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Development of the arterial pattern in the upper limb of staged human embryos: normal development and anatomic variations

M. RODRÍGUEZ-NIEDENFÜHR[1], G. J. BURTON[2], J. DEU[1] AND J. R. SAÑUDO[1]

[1] *Unit of Anatomy and Embryology, School of Medicine, Autonomous University of Barcelona, Spain, and*
[2] *Department of Anatomy, University of Cambridge, UK*

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ABSTRACT

A total of 112 human embryos (224 upper limbs) between stages 12 and 23 of development were examined. It was observed that formation of the arterial system in the upper limb takes place as a dual process. An initial capillary plexus appears from the dorsal aorta during stage 12 and develops at the same rate as the limb. At stage 13, the capillary plexus begins a maturation process involving the enlargement and differentiation of selected parts. This remodelling process starts in the aorta and continues in a proximal to distal sequence. By stage 15 the differentiation has reached the subclavian and axillary arteries, by stage 17 it has reached the brachial artery as far as the elbow, by stage 18 it has reached the forearm arteries except for the distal part of the radial, and finally by stage 21 the whole arterial pattern is present in its definitive morphology. This differentiation process parallels the development of the skeletal system chronologically. A number of arterial variations were observed, and classified as follows: superficial brachial (7.7%), accessory brachial (0.6%), brachioradial (14%), superficial brachioulnar (4.7%), superficial brachioulnoradial (0.7%), palmar pattern of the median (18.7%) and superficial brachiomedian (0.7%) arteries. They were observed in embryos belonging to stages 17–23 and were not related to a specific stage of development. Statistical comparison with the rates of variations reported in adults did not show significant differences. It is suggested that the variations arise through the persistence, enlargement and differentiation of parts of the initial network which would normally remain as capillaries or even regress.

Key words: Arterial development; embryology; arm; forearm.

INTRODUCTION

Variations in the branching pattern of the major arterial trunks have been reported with an incidence of up to 20% in human adult limbs (McCormack et al. 1953; Wankoff, 1962; Rodríguez-Niedenführ et al. 2001). If the presence of a median artery in the forearm is also included, this percentage rises even higher (Rodríguez-Niedenführ et al. 1999). However, despite their obvious clinical importance, remarkably little is known as to how or when during development these variations arise. For example, there is only one report in the literature which mentions the existence in the upper limb of an arterial variation in embryonic material (Senior, 1926).

Much of our current understanding regarding development and variations of the upper limb arteries is derived from early descriptive studies on human or laboratory animal embryos, and several theories have been proposed (Von Baer, 1828; Baader, 1866; Hochstetter, 1890, 1891; Göppert, 1904, 1910; Sabin, 1905, 1917; Rabl, 1907; Elze, 1908, 1913, 1919; Evans, 1908, 1909*a*, *b*). In humans, De Vriese (1902) described the arteries as originating from an initial capillary network associated with each of the principal nerves, whereas Müller (1903) considered they were formed by the union of superficial and deep pathways. Singer (1933) suggested that they arise from a single axial channel which represents the brachial and interosseous arteries. The first two authors considered

Correspondence to Dr José R. Sañudo, Unitat d'Anatomia i Embriologia, Universitat Autònoma de Barcelona, Campus Bellaterra, 08193-Barcelona, Spain

that the definitive arterial pattern results from the remodelling of the complex primitive networks (De Vriese, 1902; Müller, 1903), whereas Singer (1933) described a process of sprouting from the axial arterial trunk.

The differences between these reported developmental processes may be explained by the fact that the samples examined were too small, did not include all stages during which upper limb development occurs (stages 12–23; O'Rahilly & Müller, 1992) and did not include multiple embryos from each of the stages studied (De Vriese, 1902; Müller, 1903). Furthermore, Singer's study (1933), although making reference to embryonic stages, did not present details of the embryonic material examined, and its conclusions were based mainly on the findings of variation in adults, with the embryonic results published only in abstract form (Senior, 1926). The same principle of using data from studies based on adult cadavers to state hypotheses of how arterial development may take place has also been used by several other authors (Schwyzer & de Garis, 1935; Moncayo-Marques, 1941; Wankoff, 1961, 1962; Kadanoff & Balkansky, 1966; Poteat, 1986; Rodríguez-Baeza et al. 1995; Fadel & Amonoo-Kuofi, 1996; Anagnostopoulou & Venieratos, 1999; Nakatani et al. 1999).

The present study was undertaken in view of this confusion, and of the high incidence of variations. The aim was to establish the normal pattern of development of the arteries of the upper limb from a large and reliable sample of human embryos between stages 12 and 23, and to establish when and how variations occur. The most representative stages were reconstructed 3-dimensionally, and a new theory concerning arterial development in the human upper limb is proposed here.

MATERIAL AND METHODS

A total of 112 serially sectioned human embryos (224 upper limbs) belonging to the Bellaterra Collection (Prof. J. M. Domènech. Unidad de Anatomía y Embriología Humana, Universidad Autónoma de Barcelona, Spain) and the Boyd Collection (Department of Anatomy, University of Cambridge, UK) were studied. Crown-rump (CR) length and developmental stages (O'Rahilly & Müller, 1987) are shown in Table 1.

Three-dimensional computer-aided reconstruction was performed using Keops-Visilog software.

Table 1. *Crown-rump (CR) length and developmental stage of the embryos included in this study*

	CR length (mm)	Embryo	CR length (mm)	Embryo	CR length (mm)
Stage 12					
RI-5	3.5	H-86	3.8	H-710	4
Stage 13					
SS-19	5	H-875	5	SS-1	6
H-563	6				
Stage 14					
RI-1	6	H-1183	7		
Stage 15					
H-685	7.5	DO-3	8	PLA-14	8
DU	8.4	H-237	8.5	H-102	9
Stage 16					
CB	9	H-226	9	H-1228	9.5
H-67	9.5	DU-10	10	BI-6	10
H-33	10	MAR-3	10.3	DU-5	10.3
PG-3	11	H-1026	11	BI-3	12
BI-7	13				
Stage 17					
H-1069	13	H-23	13	H-854	13.5
H-8	14	H-186a	14	H-186b	14
H-883	14.5	RE-1	15	SS-30	15
Stage 18					
H-78	13.5	H-241	14	DU-9	15
H-201	15	H-673	15	H-214	15.5
FU-20	16	SS-21	16	HM-2	16
FU-17	16	H-973	16	FU-10	16.5
CB-7	17				
Stage 19					
H-640	17	H-25	17	DU-8	18
H-242	18				
Stage 20					
RI-6	19	SS-18	19	PU-3	19
SS-2	19	RI-2	19	GI-10	19
VAL-1	20	MAR-4	20	H-1106	20
H-954	20	H-951	20	H-243	20
PLA-1	21	PLA-3	21	DO-24	21
H-1011	21	H-27	21	H-960	22
H-907	22	H-594	22	H-173	22
H-767	22				
Stage 21					
DF-5	22	SS-29	22	FU-18	22
RI-8	23	H-1174	23	H-950	23
H-876	24	H-855	24	H-1103	24
Stage 22					
FU-12	24	DU-12	24	FRA-25	24
H-35	25	DF-4	26	H-238	26
H-11	26	H-211	26	H-244	26
H-583	27				
Stage 23					
DF-2	27	SS-26	28	H-983	28
H-970	28	H-585	28	H-795	28
H-1022	28.5	SS-31	29	H-179	29
H-1061	29	H-988	29	A-1	30
SAM	30	GF	30	H-180	30
H-31	30	H-209X	30		

RESULTS

Analysis of the embryonic sample enabled us to establish the morphogenetic timetable of the normal vascular development of the upper limb, and has also highlighted the existence of arterial variations in the different parts of the vascular system. As these variations were not related to a specific stage, we first present the normal development of the arterial pattern and then analyze the arterial variations observed.

Normal development

Stage 12 (3–5 mm; 26 d). By this stage the upper limb bud has initiated its outgrowth, and contains a dispersed capillary network within the undifferentiated mesenchymal tissue. No other structures (e.g. muscular or skeletal blastemas) have differentiated, and although the principal nerve trunks have arrived at the base of the limb bud, they have not yet entered it.

Stage 13 (4–6 mm; 28 d). The limb bud has continued its outgrowth, and few differences were observed in relation to the previous stage. A larger axial trunk can be observed, originating from the dorsal aorta, but when it reaches the base of the limb bud it ramifies into capillaries throughout the whole limb bud. The nerves have still not entered the bud and no skeletal or muscular elements are visible (Fig. 1*C*).

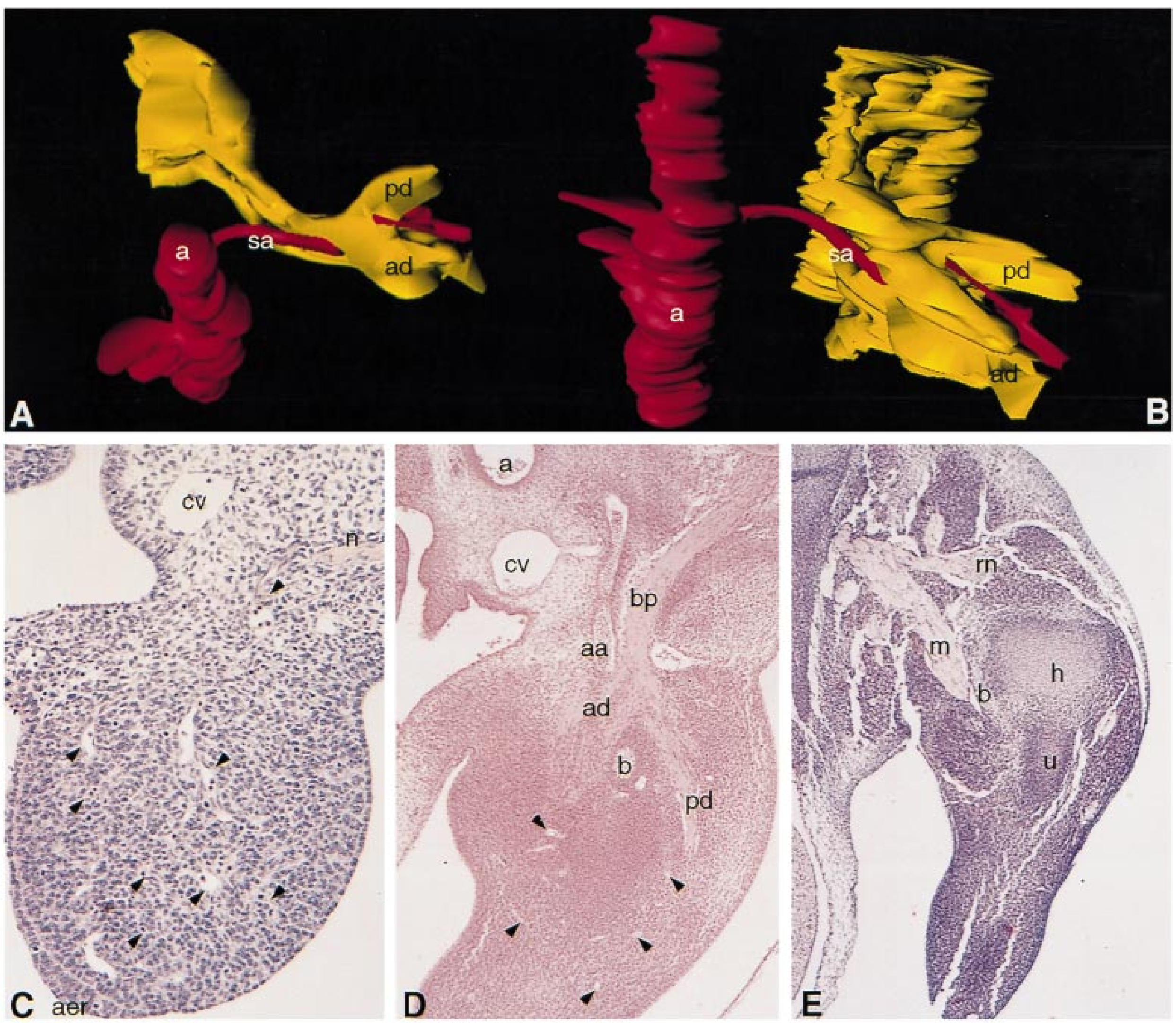

Fig. 1. Normal development of the upper limb in human embryos. (*A*) Superior view of a computer aided reconstruction of a stage 15 human embryo. (*B*) Anterior view of the reconstruction in (*A*). (*C*) Stage 13 human embryo showing disperse capillaries (arrowheads) in the limb bud. (*D*) Stage 16 human embryo showing a well developed axillary artery and the beginning of the brachial and disperse capillaries in the forearm region. (*E*) Well developed brachial artery in the elbow of a stage 17 human embryo. a, aorta; sa, subclavian artery; aa, axillary artery; b, brachial artery; bp, brachial plexus; ad, anterior division of brachial plexus; pd, posterior division of brachial plexus; cv, cardinal vein; m, median nerve; rn, radial nerve; h, humerus; u, ulna; aer, apical ectodermal ridge; n, nerve.

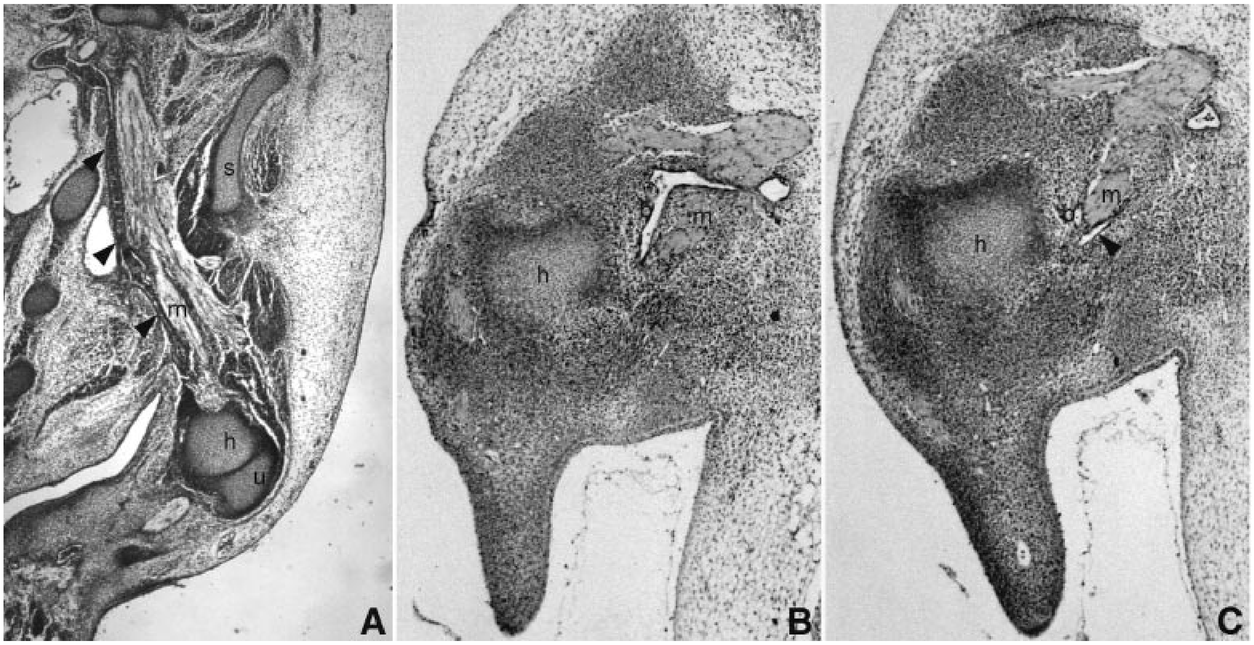

Fig. 2. (*A*) Superficial brachial artery (arrowheads) in front of the median nerve (m) in a stage 20 human embryo. (*B*) Origin of the accessory brachial artery from the axillary before crossing posteriorly the median nerve (m). (*C*) Accessory brachial artery (arrowhead) rejoining the brachial artery (b). s, scapula; h, humerus; u, ulna.

Stage 14 (5–7 mm; 32 d). The axial trunk now represents the subclavian artery which enters the limb bud, where it ramifies into capillaries. These capillaries extend along the whole limb bud. The nerves do not enter the limb bud and no differentiated skeletal or muscular elements were observed.

Stage 15 (7–9 mm; 33 d). The axial artery has extended to include both the subclavian and axillary arteries. After crossing the neural plate, it ramifies into its capillary network. The nerves have begun to enter the limb bud, joining together to form the neural plate and then branching into anterior and posterior divisions (Fig. 1*A*, *B*).

Stage 16 (8–11 mm; 37 d). By now the arterial pattern shows a well formed subclavian artery running in front of the neural plate. The neural plate has divided into 2 divisions (anterior and posterior). The anterior one forms the musculocutaneous, ulnar and median nerves while the posterior one forms the radial nerve. The artery pierces the anterior division of the neural plate to pass between the 2 divisions. Once past the neural plates the artery divides into capillaries without a defined pattern (Fig. 1*D*). An artery remaining in front of the anterior division of the neural plate was occasionally observed.

The mesenchymal tissue of the humerus has now begun to chondrify, and the ulna and radius are represented by condensed mesenchymal tissue.

Stage 17 (11–14 mm; 41 d). The axillary artery continues as the brachial artery, extending until the elbow, before ramifying into capillaries along the forearm and hand (Fig. 1*E*). The proximal portion of the brachial artery displays a well defined arterial wall, as do the proximal branches (profunda brachii). The nerves are easily recognisable as far as the hand, and the distal branching of the radial and ulnar nerves into dorsal cutaneous branches can be observed. The mesenchyme of the humerus is in a chondrified state, the ulna and radius are condensed and the mesenchyme of the carpus and metacarpus has begun to condense (Figs. 1*E*, 2*B*, 2*C*).

Stage 18 (13–17 mm; 44 d). At this stage the humerus, ulna and radius are chondrified (Fig. 3*A*, *B*). The carpus and metacarpus are represented by condensed mesenchyme. The vascular pattern is more differentiated, and well defined structures can be followed to the hand region corresponding to the ulnar, median and interosseous arteries (Fig. 3*A*, *B*). The initial part of the radial artery is clearly defined but its distal portion remains as a capillary net. The main nerves with their branches are recognisable as far as the hand (Fig. 3*A*, *B*).

Stage 19 (16–18 mm; 47 d). The skeletal elements have all chondrified, and well defined tube-like vessels are easily observed and followed through the whole upper limb until the hand, where they form the palmar arches. The distal part of the radial artery remains as a capillary plexus which is difficult to follow down to the hand. The nerves have achieved their definitive adult arrangement and can be easily recognised.

Stage 20 (18–22 mm; 50 d). From this stage on, the arterial pattern has already achieved its definitive morphology and can easily be followed until the digital arteries. The distal part of the radial artery, although remaining in a capillary state and with an undifferentiated arterial wall, may be followed with ease as far as the wrist (Fig. 4*A*–*D*).

Stage 21 (22–24 mm; 52 d), stage 22 (23–28 mm; 54 d) and stage 23 (27–31 mm; 56 d). The arterial wall continues to differentiate and is now well defined in all segments including the radial artery and the palmar arches. The skeletal and neural elements of the upper limb have achieved their definitive morphology.

Variations of the arterial pattern

Variations in the brachial artery were already detectable at stage 17 as the brachial artery has already differentiated. Therefore the incidence will be based on the embryos from stages 17 to 23 (84 embryos—168 upper limbs).

Variations concerning the forearm arteries were not detectable until stage 18. From this stage onwards, the definitive arterial pattern is observed down to the hand, except for the distal part of the radial artery. Therefore the incidence will be based on the embryos from stages 18 to 23 (75 embryos—150 upper limbs).

Adopting a recently proposed terminology for the arterial variations in the adult upper limb (Rodríguez-Niedenführ et al. 2001), the variations observed were as follows.

Superficial brachial artery, where the course of the brachial artery was anterior rather than posterior to the median nerve (Fig. 2*A*). It was observed in 13 out of 168 upper limbs (7.7%) of embryos belonging to stages 20–23.

The brachial artery adopted its superficial course above the median nerve roots in 8 cases (Fig. 2*A*) and below them in 5 cases.

A branch originating from the brachial artery remained behind the median nerve, sending off the collateral branches such as the profunda brachii, circumflex humeral and ulnar collateral arteries.

Accessory brachial artery, where a second brachial artery originates from the axillary, coursing in front of the median nerve and rejoining the brachial artery before reaching the elbow (Fig. 2*B*, *C*). It was observed in 1 of 168 upper limbs (0.6%) from an embryo belonging to stage 17.

Brachioradial artery, where the radial artery originates proximal to the elbow (Fig. 3*A*, *C*). It was observed in 21 of 150 upper limbs (14%) from embryos belonging to stages 18, 20, 21, 22, 23.

The brachioradial artery originated from the axillary artery in 5 (24%) cases and from the brachial artery in 16 (76%).

At the elbow, an anastomosis joining the brachial and brachioradial artery was observed in 3 of the 21 cases (14.3%).

Superficial brachioulnar artery, where the ulnar artery originates proximal to the elbow and courses superficial to the superficial forearm flexor muscles (Fig. 4*A*–*C*). It was observed in 7 of 150 upper limbs (4.7%) from embryos belonging to stage 18, 20, 21.

In 3 (43%) cases it originated from the axillary, while in 4 (57%) it originated from the brachial artery.

In 2 cases, this artery coexisted in the forearm with a normal ulnar artery (Fig. 4*D*). In both cases, the superficial brachioulnar artery originated from the brachial artery and ended flowing into the ulnar artery at the distal end of the forearm (Fig. 4*D*).

In 1 case, a median artery originated from the distal third of the superficial brachial artery (Fig. 4*A*, *B*).

Superficial brachioulnoradial artery, where the second brachial artery courses in front of the median nerve and divides into the radial and ulnar arteries, while the normal brachial artery continues as the interosseous trunk. It was observed in 1 of 150 upper limbs (0.7%), from a embryo belonging to stage 20.

It originated from the brachial artery below the median nerve roots.

Median artery. This artery was observed in 2 patterns as in adults (Rodríguez-Niedenführ et al. 1999). The palmar pattern consists of an artery accompanying the median nerve in the forearm and extending down to the palm (Fig. 5*A*, *B*). It was observed in 28 of 150 upper limbs (18.7%) from embryos belonging to stages 20–23.

The antebrachial pattern is a median artery which does not extend as far as the hand, and it was also observed in the current series. However, due to its high incidence in the adult (Rodríguez-Niedenführ et al. 1999) it is considered a normal feature rather than a variation and therefore it was not analysed.

Superficial brachiomedian artery, where the origin of a median artery was above the elbow level and had a superficial course in the forearm. It was observed in 1 of 150 upper limbs (0.7%), in an embryo belonging to stage 21.

DISCUSSION

The current theory regarding the development of the vascular system of the upper limb states that development begins at stage 12. Initially a capillary

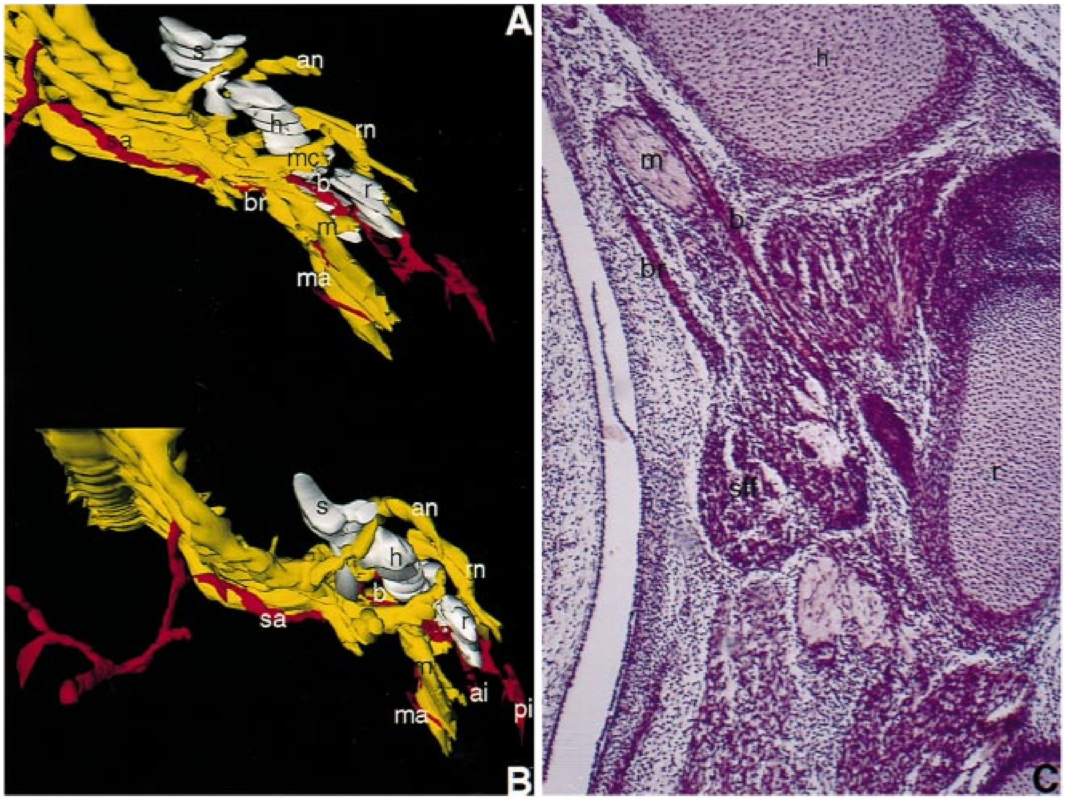

Fig. 3. (*A*, *B*) Reconstruction of a stage 18 human embryo showing the beginning of the brachioradial artery (br) but the distal part is not reconstructed as it is represented by a capillary plexus. (*C*) Brachioradial artery in a stage 21 human embryo. sa, subclavian artery; b, brachial artery; ma, median artery; ai, anterior interosseous artery; pi, posterior interosseous artery; an, axillary nerve; mc, musculocutaneous nerve; rn, radial nerve; m, median nerve; s, scapula; h, humerus; r, radius; sff, superficial forearm flexor muscles.

plexus enters the limb bud and is constantly elaborated in a distal direction as the limb grows. In later stages only one trunk, named the axial artery, supplies the limb and the terminal capillary plexus. From this axial artery, which represents the axillary, brachial and anterior interosseous arteries, the forearm arteries appear successively by means of an angiogenic sprouting mechanism. The median artery develops first, followed by the ulnar and finally the radial arteries (Lippert & Pabst, 1985; O'Rahilly & Müller, 1992; Schmidt & Lanz, 1992; Larsen, 1993; Williams, 1995; Carlson, 1999).

This theory, shown in almost any modern textbook, is an adaptation of results obtained from experimental studies (Wollard, 1922; Feinberg & Noden, 1991) and a model proposed by Singer (1933). However, this model was not based on original results, but on data published in a previous abstract proceeding (Senior, 1926) without consideration of other embryological studies (Zuckerkandl, 1894; De Vriese, 1902; Müller, 1903; Elze, 1908; Evans, 1908).

A capillary network had been described by the earlier embryologists in stage 16 embryos, extending down as far as the palmar region (De Vriese, 1902; Müller, 1903). The network was variously described as following each of the main nerves (De Vriese, 1902), or composed of superficial and deep pathways anastomosed at different levels (Müller, 1903). However, this can not be considered as the initial plexus as the limb starts developing in earlier stages (O'Rahilly & Müller, 1992).

Our results confirm that at stage 12 a capillary network arises from the dorsal aorta and reaches the limb bud. The network takes the form of a uniform 3-dimensional capillary plexus, the existence of which is supported by experimental studies based on injection techniques (Feinberg & Noden, 1991; Aizawa et al. 1999). Such studies are not complicated by artifacts, e.g. collapse of the capillaries, which can render the vessels difficult to detect in standard histological sections (Aizawa et al. 1999).

The capillary network has been shown to expand into the growing limb by angiogenesis and also by in situ differentiation of mesoderm tissue into endothelial cells (Brand-Saberi et al. 1995).

This capillary network undergoes enlargement and differentiation in a proximal to distal fashion in parallel with differentiation of the surrounding mesenchyme (Drushel et al. 1985). The morphogenetic timetable of this coupled vascular-skeletal develop-

Fig. 4. (*A*, *B*) Lateral views of a computer-aided reconstruction of a superficial brachioulnar artery (sbu) and a median artery (ma) originating from the latter. (*C*) Histological section of a stage 20 human embryo presenting an sbu. Note the course over the superficial forearm flexor muscles (sff). (*D*) Coexistence of a sbu and a normal ulnar artery (duplication of the ulnar artery). Note the sbu flowing into the ulnar artery (ua). b, brachial artery; ra, radial artery; ai, anterior interosseous artery; pb, profunda brachii artery; m, median nerve; un, ulnar nerve; h, humerus; u, ulna.

ment has been established in the chicken (Drushel et al. 1985), but no references to an equivalent timetable in the human embryo were found in the literature.

We observed that at stage 13 the subclavian artery begins to differentiate from the preexisting capillaries (Fig. 6). No well differentiated tube-like structures can be observed within the limb until stage 15, when the definitive subclavian and axillary arteries are first visible entering the limb and branching into an undifferentiated capillary network (Fig. 6). At this stage the skeletal elements of the forearm and hand are not definitely formed (O'Rahilly & Gardner, 1975), and therefore the capillary network may be still undergoing remodelling processes (Seichert & Rychter, 1971, 1972*a–c*; Caplan & Koutroupas, 1973; Caplan, 1985; Drushel et al. 1985). However, the brachial artery is acquiring its definitive morphological features as the humerus is forming in stages 16–17 as shown by our results (O'Rahilly & Gardner, 1975). By stage 17 the differentiation process has reached the elbow region, and a well developed brachial artery can be followed to the elbow level where it branches into several capillaries which ramify through the forearm (Fig. 6).

At this stage, variations in the brachial artery, such as a second brachial artery, were detected in our study, though they have not been reported previously. This second brachial artery may or may not continue into the forearm. In those cases where it did continue it could not be established whether the artery represented the radial, ulnar, median or interosseous since these arteries have not yet differentiated.

The existence of these variations indicates that they are established prior to stage 17, supporting the idea that arterial remodelling allows a later correct differentiation of the skeletal elements (Seichert & Rychter, 1971, 1972*a–c*; Caplan & Koutroupas, 1973; Caplan, 1985; Drushel et al. 1985).

As differentiation of the skeletal elements of the forearm proceeds, the forearm arteries acquire a

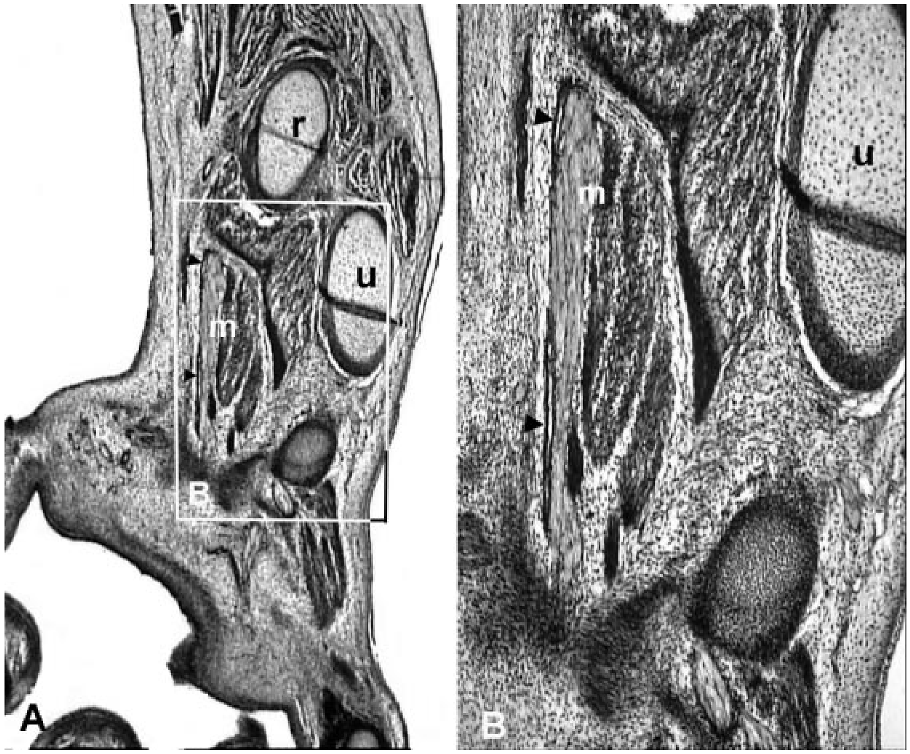

Fig. 5. Palmar pattern of a median artery (arrowheads) in a stage 21 human embryo. m, median nerve; u, ulna, r, radius.

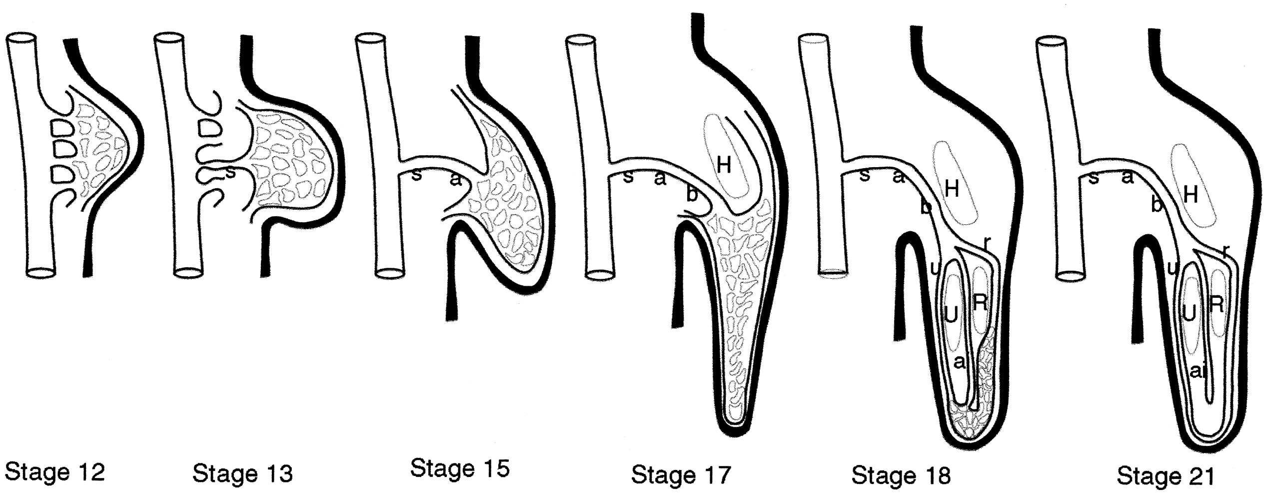

Fig. 6. Sequence of development of the arteries of the human upper limb. Note the disappearance of the plexus-like network with the appearance of the skeletal elements. s, subclavian artery; a, axillary artery; b, brachial artery; r, radial artery; u, ulnar artery; ai, anterior interosseous; H, humerus; U, ulna; R, radius.

differentiated morphology. By stage 18, well defined tube-like vessels representing the median, ulnar and interosseous arteries can be followed as far as the hand, but the radial artery remains in a capillary state and its distal portion is difficult to visualise (Fig. 6). This delayed differentiation of the radial artery may be due to the generally later differentiation of the radius and the lateral metacarpal region observed in our study (Carlson, 1999). This contrasts with the findings from previous authors who considered the radius chondrifying earlier than the ulna (O'Rahilly & Gardner, 1975).

By stage 18 we could determine the continuation in the forearm of those aberrant second brachial arteries which originated in the arm. Different variant patterns were observed with, amongst others, a second brachial artery continuing in the forearm as the radial artery (brachioradial artery). This variation has only been reported once (Senior, 1926), but the rest of the variations, such as the superficial brachial, superficial

Table 2. *Arterial variations observed in this embryonic sample and a previous adult-based sample* (*Rodríguez-Niedenführ et al. 1999, 2001*)

	Embryo (%)	Adult (%)
Superficial brachial artery	7.7	4.9
Accessory brachial artery	0.7	0.25
Brachioradial	14	13.8
Superficial brachioulnar artery	4.7	4.2
Brachioulnar artery	–	0.26
Superficial brachioulnoradial artery	0.7	0.5
Superficial radial artery	–	0.52
Median artery (palmar pattern)	18.7	12
Superficial brachiomedian artery	0.7	–

Chi-squared test did not show statistically significant differences ($P > 0.05$) between the superficial brachial, brachioradial, superficial brachioulnar or median arteries.

brachioulnar or superficial brachiomedian, have not previously been reported in human embryos.

By stage 21, the radial artery has also acquired its final differentiated state and therefore we can now consider that the definitive adult pattern is established (Fig. 6). This is considerably later than the stages 18–19 proposed by Müller (1903). It is noteworthy that Müller (1903) did not analyse the palmar arches, and therefore his results cannot be considered definitive for all vascular elements in the limb, only for those of the arm and forearm.

The arterial variations affecting the distal course of the radial artery, namely superficial radial or superficial brachioradial artery (Wood et al. 1997; Rodríguez-Niedenführ et al. 2001), were not observed in the present study but have to be established before stage 21 as by then the radial artery has already acquired its definitive morphology.

We have shown that the different arterial variations can be observed in any of the stages from 17 to 23 and are therefore not characteristic of a specific developmental period (Singer, 1933). Furthermore, a statistical comparison of the arterial variations observed in this study and in a previous one based on human adults (Rodríguez-Niedenführ et al. 1999, 2000, 2001) has shown that there are no significant differences between the embryonic (stages 17–23) and adult samples (Table 2). This fact has not previously been reported as no large samples of embryonic material have been studied. Indeed, only one arterial variation observed in the embryonic period has been published (Senior, 1926).

It may be concluded that the development of the arterial pattern in the human upper limb takes place by a combined process. An initial capillary network expands into the growing limb bud (stage 12) and, at the same time, the proximal parts of this network originating from the dorsal aorta begin to enlarge and differentiation of the arterial wall commences (stage 13). It is suggested that the persistence, enlargement and differentiation of capillaries forming the initial capillary plexus, which would normally remain in a capillary state or even regress, gives rise to arterial variations of the definitive arterial pattern, rather than the sprouting of aberrant vessels (Singer, 1933; O'Rahilly & Müller, 1992; Schmidt & Lanz, 1992; Larsen, 1993; Williams, 1995; Carlson, 1999).

The proximal to distal differentiation sequence (stages 13–21), as well as the postero-anterior polarity in the development of the vascular pattern (the ulnar, interosseous and median arteries differentiate earlier than the radial, stages 18–21), may imply the existence of similar developmental mechanisms which control the development of the skeletal system (Cohn & Bright, 1999). The influence of vascular development on muscular development has also been proposed (Caplan & Koutroupas, 1973; Mrázková, 1989).

Our results, therefore, suggest that the sprouting theory described in many of the embryological and anatomical textbooks (O'Rahilly and Müller, 1992; Schmidt and Lanz, 1992; Williams, 1995; Larsen, 1993; Carlson, 1999) is obsolete. The new findings suggest that the arterial pattern of the upper limb develops from an initial capillary plexus by a proximal to distal differentiation (in the forearm with a posterior-anterior polaritiy) due to the maintenance, enlargement and differentiation of certain capillary vessels, and the regression of others. Arterial variations may be explained on the basis of this theory by modifications of the normal pattern of capillary maintenance and regression.

Although our knowledge concerning limb development is increasing rapidly, there is still much to learn regarding the factors which determine the definitive vascular pattern of the upper limb. On the one hand, it has been suggested that chemical factors such as oxygenation and nutrient requirements, as well as haemodynamic forces, are important regulators (Arey, 1963; Caplan, 1985). On the other hand, the fact that the arterial pattern presents a highly reproducible and evolutionarily conserved pattern suggests that the underlying mechanisms must also have a genetic basis, for haphazard development would show a greater variability in the adult (Weinstein, 1999). However, it has not yet been clarified what influences could determine the selection of those capillaries which will undergo enlargement and differentiation, and those which will remain as capillaries or even regress, thus creating the normal or variant arterial patterns.

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