

# Spinal cord arteriosclerosis and progressive vascular myelopathy

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Spinal cord arteriosclerosis is considered to be infrequent compared with atheromatosis in other parts of the body. Whereas Staemmler (1939) could not observe any atheromatous changes in the spinal cords of 700 unselected cadavers, Nunes Vicente (1964) noted mild arteriosclerosis of major spinal vessels in 13 out of 200 consecutive necropsy cases. Mannen (1963) even reported the incidence of 2.6% atheromatous plaques in the anterior spinal artery of 300 unselected cases upon which necropsies were performed in a geriatric hospital. Moderate to severe atheroma of spinal cord vessels has been observed incidentally but only exceptionally has spinal cord infarction been caused by documented occlusion of spinal arteries (Thill, 1923; Zeitlin and Lichtenstien, 1936; Antoni, 1941; Garstka, 1953; Hogan and Romanul, 1966; Jellinger, 1966, 1967). Angiosclerosis of the small intramedullary arteries as a local variant of atheromatosis is also extremely rare (Arendt and Wünscher, 1954). The relationship between thickening of the small intramedullary vessels in advanced age, known as 'perisclerosis', 'hyalinosis', or 'fibrosis' and arteriosclerosis, however, has been uniformly denied (Lüthy and Zollinger, 1946; Stochdorph and Meessen, 1957).

On the other hand, spinal cord lesions due to arteriosclerosis have been known since the late nineteenth century (Demange, 1884; Campbell, 1894) but have subsequently received only an occasional mention in the literature. Reviewing myelopathy due to vascular diseases, Keschner and Davison (1933) found only two cases referable to arteriosclerosis in 200 instances of cerebral atherosclerosis. Recent reports, however, suggest that the condition may be far more common than was formerly supposed (Jellinger and Neumayer, 1962;

Hughes and Brownell, 1966). Recently we reported on more than 60 cases, all verified at necropsy, in which a complex neurological syndrome, often referable to a combined lesion of the upper and lower motor neurone, was associated with generalized arteriosclerosis and severe aortic atheroma without thrombosis or occlusion of the spinal tributaries (Jellinger and Neumayer, 1966). The pathogenesis of this rarely diagnosed condition is obscure as, till now, there have been neither sufficient observations regarding the incidence of spinal cord atherosclerosis nor relevant data on the changes of spinal vessels in old age, generalized arteriosclerosis, and systemic hypertension.

In this communication the incidence of arteriosclerotic changes and vascular fibrosis in the spinal cords of 1,037 necropsied cases described in the files of the Neurological and Pathological Institutes of Vienna University is reported and correlated with the age and the frequency of atherosclerosis of the aorta, the coronary and cerebral arteries, as well as the incidence of cerebrovascular lesions and systemic hypertension. Inflammatory vascular processes (syphilis, panarteritis nodosa) and their consequences are not included. Table I sets out the age distribution of the examined cases. In addition, corroborative studies were made of 76 necropsy cases of vasocirculatory myelopathy in advanced age, and in the remaining series of necropsied cases of the same ages without vascular disorders of the spinal cord.

## MATERIAL AND METHODS

For the examination of the spinal cord vessels serial sections of at least six to 30 blocks of various segments of the spinal cord stained with haematoxylin and eosin, cresyl violet or Nissl's method, Van Gieson's elastica

TABLE I  
AGE DISTRIBUTION OF THE EXAMINED NECROPSY CASES

	Age Group								Total	
	0-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80		81-90
Vascular myelopathy	200	80	103	103	116	170	180	77	8	1,037
	—	—	—	—	3	9	33	28	3	76

technique, and Heidenhain's or Klüver-Barrera's myelin method were available. Selected sections were stained with Azan or Masson's trichrome technique, Weigert's method for fibrin, P.A.S., toluidin blue, Gomori's silver impregnation, Bodian's stain for neurofibrils, and the coupled tetrazonium method. Frozen sections were stained with Sudan III, Sudan-black B, and Spielmeier's myelin stain.

The classification of the vascular lesions of the spinal cord followed the usual pathological criteria recently summarized for the cerebral vessels by Arendt and Bachmann (1966): intimal fibrosis (collagenization), hypertrophy of the internal elastic lamina, adventitial fibrosis, and combined atheromatous changes. The intensity of arteriosclerosis of the spinal arteries was graded as follows: 0 normal, 1+ mild involvement (slight circular or sectional intimal fibrosis and/or duplication and splitting of the internal elastic fibres with or without adventitial fibrosis), 2+ moderate sclerosis (same lesions of greater intensity without much narrowing of the lumen), 3+ severe changes (plaque-like intimal cushions and hypertrophy of the internal elastic layer with narrowing of the lumen), 4+ typical atheroma (containing cholesterol crystals with stenosis or thrombosis of the vessel). Regarding fibrotic thickening of the sulcal and intramedullary vessels, five degrees of intensity were considered: 0 normal, 1+ mild changes (slight thickening of the vessel wall with condensation of perivascular connective tissue without narrowing of the lumen), 2+ moderate lesions (thickening of the vessel wall up to twice the normal calibre with slight narrowing of the lumen), 3+ considerable (higher degree of lesions with considerable narrowing of the lumen), 4+ severe lesions (extreme

thickening of the vessel wall with obstruction causing almost complete stenosis of the lumen). Similar criteria were used to grade adventitial fibrosis of the vessels of the spinal leptomeninges.

Complete necropsy records were available for 407 cases aged over 21 from the 757 cases in these age groups. They were examined to assess the incidence of aortic atheroma, including aortic thrombosis, and of coronary and cerebral atheromatosis, grading the conditions according to the four degrees of intensity of the coding guide of the World Federation of Neurology (1959), and also in relation to the frequency of cerebrovascular lesions and the necropsy findings of systemic hypertension (Table II).

## RESULTS

Arteriosclerotic changes in the major spinal arteries were seen in 12.7% of our total material, *i.e.*, in 22.2% of the age group over 41 years and in 27.1% from those over 61 years respectively. Of these, however, 10.5% showed only mild intimal fibrosis and/or hypertrophy of the internal elastic lamina without much narrowing of the lumen (Fig. 1a). These lesions had always to be clearly distinguished from the 'physiological' intimal cushions in spinal arteries (Hassler, 1961). Moderate, non-stenosing atherosclerosis (Fig. 1b) was noted in 1.8%. Only two cases showed proliferative lesions with obstruction (Fig. 1c) and another two typical atheromatous plaques (Fig. 1d), indicating an incidence of 0.4% of severe atherosclerosis in major spinal vessels. As

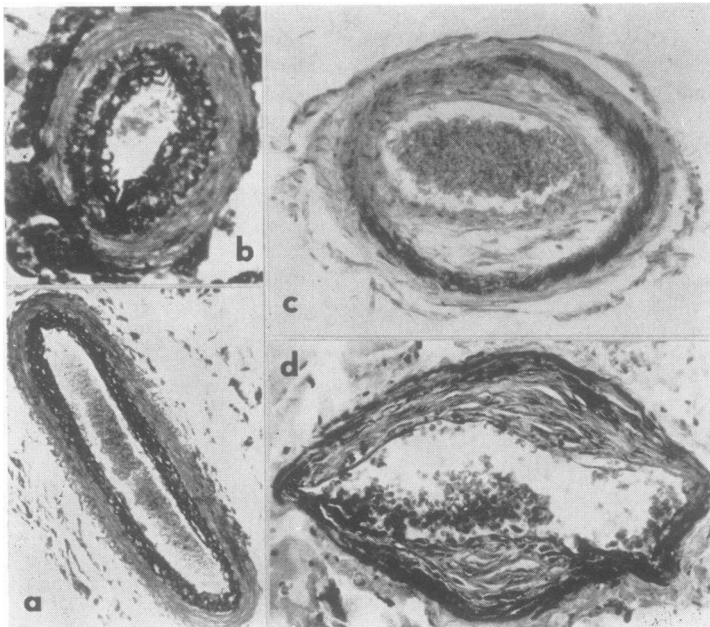


FIG. 1. Arteriosclerosis of major spinal arteries.

(a) Mild hypertrophy of internal elastic lamella and slight thickening of the intima in anterior spinal artery at the T 11 level. NI 131/63. Van Gieson elastica stain  $\times 44$ .

(b) Moderate intimal fibrosis and thickening of internal elastic lamella with slight narrowing of lumen in posterolateral spinal artery at the cervical level. NI 42/61 Van Gieson stain  $\times 140$ .

(c) Proliferation of subintimal connective tissue with partial obliteration of posterior spinal artery at midthoracic level. NI 154/59. Haematoxylin and eosin stain  $\times 140$ .

(d) Atheroma of anterior spinal artery at the T 11 level in progressive myelopathy in a 66-year-old sclerotic woman. NI 49/66. Haematoxylin and eosin stain  $\times 200$ .

TABLE II

CORRELATIVE DATA ON SPINAL AND GENERALIZED ATHEROSCLEROSIS

Author	Material	Analysis of Material
Keschner and Davison (1933)	Cerebral sclerosis 200 cases	Spinal sclerosis and myelopathy ..... 1%
Staemmler (1939)	Unselected necropsies 700 cases (502 aged over 41yr. or 283 aged over 61 yr.)	Spinal atherosclerosis ..... 0 Pial artery atheroma ..... 1.4% Intermedullary arteriolosclerosis, rare Severe generalized atheromatosis, systemic hypertension ..... 10% Sclerotic plaques (anterior spinal artery) ..... 2.6% Vascular myelopathies ..... 9% Cerebrovascular lesions ..... 80%
Mannen (1963)	Geriatric necropsies 300 cases	Spinal sclerosis (11 cases + 2 cases ++). . . . . 6.5% Cerebral sclerosis ..... 37.5% Coronary sclerosis ..... 36.0% Aortic atheroma ..... 70.0% Cerebrovascular lesions ..... 8.0% Systemic hypertension ..... 8.5% Spinal sclerosis (132 cases) ..... 12.71% " " mild (109 cases) ..... 10.5% " " moderate (19 cases) ..... 1.83% " " severe (9 cases) ..... 0.38%
Nunes Viscente (1964)	Consecutive necropsies 200 cases (122 aged over 41 yr. or 50 aged over 61 yr.)	Cerebral sclerosis ..... 39.3% Coronary sclerosis ..... 37.2% Aortic atheroma ..... 45.2% Cerebrovascular lesions ..... 7.6% Systemic hypertension ..... 8.2%
Jellinger (1966)	Neurological necropsies 1,037 cases	

to the age groups over 41 and 61 years respectively, this corresponds to 18 and 20% mild, 3.4 and 5.3% moderate, and 0.7 and 1.5% severe spinal cord atheromatosis, the total incidence of moderate to severe atheroma being 2.2% in the present series (see Table II).

Thus the frequency of arteriosclerosis of the spinal cord was approximately twice as high as in the series of Nunes Vicente (1964). As the percentage of generalized and cerebral atherosclerosis was very similar in both series, this difference in part may be due to deviations caused by methods of examination, e.g., number of spinal cord sections examined. In

Mannen's (1963, 1966) series of necropsies in geriatric cases, however, the incidence of severe atheroma of spinal arteries was somewhat higher than in our material. No statistical data on mild atherosclerosis are available, although Mannen noted a thickening of the arterial wall in most cases, sometimes associated with duplication and splitting of the internal elastic fibres. Some comparative figures for the spinal cord and generalized atherosclerosis are given in Table II.

Although the presented results are derived from necropsy material mainly from cases of neurological disease, good agreement of our data on generalized

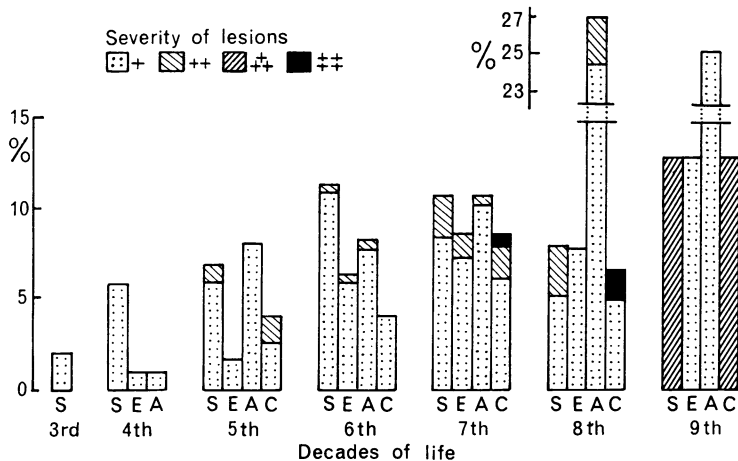


FIG. 2. Incidence of arteriosclerotic changes in major spinal arteries in different age groups of 1,037 unselected necropsy cases. S subintimal fibrosis. E elastic hypertrophy. A adventitial fibrosis C combined sclerosis.

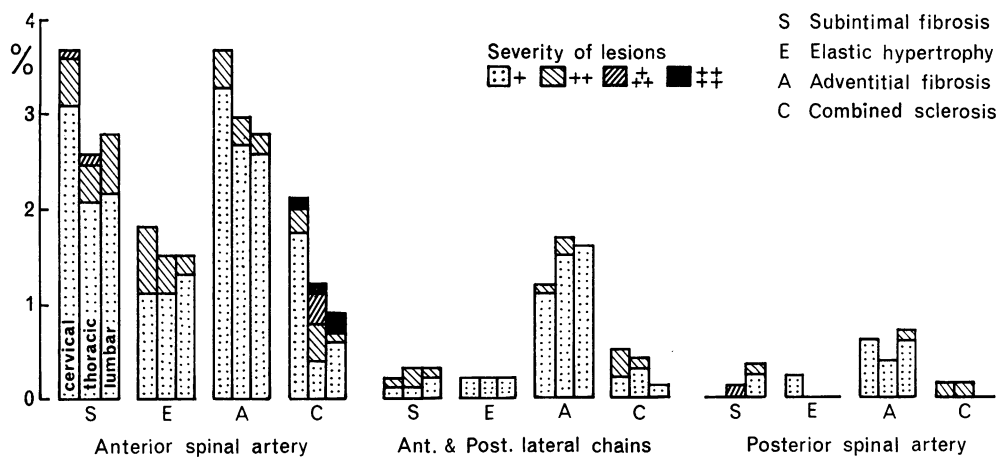


FIG. 3. Localization of atherosclerotic changes in major spinal arteries.

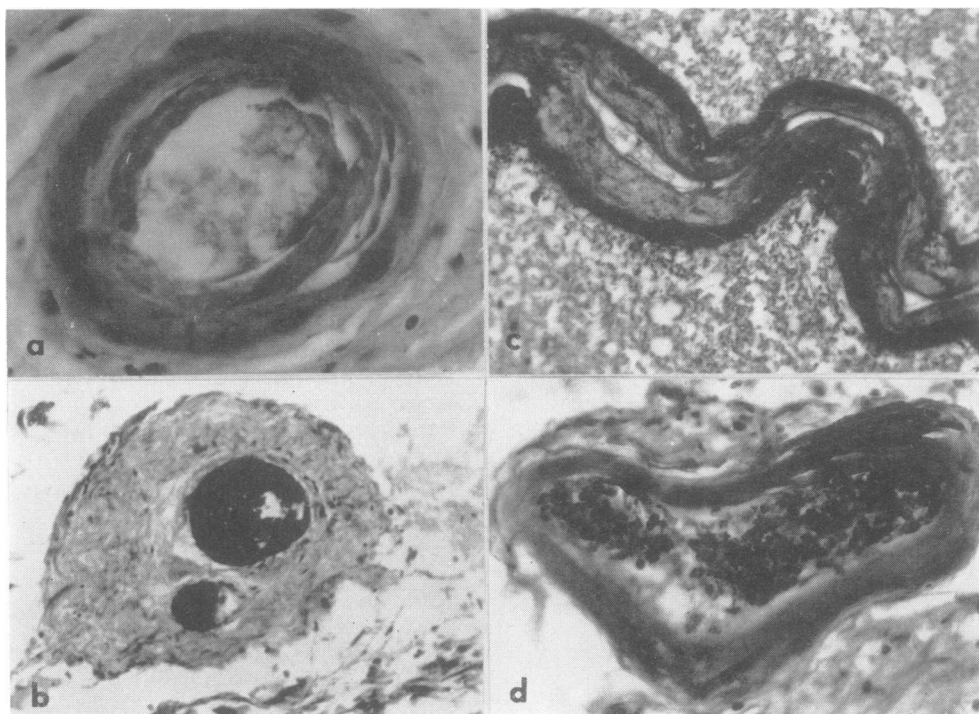


FIG. 4. Lesions of small spinal vessels.

(a) Arteriosclerosis of sulco-commissural artery in systemic hypertension. NI 4522-38. Haematoxylin and eosin stain  $\times 280$ .

(b) Severe adventitial fibrosis of small dorsal pial vein in sclerotic myelopathy. AH 25/64. Van Gieson elastica stain  $\times 250$ .

(c) Severe fibrosis of dorsal fissural vessel in the cervical region with extreme narrowing of lumen. NI 159/59. Van Gieson elastica stain  $\times 250$ .

(d) Fibrinoid degeneration of small pial vessel in hypertonic man aged 86 with severe myelopathy. Haematoxylin and eosin stain  $\times 360$ .

and cerebral atherosclerosis with large statistical series allow of a correlation between our findings and those in unselected necropsy series. The mean frequency of 39.3% for cerebral atherosclerosis in our total series, *e.g.*, corresponds well with recent data of Zschoch (1966) derived from more than 13,000 consecutive necropsies, indicating an incidence of 39.44% for cerebral atheromatosis.

No relevant correlation was found between sclerotic changes in spinal arteries and atheromatosis of the rest of the body. That spinal cord atherosclerosis is not dependent on age has been confirmed by ranging the various lesions of the major spinal vessels according to decades (Fig. 2). As to the site of atherosclerotic changes, in agreement with Mannen (1966), the anterior spinal artery was found to be predominantly affected, and the incidence of lesions remarkably decreased *via* the anterior and posterior lateral chains to the posterior spinal artery (Fig. 3). The clear correlation between the frequency of sclerotic changes and the calibre of the affected vessels lends support to the suggestion that mechanical factors of circulation are of some importance for the pathogenesis of arteriosclerosis (Staemmler, 1939). Although atheromatous plaques of the anterior spinal artery were found at the level of the lower thoracic and upper lumbar cord, in general, the sclerotic lesions of this artery were more pronounced in the cervical region (Fig. 3). This fact is supported by Mannen's (1966) data on the average ratio of the vascular wall to the diameter of the lumen, indicating a higher degree of obstruction in the cervical region than elsewhere.

Atheroma of the radicular tributaries seems to be extremely rare and was only noted once in our whole series. Occlusive and proliferative changes described in small pial vessels over infarcted brain in the border zones of arterial supply (Romanul and Abramovicz, 1964) were never found in the spinal cord. Calcification of the media in dorsolateral spinal arteries was detected in two patients, one of whom had suffered from paraplegia with sensory loss below T8 due to myelonecrosis probably attributable to severe calcareous arachnopathy.

Arteriosclerotic changes of small intramedullary vessels are much more infrequent than in the major spinal arteries. In our material spinal arteriolo-sclerosis was just an exceptional finding in the sulco-commissural arteries (Fig. 4a) and small branches of the spinal grey matter usually associated with severe generalized atherosclerosis and systemic hypertension. Contrary to the findings of Arendt and Wünsch (1954) we never were able to detect senile 'kongophilic' or 'drusige' angiopathy (Schlote, 1965) and genuine hyalinosis, *i.e.*, hypertensive angiopathy (Anders and Eicke, 1940) in the spinal cords examined.

The comparatively rare atheromatous changes of spinal arteries are opposed by diffuse mural thickening of the small intramedullary and radicular branches, those in the posterior and anterior sulcus, and the pial veins and capillaries, the frequent occurrence and severity of which in advanced age are well known (Campbell, 1894; Stern, 1936; Bailey, 1953; Morrison, 1959). These lesions, known under the synonyms mentioned above, by morphological and histochemical criteria (*c.f.* Arendt and Bachmann, 1966) may be characterized as fibrosis of the extra- and intramedullary vessels. In the spinal cord this condition is usually much more pronounced than are identical changes of the small pial and intracerebral vessels in the senile brain (Stochdorph and Meessen, 1957; Baker and Iannone, 1959). Considered as sequelae of chronic relapsing oedema or of hypertension secondary to haemodynamic disturbances (Zollinger, 1959; Hughes and Brownell, 1966), or occurring as symptomatic vascular changes in degenerative, inflammatory, and demyelinating disorders of the central nervous system, these fibrotic lesions are not specific for any particular disease.

In vessels of the leptomeninges, fibrosis mainly consists of variable thickening of the adventitia with condensation of the surrounding connective tissue (adventitial fibrosis) or complete acellular, often collagenous, transformation of the vessel wall (Fig. 4b) rarely leading to stenosis. Fibrinoid degeneration of pial vessels occasionally described as 'hyalinosis' in senile spinal cords (Lanza, 1938; Graux, Guazzi, and Gesquier, 1962) was noted in two cases of hypertension aged over 80 in combination with severe generalized atherosclerosis (Fig. 4d). In sulcal branches and intramedullary vessels, complete acellular and structureless thickening of the walls without evidence of fibrinoid or hyalin degeneration or angioneclerosis often does not permit of clear distinction between arterioles and veins. Transformation of the vessels into homogenous, slightly eosinophilic and strongly P.A.S.-positive tubes of a bright red when stained by Gieson's method and a blue tint with Azan and Mallory's method is usually accompanied by condensation of loose perivascular connective tissue in the perivascular spaces. Severe fibrotic thickening may result in extreme narrowing of the lumen, the intima remaining intact (Fig. 4c).

Fibrosis of the extramedullary vessels favours the dorsal pial veins with increasing severity from cervical to lumbosacral region (Fig. 5a). Fibrosis of the intramedullary and sulcal branches, usually predominating in the dorsal fissure and in the posterior and posterolateral columns, revealed a clear cervical predilection with an inverse caudal decrease of intensity (Fig. 5b). These latter findings are opposed to the observations of Lanza (1938) who emphasized

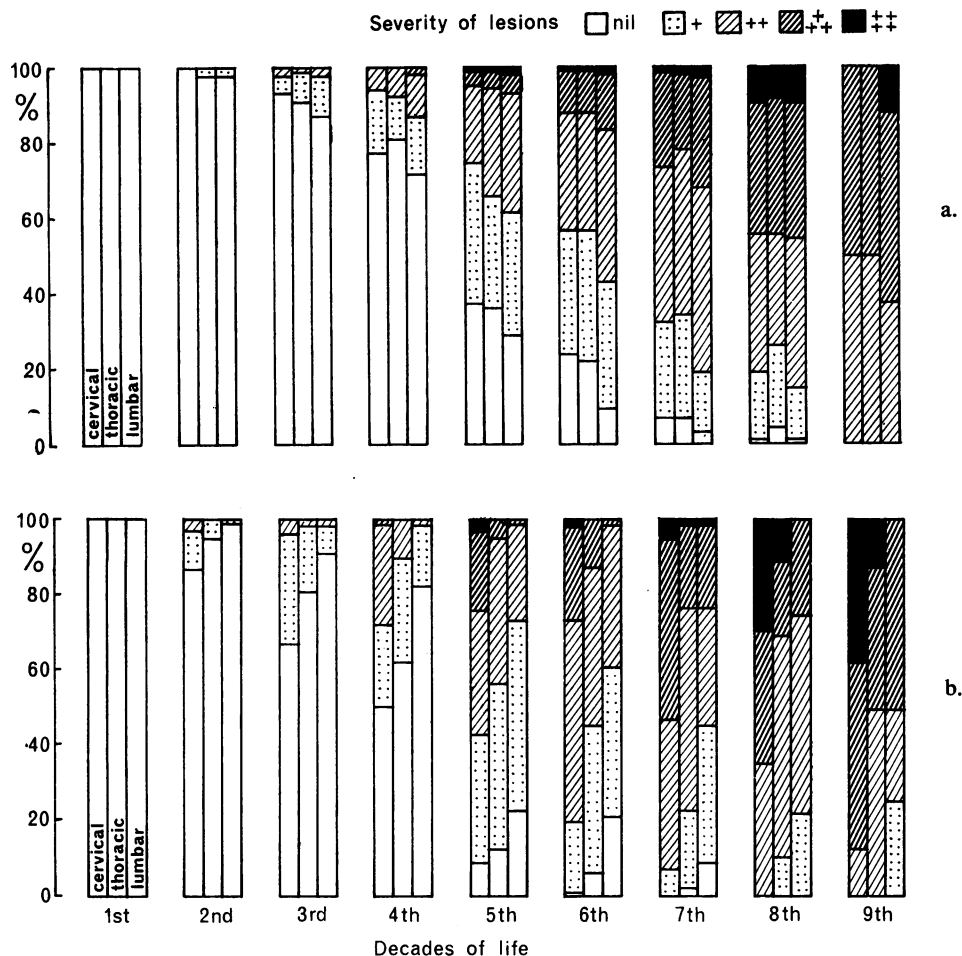


FIG. 5(a). Incidence of fibrosis of the pial veins in 1,000 unselected spinal cords.

(b) Incidence of fibrosis of intramedullary vessels in 1,037 unselected necropsy cases.

that intramedullary vessels in the lumbosacral cord were favoured, probably related to aortic atheroma. Though there is a large local and individual variability in intramedullary vascular fibrosis, we rarely noted severe stenosing lesions in the caudal parts of the spinal cord. High degrees of fibrosis of intramedullary arterioles, veins, and capillaries, however, were often encountered in the cervical intumescence and the uppermost thoracic segments.

In accordance with the observations of Nunes Vicente (1964) we saw an approximately linear relationship between fibrosis of the intra- and extramedullary spinal vessels and advancing age (Fig. 5a and b) although these changes are not considered as the normal accompaniment of aging. A negative association between spinal vascular fibrosis and generalized atherosclerosis and systemic hyper-

tension was established, but thickening of intramedullary vessels was much more pronounced in arteriosclerotic myelopathies than in other cases of the same age.

Interesting results of some pathogenic value were brought about by correlating investigations in 76 necropsy cases of 'progressive vasocirculatory myelopathy of advanced age' (Jellinger and Neumayer, 1962, 1966) with the rest of the series without vascular disorders of the spinal cord. The myelopathy group, considered as a clinico-pathological entity, comprises above all observations of subacute or chronic spinal cord ischaemia caused by insufficiency of arterial supply attributable to atherosclerosis. This group of chronic lesions of the spinal cord was formerly known as 'senile paraplegia' (Leyden, 1892) or 'spastic paraparesis of the arteriosclerotic'.

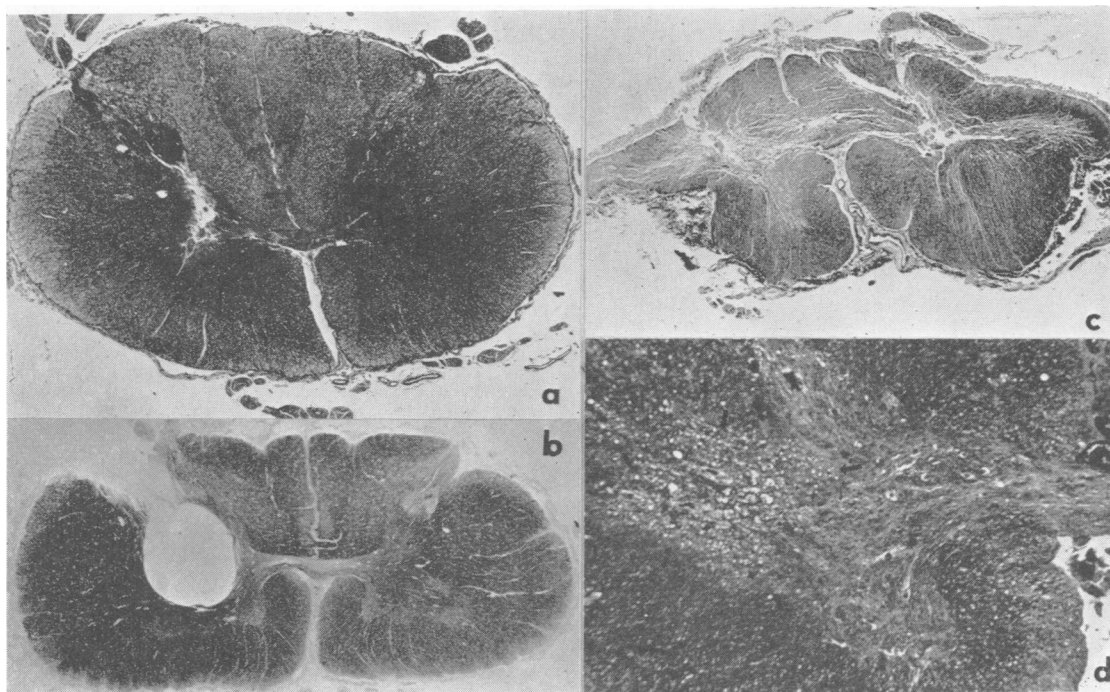


FIG. 6. Progressive vascular myelopathy due to arteriosclerosis.

(a) Cystic necrosis in intermediary grey matter between C 6 and C 7 level. Spongy degeneration of marginal white matter and pallor of posterior columns. Man aged 66 with severe atherosclerosis and subacute myelopathy. Heidenhain stain  $\times 75$ .

(b) A reactive sharp-lined cyst due to old infarct in intermediary grey matter and posterior column at the C 5 to C 6 level in man aged 77 with progressive myatrophies. NI 89/66. Kluver-Barrera stain  $\times 8$ .

(c) Central spongy necrosis of grey matter and adjacent parts of posterior and posterolateral white columns at the T 2 level in hypertonic man aged 77 with progressive incomplete transverse syndrome. AH 4/60. Heidenhain stain  $\times 7$ .

(d) Small focal infarction in central grey matter of anterior horn and intermediary region at the T 5 level in man aged 66 with paraplegia of five years' duration associated with malignant hypertension. NI 35/57. Heidenhain stain  $\times 20$ .

The often ill-defined clinical picture of 'arteriosclerotic myelopathy' is accompanied by a picture similar to late forms of nuclear myatrophy (so-called pseudo-myatrophic lateral sclerosis of vascular origin) or atypical para- or quadriplegia with signs referable to lesions of the upper and lower motor neurone or occasionally by subacute incomplete transverse syndromes (Keschner and Davison, 1933; Jellinger and Neumayer, 1966; Hughes and Brownell, 1966). The chief alterations in the spinal cord are found in the grey matter. Their morphological features are often focal, 'rarefaction necrosis', with only a slight tendency towards degradation and glial organization located in the spinal grey matter. They prefer the intermediary regions corresponding to Rexed's (1964) laminae VII and VIII and extend to the anterior and posterior horns (Fig. 6a and b). This damage may result in simple atrophy of the nerve cell parenchyma accompanied by moderate cellular and fibrillary

gliosis, spongy areas of disintegration or the formation of cysts with a minor glial reaction (Fig. 6b) — a patchy lacunar state similar to the cerebral *état criblé* or perivascular lacunae in the basal ganglia. Like these well-known lesions in the arteriosclerotic brain, we consider them to be secondary to a rarefaction and consecutive resorption of tissue caused by chronic relative arterial ischaemia. Presumably lesser degrees of arterial insufficiency than operate in spinal infarction or softenings are responsible, and an additional factor of relative tissue sensitivity to hypoxia becomes important. The dominating factor is the unsystematized distribution of these 'rarefaction necroses'. These irregularly placed lesions of the grey matter are often small and may even affect one half to one third of one spinal segment. They may be accompanied by moderate damage to the marginal white matter or by degeneration of the posterior columns (Hughes and Brownell, 1966). Occasionally a pencil-like necrosis of the central grey

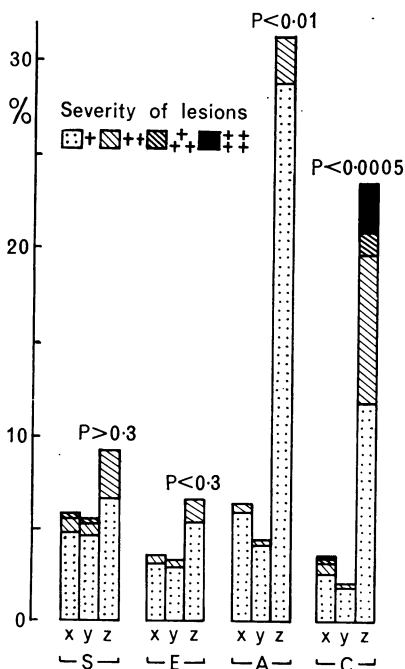


FIG. 7. Correlation of incidence and severity of atherosclerotic changes of the major spinal arteries in 1,037 unselected necropsy cases (x), 961 necropsy cases without vascular disorders of the spinal cord (y), and 76 necropsy cases of vascular myelopathy due to arteriosclerosis (z). S subintimal fibrosis. E elastic hypertrophy. A adventitial fibrosis. C combined sclerosis.

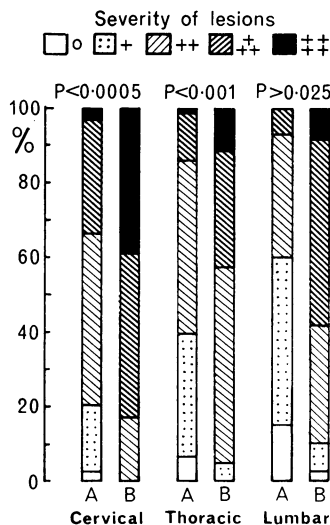


FIG. 8. Correlation of incidence and severity of fibrosis of intramedullary vessels in 961 unselected necropsy cases without vascular disorders of the spinal cord (A) and 76 cases of vascular myelopathy due to arteriosclerosis (B).

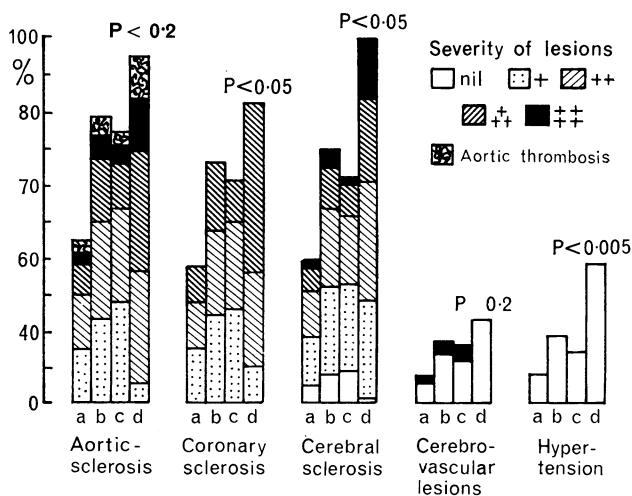


FIG. 9. Correlations of incidence and severity of generalized atherosclerosis, cerebrovascular lesions, and systemic hypertension in necropsy series without vascular lesions of the spinal cord (a-c), and in 76 cases of vascular myelopathy due to arteriosclerosis (d). a ages 0-80 years inclusive (1,037 cases). b ages 0-40 years inclusive (407 cases). c without vascular myelopathy (331 cases). d with vascular myelopathy (76 cases).



matter in the lower cervical and upper thoracic region is found (Fig. 6c), whereas in rare instances small focal infarctions of variable localization were seen (Fig. 6d). Mannen (1966) noted similar lesions in six of 25 cases of arteriosclerotic myelopathy, the clinical manifestations of which, however, were not always definite. Myelopathies attributable with certainty to severe bony and cartilaginous deformities in cervical spondylosis (Hughes, 1966) are not included in this series.

Statistical evaluation of both groups showed no relevant differences in the frequency and severity of intimal fibrosis and hypertrophy of the elastica of the major spinal arteries. In the myelopathy group, however, there was a significant preponderance of adventitial fibrosis, which is not regarded as a sclerotic change, and a highly significant occurrence of atherosclerosis in the spinal arteries (Fig. 7). A highly significant positive association between myelopathy and fibrosis of the small intramedullary vessels was established, its significance decreasing from cervical to caudal cord levels (Fig. 8).

A statistical comparison of generalized atherosclerosis revealed a significant preponderance of coronary and cerebral atheromatosis in the myelopathy group and its highly significant association with necropsy findings of systemic hypertension. There was only a slight irrelevant preponderance of aortic atheroma and aortic thrombosis and of cerebrovascular lesions in the myelopathy group as compared with the large series without vascular disorders of the spinal cord (Fig. 9).

#### DISCUSSION

The reported findings prove the infrequent incidence of arteriosclerosis in major spinal arteries with the extremely rare occurrence of moderate to severe atheroma, the incidence of which in the examined series represents approximately 5% of its mean frequency in cerebral arteries. Up to now, no statistical observations exist regarding the incidence of vascular disorders of the spinal cord except some correlative data with cerebrovascular lesions. In the material of Keschner and Davison (1933) there were two sclerotic myelopathies out of 200 cases of cerebral arteriosclerosis, indicating an incidence of 1% for spinal cord damage due to arteriosclerosis. In Mannen's (1966) geriatric material the incidence of cerebrovascular syndromes was 80% compared with one of 9% for vascular myelopathies with multiple small ischaemic softenings comparable with the 'rarefaction necroses' mentioned above. Mannen, however, observed no spinal cord infarction caused by occlusion of major spinal tributaries or dissecting aneurysm of the aorta. Nunes Vicente (1964)

reported an incidence of 2% for spinal cord infarctions of various origins and of 9% for cerebrovascular accidents in 200 unselected necropsies. On the other hand, Blackwood (1958) found no examples of arterial softening of the cord in 3,737 post-mortem examinations from 1909 to 1958 at the National Hospital, Queen Square, London. According to our personal experience in a series of about 200 instances of spinal cord damage, considered as being referable to vascular and/or circulatory disorders in a wider sense, only two cases (1%) were due to infarctions resulting from local atheroma in major spinal arteries. For comparison, 3.5% of myelonecroses were caused by aortic lesions, whereas 2.5% of cases of spinal cord damage occurred in combination with panarteritis nodosa. Considering the percentage of moderate to severe spinal cord atherosclerosis in our total material it can be suggested that only about 5% to 10% of atheromas in major spinal arteries may result in typical spinal cord infarcts. This confirms the minor importance of local atherosclerosis for the pathogenesis of acute vascular disorders of the spinal cord.

Our correlative statistical investigations, however, indicate a certain significance for spinal cord arteriosclerosis as a contributory factor in the comparatively frequent manifestation of circulatory disorders of the spinal cord in generalized atheromatosis, systemic hypertension, or other cardiovascular dysfunctions. This seems the more important because chronic spinal cord ischaemia due to atherosclerosis seems to be far more common than was formerly suggested. Progressive myelopathies referable to arteriosclerosis represented almost one-third of our total necropsy material of probable vasocirculatory disorder of the spinal cord, and about one-fifth of Hughes' relevant cases (1966). Contrary to rare spinal cord infarctions resulting from documented interference with spinal blood flow due to occlusion of spinal tributaries, including the aorta and its segmental branches (Gruner and Lapresle, 1962; Hughes, 1966; Jellinger, 1966), the site of the non-systemic ischaemic lesions in vascular myelopathy shows neither a relevant relationship to the segmentary pattern of spinal vascular supply nor to the organic impairment of the major spinal arteries (Jellinger and Neumayer, 1962, 1966; Mannen, 1933). This indicates that the underlying disorders are predominantly located in the extramedullary feeding system of the spinal cord.

The obvious cause of the spinal cord damage thought to be due to chronic diminution in its total blood supply is the severe arteriosclerosis present in every case, and particularly evident as severe atheroma or even thrombosis of the abdominal aorta from which the blood supply of the caudal part of

the spinal cord arises (Gruner and Lapresle, 1962; Hughes and Brownell, 1966). Dissection of the intercostal arteries and the lumbar spinal branches usually failed to demonstrate any thrombosis or occlusion but frequently the mouths of these vessels were buried in plaques of calcified or ulcerating atheroma. As the segmentary arteries do not form an angle with the aorta but an elbow-like arch which is almost 90°, partial blocking of their orifices may lower considerably the blood pressure in the spinal arterial bed. Thus an interruption or severe diminution of the blood supply to the spinal cord might be caused without any occlusion of spinal tributaries (Gonzalo-Sanz, 1962). Nothing, however, is known so far of the 'critical' minimum blood pressure in the capillary bed of the human spinal cord, where blood flow reaches a critical level, that is to say, when the average O<sub>2</sub> uptake begins to decrease and severe neurological disturbances occur. Whereas a decrease of arterial blood pressure in the canine aorta below 15 mm.Hg for one hour causes ischaemic lesions in the spinal cord (Blaisdell and Cooley, 1962), extensive mobilization of the canine aorta from the posterior parietes was not usually associated with permanent neurological symptoms when the parietal blood pressure in the intercostal arteries did not fall below 30 mm.Hg (Killen and Adkins, 1965). These experimental conditions associated with a comparatively rapid fall in blood pressure are not considered to be relevant for the chronic and slow lowering of the spinal cord blood flow in man due to arteriosclerosis and general circulatory disorders. Although the experimental data of Otomo, Wolbarsht, Van Buskirk, and Davidson (1960), Bartsch and Swank (1967), and Czanyak (1967) lend support to the suggestion that spinal cord blood flow similar to the regulation of brain circulation chiefly depends on the systemic blood pressure, very little is known of the autoregulation of spinal cord circulation. Therefore any pathogenic interpretation of spinal cord damage in association with atherosclerosis up to the present rests on the pathological and morphological findings in the spinal cord and its feeding system.

A thorough evaluation of the site and distribution of chronic ischaemic spinal cord lesions in 60 necropsy cases of progressive myelopathy referable to arteriosclerosis revealed a most striking preference for damage to the cervical intumescence and the upper thoracic region between C 5-6 and T 2 (Jellinger, 1966, 1967). This corresponds well with the findings of Mannen (1966) who noted a favoured site for small softenings in sclerotic myelopathy at the level of the cervical cord, especially in C 5 to C 8. In spite of severe aortic sclerosis with ulcerating atheroma and sometimes lower aortic thrombosis, ischaemic damage to the thoraco-lumbar cord was

comparatively rare in our series. In some cases this might be due to a special pattern of vascularization of the caudal parts of the spinal cord providing collateral supply via accessory lower lumbar branches (Lazorthes, Gouazé, Bastide, Sontoul, Zadeh, and Santini, 1966). Recently Garland, Breenberg, and Harriman (1966), in a case of spinal cord malacia with ischaemic lesions at various levels of the lumbosacral cord, found stenosis of the anterior spinal artery at one lumbar level which was discussed as one aetiological factor of insufficiency of arterial supply.

The predilection for chronic ischaemic damage to be in the cervical cord indicates that the most severe decrease in blood flow occurred in the spinal territory where the vertebral arteries are the source of supply. This appears the more surprising as the anatomical pattern of arterial supply to the cervical cord is thought to provide almost perfect protection of this part from the complications of atherosclerosis (Turnbull, Breig, and Hassler, 1966). On the other hand, it is well known that occlusion, stenosis, and other impairments of the vertebral arteries are accompanied by cervical infarction on myelopathy (Hughes, 1966). In spite of the vertebral arteries being frequently affected by severe atherosclerosis (Hutchinson and Yates, 1956; Fisher, Gore, Okabe, and White, 1965) and the critical reduction in their blood flow due to various positions of the neck (Chrast and Korbicka, 1962), the causes of the preferential damage to the spinal territory of supply of the vertebral arteries in chronic myelopathy associated with arteriosclerosis is not yet elucidated since we lack detailed angiographical and morphological data regarding the extracranial part of this artery. Whereas cases with severe cervical spondylosis as one possible cause of myelopathy were not included in the series examined, moderate bony and cartilaginous deformation of the cervical spine were noted in 12% of this myelopathy group. They should therefore be taken into account as a contributory factor to spinal cord damage due to direct mechanical impairment or vasocirculatory disorders (c.f. Taylor, 1964; Hughes, 1966; Breig, Turnbull, and Hassler, 1966). Whether there is a local correlation of spinal cord lesions with the cervical preference of atherosclerosis of the anterior spinal artery and fibrosis of the small intramedullary vessels needs further discussion.

Fibrotic thickening and stenosis of intramedullary vessels, which is regarded as secondary to a diminution of the total blood supply, is probably comparable to 'adaptation sclerosis' (Stammmer, 1939; Zollinger, 1967) and itself causes general and local increase of vascular resistance in the spinal cord. Therefore it results in considerable reduction of the regional

blood flow, as was demonstrated in senile brains by Lassen, Høedt-Rasmussen, Sorensen, Skinhøj, Cronquist, Bodfors, Eng, and Ingvar (1963). Moreover, these vascular changes cause a 'rigidity' of nutrition and haemodynamic adaptation of the spinal vascular system that in a critical diminution of blood flow due to extramedullary disorders, e.g., aortic atheroma, cardiac failure, or vasocirculatory insufficiency, may result in ischaemia of the spinal cord. The 'critical zones' of arterial supply are usually affected first. These are the intermediary grey matter, and, as in relation to the longitudinal extension of the cord, the cervical-thoracic region, being the overlapping zone between the territories of supply of the vertebral and subclavian artery and the aorta respectively (Jellinger, 1966, 1967). Fibrosis of the intramedullary vessels, in addition to the rare atherosclerosis of the major spinal arteries, therefore is regarded as an important factor contributing to a higher vulnerability of the spinal cord in elderly and sclerotic patients towards vasocirculatory disorders of mainly extramedullary origin which cause critical decrease in spinal cord blood flow.

The thorough analysis of spinal cord arteriosclerosis and of progressive myelopathy combined with atherosclerosis indicates that a very complex combination of organic and vascular disorders originating within and without the medulla must be considered as factors in the pathogenesis of spinal cord lesions attributable to arteriosclerosis and systemic hypertension. Further correlative clinicopathological and experimental studies will be necessary to elucidate the mechanisms of chronic spinal cord ischaemia from arteriosclerosis.

#### SUMMARY

Histological examination of 1,037 unselected neurological necropsy cases revealed a mean frequency of 10.5% for mild arteriosclerotic changes and of 2.2% for moderate to severe atheroma in the major spinal arteries, the incidence of macroscopically detected cerebral atherosclerosis being 39.3%. Arteriosclerosis of vessels of the spinal cord does not depend upon age and shows a negative correlation with atherosclerosis in the rest of the body. Atheroma of radicular tributaries and intramedullary arteriosclerosis are extremely infrequent. The comparatively rare incidence of atherosclerosis of the spinal cord is opposed by frequent fibrotic thickening and narrowing of the small intra- and extramedullary vessels, the occurrence and severity of which is clearly related to advancing age. Relevant correlations of fibrosis of the small vessels of the spinal cord not specific for any particular disease to generalized atherosclerosis were not established.

Although atheroma of the spinal arteries exceptionally result in spinal cord infarction, correlative studies gave good evidence suggesting arteriosclerosis and fibrosis of the spinal vessels as important contributory factors in chronic ischaemia of the spinal cord referable to haemodynamic disorders, chiefly of extramedullary origin, in generalized atherosclerosis, aortic atheroma, and systemic hypertension. Progressive myelopathy due to arteriosclerosis is suggested to be far more common than was formerly supposed. The pathogenesis is discussed with special reference to the favoured site for chronic ischaemic damage in the lower cervical and upper thoracic spinal cord, indicating a chronic decrease in spinal blood flow predominantly in the spinal territory supplying the vertebral arteries. A pathological analysis of a larger series of observations of this clinically ill-defined condition suggested a complex combination of vasocirculatory disorders of extra- and intra-medullary origin due to arteriosclerosis, whereas cervical spondylosis in this type of myelopathy was found to be of minor importance.

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