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Neuroanatomical localization of myelin basic protein in the late first and early second trimester human foetal spinal cord and brainstem

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Summary

The temporal and spatial expression of myelin basic protein in the first and second trimester human foetal spinal cord and brainstem from 9 to 20 gestational weeks was determined by immunocytochemistry in sections of cervical, thoracic and lumbosacral levels from 41 human foetal spinal cords and ten brainstems. Myelin basic protein-positive oligodendrocytes were observed peripheral to the ependyma at 9–10 gestational weeks. Oligodendrocytes expressing myelin basic protein were seen at 10–12 gestational weeks in the anterior and lateral funiculi. Myelin basic protein was detected later in the posterior funiculi than in the anterolateral white matter and most spinal cord tracts could not be identified by means of variation in myelin basic protein expression. Mylein basic protein was found in the midline of the brainstem at ten gestational weeks and spread laterally during the second trimester. We conclude that in the human foetal spinal cord, myelin basic protein is present by 10 gestational weeks in the anterolateral cervical spinal cord and midline of the brainstem. It is expressed in a rostral-to-caudal and anterolateral-to-posterior manner in most tracts of the spinal cord. However, an exception to these findings is that the fasciculus gracilis, upon developing into a defined region, had more myelin basic protein-positive cells at the lumbar level than in more rostral regions. Definition of the kinetics of myelin basic protein expression in the normal human foetal spinal cord provides a baseline for study of aberrant myelination and demyelination.

Introduction

Myelination has been studied by histochemical methods in many animals, including sheep, opossum, cat, and chicken (Tilney & Casamajor, 1924; Langworthy, 1928; Romanes, 1947; Bensted *et al.*, 1957; Barlow, 1969). Myelin is first observed in these animals in the spinal cord and brainstem (Tilney & Casamajor, 1924; Langworthy 1928; Romanes, 1947; Barlow, 1969). In particular, the earliest traces of myelin are found in the ventral roots and anterior funiculi of the spinal cord, as well as the medial longitudinal fasciculus (MLF), reticular formation and vestibular connections in the brainstem (Tilney & Casamajor, 1924; Langworthy, 1928; Romanes, 1947; Bensted *et al.*, 1957; Barlow, 1969). During development, myelin appears later in the posterior funiculi of the spinal cord and the cervical and thoracic levels always contain more myelin than the lumbosacral level (Langworthy, 1928; Romanes, 1947; Bensted *et al.*, 1957; Barlow, 1969). Recent studies using immunocytochemical methods with antibodies against myelin-associated proteins have revealed a similar pattern in neonatal rats (Rozeik & Von Keyserlingk, 1987; Schwab & Schnell, 1989).

Although myelination in humans has also been studied by histochemical methods, these studies have generally been limited to autopsy material obtained from children, neonates and foetuses older than 20 gestational weeks (GW) (Langworthy, 1933; Yakovlev & Lecours, 1967; Rorke & Riggs, 1969; Gilles *et al.*, 1983). Studies of myelination in the human foetus less than 20 GW, when this process is in fact initiated, have not been performed using newer techniques and reagents presently available. Therefore, temporal and spatial expression of myelin basic protein (MBP) in the human foetus remains controversial. Although some evidence exists that the MLF contains myelin at the end of the first trimester (Lucas Keene & Hewer, 1931; Gilles, 1976) and MBP has been identified in the human foetal spinal cord (HFSC) as early as 8–10 GW by one group (Tohyama *et al.*, 1991), another study did not find MBP at this time (Sasaki *et al.*, 1988). Limited ultrastructural studies of the HFSC have revealed

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myelinated axons at 11–16 GW (Gamble, 1969; Choi, 1981; Choi & Kim, 1984, 1985; Weidenheim *et al.*, 1992). In an attempt to resolve some of these issues, the present study explored the relationship of MBP expression over the entire length of the HFSC before 20 GW and compared the results with myelination in the brainstem.

Methods

Source of foetal tissue

The present study is part of an ongoing research protocol that has been approved by the Albert Einstein College of Medicine Committee on Clinical Investigation and the City of New York Health and Hospitals Corporation. Informed consent was obtained from all participants. Foetal tissues from abortuses of normal women were collected after elective pregnancy termination.

For this study, 41 spinal cords from 9 to 20 GW abortuses (Table 1) were obtained within 10 min of foetal demise. The age of the abortus was determined by multiple parameters including the date of the last menstrual period by history, uterine size by bimanual and abdominal examination, ultrasonography using predominantly the maximum biparietal diameter and, post-abortally, by measurement of foetal foot length. If a conflict arose between the various measures of gestational age, foetal foot length was accepted as the standard (Hern, 1984). The reference point for calculation of gestational age is the women's last menstrual period. Spinal columns were fixed in Bouin's solution. After overnight fixation, the spinal cord was dissected from the vertebral column and transferred to 30% sucrose. The cervical and lumbar enlargements and the thoracic spinal cord were identified. Subsequently, cross-sections of all three levels were made at 40 μm using a Vibratome 1000 Sectioning System (Technical Products International, Inc., St. Louis, MO, USA).

Table 1. Description of specimens.

GW	*No. with 3 levels*	*No. with 2 levels*	*No. with brainstem*	*Total*
9–10	1	0	0	1
10	4	1	1	5
10–11	1	0	0	1
11	4	1	1	5
12	5	1	4	6
13	2	1	0	3
14	3	1	0	4
15	3	2	3	5
16	3	2	1	5
17	2	1	0	3
18	1	0	0	1
19	1	0	0	1
20	1	0	0	1

GW = Gestational weeks

For the 9–10 GW specimen, the spinal cord was divided into rostral, middle and caudal thirds corresponding to cervical, thoracic and lumbar levels, and Vibratome sections made at 60–70 μm.

Multiple levels from 41 spinal cords were available for immunocytochemistry (Table 1). Of these, three levels were available from 31 spinal cords and two levels, from ten spinal cords. Brainstem (mostly medulla) sections from ten cases were studied; sections of upper and lower medulla were available from one specimen of 15 GW. Sections of pons or ponto-medullary junction were available from one specimen each at 11, 15 and 16 GW; sections of midbrain were available from one specimen each at 11 and 16 GW.

Immunocytochemistry

Antibody to MBP was obtained from Boehringer-Mannheim Corporation, Indianapolis, IN, USA, and used at dilutions of 1:800 to 1:1600. Standard methods were used for immunocytochemical staining (Polak & Van Noorden, 1983). Free-floating tissue sections were treated with 0.3% H_2O_2 in absolute methanol for 30 min to block endogenous peroxidase activity. After washing, nonspecific-protein binding was blocked with 5% normal horse serum. The sections were incubated with the primary antibody 16 h at 4° C, with a 4 h period at room temperature thereafter. Primary antibody was detected with the avidin-biotin-peroxidase conjugate method using Vectastain kits (Vector Laboratories, Burlingame, CA, USA) as the source of biotinylated secondary antibody and ABC complex. The manufacturer's instructions were followed. Sections were developed with diaminobenzidine. Stained sections were mounted on glass slides, dehydrated and coverslipped in Permount.

A positive control from a well-myelinated specimen was included in every experiment, as were substitution controls which used antibodies to antigens not associated with myelin including vimentin and glial fibrillary acidic protein (GFAP) (Boehringer Mannheim Corporation). The antibody to vimentin was used at 1:800 and the antibody to GFAP at 1:200. Some sections were also stained with SMI31 antibody (Sternberger Monoclonals, Inc., Baltimore, MD, USA) against a phosphorylated epitope found on medium and high molecular weight neurofilaments. SMI31 was used at a dilution of 1:40 000.

Results

Spinal cord

MBP expression in several anatomic areas of the developing spinal cord is summarized in Table 2.

In the 9–10 GW specimen, several aggregates of MBP-positive material suggestive of the lacy oligodendrocytes described in tissue culture were observed just beneath the ependyma of the mid-portion of the central canal in the upper one-third of the spinal cord (Fig. 1). MBP-positive structures were not observed in the lower levels at this time.

In the ten GW specimens, occasional MBP-positive process-bearing cells consistent with lacy oligo-

Table 2. MBP expression in several anatomic locations between 10 and 20 GW.

GW	Level	*Subependymal area*	*Anterior funiculus*	*Anterior root*	*Anterolateral funiculus*	*Posterior funiculus*
9–10	C	+	0	0	0	0
	T	0	0	0	0	0
	L	0	0	0	0	0
10	C	+	+	0	+	0
	T	+	+	0	0	0
	L	+	+	0	0	0
11	C	+	+	+	+	+
	T	+	+	+	+	+
	L	0	+	0	0	+
12	C	+	+	+	+	+
	T	+	+	+	+	+
	L	+	+	+ (rare)	+	+
13	C	+	+	+	+	+
	T	+	+	+	+	+
	L	+	+	+	+	+
14	C	+	++	+	+	+
	T	+	+	+	+	+
	L	+	+	+	+	+
15	C	+	++	+	++	+
	T	+	++	+	++	+
	L	0	++	+	++	++
16	C	0	++	+	++	++
	T	0	++	+	++	++
	L	0	++	+	++	++
17	C	0	++	+	++	++
	T	0	++	+	++	++
	L	0	+	+	+	++
18	C	0	++	+	++	++
	T	0	+	+	+	+
	L	0	+	+	+	++
19	C	0	++	+	++	++
	T	0	++	+	++	++
	L	0	+	+	++	++
20	C	0	+++	Not seen	+++	++
	T	0	+++	Not seen	+++	++
	L	0	++	Not seen	++	++

GW = Gestational weeks
For the 9–10 GW specimen, *C* = upper third, *T* = middle third, *L* = lower third, as explained in the text. Otherwise, C = cervical, *T* = thoracic and L = lumbosacral.
Explanation of grading: 0 = absent MBP expression; + = few MBP-positive structures; ++ = moderate MBP expression; +++ = marked MBP expression.

dendrocytes were present in the anterior funiculi at the cervical level in all four cases studied (Fig. 2). The anterolateral funiculi contained MBP-positive structures in four out of five specimens. Short, longitudinally-sectioned MBP-positive tubules were found in the region of the anterior roots in three out of five cases (Fig. 2a). The posterior half of the lateral funiculus did not have MBP-positive cells or lamellae, and the posterior funiculi were unstained in all five cases. A spatial gradation of MBP expression was observed; the thoracic levels, at this age, contained less MBP, and the lumbar levels, even less. Myelin basic protein-positive cells could be observed in the subventricular region.

At 11 GW, MBP-positive structures consistent with process-bearing cells could be identified in the posterior funiculi in three out of five cases; MBP-positive cells and processes were present in the anterior funiculi as described above. In addition, rare positive cells were present in the lateral funiculus, especially its anterior half. Only one out of five samples contained a rare positive cell in the posterior half of the lateral

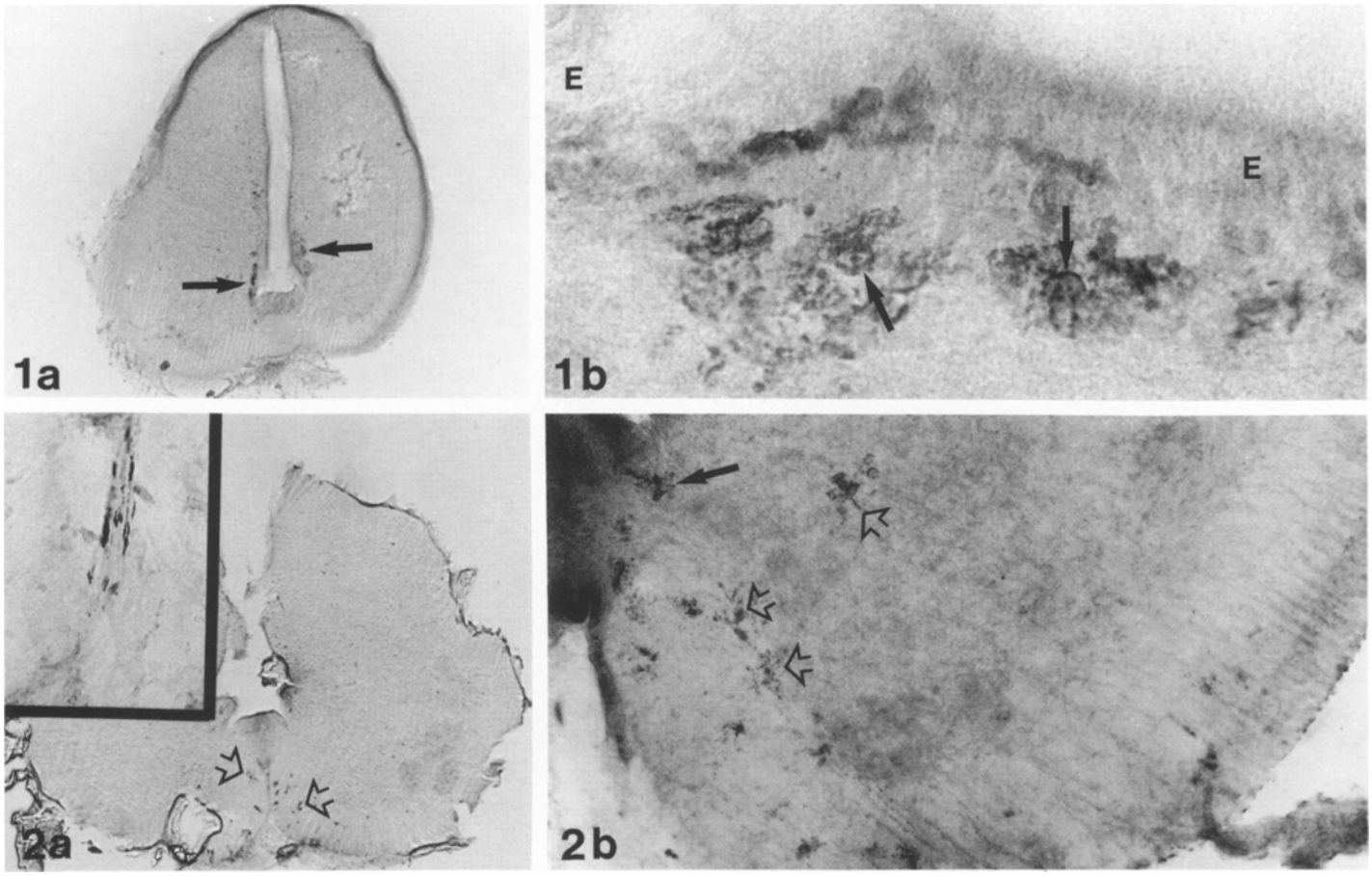

Fig. 1. (a) Differentiated oligodendrocytes (arrows) are present just beneath the ependyma of the central canal of the upper third of the spinal cord in the 9–10 GW specimen. The anterior portion of the spinal cord is inferior. × 30. This and all subsequent figures show sections immunostained for MBP. (b) Detail of MBP-positive cells beneath ependyma (E). Clusters of MBP-positive processes are present, and nuclear outlines are seen (arrows). × 467.

Fig. 2. (a) Myelin basic protein expression in the anterior funiculi of the cervical level of a 10/11 GW spinal cord. The anterior funiculi are inferior in the illustration. Arrows mark the dark-staining oligodendrocytes. × 35. Inset: MBP-positive internodes of the anterior root fibres of an 11 GW cervical spinal cord. × 275. (b) In this picture, the anterior funiculus of the spinal cord is inferior; the anterior median sulcus is at the left side and the lateral funiculus, at the right side. The anterior funiculus of 10 GW spinal cord contains MBP-positive cells (open arrows). The open arrow furthest to the right shows a positive cell in the grey matter. At the long arrow, a positive cell is noted just beneath the ependyma of the central canal. These cells have the morphology of so-called 'lacy oligodendrocytes' described in tissue culture. × 133.

funiculus. More MBP was expressed at the cervical and thoracic levels of the spinal cord than at the lumbosacral level (Fig. 3).

Between 11 and 14 GW, there was a gradual increase in the numbers of oligodendrocytes and myelin tubules in all three funiculi (Fig. 4). At a given level of the spinal cord, more MBP-positive structures were always present in the anterior and anterolateral white matter than in the posterior funiculi and the posterior part of the lateral funiculi. Also, the cervical and thoracic levels contained more MBP-positive cells than the lumbosacral level. Occasional MBP-positive cells could be observed in the subependymal area.

By 15 GW, more MBP was present in the anterior and anterolateral white matter than in the more posterior white matter at any given level, and MBP expression was greater in the cervical and thoracic levels of the anterior and anterolateral funiculi than at the lumbosacral level. The anterior funiculus of the cervical level showed a uniform distribution of MBP-positive oligodendrocytes and myelin lamellae (Fig. 5a). More MBP-positive cells were present in the anterior half of the lateral funiculus than in its posterior half. In the posterior funiculi, the cuneate fasciculus had many interwoven MBP-positive processes and numerous lacy oligodendrocytes, but the gracile fasciculus contained only scattered MBP-positive oligodendrocytes (Fig. 5a). The thoracic level showed a uniform distribution of MBP-positive structures in the anterior and anterolateral funiculi (Fig. 5b), and the

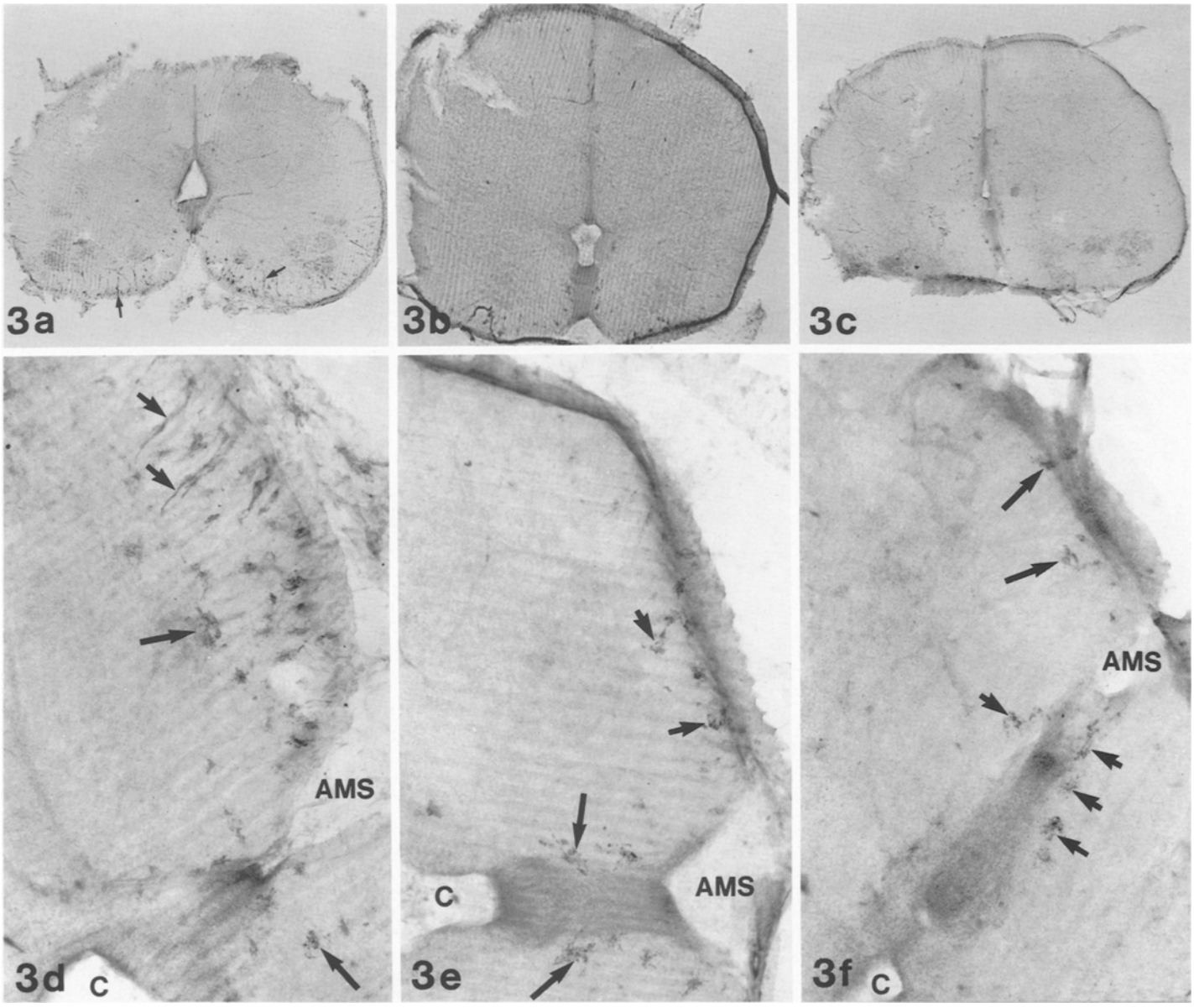

Fig. 3. Spinal cord (11 GW). In (a), (b) and (c) the anterior funiculi are inferior. (a) At the cervical level, dark MBP positive cells are present in the anterior and lateral funiculi. Elongated dark structures (arrows) are the anterior root fibres. × 25. (b) Fewer MBP-positive cells are seen in the anterior and anterolateral funiculi of the thoracic spinal cord. × 35. (c) Very few MBP-positive cells are visible in the anterior funiculus at lumbar level. × 27. (d) Detail of anterior and anterolateral funiculus at cervical level showing MBP-positive oligodendrocytes (long arrows) and short myelinated segments of anterior roots (short arrows). C indicates central canal and AMS marks the anterior median sulcus. × 114. (e) Similar view of thoracic cord. There is less MBP expression than at the cervical level. Long arrows mark oligodendrocytes adjacent to the anterior portion of the central canal (C), and short arrows mark oligodendrocytes ventrally (adjacent to a fold in the tissue). × 122. (f) Similar view of lumbosacral spinal cord. Even fewer MBP-positive structures are present. Short arrows mark some oligodendrocytes adjacent to the anterior median sulcus and long arrows mark more ventral oligodendrocytes. × 140.

posterior funiculi contained discrete oligodendrocytes and short MBP-positive myelin tubules; the cuneate tract contained more MBP than the gracile tract. The posterior half of the lateral funiculus had very little MBP. The lumbar levels contained oligodendrocytes and myelin tubules in all three funiculi (Fig. 5c), and there were more MBP-positive structures at this age than previously. Interestingly, the gracile tract contained more MBP a the lumbosacral level than at the cervical and thoracic levels. Occasional MBP-positive cells couls be seen in the subependymal area.

At 16 GW, there was a spatial gradient in MBP expression from the cervical level caudally in four out of five cases. The fasciculus gracilis was the single

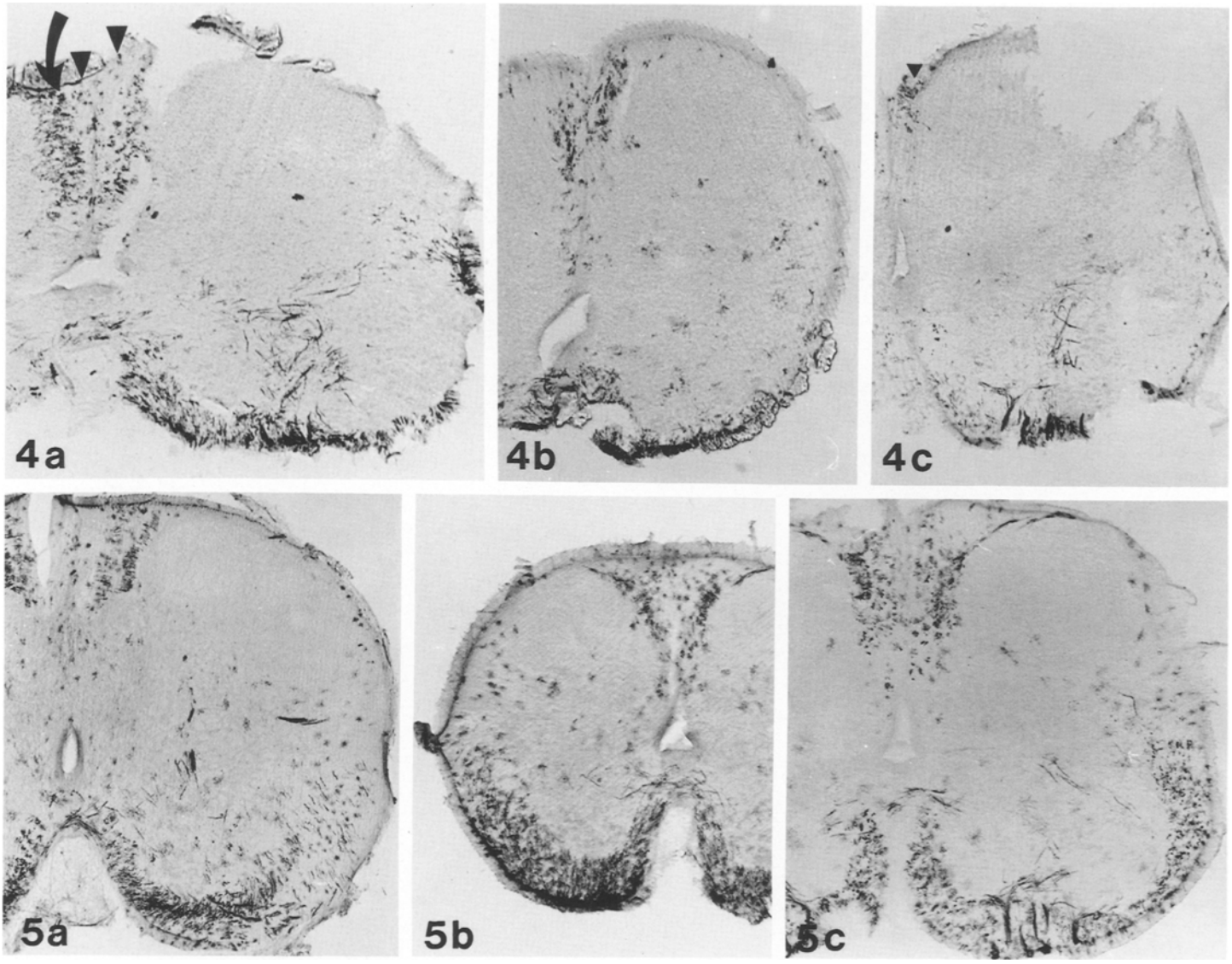

Fig. 4. Spinal cord (14 GW). Anterior funiculi are inferior in this and all subsequent illustrations. (a) At the cervical level, the anterior and anterolateral funiculi contain numerous myelinated fibres, and the posterior funiculi contain MBP, but to a lesser extent. The fasciculus cuneatus (arrow) has more MBP reaction product than the fasciculus gracilis (arrowheads). × 41. (b) At the thoracic level, more reaction product is present in the anterior than the lateral funiculus. There is edge artefact ventrally. × 39. (c) The lumbar level contains less MBP than the more rostral levels. Small amounts of MBP are present in the fasciculus gracilis (arrowhead). × 35.

Fig. 5. Spinal cord (15 GW). (a) At high cervical level, more MBP is present anteriorly than laterally. The fasciculus cuneatus contains MBP-positive fibres, while the fasciculus gracilis has short fibres and cells. A portion of the anterior funiculus not expressing MBP probably corresponds to the crossing of the pyramidal tracts and/or the anterior corticospinal tract. × 29. (b) An anterior-posterior gradient is seen at the thoracic level. In this specimen, it is difficult to see a difference in amount of MBP expression between the cervical and thoracic levels. There is edge artefact ventrally. × 30. (c) MBP expression is less intense at the lumbar level than at more rostral levels. × 37.

Fig. 6. Spinal cord (20 GW). The intensity of MBP expression is similar at all three levels. (a) This high cervical level includes fascicles of the spinal accessory nerve (arrows). The pale area in the anterior funiculus (arrowhead) represents the site of crossing fibres of the corticospinal tract. The pale fasciculus gracilis contrasts to the well-myelinated fasciculus cuneatus at the cervical level. × 28. (b) At the thoracic level, a pale region of the lateral funiculus (arrow) corresponds to the future corticospinal tract. × 39. (c) At the lumbosacral level, the fasciculus gracilis contains much MBP. The posterior portion of the lateral funiculus, the ending of the future corticospinal tract, is paler than the rest of the lateral funiculus. × 32.

Fig. 7. At 10 GW, only a few lacy oligodendrocytes (arrowheads) are seen in the midline of the medulla. × 115.

Fig. 8. By 12 GW, many oligodendrocytes are seen in the midline and a few laterally. × 28.

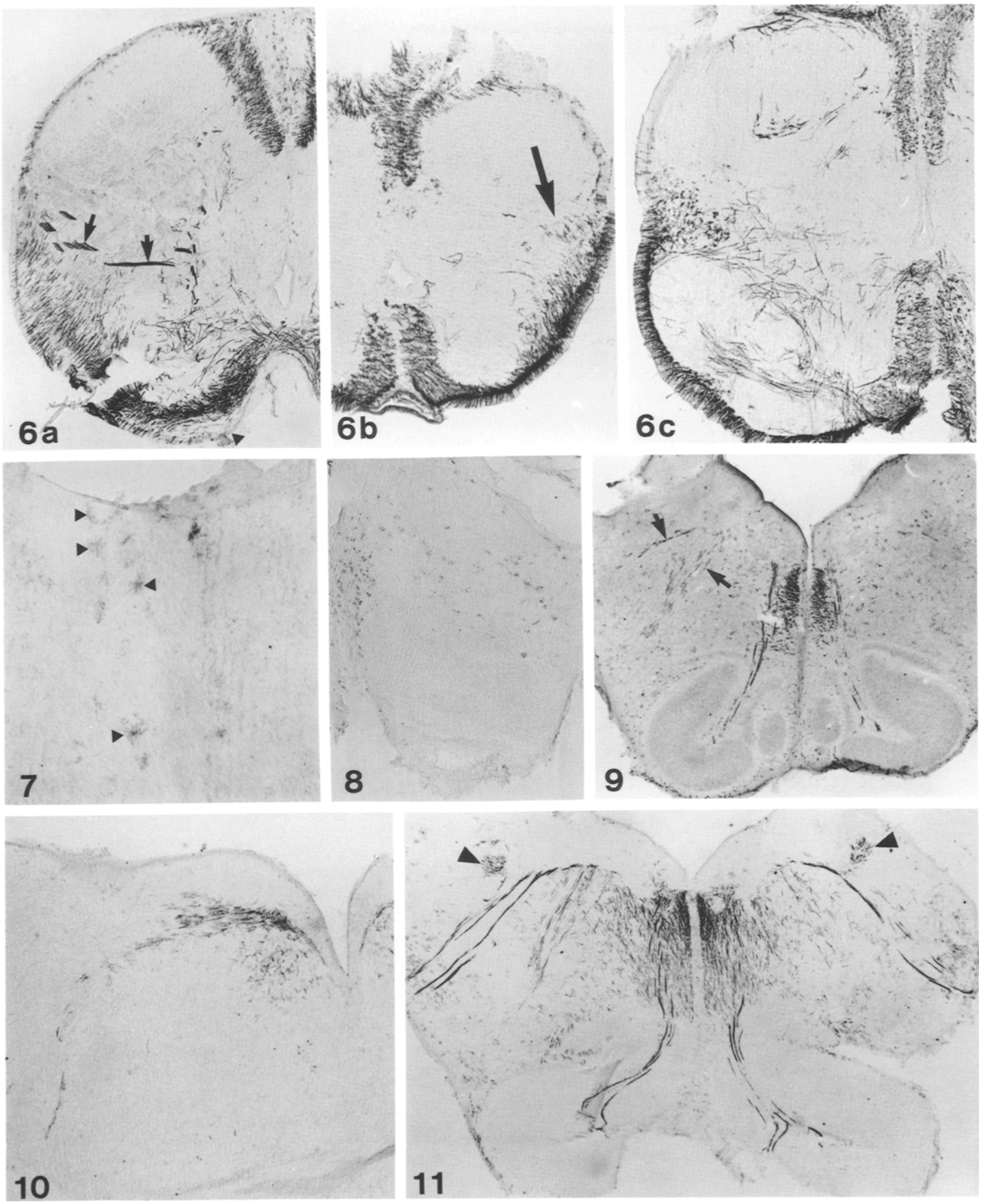

Fig. 9. At 15 GW, the medial longitudinal fasciculus, and fascicles of cranial nerves X (arrows) and XII are easily identified. × 14.

Fig. 10. A section of pons from a 16 GW specimen shows the facial nerve looping around the MLF. × 18.

Fig. 11. At 20 GW, cranial nerves X and XII are easily found. Fibres of the vestibular nerve are myelinated bilaterally (arrowheads). The MLF is well-myelinated and the medial lemniscus expresses MBP in its ventral half. Many lacy oligodendrocytes are present in the reticular formation. × 12.

exception to the rostro-caudal gradient of MBP expression; here, MBP was expressed more strongly at the lumbosacral than the cervical and thoracic levels. In addition, when the spatial distribution of MBP was observed at any given level of spinal cord, the previously observed anterolateral to posterior gradient of MBP expression was much less marked than it had been in the younger specimens. Myelin basic protein-positive cells were not localized to the subependymal area around the central canal.

From 17 to 20 GW, there was a gradual increase in MBP expression in all areas of the spinal cord. It became difficult to distinguish the three levels of the cord on the basis of density of MBP expression (Fig. 6). However, the posterior portion of the lateral funiculus, the site of the future lateral corticospinal tract (CST), and the cervical portion of the fasciculus gracilis expressed very little MBP even at 20 GW (Fig. 6). Myelin basic protein-positive cells did not localize to the subependymal area.

During the period from 10 to 20 GW, it was not possible to distinguish the various functional tracts of the spinal cord, with the exception of the unmyelinated anterior and lateral CST. After 15 GW, the fasciculus cuneatus could be distinguished from the fasciculus gracilis which expressed more MBP at the lumbosacral levels (Figs 5, 6). In some specimens, the anterior spinal roots and dorsal roots could be observed. Anterior root fibres contained MBP beginning at 11 GW (Fig. 3d). Dorsal root fibres were delineated by this method between 12 and 14 GW.

Lacy oligodendrocytes and short myelinated segments were scattered randomly in the grey columns beginning at 12 GW and increased in number as development proceeded.

Brainstem

At 10 GW, a few lacy oligodendrocytes were observed in the midline of the medulla dorsally in the region of the medial longitudinal fasciculus (MLF) and medial lemniscus (Fig. 7).

By 11 GW, lacy oligodendrocytes were present in the midline of the medulla, pons and midbrain. Despite examination of corresponding sections stained for neurofilaments, which permitted identification of nerve fibre bundles, it was not possible to identify the tracts containing myelin with any certainty; they probably represented the future MLF in the medulla and pons, and the third cranial nerve in the midbrain.

By 12 GW, short myelinated segments formed a fibre bundle in two out of four cases in the midline of the medulla in the MLF (Fig. 8). A collection of lacy oligodendrocytes was present in the medial lemniscus. In the other two cases, aggregates of lacy oligodendrocytes marked the location of the MLF. In addition, fascicles of the hypoglossal nerve could be identified in two out of four cases. Fascicles of the vagus nerve were observed in one out of four cases. The fasciculus gracilis contained lacy oligodendrocytes. Also, lacy oligodendrocytes were present in the neuropil laterally (Fig. 8).

The 15 GW specimens included one specimen with a section of medulla and one specimen with sections of medulla and cervico-medullary junction. Again, myelinated fibres were seen in the MLF and hypoglossal and vagus nerves (Fig. 9). Lacy oligodendrocytes were seen in the medial lemniscus and lateral grey matter. At the cervico-medullary junction, fewer MBP-positive structures were seen in the dorsal columns than in the cervical spinal cord.

At 16 GW, MBP expression in the medulla was not significantly different from that at 15 GW. At the ponto-medullary junction, the facial nerve could be identified near the MLF (Fig. 10); there were scattered lacy oligodendrocytes lateral to the facial nerve. In the midbrain, a few scattered lacy oligodendroglia were present.

At 20 GW, MBP expression was more extensive in the medulla (Fig. 11), and major landmarks, including cranial nerves X and XII, a portion of the vestibular nerve, the MLF and the dorsal half of the medial lemniscus, were easily identified.

Discussion

The results of this study further the understanding of the development and differentiation of human oligodendrocytes and myelin. It is of interest to note that MBP-positive structures can be identified as early as 9–10 GW in the subependymal region of the HFSC. These findings might suggest that oligodendrocytes may originate from progenitor cells in this area; the work of others in rodents (LeVine & Goldman, 1988a,b; Warf *et al.*, 1991) supports this idea. In this connection, MBP has been identified in rat oligodendrocytes before the onset of myelination (Sternberger *et al.*, 1978). However, if this theory is applicable to the HFSC, a greater concentration of MBP-positive cells might be expected in this area than was noted. Elucidation of this point will require additional work using other markers of oligodendrocyte differentiation.

By ten GW, MBP-positive oligodendrocytes are observed in the anterior and lateral funiculi of the HFSC. Myelin basic protein expression appears to increase rapidly and by 11 GW, the posterior funiculi also contain oligodendrocytes and anterior root fibres can be identified. Positive dorsal root fibres are seen at 12–14 GW, and scattered lacy oligodendrocytes are present in the grey matter from 12 GW onward. The lateral CST is largely unmyelinated during the second trimester, though rare MBP-positivity is present in this

tract. Myelin basic protein expression increases in all locations during the remainder of the second trimester. During this time, expression is more intense at the cervical level than at the thoracic or lumbar levels in the anterior and anterolateral funiculi. In the fasciculus gracilis, MBP expression is more intense at the lumbosacral levels of the spinal cord. There is also more MBP expression in the anterior and anterolateral funiculi than in the posterior and posterior half of the lateral funiculi at any given level.

In general, the spatial gradient of myelination in the HFSC is rostral to caudal and antero-lateral to dorsal; the differences are more marked earlier in gestation, and are difficult to detect after 16 GW. This pattern is similar to that observed in other animals (Langworthy, 1928; Romanes, 1947; Bensted *et al.*, 1957; Barlow, 1969; Schwab & Schnell, 1989; Warf *et al.*, 1991). Most earlier studies of human myelination in foetuses of these ages have merely mentioned that myelin is present in the spinal cord without investigating its spatial distribution or increase over time (Gamble, 1969; Choi, 1981; Choi & Kim, 1984, 1985; Tohyama *et al.*, 1991). However, studies of older human specimens have suggested that the spatial-temporal gradient of spinal cord myelination does proceed as discussed above (Langworthy, 1933; Gilles *et al.*, 1983).

Myelin basic protein is also expressed in the MLF of the medulla and in the pontine midline during the late first and early second trimester. In the older specimens of medulla, a few fascicles of the hypoglossal and vagus nerves contained MBP by 12 GW, and lacy oligodendrocytes could be seen in the medial lemniscus, fasciculus gracilis, and reticular formation as well. The variability in MBP expression observed in the brainstem may reflect biological variability in myelination, as previously noted by others (Rorke & Riggs, 1969; Gilles *et al.*, 1983). A similar variability was observed in the spinal cord sections.

No differences in MBP expression are found among the several ascending and descending tracts of the anterior and anterolateral white matter of a given level of the spinal cord during the late first and second trimester. This finding suggests that myelination in the HFSC may be independent of axonal growth, at least in some tracts. However, separate foci of MBP expression are observed in the brainstem midline, representing early myelination of the MLF, medial lemniscus and tenth and twelfth cranial nerves. The factors responsible for the induction of MBP expression in the CNS are uncertain, and multiple signals may be involved (Schwab & Schnell, 1989). Although some investigators have isolated an oligodendroglial growth factor from neuronal cell lines, the relationship of this factor to myelination *in vivo* requires further investigation (Giulian *et al.*, 1991).

Myelin basic protein is expressed earlier and to a much greater extent in the white matter of the HFSC and brainstem than in the grey matter. Indeed, except for cranial and spinal nerve roots, only scattered lacy oligodendrocytes were observed in the grey matter during the study period. Again, this observation is in accord with previous work in mice (Jordan *et al.*, 1989).

This study not only provides new and additional information about myelination in the normal human foetal spinal cord, but also provides normative data against which pathological conditions can be measured. Biological differences in oligodendrocytes and myelin in the several spinal cord tracts, as shown by their differing patterns of expression and kinetics of myelination, could be reflected in their selective vulnerability to various types of injury. This last point may have special significance for the understanding of dysmyelination, demyelination and the neuropathology of paediatric AIDS.

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