

XXXVI.—The Middle Cells of the Grey Matter of the Spinal Cord.

By J. H. Harvey Pirie, B.Sc., M.D., M.R.C.P. Ed. Abstract of Thesis for the Degree of M.D. Edin. Univ., 1907. (*From the Pathological Department of the Royal Infirmary, Edinburgh.*) Communicated by Dr ALEXANDER BRUCE. (With Two Plates.)

(MS. received February 6, 1908. Read February 17, 1908.)

THESE cells were first described and recognised as a separate and distinct group by Waldeyer (1). From his paper the following notes are taken:—“The middle cells are found at the junction of the anterior and posterior cornua, but especially in the former. They are small and medium-sized polygonal cells, arranged sometimes in a fairly compact group, sometimes more loosely scattered over a wider area. They are never so closely aggregated as are the cells of Clarke’s column or those of the intermedio-lateral tract (Seitenhorn), but they are close enough to be regarded, especially in the upper cervical region, as a special nucleus of cells. Their situation varies somewhat in the different regions of the cord. As a group, they are most distinct in the upper cervical region. They lie here closely compacted to the outer side of, or a little in front of, Clarke’s column. In the lower cervical region they form a less distinct group near Clarke’s column, but quite internal to the postero-lateral motor group. In the upper dorsal region they are also abundant. They are situated laterally, and even somewhat posteriorly, to Clarke’s column, extending into the posterior horn and into the scattered cells (Zerstreuungszellen) of the anterior cornu without a distinct limit. They are always quite distinctly internal to the margin of the grey matter. With the growth of Clarke’s column in the dorsal cord the middle cells become fewer. In the lower dorsal region they again become more numerous, no longer form a distinct group, but are more in their former position on the outer or antero-external aspect of Clarke’s column, in great numbers. Similarly in the lumbar cord, though less abundantly developed. In the sacral cord there is a group of cells which, from their character and situation, are probably middle cells, but at this level no characteristic distribution of the various cell groups is recognisable.”

Other small cells in the grey matter of the cord named by Waldeyer must also be referred to. His account of the intermedio-lateral tract is sufficiently noticed in Bruce’s paper on that tract (2). The cells which he

calls "scattered cells" (Zerstreutenzellen) "form no definite group. They are situated—(1) in the anterior horns; (2) in the neighbourhood of the central canal; (3) in the Rolandic substance of the posterior horns; (4) in the white matter."

Those in the anterior horn and in the neighbourhood of the central canal I have not been able definitely to separate from the middle cells, and have included them in my description of that group. But, for clearness, the small cells in the anterior horn are sometimes referred to as the scattered cells; those in the neighbourhood of the central canal as the para-central cells—using topographically a term introduced by Onuf and Collins (3), without meaning to convey that they are the same cells which these authors describe (in the cat) as lying "ventrad of Clarke's column, on each side of the central canal, and showing in longitudinal sections a segmented arrangement." In man, they further state that "this group seems to have lost its individuality and to form part of Clarke's column, except at certain levels (upper dorsal and middle sacral) where a cell group is seen which apparently corresponds to the para-central group, although situated considerably more laterally than in the cat." Elsewhere they speak of the cells of the intermediate zone (apparently the middle cells) as "for the most part small, approaching in shape and structure to the cells of the lateral horn and of the para-central group."

Waldeyer classified the small cells of the posterior horn which "lie posterior to the level of the hindmost part of Clarke's column, but do not form any well-marked group, and are not always present, as (1) Basal, (2) Central, (3) Marginal. They are seldom or never all present together, and are never in large groups, often only single cells, or at most two or three cells. The Basal cells lie immediately behind Clarke's column, middle cells, and lateral horn cells; the Central cells in the posterior horn nucleus; the Marginal cells on the inner and outer borders respectively of the posterior horn, the inner being apparently the more abundant." I have been much puzzled over these cells in the foetal cord: sometimes they can be distinguished according to Waldeyer's subdivisions, but very often it is impossible to separate them from the reticular group of the intermedio-lateral tract, on the one hand, and from the middle cells, on the other. In appearance and size they are all much alike; and as regards position, the outer marginal cells might be simply a continuation backwards of the reticular group, while the basal, and sometimes even the more central and inner marginal cells, are often directly continuous as a group with the middle cells. I have observed at all levels of the cord, but especially in the lumbar segments in all of the situations of these posterior horn cells, certain large

cells, resembling, both in size and appearance, the motor cells of the anterior cornua. They are usually single, but, rarely, two may occur together.

Argutinski's observations (4) must now be referred to. His description of the middle cells of the new-born child is fuller than that of Waldeyer, but differs from his in several points. In particular, he finds a regular and sharply defined segmentation of the middle cell column, but limits the system to the dorsal portion of the cord. After a careful and thorough examination of the spinal cord both in longitudinal and in transverse sections—including serial sections of a complete cord—I am convinced that this segmentation of the middle cells does not exist, and, further, that what Argutinski has described is the reticular group of the intermedio-lateral tract. His description is too long to quote in its entirety; briefly, it is that of a double chain of segmented cell columns (*Seitenhornzellen* and *Mittelzellen*), limited to the dorsal portion of the cord, the segmentation of the two columns being parallel, but sharper in the middle cell group. His description is based principally on the examination of longitudinal sections, although, as he himself states, conclusions as to position can only be drawn from transverse sections. That this double chain exists I fully admit, but I hold that it is formed of the two constituent groups of the intermedio-lateral tract, and not of the middle cells and lateral horn cells. Waldeyer, as pointed out by Bruce, includes the reticular group of cells in his *Seitenhornzellen*. Argutinski does not do so; he only includes the apical group of the intermedio-lateral tract under that heading. If, throughout his paper, we read for "*Seitenhornzellen*," apical cells or apical group, and for "*Mittelzellen*," reticular cells or reticular group, we get an excellent description of the complete intermedio-lateral tract. The points of agreement between his "*Mittelzellen*" and the reticular group of cells as described by Bruce (whose observations I entirely corroborate, except in some small points, probably due solely to the difference in age of the subjects from whom the cords were obtained) are as follows:—

- (1) Longitudinally limited almost to the dorsal portion of the cord.
- (2) Lie very near to the lateral horn cells (apical group), sometimes even in direct contact with them.
- (3) Lie posterior and internal to the lateral horn cells, usually close to the re-entrant reticular angle.
- (4) Direction of cells—chiefly inwards and forwards.
- (5) Shape of cells—like the lateral horn cells (apical group), but broader.
- (6) Parallel segmentation of the apical and reticular groups (*Seitenhorn-* and *Mittelzellen* of Argutinski), the segmentation being a much sharper one in the latter of the two groups.

There are two points of non-agreement in the description:—

1. Argutinski's middle cells never approach quite close to the lateral columns—a point which he insists on strongly, as distinguishing them from the Seitenhornzellen. Well, in the cord of the new-born I find that the reticular group not infrequently does lie a little way from the edge of the grey matter, sometimes even a considerable distance (particularly in D 3 and D 12). Moreover, from the shape which the reticular group so often has, it is obvious from the accompanying diagram (fig. 1) that many frontal longitudinal sections would show the reticular group quite internal to the edge of the grey matter. But I cannot agree with nor explain his statement that the group *never* approaches quite to the lateral columns.

2. He describes his cells as sometimes departing from their usual

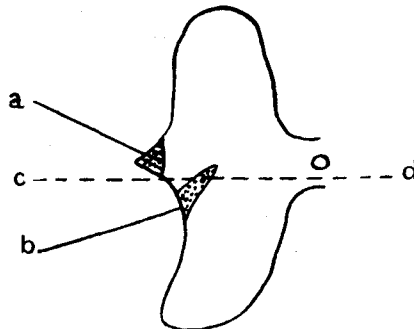


FIG. 1.

- a.* Apical group of the intermedio-lateral tract.
- b.* Reticular group of the intermedio-lateral tract.
- c.d.* Line of a frontal longitudinal section which would show the reticular group quite internal to the edge of the grey matter, and in a position more usually occupied by middle cells.

position, and being found more or less mesially, or even in the region of the anterior horn cells or Clarke's column cells, and that all transitions may be found between these positions. It is obvious that here he must be referring to the real middle cells of Waldeyer, and I am in complete agreement with this statement. But when he says, further, that if the cell group is seen lying closer to the middle line, his middle cell group (reticular group) is absent from the usual place, I must part company from him, and can only differ without explaining. But certainly I have often observed a reticular group in its usual situation and a group of middle cells present in another part of the same section.

So far as I am aware, no other writers have given any further account of the middle cells of the spinal cord.

The present investigation was made on the spinal cord of a full-time healthy foetus. The cord was hardened in absolute alcohol and divided

into root segments by cutting transversely just below the lowest fibre of each nerve root. The segments were embedded in paraffin and each cut into serial sections; the sections were then stained with Giemsa's stain (azure blue and eosin). Special means were taken to see that each segment was cut and mounted so that the sections were numbered serially from above downwards, and that there was no confusion between right and left sides. There were in all nearly 16,000 sections. At first, when the possibility of the middle cells having a segmented arrangement was before me, I attempted to enumerate them, with the idea of representing the numbers graphically, but it soon became evident that no such segmented

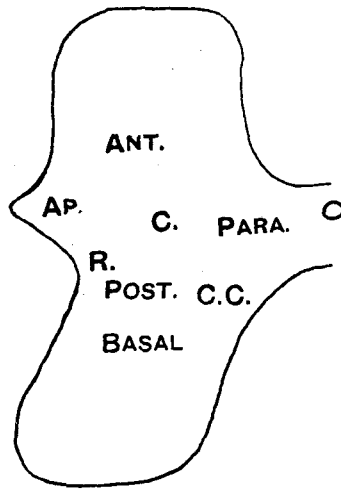


FIG. 2.

- | | |
|--|---|
| C. = Central area. | C.C. Clarke's column area. |
| ANT. Anterior central area in the base of the anterior horn. | Postr. Post-central area. |
| PARA. Para-central area. | R. Reticular area and area of the formation of the reticularis. |
| AP. Apical or lateral horn area. | BASAL. Posterior basal area. |

character existed; and further, that the task of counting all the cells was too herculean to attempt. I therefore contented myself with noting the position and arrangement of the middle cells throughout the whole series of sections, summing up the results for each 25 as I went along, and again for each segment. By this method, I consider, a very accurate idea of their distribution has been obtained.

Some difficulty was felt with regard to nomenclature and division of the grey matter into areas. Waldeyer recognises three regions of the grey matter: a free anterior horn, a middle region, and a free posterior horn. The middle region is defined as including the central canal with transverse commissures, the lateral horn, the region of the middle cells, and Clarke's column. Everything in front is the free anterior horn; everything

behind, the free posterior horn. But it is evident that to describe in detail the position of the middle cells, some other plan must be adopted; and the terms which I have used in the description are best explained by reference to the accompanying diagram (fig. 2).

At most levels these different areas or regions can be recognised, but they are quite arbitrary, and only employed for topographical convenience, and it seems futile to attempt to define any exact boundaries for them. The middle cells are certainly not in the least regardful of boundary-line between these regions. In the cervical and lumbo-sacral enlargements there is, of course, no apical region; Clarke's column, though not always represented by cells of that column, still has its "area" there; in addition, an external central area might perhaps be added. I shall now go on to the description of the middle cells as found in the various segments of the cord.

C 1.—See fig. 3.—Vary considerably in number, on the whole fairly abundant, either scattered diffusely or in loose groups. In the base of the anterior horn always some scattered cells. The commonest group is a central one, tending to extend into the basal area, and especially into the para-central area; may be 30 or more cells, forming a not very compact group. Frequently a small group in the position corresponding to that of the lateral horn. Merely a few scattered cells in the reticular formation, post-central area, and region of Clarke's column. The cells vary in size in all areas; those in anterior horn on the whole larger than the others, and sometimes with difficulty distinguished from motor cells, but they are never in such compact groups. They are all of polygonal or rounded polygonal outline, and their mode of occurrence is typical, *i.e.* irregular and casual—any group that may be found can never be traced through more than three or four sections at most; there is never any sign of regular segmentation such as is seen in the intermedio-lateral tract of the dorsal region.

C 2.—Cells fewer in number than in C 1. A central group of from 12–15 cells is a very common feature of the segment; in fact, for long stretches it seems to be almost constant, particularly on the right side. Sometimes it is more para-central than central. A small group at or just in front of the apex—such as it is—of the lateral horn is also common. In the other areas their appearances are much as in C 1.

C 3.—See fig. 11, Plate I.—Cells not very abundant, characteristically scattered, sometimes thickly, more often thinly. Small aggregations may be found in the area of Clarke's column, the post-central region, and in the base of the anterior horn, either near the outer edge or nearer the centre, but none of them are very compact or very large. A central or central-

para-central group is the most common. In other regions only scattered cells occur. In size they appear to be of mixed sizes in all areas; their distribution lengthwise is typical of the middle cells—here one section, gone the next.

C 4.—The description given of C 3 applies practically unchanged to this segment, although, with the growth of the lateral motor group, the middle cells disappear from the outer portion of the base of the anterior horn, but they may still be seen between the motor nuclei. On the whole, the cells are both rather more numerous and rather larger than in C 3,

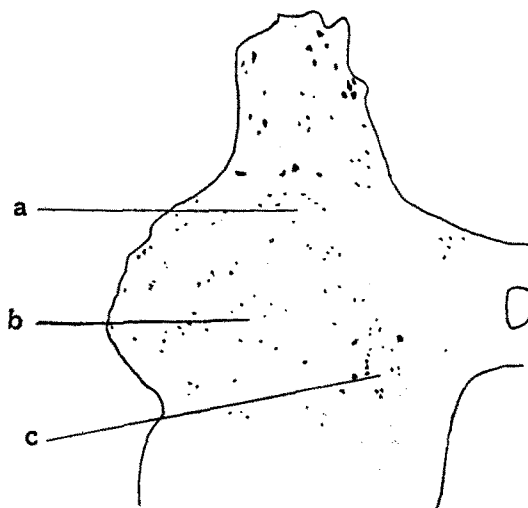


FIG. 3.*

C 1—162 L ($\times 33$).

- a. Scattered cells in the base of the anterior horn.
- b. Middle cells scattered over the area of the lateral horn and the reticular formation.
- c. Group of middle cells in the posterior part of the central-para-central area, including a few of larger size than elsewhere, all the others being small.

particularly the more anterior cells, though here also the difference in size between these and the others is not at all marked.

C 5.—Cells increasing in number, descending the segment, also tending to be more grouped. Anterior to the frontal plane of the central canal few and scattered, but often of larger size than elsewhere, sometimes not much smaller than motor cells. In the reticular formation, scattered at first and sometimes outlying in the white matter, oftener small groups in the lower part. A central group more often in upper part than in lower. In lower part of the segment frequently a well-marked band of cells stretching

* These figures in the text are traced from photographs, and give exact position of cells and approximately their relative sizes and shapes. The numbering is as follows:—C 1—162 L means the 162nd serial section from the top of the first cervical segment, the left side.

through the reticular and post-central areas to the central or even para-central region. Along this band, aggregations of cells may be present in any part, most often post-centrally. Very few in the region of Clarke's column. Inconstancy of their appearance a typical feature, as always. Medium and small-sized cells mixed, the more anterior being generally larger than the others.

C 6.—See fig. 12, Plate I.—Cells, on the whole, abundant. In individual sections they may be few or many, scattered or grouped. Most numerous about junction of central and post-central areas (these two regions are not very distinct in the cervical enlargement). A small reticular group also common. More often, simply scattered cells in the other areas. There is a distinctly large proportion of big cells in this segment, not only anteriorly, but also more posteriorly, although here they are mingled with others, smaller and more rounded than polygonal in outline.

C 7.—Cells abundant, especially along a broad band from the reticular angle to the central canal, but particularly, as in lower C 6, in the post-central areas. More often, just scattered cells anteriorly and in Clarke's column areas, although there are often cells lying rather behind the region of Clarke's column (posterior basal?). No trace of any regular segmentation. In size and shape the anterior cells are fairly large and polygonal, the central and post-central of large and medium sizes, the reticular and posterior basal medium-sized and more rounded.

C 8.—See fig. 4.—Upper part as in C 7. In the lower, cells diminish in number and are more scattered, although small groups may be seen in any of the usual positions. In the lower, also, middle cells are more often seen lying between the anterior and lateral motor nuclei. In size they are much as in C 7. Cells are not more common in the reticular formation, nor is there any sign of segmentation or special grouping here. Very few cells in region of Clarke's column.

D 1.—Cells of the bigger type in base of anterior horn and (in upper part) between median and lateral motor groups. Medium-sized cells in central, para-central, and post-central areas, also in the *formatio reticularis*, also a few at the base of the posterior horn. Most abundant, and often persisting through a number of sections, just internal and a little anterior to the reticular angle, but never so closely packed as the cells of the *intermedio-lateral tract*. The medium-sized cells individually closely resemble those of that tract, and sometimes it is impossible to say to which series any particular cell is to be allotted. Many of the post-central cells behind and external to Clarke's column are of a smaller, more rounded type.

D 2.—See fig. 5.—Anterior cells, sometimes in small groups, but usually scattered. On the whole, larger than the others, but cannot be definitely separated from the central middle cells either by this or by another feature which helps to distinguish them, viz. the fact that they are often elongated along one axis. The long axis may have any orientation. The other middle cells may be scattered thickly or thinly, but often small, but not very compact, groups of from 6 to 18 cells are seen. Groups, when traced through two or three sections, often disappear or shift in position—there is no constancy. A central group is the most common, next most a post-central,

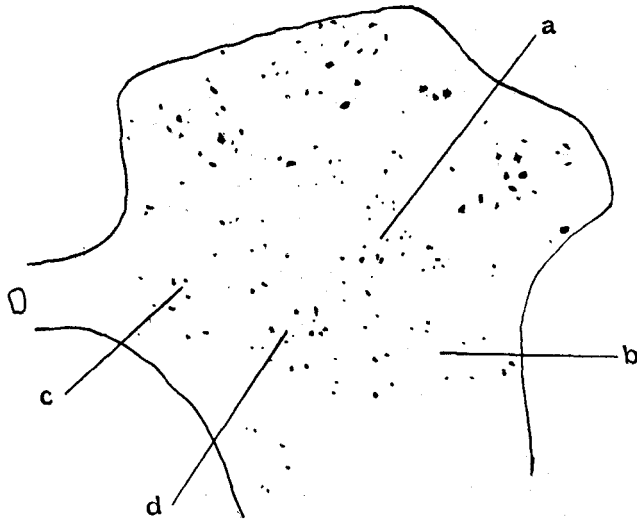


FIG. 4.

C 8—88 R ($\times 32$).

- a. An external central group of middle cells, extending between the motor groups.
- b. A few cells in the reticular area.
- c. Small para-central group.
- d. Central post-central group.

A few small cells in area of Clarke's column and anterior "scattered" cells.

on the outer side of and behind Clarke's column. In the upper part more especially there are often cells in the reticular formation which, from their size, character, and casual occurrence, are probably not cells of the intermedio-lateral tract, but middle cells. In appearance and size, however, the individual cells are very much alike.

D 3.—Cells erratically distributed as usual, sometimes scattered, sometimes in small groups. Chiefly polygonal, about the same size as those of the apical group of the intermedio-lateral tract, but staining rather more darkly; others smaller, and rather more rounded in central and post-central areas. In base of anterior horn they are not markedly larger than else-

where, but are frequently elongated in one direction. Both central and post-central cells are sometimes with difficulty separated from the reticular group of the intermedio-lateral tract, especially when there are isolated cells of the latter group left stranded in the central area, a feature which is not uncommon in this segment.

D 4.—See fig. 13, Plate II.—Appearances very much as in D 3. Central grouplets are the commonest, but para-central and post-central are not uncommon. In other regions they are chiefly just loosely scattered cells.

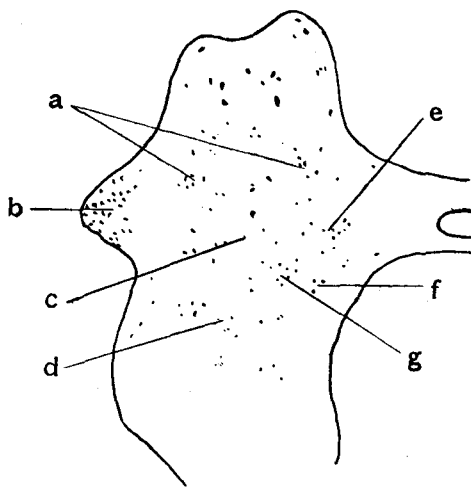


FIG. 5.

D 2—173 L ($\times 32$).

- a. Two small groups of anterior middle cells.
- b. Apical group of intermedio-lateral tract.
- c. Scattered middle cells in central area.
- d. Posterior basal cells, indistinguishable from middle cells.
- e. Para-central group of middle cells.
- f. Three cells of Clarke's column.
- g. Post-central group of middle cells.

D 5.—Anterior scattered cells, not abundant; they vary considerably in size, and at times it is difficult to distinguish some of them from motor cells, on the one hand, and from reticular group (intermedio-lateral tract) cells, on the other. In other regions, also, not abundant; may be disposed anywhere around the whorl of fibres surrounding Clarke's column, in front as a para-central group, to the outer side or even behind as a central or post-central group. The occurrence of any group is, as usual, short-lived. Most cells are distinctly polygonal; the anterior often have one long axis, while some of the central and post-central are almost rounded.

D 6.—Cells nowhere numerous. Usual erratic distribution, scattered or grouped; small groups in base of anterior horn or centrally are probably the most frequent. With the still further relative increase in size of

Clarke's column, the post-central cells are often crowded into the form of a band on the outer aspect of Clarke's column.

D 7.—See fig. 6.—Middle cells appear to be relatively, though not absolutely, abundant in this segment. In appearance, they are practically indistinguishable from apical group cells of the intermedio-lateral tract. The post-central cells, which may extend to quite behind Clarke's column, or into the formatio reticularis in the absence of the reticular group cells, are frequently of the smaller, more rounded type.

D 8.—Similar to D 7. Cells moderately abundant, and with all the usual characteristics—erratic, irregular distribution, scattered thickly or thinly, or aggregated into loose groups in any of the possible sites.

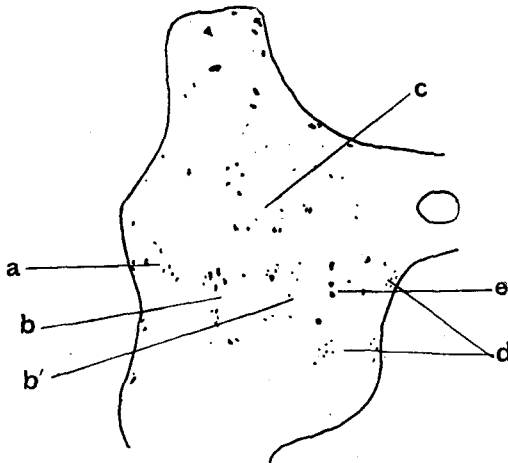


FIG. 6.

D 7—438 L ($\times 40$).

- a. Intermedio-lateral tract—a few cells only.
- b. Large post-central middle cells.
- b'. Small post-central middle cells.
- c. Scattered middle cells in anterior and central areas.
- d. Small cells behind and to inner side of Clarke's column.
- e. Clarke's column.

D 9.—As before. The post-central cells, though sometimes of medium size and definite polygonal shape, are, more than in any other segment, mainly of the small, rounded type.

D 10.—In the lower part of the segment the cells are increasing somewhat both in number and size. The post-central cells (in contrast to D 9) tend to be large, and are often hard to distinguish from the reticular group, which is not very sharply circumscribed on its inner aspect.

D 11.—Anterior and central cells more numerous, either scattered or in small groups, very similar individually to cells of the apical group, although the anterior ones are sometimes more elongated. The post-central cells may

also be similar, and difficult to separate from the innermost cells of the reticular group, but many are smaller and more rounded. They may form a band round Clarke's column, and may lie directly behind it. The middle cell distribution is everywhere casual and erratic.

D 12.—See fig. 7.—Very similar to D 11. With the great increase of Clarke's column, the post-central cells are crowded characteristically into band form.

L 1.—See fig. 8.—Increase in size and number along with the other cell-

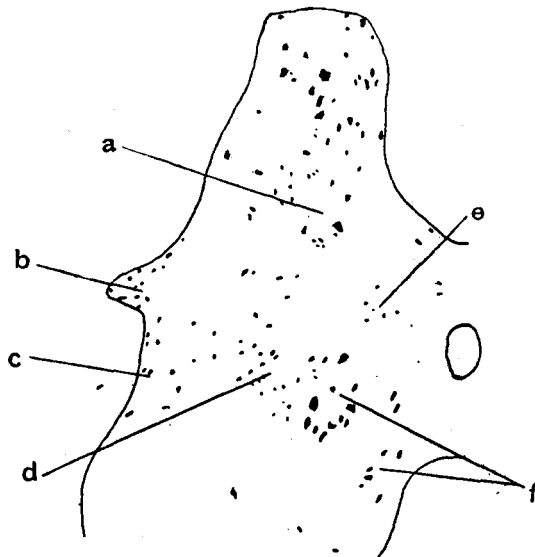


FIG. 7.

D 12—104 L ($\times 40$).

- a.* Abundant anterior middle cells, large and small.
- b.* Apical group, intermedio-lateral tract.
- c.* A few cells representing the reticular group of the intermedio-lateral tract.
- d.* Large group of post-central middle cells.
- e.* Small para-central group.
- f.* Clarke's column.

There are only a few scattered middle cells in the central area.

systems. Anterior cells particularly numerous, either as groups in various parts of the base of the anterior horn, or very commonly scattered thickly over it. Central cells also common, of typical middle cell character as regards their occurrence. Both anterior and central cells are polygonal, very like the intermedio-lateral tract cells individually, and not always readily separable from that tract when lying near its boundaries. Post-centrally, they are also mostly of the same type, but both here and occasionally in the reticular formation there are some of the smaller, more rounded cells.

L 2.—A large increase in the number of middle cells, *pari passu* with that of the grey matter. Many of the individual cells are also larger. The cells may be in groups or scattered irregularly over the basal and

inner portions of the anterior horn, in the area corresponding to the position of the now dwindling apical group, or extending right to the margin of the grey matter between the apical and reticular groups of the intermedio-lateral tract. They are also present in the region sometimes occupied by the tip of the triangular-shaped reticular group, and are not always readily distinguished from it. The post-central cells are, on the whole, smaller than the others, but most are polygonal in outline, although some are rounded; they usually form a band on the outer side of Clarke's column.

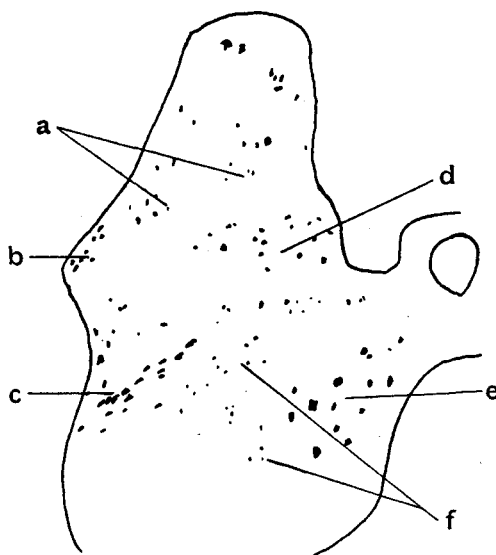


FIG. 8.

L 1—433 L ($\times 40$).

- a. Anterior middle cells.
- b. Apical group, intermedio-lateral tract.
- c. Reticular group, intermedio-lateral tract, of large cells, extending well into central area.
- d. Group of fairly large middle cells.
- e. Clarke's column.
- f. Small, rounded, post-central middle cells.

L 3.—See fig. 14, Plate II.—The middle cells now form a striking feature of the section. They are very numerous, and may be present anywhere in the posterior part of the anterior horn, central area, and base of the posterior horn. They have also invaded the areas occupied at higher level by the reticular group and by Clarke's column, but in the latter position they are never very numerous. They may be scattered or forming loose groups in any part of this wide field, but, as at other levels, these groups never persist through more than three or four consecutive sections. Groups may be present in the reticular formation, but they have none of the characters of the reticular group of the intermedio-lateral tract (which dies out in the

upper fourth of this segment) and all those of the middle cell system. In size and shape there is great variation. Many are large, polygonal cells, larger than intermedio-lateral tract cells; the post-central ones are very often smaller and more rounded in outline, but quite a fair proportion are as large and distinctly multipolar as the central and anterior cells.

L 4.—Much as in L 3. In the lower part the middle cells are extending rather further forwards on the median aspect of the anterior horn. In the reticular formation groups are rare, but a few cells are generally to be seen.

L 5.—[Note, segment destroyed; description taken from examination of



FIG. 9.

S 1—357 R ($\times 32$).
a. Motor cells.

The middle cells are scattered thickly over whole area not occupied by motor cells, the only other cells present. They are perhaps most abundant and of largest size in the central and reticular areas.

a segment obtained from another cord of practically identical age.]—Very similar to L 3 and L 4. Individual sections may show few or many cells, and scattered or aggregated in any part of the base of anterior horn, central area, or base of posterior horn. They are extending further forwards now in the outer part of the lateral enlargement. The same variations in size.

S 1.—See fig. 9.—The distribution is much as in the lower lumbar segments. Usually abundant, and anywhere within the large area shown in the accompanying figure. In the Clarke's column area they are fairly common, though not so abundant as in other parts. In the lower part of

the segment, with the disappearance of the median motor group, the middle cells extend forwards almost to the antero-internal angle of the anterior horn, and may be very abundant in the anterior area.

S 2.—Area of distribution proportionately larger than in S 1, extending further forwards and relatively further outwards in the anterior horn. Although individual sections may be picked out with few cells, they are on the whole very numerous. Vary much in size. Scattered diffusely or forming loose groups in almost any part, but anterior, central, and reticular

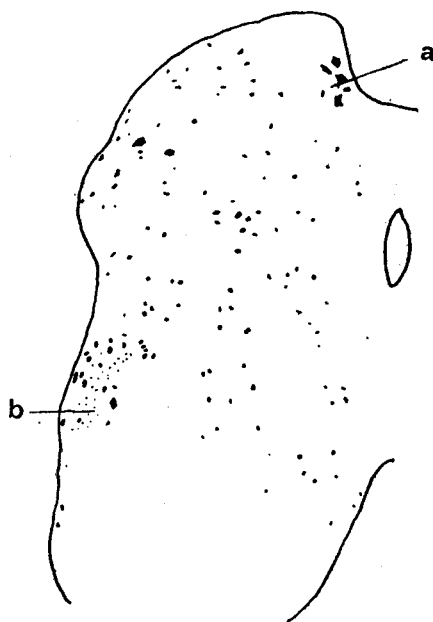


FIG. 10.

S 4—210 L ($\times 33$).

a. Anterior median motor group.

b. Small round cells in posterior part of reticular formation, apparently the representatives of the sacral intermedio-lateral tract.

The middle cells occur as fairly large cells over the whole of the anterior horn except where group *a* is; also in the central and post-central areas and area of Clarke's column. In the reticular area they are mingled with group *b*.

are perhaps the most common. Have much the same variations in size and irregularity of occurrence in all areas.

S 3.—Area of distribution as in S 2. Cells diminishing in number in lower end, where they are only found thickly in the base of the anterior horn. Distinct groups are now rather rare; at places they may be thickly scattered rather than grouped.

S 4.—See fig. 10.—With the gradual dying out of the motor group, the middle cell area gradually comes to take in the whole anterior cornua, as

well as its more usual limits. At the same time the cells become progressively fewer in number and also smaller in size. More scattered than forming definite groups; may be in any part, but most abundant in the anterior horn, and here also, on the whole, larger than in central and post-central regions. In the reticular area are cells indistinguishable in every way from other middle cells, but mingled irregularly with others which are quite different, sometimes the one set, sometimes the other predominating. [Those cells, probably representing the intermedio-lateral tract, are much smaller, pale, and almost circular in outline. They seem to consist almost entirely of nucleus. They appear first in the extreme lower end of S 3.] In character and irregularity of occurrence the middle cells are as in other segments.

S 5.—Cells gradually diminishing in number. At the lower end only occasional in their occurrence—one or two cells only. May be found in any part of the grey matter, but chiefly in two situations: firstly, the extreme anterior part of the anterior horn; secondly, near the reticular angle, along with cells of the intermedio-lateral tract, as in S 4. In the first-named area they are usually larger in size.

Coccygeal Segment.—At its upper end there are some straggling middle cells both anteriorly and near the reticular formation; they gradually become rarer and rarer. Some of the intermedio-lateral tract cells seem also to be present.

SUMMARY.

The middle cells are present throughout the whole length of the spinal cord. They are situated in the middle region of the grey matter, between the free anterior and free posterior cornua; but they sometimes also extend into the regions usually occupied by the anterior cornual cells, by the intermedio-lateral tract or by Clarke's column. The small cells in the base of the anterior horn (scattered cells) cannot be sharply separated from the middle cells, nor can most of the small cells about the base of the free posterior horn.

Although some of the middle cells may be found in all this wide area of distribution at practically any level of the cord, there are certain arrangements of cells which may be looked upon as typical of each segment, or at least of each region of the cord. In the upper cervical region they are not on the whole very abundant (this differs from Waldeyer's account), but are best developed in the central and para-central fields. In the cervical enlargement they are much more numerous, particularly within a broad band extending from the *formatio reticularis* to about the anterior grey commissure. Throughout the dorsal region they are again com-

paratively few in number, and may be scattered irregularly; but small groups are often found, most commonly in the central area, about on a level with the central canal, and in the post-central area, between Clarke's column and the reticular group of the intermedio-lateral tract. In the lumbar segments the middle cells are abundant, particularly centrally and in the base of the anterior horn. Their field extends anteriorly, until in the lower sacral region they come to be found over the whole area of the anterior cornua in addition to their more usual situations.

At all levels, as studied in serial sections, the distribution of the middle cells is seemingly erratic and casual. No regular plan of arrangement can be made out, and there is most certainly no segmentation (as Argutinski described) like that so well seen in the intermedio-lateral tract. The cells are sometimes just dotted here and there singly; sometimes they are scattered fairly thickly and evenly over the whole or part of the regions they are to be found in; or, again, they may occur more thickly in one part, or be aggregated into a distinct little cell group or nest, but even then these cell groups are seldom so closely packed as are the cell groups of the intermedio-lateral tract. The duration of any one of these types of cell arrangement is inconstant; and although there are levels where cells seem for a bit to be almost persistent in one place, this much can be stated as a general rule, that no middle cell group lasts through more than a very few serial sections. If traced further, the group is found either to shift to some other area or to die out altogether. Occasionally there appears to be a variation in number of cells parallel with the oscillations of the intermedio-lateral tract, but closer study shows that this is by no means absolute, and is probably only a local accidental variation.

Without expressing any opinion as regards function, I am inclined to divide the cells I have described collectively as middle cells into three groups, basing this division merely on the distribution and arrangement of the cells and on the microscopic appearances of the cell bodies. These divisions are, however, not very sharply defined either as regards the character of the individual cells or in the cell distribution. Still they seem to warrant such a division being made, and to suggest at least that the cells of the three groups may be functionally different. The groups I would make are—

(1) The middle cells proper, or central cells, occurring chiefly in the central area of the grey matter. These cells are of medium size and very similar to those of the apical group of the intermedio-lateral tract, multipolar, polygonal or rounded polygonal in outline, with a comparatively large nucleus and a few chromatic granules round it in the cell substance.

Sometimes scattered, but more often present as a small clump of cells. With them may be included the cells in the para-central area, which, although sometimes forming a distinct and separate aggregation of cells, can mostly not be separated off from the central cells. Many of the cells occurring in the reticular area at levels where the reticular group of the intermedio-lateral tract is not present (especially in the lower cervical region) may probably also be included here.

(2) Anterior central cells in the base of the anterior horn—one of Waldeyer's "scattered" cell groups. As this name implies, these are often simply scattered over the area in question, but sometimes they are gathered into small cell-nests, but rarely very compact ones. Although there is no sharp boundary between them posteriorly and the central cells, they are in the main larger cells, and are further distinguished by their shape. They are not so often definitely multipolar and of approximately equal diameter in different directions, but more frequently *appear* to be bipolar, with long-drawn-out processes. The axis of elongation may be variously oriented. With these would fall to be included the middle cells in the external central area of the lateral enlargements, particularly in the lumbo-sacral cord. Possibly also some of the para-central cells should be classed with this group, and not with the previous one.

(3) Post-central cells. These lie in the area between Clarke's column and the formatio-reticularis, or in the corresponding region of the grey matter at level where Clarke's column is unrepresented. As with the anterior central cell, there is no sharp boundary between this series and the central middle cells. They are often continuous, or the cells may lie betwixt and between the two areas. But although many of the posterior cells may be as large, they are distinguished on the whole by being smaller in size than the central cells and less definitely polygonal, more rounded in outline. They are generally present either as a small clump or as a band of cells on the outer and posterior aspects of Clarke's column. Posteriorly, it is very difficult to separate this group from the posterior-basal and posterior-marginal cells of Waldeyer. With this group may be included cells present in the area of Clarke's column, particularly when that column is absent or only represented by occasional cells. Also some of the small cells found in the reticular formation, especially those lying between (vertically) the nuclei of the reticular group of the intermedio-lateral tract.

These subdivisions may require modification from subsequent investigations, particularly by tracing the course and termination of the cell processes. I have attempted to do this by means of Cajal's silver impregnation methods, but, so far, have not succeeded. All I can affirm is that the fibres

arising from the middle cells run in a variety of directions to begin with; but as some could be traced far enough to be seen doubling more or less sharply upon themselves, this gives no real clue to their destination. In no case could I follow any one to a termination. In some cells there was observed an endo-cellular fibrillary network, similar to that in the large motor cells of the anterior horn. In this particular cord the following figures give approximate average diameter of the cells of the different groups:—

Anterior motor cells	·023-·035 mm.	
Anterior central middle cells	·018-·023 mm.	
Central middle cells	·015-·018 mm.	
Post-central middle cells	·011-·015 mm.	
Apical group	} intermedio-lateral tract	·016 mm.
Reticular group		·018 mm. In lower sacral ·010 mm.
Clarke's column	·020-·027 mm.	

In conclusion, I have to express my thanks to Dr Alexander Bruce for suggesting this subject for a thesis; to Dr Theodore Shennan, in whose laboratory the preparation of the sections was carried out; to Mr Henry Wade for the use of micro-photographic apparatus; and lastly to the Carnegie Trust, since this thesis is part of work done under the terms of a grant from the Trust for original research.

7th July 1908.—Since this paper was read before the Society, Jacobsohn has published a paper dealing with the cells of the spinal cord ("Über die Kerne des menschlichen Rückenmarks," *Anhang z. d. Abhandl. d. königl. Preuss. Akad. der Wissenschaft*, 1908).

He describes the middle cells as the *Tractus Cellularum*, scattered over the whole grey matter, and forming no very definite groups or nuclei, but three series may be distinguished—(a) an antero-median group, lying along inner edge of the anterior horn; (b) a postero-median group, the smallest of the three, and also composed of the smallest cells, in the position of, amongst, or surrounding Clarke's column; (c) a lateral intercornual series, the largest, near the formatio-reticularis, and in the outer part of the base of the posterior horn. All three series are indefinitely bounded towards the centre of the grey matter, and may meet there.

It must be noted, however, that this author, in addition to a thoracic and a sacral sympathetic nucleus (intermedio-lateral tract), describes a third or lumbo-sacral median sympathetic nucleus, extending from L 4 to the coccygeal segment, which would include practically all the cells which I have described as an extension of the middle cells into the lateral enlargement of the anterior horn as the motor groups die out.

REFERENCES.

- (1) WALDEYER, "Das Gorilla-Rückenmark," *Abhand. d. könig. Akad. d. Wiss. zu Berlin*, 1888.
- (2) BRUCE, "Distribution of the Cells in the Intermedio-lateral Tract of the Spinal Cord," *Trans. Roy. Soc. Edin.*, vol. xlv., pt. i., No. 5, 1906.
- (3) ONUF and COLLINS, *The Sympathetic Nervous System*, 1900.
- (4) ARGUTINSKI, "On a regular segmentation in the grey matter of the spinal cord in the new-born and on the Middle Cells," *Arch. f. micros. Anat.*, xlviii, 1897, p. 496.

DESCRIPTIONS OF FIGURES.

[Photographs untouched save outlining of the grey matter.]

PLATE I.

Fig. 11. C 3—200 L ($\times 33$).

The middle cells are scattered in the base of the anterior horn and in the areas of the lateral horn and reticular formation, those in the anterior horn being of larger size. They form a fairly compact group in the central area, and there is also a group of smaller-sized cells in Clarke's column area.

Fig. 12. C 6—274 L ($\times 32$).

The middle cells occur in the manner most characteristic of the cervical enlargement, viz. as a broad band of cells stretching from the reticular angle towards the central canal. There are also some scattered cells anterior to this, and a very few small cells in the area of Clarke's column and base of posterior horn.

PLATE II.

Fig. 13. D 4—23 R ($\times 40$).

Shows apical group of intermedio-lateral tract occupying most of the lateral horn, and with some outlying cells in the white matter. The reticular group cells are larger in size, tend to be elongated along a line running inwards and forwards from the reticular angle, and the group lies some way internal to the edge of the grey matter. There are a very few scattered cells in the base of the anterior horn; some centrally, near the tip of the reticular group, and a small group of smaller, more rounded, post-central middle cells.

Fig. 14. L 3—259 L ($\times 32$).

The middle cells form a large central aggregation. There are small groups post-centrally and behind the anterior median motor group.

A few cells in the reticular area and base of posterior horn.

(Issued separately September 2, 1908.)

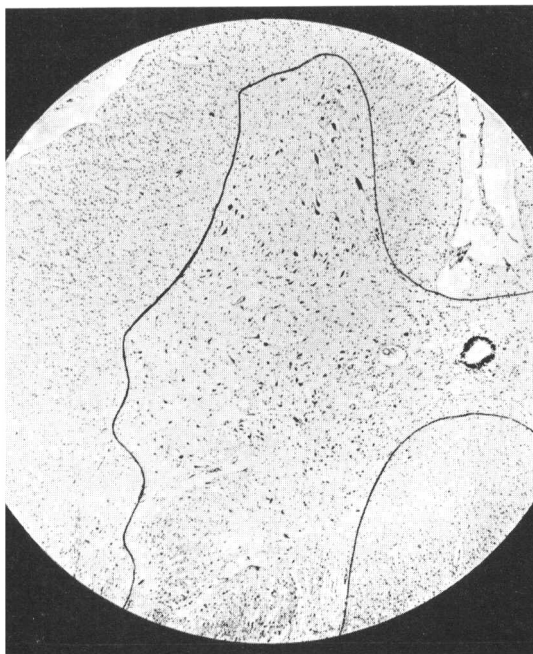


FIG. 11.

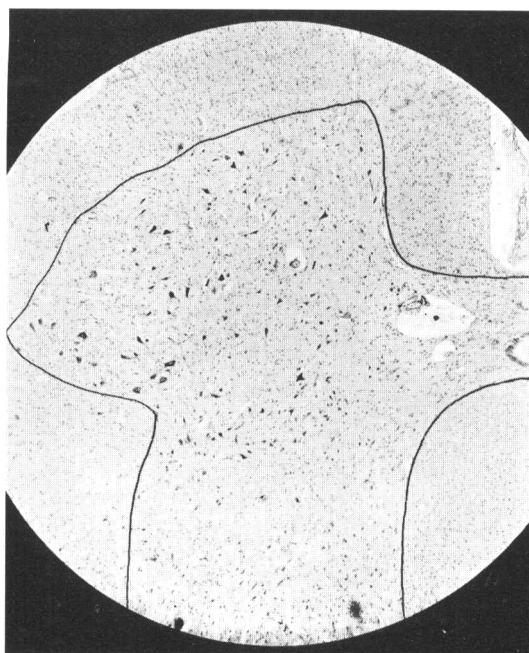


FIG. 12.

DR J. H. HARVEY PIRIE,

[Plate I.

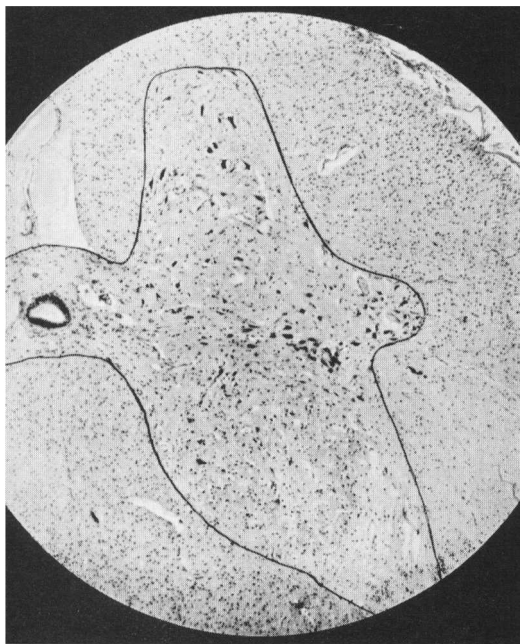


FIG. 13.

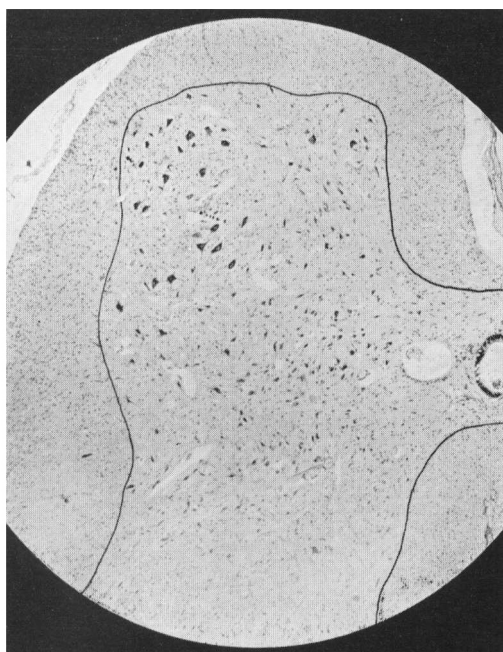


FIG. 14.

DR J. H. HARVEY PINIE.

[Plate II.