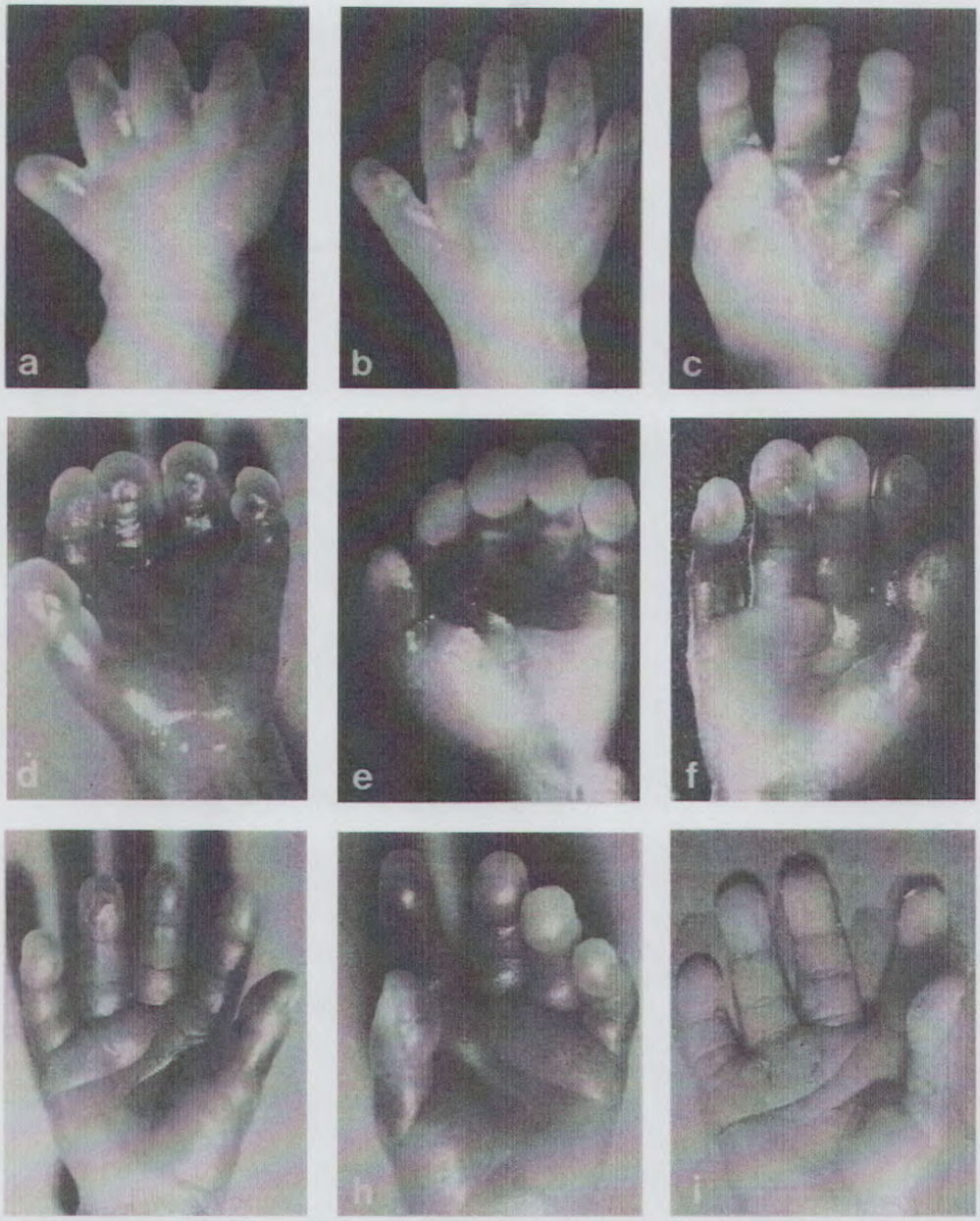

Fig 2. Fetal hands from 7 to 18 weeks of gestation. **a,** 7 weeks; **b,** 8 weeks; **c,** 9 weeks; **d,** 10 weeks; **e,** 11 weeks; **f,** 12 weeks; **g,** 13 weeks; **h,** 14 weeks; **i,** 18 weeks.

to the distal interphalangeal flexion crease (most commonly on the middle finger) in patients with sickle cell disease. DeJong and Platou[6] reported this finding in 34% of patients with sickle cell disease in comparison with 7% of healthy black individuals. Zizmor[7] observed this crease in 90% of patients with sickle cell disease in comparison with 10% of control subjects. On the basis of the evidence noted above and our clinical experience, we conclude that genetic factors probably do play a role in the formation of digital creases but that fetal hand movement is necessary for normal development of these flexion creases to occur.

Two other recent studies have investigated the development of human palmar and digital creases. Lacroix et al.[8] used scanning electron microscopy of 50 fetal hands to develop a method of rapid estimation of fetal age based on the appearance of the hand; fetal age was roughly estimated by weeks of amenorrhea. Kimura and Kitagawa[3] examined 150 fetal hands from 6 to 20 weeks of gestation.

Table. Development of hand creases and pads: Numbers of fetuses in which the specific crease or pad was present at each week of gestation

Gestation (wk)	No. of fetuses examined	DIC	PIC	MCPC	DTC	PTC	TC	Digital pads	Interdigital pads
7	4	1	1	1	0	0	1	0	0
8	17	11	4	8	0	0	2	9	10
9	23	22	19	22	6	4	18	22	19
10	11	11	11	11	7	2	11	11	9
11	13	13	13	13	11	8	13	13	8
12	12	12	12	12	12	11	12	12	1
13	5	5	5	5	4	4	5	3	1
14	4	4	4	4	4	3	4	3	0
15	2	2	2	2	2	2	2	0	0
16	1	1	1	1	1	1	1	0	0
17	4	4	4	4	3	4	4	0	0
18	3	3	3	3	3	3	3	0	0
19	1	1	1	1	1	1	1	0	0

DIC, Distal interphalangeal crease; PIC, proximal interphalangeal crease; MCPC, metacarpophalangeal crease; DTC, distal transverse crease; PTC, proximal transverse crease; TC, thenar crease.

The estimation of fetal age was based on hand length and the morphologic features of the hand reported by Lacroix et al. and thus depended on the accuracy of the previous study. In our investigation, each fetus was dated by a combination of menstrual period dates and ultrasound examination before termination of the pregnancy. Additionally, we examined more hands from 8 to 12 weeks, and we documented our data regarding timing interpretation by using a scoring system. Therefore our study refines the knowledge regarding the critical period of hand crease development.

Examination of palmar and digital creases may yield useful information in several situations. Alterations of these creases may serve as diagnostic clues in many congenital malformation syndromes, such as Down syndrome, trisomy 18, and Cornelia de Lange syndrome. An unusual crease pattern may reflect an underlying bone or joint abnormality. Hypoplastic or absent flexion creases in structurally normal hands are often seen in conditions associated with diminished movement, such as arthrogryposis or severe neurologic impairment. Palmar crease alterations have been reported in a number of other conditions, including congenital rubella syndrome,[9-11] childhood leukemia,[12-14] hyperactivity,[15] prematurity,[16] small-for-gestational-age infants,[16] infants born to mothers on methadone maintenance,[16] and children with developmental problems.[17] Alteration of crease patterning suggests that the cause and pathogenesis are prenatal in origin. Therefore we believe that careful inspection of hand creases should be particularly done as a part of the examination of patients with multiple congenital anomalies, hand malformations, neurologic abnormalities, or exposure to teratogens.

The baby that was mentioned in the introduction of this article was exposed to carbon monoxide at 11 fetal weeks of gestation and had total absence of digital creases. Finger creases are first visible at 8 weeks and are well defined by 10 weeks, so we concluded that the carbon monoxide exposure could not explain the absence of finger creases in this baby.

Our observations confirm that palmar and digital creases develop between 8 and 13 fetal weeks. A hand malformation or specific insult that occurs before the time of crease development and that alters the form or function of the fetal hand can result in secondary alterations in the crease patterns of the hand. Although genetic factors may play a role in the development of digital creases, fetal hand movement is necessary for normal formation of these flexion creases to occur.

We thank Nancy Chandler and Steven Leitch for technical assistance.

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Clinical and laboratory observations

Effect of a lipid emulsion (Intralipid) on polymorphonuclear leukocyte functions in the neonate

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The lipid emulsion Intralipid is widely used in neonatal intensive care units for parenteral nutrition to provide essential fatty acids and high caloric intake. In adults, both depression and stimulation of chemotaxis, random motility, and oxidative metabolic function have been reported after in vivo or in vitro treatment.[1-6] We reported no impairment of oxidative-metabolic and chemotactic functions when neonatal PMNs were incubated in vitro with 25, 50, or 100 mg/ml of Intralipid for 30 minutes.[7] Wheeler et al.[8] reported no abnormality of chemiluminescence after a single-dose Intralipid infusion of 1 gm/kg/24 hr in 14 premature and term neonates.

CBC	Complete blood (cell) count
HBSS	Hanks balanced salt solution
PMN	Polymorphonuclear neutrophil leukocyte
RDS	Respiratory distress syndrome
TG	Triglyceride
TTNB	Transient tachypnea of the newborn

We therefore studied chemiluminescence and chemotaxis in high-risk neonates after the infusion of a single dose and after long-term administration of Intralipid.

Presented in part at the 3rd annual Greater New York Conference on Perinatal Research, Glen Cove, N.Y., Nov. 20, 1986, and at the 28th annual American College of Nutrition meeting, Symposium on Advances in Clinical Nutrition, St. Charles, Ill., Sept. 22, 1987.

Submitted for publication Jan. 6, 1987; accepted Jan. 20, 1988.

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