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Extrinsic and intrinsic blood supply and histomorphological changes associated with age in the cerebral arteries and brain nuclei in dog (Canis familiaris) and pig (Sus scrofa domestica)

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EXTRINSIC AND INTRINSIC BLOOD SUPPLY AND HISTOMORPHOLOGICAL CHANGES ASSOCIATED WITH AGE IN THE CEREBRAL ARTERIES AND BRAIN NUCLEI IN DOG (CANIS FAMILIARIS) AND PIG (SUS SCROFA DOMESTICA).

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Extrinsic and intrinsic blood supply and histomorphological changes associated with age in the cerebral arteries and brain nuclei in dog (Canis familiaris) and pig (Sus scrofa domestica)

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INTRODUCTION

The present investigation was envisaged to pursue studies on the brain as a part of the gerontological work being carried on in the Department of Veterinary Anatomy at Iowa State University for the last twelve years. The project was developed to study normal aging process in the different organs of the dog and pig, specially maintained for such gerontological studies.

The present work was undertaken to study the extrinsic and intrinsic blood supply to the brain, histomorphological age change in the cerebral arteries and age-associated changes in different nuclei and cortices of the brain in the dog and pig. An attempt was also made to compare these changes with those reported in other species of domestic animals and in the human.

The blood supply to the brain, in the above species, was included in view of the lack of information about its intrinsic distribution. The extrinsic blood vessels have been studied extensively by many authors dating as early as late nineteenth century. The works published so far do not contain sufficient information regarding the internal distribution and nuclear areas supplied and do not recognize many branches which have already been recognized in the human. Various workers put forth conflicting terminology which

required clarification. N.A.V. (1968) attempted to form a universal nomenclature for all domestic animals in line with the already accepted one in the human. A number of books on Veterinary Anatomy mentioned about the blood supply to the brain in the dog and pig which was too concise and was from a comparison point of view with other domestic species. The only exception to the above was the publication by Miller, et al. (1964) who mentioned about the extrinsic blood supply in the case of dog. The present attempt, to study the extrinsic and intrinsic blood supply to the brain in both species, to discuss their nomenclature and to propose the acceptance of important extrinsic and intrinsic vessels present in the domestic animals, may serve useful for future work in this line. The intrinsic blood supply was incorporated to detail out the different sources of the blood supply to different nuclear areas and fiber tracts. The above investigation was thought useful because of its paucity in the literature as well as its significance not only from the academic point of view but also from its importance in the applied and experimental works in the field of neuroanatomy, neurophysiology, neuropharmaceology and biomedical sciences. It was thought that the above information will stimulate the correlative studies for further experimental work in the above fields for which the dog and pig serve as suitable experimental subjects.

Histomorphological age changes in the aorta and its major branches as well as the arteries of different organs of the dog and pig have been studied or are in the process of investigation in the Department of Veterinary Anatomy at Iowa State University. A number of studies on the cerebral arteries have been reported by various authors, but invariably these studies were done on the tissues collected from autopsy or from the experimental animals. The studies done or in progress in the above-mentioned department were an exception to the latter as the animals included were specially raised for the normal aging studies, their diet and habitat were the same, their genetic history as well as other relevant records were maintained. The present work employed the dogs and pigs from the above colonies and formed a segment of the gerontological project being conducted. The connective tissue changes in the arterial wall were incorporated. The recognition of the above changes was thought to be important in the aging cerebral arteries as such changes might be predisposing the arterial wall to undergo narrowing or hardening by developing fibrosis and intimal thickening. In addition to the above, the comparative evaluation of the changes in the vascular wall of the cerebral arteries in the dog and pig were incorporated to elucidate the difference in the response of the arterial wall to aging in these species.

A number of studies on the aging pigment (lipofuscin) in the nervous tissue have been reported in different animals. The studies on the lipofuscin pigment in the brain stem nuclei, spinal cord, dorsal root ganglia and paravertebral ganglia of the dog and pig have been conducted in this department. These investigations contributed a great deal to the understanding of the possible origin of the pigment and its magnitude in different areas of the nervous tissue. The present study was extended to investigate further into the problem by including the cortices and other nuclear areas in the above species. The study also included quantitative estimation of the intraneuronal volume of the pigment in different areas, distribution of the pigment per unit area as well as the percentage of the neurones containing the pigment in different age groups.

As indicated earlier, gerontological studies on the different organs and tissues of the dog and pig already conducted and being pursued in the Department of Veterinary Anatomy at Iowa State University will comprise a most valuable contribution to the understanding of the aging process and will enable one to distinguish between the pathological changes and age changes in the above species at different ages.

The different gerontological studies in this department on brain, spinal cord, kidney, adrenal, pancreas, hypophysis,

female genital tract, salivary glands and blood vessels including the aorta, were studied or being studied at present from the same animals in most of the cases. The age changes in the different organs and tissues when correlated and compiled together will form a most exhaustive and rare treatise on the age changes in the dog and pig.

REVIEW OF LITERATURE

Blood Supply to the Brain of the Dog and Pig

The study of the blood supply to the brain was first recorded by Alcmaeon (500 B.C.) who studied the optic nerve and distribution of the blood vessels to the brain. Hippocrates (400 B.C.) mentioned the blood vessels supplying the brain of goat in his treatise. He mentioned that the arteries contained air. Herophilus (300-250 B.C.) recognized that the brain was the central organ of the nervous system, a seat of intelligence. He coined the term "rete mirabile" for the arterial plexus observed at the base of the brain. Leonardo-da-Vinci (1452-1518) also described the rete in ruminants. Berengario-de-Carpi (1490) denied the presence of a rete mirabile at the base of the brain in man as was thought earlier. He was supported by Vesalius (1538).

Willis (1664), in his fundamental work on the anatomy of the brain confirmed the views of the above workers. He stressed the importance of the regulation against too sudden changes in the blood supply to the brain. He noted that the circulus arteriosus at the base of the brain was present for a smooth and continuous cerebral blood supply.

Rapp (1827) attempted to generalize about the presence of the rete to function and thought that it was present in animals in which arteria vertebralis was not directed to

supply the brain. Tandler (1899) while studying the comparative blood supply to the mammalian head observed that the circulus arteriosus can be supplied either only through the arteria vertebralis or, in other extremes, by the arteria carotis interna but all possible intermediate stages can be observed in mammals. He observed that the rete mirabile was present in most of the Artiodactyles and Carnivores. Tandler (1906) observed the formation of the rete mirabile embryologically. He described that the arteria carotis interna gave small vascular buds which progressively enlarged, ramified, and anastomosed among themselves. The rete was completed by a contribution from the ramus anastomoticus, a branch of the arteria maxillaris interna.

Hofmann (1900) studied the comparative blood supply to the head of the vertebrates and noted varied patterns of arterial contributions to the brain in the above group. He observed the presence of a rete mirabile in Artiodactyles and Carnivores included in his studies. de Vriese (1905) recognized that in Artiodactyles the cerebral arteries took their origin from the rete mirabile in the adult stage whereas in the embryonic stages the patent arteria carotis interna influenced the cerebral supply which progressively shut off due to its obliteration in late fetal and early postnatal stages. He recognized a rete in Carnivores also.

Chauveau and Arloing (1905) mentioned that the internal carotid artery in the dog anastomosed with a branch from the arteria carotis externa. It anastomosed on the side of the pituitary fossa with a division of the arteria sphenospinalis and returning branches of the arteria ophthalamica, forming a small plexus similar to that observed in ruminants and from which proceeded the cerebral arteries. The arteria occipitalis, at the level of the atlantal transverse process, divided to give off an arteria occipito-muscularis and arteria cerebrospinalis. They recognized that arteria sphenospinous and arteria ophthalamica anastomosed with the arteria carotis interna. Regarding the arteria carotis interna in the pig they mentioned that a rete was formed by the above arteries after it entered the cranial cavity. It was joined by the ophthalmic branch of the arteria maxillaris interna.

Canova (1909) studied the blood supply to the head of the sheep and goat. He confirmed the views of earlier workers regarding the involution of the arteria carotis interna and formation of the rete. Bruckner (1909) studied the blood supply to the head of the dog and found that the arteria carotis interna joined with its fellow of the opposite side by an arterial stump, the arteria intercarotica, in one specimen. He recognized a ramus anastomoticus extending between the arteria carotis interna and arteria ophthalmic externa.

Dandy and Goetsch (1911) asserted that the pituitary gland of the dog received its blood supply from various sources. They found that the anterior lobe received its blood supply from the anterior half of the circle as well as directly from the arteria carotis interna. The posterior lobe received vessels directly from the arteria carotis interna. The intermediate lobe received vessels through the stalk, adjacent brain areas and vessels supplying the posterior lobe. Stopford (1916a,b) observed that the blood supply to the medulla oblongata and pons of man was contributed by a complete set of branches given by the arteria cerebelli inferioris anterior, arteria cerebelli inferioris posterior, arteria cerebelli superioris and other collateral branches from the basilar and vertebral arteries.

Jenke (1919) studied the blood supply to the brain of the pig and dog and noted the obliteration of the internal carotid artery and presence of the rete mirabile in the pig. He described the branch of the internal carotid artery as an anterior ramus giving off the middle and anterior cerebral artery, whereas the posterior ramus continued caudally. The terminal branch of the arteria basilaris gave off the posterior cerebral and anterior cerebellar arteries in both species.

Fazzari (1929) described the origin and distribution of the cerebellar arteries in man and domestic animals. He noted

the presence of the arteria cerebellaris anterior accessorius in the sheep. In addition to the arterial cerebellaris anterior and posterior, an arteria vertebrocerebellaris was recognized by him in the dog and man. This artery was absent in sheep.

Bruni and Zimmerl (1951) gave the general pattern of the blood supply to the swine and canine brain. They mentioned the association of the rete mirabile to the cerebral blood supply in the pig.

Basir (1932) found that the anterior lobe of the pituitary gland in the dog was supplied by the branch of the circulus arteriosus. The pars nervosa got its supply from the arteria lobar caudalis (posterior lobar artery) given by the arteria carotis interna. This also supplied the infundibular stalk and cavity. Abbie (1933, 1934) studied the comparative anatomy of the choroidal arteries and forebrain arteries in the vertebrates. While dealing with the subprimates he mentioned that there were two sets of choroidal arteries, anterior and posterior, the latter were also designated separately into two or three different choroidal arteries based on the topography and origin. He recognized that the cerebral arteries have not undergone much change in their origin except the posterior cerebral artery, the origin of which shifted backwards. Shellshear (1920, 1927, 1930) while studying the brain arteries postulated that the cerebral arteries

were formed in definite relation to the function and that the distribution of arteries obeyed the ontogenetic and phylogenetic laws.

Ask-Upmark (1935) in his extensive study on the carotid sinus and cerebral circulation stated that the rete mirabile was present in those animals in which the arteria carotis externa took over the blood supply to the brain from the arteria carotis interna, depending on the development of the rete mirabile which was extensive or meager.

Wislocki (1937) observed the blood supply of the pituitary gland in the cat and found two sets of arteries, arteriae hypophysiales superiores and inferiores, supplying it. Zhedenov (1937) studied the obliteration of the internal carotid artery and formation of the rete mirabile in the ox. He divided the rete into anterior and posterior portions.

Ellenberger and Baum (1943) and Zietzschmann (1943) included the works of various earlier workers and described the blood supply to the brain of domestic animals. They included the rete mirabile in both animals in agreement with the already reviewed workers. According to them, the arteria choroidea rostralis, arteria cerebri media and arteria cerebri rostralis arose from the ramus communicans rostralis. They recognized an arteria cerebri profunda arising from the ramus communicans caudalis.

Nilges (1944) studied the arterial supply to the cornu ammonis (hippocampus) in various animals including the dog and found that the arteria choroidea rostralis and arteria cerebri caudalis were the main sources of supply to the above.

Miller (1948) mentioned the formation of the circulus arteriosus by the branches of the arteria carotis interna and arteria basilaris, but did not mention the detailed course of the vessels and their supply to different parts of the brain.

Legait and Radacot (1949) studied the modification of the cerebral circulation in domestic animals including the pig and dog, based on the involution or patency of the arteria carotis interna and main source of blood supply to the brain.

McDonald and Potter (1951) observed that in the rabbit, the distribution of carotid and vertebral blood formed an equilibrium in the arteria communicans caudalis. This equilibrium could be shifted forward or backward depending upon the occlusion of the internal carotid or vertebral arteries.

Jewell (1952) in the dog, observed various anastomoses between the intracranial and extracranial circulation. He noted that the occipitovertebral anastomosis and anastomosis between the arteria anastomotica and arteria carotis interna were the important routes by way of which the blood might

reach the brain. Daniel, et al. (1953) studied the formation of the rete in various animals including the dog and the pig. They observed that the rete in the pig was contributed by the arteria pharyngeus ascendens, ramus anastoticus, arteria anastomotica and arteria carotis interna, whereas in the case of the dog the major contribution in the formation of a small rete was from the arteria carotis interna, arteria anastomotica and the ramus anastomoticus.

Jewell and Verney (1957) studied the neurohypophyseal osmoreceptors in the dog. They observed that the internal carotid blood in the dog distributed to the anterior hypothalamic areas whereas the vertebral blood supplied the most of the hypothalamus and thalamus backwards. The arteria carotis interna supplied the pituitary as a whole.

Bradley and Grahame(1959) described the blood supply to the brain of the dog from three sources, two internal carotids and a single arteria basilaris. They regarded the arteria cerebri caudalis as a terminal branch of the arteria basilaris. They mentioned the fusion of the anterior cerebral arteries completing the anterior part of the circulus arteriosus. They described various anastomoses between the arteries associated with cerebral blood supply but did not mention the arteria intercarotica as described by various workers.

de la Torre, et al. (1959) studied the cranial circulation in dog radiographically. They observed that two anterior

cerebral arteries joined together to form an arteria communicans rostralis and noted that both arteriae cerebri rostrales got filled with unilateral injections. They regarded that the arteria communicans caudalis was a caudal continuation of the arteria carotis interna. They also observed the presence of an anastomosis between the two arteriae carotis internae just behind the hypophysis. Jewell and Verney (1957) also noted the same vessel and called it as arteria hypophysialis caudalis

Becker (1960), described the details of the blood supply to the head in the pig. He noted that the arteria carotis interna was not the main supply to the brain but was supplemented by branches from the arteria maxillaris interna. The anterior ramus of the arteria carotis interna gave off arteria ophthalamica interna and arteria choroidea rostralis. He observed the arteria communicans rostralis between two arteriae cerebri rostrales.

Popesko (1960) described the blood supply to the brain of the pig in his atlas. He illustrated arteria cerebri caudalis as arteria cerebri profunda. He recognized the rostral continuation of arteria carotis cerebri as ramus nasalis. He also recognized an arteria communicans rostralis and arteria ethmoidalis interna.

de la Torre and Netsky (1960) concluded that the persistent arteria maxillaris was the homologue of the proximal part

of the maxillocarotid anastomotic artery of the dog. The embryonic vividian and stapedial arteries of man were their distal homologues. The circle of Willis of dog resembled the circle in human fetus. They confirmed their earlier observations about different cerebral branches in the dog.

de la Torre, et al. (1962) in their radiographic study on the cerebral arteries in the dog found that the arteria basilaris was formed by the vertebro-occipital anastomosis. It gave off cerebellar and pontine branches and divided to terminate as arteriae communicans caudales.

Nickle and Schwarz (1963) reviewed the arteries of the head in domesticated animals based on the findings of earlier workers.

Goetzen (1964) studied the cerebellar arteries and their contribution to the cerebellar nuclei in the dog, calf, and sheep. He found that the arteria cerebelli superioris was the main source of their blood supply; however, other cerebellar branches also served as additional and variable source. Sisson and Grossman (1953) wrote about the cerebral arteries of the dog and pig without giving any details regarding their course and areas of specific supply.

Miller, et al. (1964) gave an accurate description of the cerebral arteries of the dog, but did not mention about their subsequent distribution and divisions for the supply to the internal structures of the brain. Haines, et al. (1969)

regarded the term proximal anterior cerebral artery be applied to the portion of the arteria carotis interna and its common trunk and the term distal anterior cerebral artery for those portions of the vessel distal to the bifurcation of the common trunk.

Flechsig and Zintzsch(1969) studied the formation of the rete mirabile epidurale and recognized that the ramus communicans nasalis gave off arteria ophthalamica interna, arteria choroidea nasalis, arteria cerebri media, and arteria cerebri nasalis. From the latter an unpaired arteria corporis callosi was formed and arteria ethmoidea interna was given off. According to them ramus communicans caudalis gave off the arteria cerebri profunda (arteria cerebri posterior of Tandler, 1906) and arteria cerebelli nasalis. They mentioned that the rami communicans caudales joined to form the arteria basilaris cerebri.

Histomorphological Changes in the Cerebral Arteries with Age

The changes in the arteries in general have been reviewed by many authors like Winternitz, et al. (1938), Altschul (1950), Steele (1952), Lansing (1959), Bourne (1961), Sandler and Bourne (1963), Lindsay and Chaikoff (1963), Adams (1964), and Roberts and Straus (1965).

Jores (1904), Hueck (1920), Burger and Schlomka (1928), Winternitz, et al. (1938), Aschoff (1939), and Simms (1942)

were few of the earlier workers who proposed that the intimal and arteriosclerotic changes were the result of physiological aging process and may or may not be modified by additional vasoactive factors. The above view has also been put forth recently by a number of workers; Buerger and Hevelke (1956), Movat, et al. (1958), Lindsay and Chaikoff (1963), Getty and Skold (1962), Getty (1965, 1966), Jones and Zook (1965), Skold, et al. (1966), and Klassen, et al. (1968). However, White, et al. (1950), Baker (1961), Flora, et al. (1968), and others regarded age as a secondary factor associated with other primary factors.

The histomorphological changes in the arteries have been classified by various workers, using different terminology - arteriosclerosis and atherosclerosis. Lobstein (1829, 1835) introduced the term arteriosclerosis and defined it as the increasing hardness and brittleness of the arterial wall. Anitschkow (1933) defined it as a chronic disease of large arteries characterized by focal thickenings of the intima, proliferation of connective tissue and accumulation of lipids, often complicated with calcification and ulcerations. Adams (1964) mentioned that the arteriosclerosis comprised of degenerative conditions of both tunica intima and tunica media. Dahme (1965a) stated that arteriosclerosis encompassed all chronic arterial metamorphoses which consist of induration, loss of elasticity and narrowing of arterial lumen, involving

hyperplastic and degenerative changes of the arterial intima and media and their tissue constituents.

The term atherosclerosis was coined by Marchand (1904), who suggested that the changes led to the formation of simple atheroma along with the increased proliferation of fibrous tissue, degenerative changes in the elastic fibers and calcification. According to him the lipid of the plaque was derived from the blood. W.H.O (1958) defined it in the following words: Atherosclerosis is a variable combination of changes of the intima of arteries (as distinct from the arterioles) consisting of the focal accumulation of lipids, complex carbohydrates, blood, blood products, fibrous tissue, and calcium deposits and associated with medial changes.

According to Korenchersky (1961) the process of atherosclerosis began with deposition of lipids, primarily in the intima, with subsequent impregnation of the affected areas by the calcium salts. Development of necrotic nests, ulcerations and formation of atheromatous plaques followed. Schettler (1961) regarded atherosclerosis in general as a chronic progressive rebuilding process in the arterial wall which may lead to hardening, loss of elasticity, and diminution of the lumen and thus to the impairment of the function of affected organs.

According to Schallok (1962) the term arteriosclerosis embraced all pathological processes which led to the hardening

of the arteries. According to these authors, widening of the vessels and an increased tortuosity (in smaller arteries) were probably enhanced in physiosclerosis, which occurred as a consequence of aging but which often was combined with atherosclerosis.

Adams (1964) defined it as a multifocal, proliferative and degenerative process affecting tunica intima and inner part of tunica media, of both large elastic arteries and certain muscular arteries in senescent individuals.

A number of studies regarding the intimal proliferation and arteriosclerosis have been conducted on the aorta and coronary arteries of man and animals. The occurrence of the changes were not new to mankind and were in prevalence in the arteries of the Egyptians (mummies) dated between 1580 B.C and A.D. 525, (Ruffer, 1911). The frequency and severity of the intimal proliferation with lipid deposition was approximately similar to the rate and extent as it is today.

Jores (1924), Wilens (1951), Duff and MacMillan (1951), Movat, et al. (1958) and Bertelsen and Jensen (1960) were among many of the workers who studied the changes in the aorta of man. They observed that there was increased intimal thickening associated with lipid deposition leading to the plaque formation. They also observed that there was gradual decrease in the elastic fibers, represented by the reduplication of internal elastic lamina and disintegration of the

elastic fibers in the medial wall. Similar studies were carried out by Duff and MacMillan (1951), Moon and Rinehart (1952), Dock (1946), Levene (1956), Moon (1959), Robertson (1960a,b) and Geer, et al. (1961) on the coronary arteries in man. They observed a lesser degree of involvement of the coronary arteries in comparison to the aorta.

Changes in the connective tissue of the human aorta have been studied by Taylor (1953), Bertelsen (1961), Bertelsen and Jensen (1960), and Zugbie and Brown (1960), who reported that fraying and reduplication increased in severity throughout all age groups.

The fragmentation of elastic fibers and accompanying increased mucopolysaccharides at least up to fifth decade after which it was constant or decreased due to medial fibrosis, was reported by Bunting and Bunting (1953), Taylor (1953), and Bertelsen and Jensen (1960).

Coronary arteries and aorta of the dog and pig

The studies carried out by Kollisch (1910) and Strauch (1916) indicated that in the dog aortic involvement with fatty streak and oval plaque formation was very evident, more so in the older specimens. There was consistent presence of the splitting and fragmentation of the internal elastic lamina which was followed by intimal proliferative and hyalinization. Krause (1922) and Nieberle (1930) found the intimal

plaques and calcific deposits in the arterial media. Zinserling (1932) noted that primary intimal sclerosis preceded lipid deposition and that the alteration of the connective tissue as well as cholesterol deposition in the vascular wall was significant in the dog.

Morehead and Little (1945) studied the aorta of healthy dogs and found focal loss of elastic tissue and hyperplasia of smooth muscle cells with fibrosis of media and localized calcification. Bloom (1946) observed that the arterial media of the dog showed connective tissue proliferation. The xanthomatosis was due to the presence of foam cells in the smooth muscle cells of the coronary arteries. Lindsay, et al. (1952a, b) observed that the coronary arteries and aorta of older dogs had intimal thickenings, due to the accumulation of the mucoid ground substance. The intimal plaques were observed to have collagen, reticulum and elastic fibers, which were gradually replaced by the mucopolysaccharide ground substance. There was loss of elastic tissue in the media, replacement by collagen and cystic deposition of acid mucopolysaccharides. Lindsay and Chaikoff (1963, 1966) in their further studies on the incidence and involvement of different arteries in the animals observed that the degenerative changes and fibrosis of the vascular wall in animals were predominating and lipid accumulation was clearly a secondary phenomenon. They emphasized the importance and prevalence of elastic

tissue degeneration, changes in ground substance and fibrous intimal proliferation in the initiation of naturally occurring arteriosclerosis in animals as opposed to experimental studies. Getty (1965, 1966) studied the different arteries of the dog and pig, especially raised for gerontological studies, found that in the dog under five years of age the intimal thickenings and plaques were characterized by excessive amount of elastic fibers and smooth muscle cells but little of connective tissue infiltration. According to him lipid accumulation was secondary seen in older age animals.

Davies and Reinert (1965) reported that the arteriosclerosis was uncommon in the dogs under one year of age. However, it was frequent in older dogs and was evidenced by the excessive presence of collagen, elastin and mucopolysaccharides. Luginbuhl, et al. (1965), Waters (1965), Dahme (1957, 1962, 1964, 1965b), Detweiler and Luginbuhl (1967), observed the intimal proliferation, duplication of elastic membrane, proliferation of smooth muscle cells, fibrosis and deposition of the acid mucopolysaccharides in the aorta and coronary arteries of the dog. Dahme (1962) and Braunmuhl (1956) also observed the deposition of amyloid in coronary arteries.

Gottlieb and Lalich (1954) observed that the aorta of the pig showed fibrous connective tissue plaques. These plaques contained sudanophilic material in addition to the fibroblasts. A number of experimental studies were carried

out by Bradgon, et al. (1957), Moreland (1965) and French and Jennings (1965), who found that the frequency of the intimal involvement increased and appeared earlier by feeding butter feeds and egg yolks than under natural diet. Jennings, et al. (1961), French, et al. (1963, 1965), and French and Jennings (1965) studied the changes in the coronary arteries and aorta of the pig. They observed that the changes are comparable to those observed in man but vary in degree. The initial changes consisted in the fragmentation of internal elastic lamina and migration of few smooth muscle cells followed by intimal thickenings. This was characterized by the initial predominance of smooth muscle cells followed by accumulation of fat, collagen and frequent calcification. Vacuolated cells were also observed as constituents of the atherosclerotic thickenings.

Skold (1962), Skold and Getty (1961), Skold, et al. (1966), and Getty and Skold (1962), studied spontaneous atherosclerosis in the aorta, coronary arteries, pulmonary arteries and iliac arteries of the swine. They found atherosclerotic plaques in the abdominal aorta, iliac arteries and orifices of coronary arteries. The plaques in the coronary arteries, thoracic aorta and ascending aorta were inconsistent and were absent in the pulmonary arteries. The plaques observed were associated with foamy macrophages, fragmentation

of the internal elastic lamina and lipid accumulation. Murphy, et al. (1962) also made similar observations on the aorta of swine.

Getty (1965, 1966) studied the aging of the various arteries of the dog and pig including aortas and coronary arteries. He observed that aorta were involved first followed by coronary arteries. The pig was observed to have earlier fatty infiltration in the intimal plaque than in the dog. The changes were comparable to the changes in man.

Campbell (1965), Jones and Zook (1965), Luginbuhl and Jones (1965a,b), Luginbuhl (1965, 1966), Moreland (1965), Zugbie (1965), Detweiler and Luginbuhl (1967) studied the involvement of the aorta and coronary arteries and found that the aorta was generally involved. The abdominal portion of the aorta was more involved than the thoracic. The atherosclerotic changes varied in degree and severity ascending with age. There was duplication of the internal elastic lamina with proliferation of smooth muscle cells in intimal thickening. The foam cells were always associated in the lesions and the calcification of intima and media was also reported by the above workers.

Cerebral arteries of man

The studies regarding the morphological changes in the cerebral arteries in man were carried out as early as 1884 by

Obersteiner. He found that the tunica media had fatty deposits and tunica adventitia developed calcareous deposits occasionally. He also included intracerebral arteries of young and old subjects in his study. Triepel (1896) observed that there was a decrease in the elastic constituents in the cerebral arteries in old age and this was preceded by the splitting of the internal elastic lamina resulting in the vascular degenerative changes. Binswanger and Schaxel (1917) noted that there were quantitative changes in the cerebral arteries of man. The changes recorded were decrease and termination in the growth of elastic tissue after fifty years of age, beyond which the medial smooth muscle cells and elastic fibers decreased. There was continuous increase in production of collagen with age contrary to the above changes in the cerebral arteries.

Ranke (1915), Hackel (1928), and Benninghoff (1930) studied the cerebral arteries and found that internal elastic lamina became laminated early in life. They observed that the elastic tissue did not increase but was replaced by connective tissue which appeared in the spaces left by the degenerated elastic tissue. Splitting of the internal elastic lamina was observed to occur with the proliferative changes.

Tuthill (1933) studied the large vessels of the circle of Willis and felt that the earliest degenerative change consisted of splitting of the elastic lamina, followed by

proliferation of connective tissue. According to his observations fat was deposited secondarily.

Wolkoff (1933) studied the human cerebral arteries ranging from two years of age to eighty-one years and found that the atherosclerotic lesions were present increasingly from fourth decade onwards. He classified them as lipid spots, lipid plaques and fibrous plaques, depending on their connective tissue composition and severity.

Baker (1937), Baker and Iannone (1959a,b,c) studied the cerebral arteries of man. They confirmed the findings of the earlier workers and related their increased frequency to age. They found intimal plaques more frequent in the internal carotid artery and upper portion of the basilar artery. The smaller arteries showed similar changes but were accompanied by fibrosis.

Seitelberger (1954) reported age changes in the small cerebral arteries and found that the entire medial layer was replaced by hyaline material and the vessels became absolutely fibrous in elderly persons.

Moosy (1959) carried out studies which indicated that the cerebral atherosclerotic changes occurred from third decade onwards, the severity of which increased from the fourth decade to the tenth.

Blumenthal, et al. (1954) studied the age changes in the basilar artery of the man in different age groups. They

observed increased intimal proliferation, atrophy of medial muscle cells, duplication of elastic lamina, lipid deposition in the intima and focal calcification of tunica media, with age.

Winter, et al. (1958) observed increase of the atherosclerotic lesions in the cerebral arteries with age, which became rapid after the fourth decade and increased up to the ninth decade.

McGill, et al. (1963) observed that the lesions of the intracranial cerebral arteries developed fibrous plaques with considerable collagen deposition and associated lipid. The first signs of atherosclerotic changes in the intima were observed in the third decade which then onwards increased steadily. The intimal fatty streaks accompanied the thickened intima. Flora, et al. (1967) studied the fine structural changes and observed increased ground substance with accumulation of numerous smooth muscle cells in the intima. Extra- and intracellular lipid was observed later in the smooth muscle cells. The former changes preceded the development of lipid-containing deposits.

Flora, et al. (1968) observed that atherosclerotic lesions were present in cerebral arteries of infants which increased steadily from the third decade to the ninth decade where 98 percent of the subjects showed some involvement.

They stressed the importance of age but not as a sole determining factor.

Klassen, et al. (1968) found intimal cellular thickenings in the aging human cerebral arteries. They observed the intimal proliferation, reduplication of internal elastic lamina, lamellar elastosis and focal calcification of cerebral arteries progressively increasing with age.

Cerebral arteries of the dog and pig

Braunmuhl (1956) studied the cerebral arteries of the dogs at varying ages. He observed that in old dogs there was a formation of the senile plaques. The arteries underwent changes like internal elastic reduplication, degeneration of the elastic elements and fibrosis. He found that the arteries got hyalinized and showed amyloid depositions. Dahme (1957, 1962, 1964, 1965a, b) studied the cerebral arteries of the dog and pig and observed similar changes but stressed that the degeneration of the media in the meningeal and cerebral arteries of dog was common and led to the loss of contractibility. He also observed the amyloid-like substance in the cerebro-meningeal arteries, the involvement of which increased with age.

Getty (1965, 1966) reported the histomorphological age changes in the cerebral arteries of the pig. He found intimal plaques in the anterior and middle cerebral arteries as well as in the basilar artery of aging hogs.

Luginbuhl (1962, 1965, 1966) and Luginbuhl and Jones (1965a,b) noted that the cerebral arteries of swine particularly anterior and middle cerebral arteries underwent extensive narrowing. They found lesser degree of involvement in posterior cerebral and basilar arteries. The intimal thickening was associated with a greater amount of fibrous tissue. There was fragmentation and duplication of internal elastic lamina. The intima contained smooth muscle cells embedded in the interstices of the elastic, reticular, and collagen fibers and matrix of ground substance. Foam cells were also observed by them. The incidence of cerebral intimal thickenings in the pig were more frequent than in the coronary arteries.

Luginbuhl (1966) and Luginbuhl, et al. (1965) studied the cerebral arteries of the dog and found that fibrosis was frequently associated with fibrosis of the media. According to them the arteriosclerotic changes in the cerebral arteries of the dog were rare; however, fibrosis of the intima, media or adventitia were observed more frequently in older dogs.

Fankhauser, et al. (1965) and Detweiler and Luginbuhl (1967) studied the cerebral arteries of the dog and pig and agreed with the earlier views of the various workers that in the dog there was fibrosis of different layers whereas in the pig only intimal proliferation was very much pronounced. They observed intimal thickenings in all cerebral arteries of the

pig to a greater or lesser extent but none in the basilar artery. They observed the occurrence of the foam cells in the atherosclerotic thickenings along with the extensive production of collagen fibers.

Occurrence of Lipofuscin Pigment

Lipofuscin pigment has received much attention in recent years due to its potential relation with the process of aging. The pigment granules were first observed by Hannover (1842) in nervous tissue. White (1899), Hodge (1894), Pilez (1895), and Obersteiner (1903) recognized the presence of the pigment in different parts of the nervous system as increasing with age.

Muhlmann (1910) noted the increase in the accumulation of lipoidal granules in the neurons with advancing age in man and the guinea pig. Dolley (1911) reported the presence of the pigment in purkinje cells of the cerebellum of the dog, Ellis (1920) in the dentate nucleus of the human, and Harms (1924) in the cerebellum of the dog. The occurrence of the pigment in different parts of the nervous tissue was investigated by Bethe and Fluck (1937; in ganglionic cells) and Andrew (1941; in the trigeminal ganglion, spinal cord and brain of the mouse). The term lipofuscin was first coined by Borst (1922).

The presence of the lipofuscin pigment and its increasing accumulation with age in the inferior olivary nucleus of man was observed by Levi (1946). Turex (1940) observed increasing deposition of the lipofuscin pigment in the gasserian ganglion of man with age. Altschul (1943) noted variable manners of disposition of the pigment in the neurons of the basal ganglia, substantia innominata and corpus subthalamicus. Vogt and Vogt (1946)stated that the sequence of the morphological age-related changes are characteristically different in each cell type and have specific courses of intracellular pigmentation. Dixon and Herbertson (1950) observed PAS positive granular material in the central nervous system of man and designated it as the "wear and tear" pigment. Hopker (1951) noted the pigmentation in brain stem nuclei and the dentate nucleus of cerebellum.

According to Gatenby and Moussa (1951), the pigment appeared first in the sympathetic and spinal ganglia and later in the cerebellar cortex, spinal cord and cerebral cortex. Hermann (1952) noted a progressive deposition of the pigment in the neurons of the sympathetic and vagal ganglia with age. Balthazar (1952), D'Angelo, et al. (1956), and Wahren (1957) also found the aging pigment in different areas of the brain. Wahren (1957) described the occurrence of lipofuscin pigment in pallidum and nucleus tuberolateralis at different age intervals.

Sulkin and Kuntz (1952) and Sulkin (1955) observed the varying degree and frequency of pigment distribution in different nuclei of the nervous system in man and dog. Strehler, et al. (1959) studied the quantitative increase of the lipofuscin pigment in the cardiac muscle and found an increasing trend with age. Wilcox (1959) regarded the presence of lipofuscin in the cranial nerve nuclei of mice as the only significant age change. Brody (1960) found a greater increase of pigment deposition in the larger neurons of the cerebral cortex than in the smaller. He reported the largest accumulation in the precentral cortex and the lowest in the striate cortex.

Whiteford (1964) and Whiteford and Getty (1966) studied the aging pigment in the brain stem nuclei of the dog and pig. They found that the pigment increased with age, appearing first at the age of two and a half years in significant amounts in the dog and at two years of age in the pig. Samorajski, et al. (1965) observed that the initial deposition and basic morphologic characteristics of the pigment, even in old age, may vary in different nuclei of the central nervous system within the same age group. Their observation was identical with Bondareff (1957, 1959, 1964), Friede (1962), and Issidorides and Shanklin (1961). Rolsten and Samorajski (1966) stressed the progressive accumulation of lipofuscin pigment with age in the central nervous system and adrenal

glands of mice, which was further investigated and confirmed by Samorajski and Ordy (1967) and Samorajski, et al. (1968). Getty (1966), Few (1966), and Few and Getty (1967) observed the pigment in the spinal cord, dorsal root ganglia and autonomic ganglia of the dog and pig. They concurred with earlier observations of Whiteford (1964) and Whiteford and Getty (1966) on the brain stem nuclei. Munnell (1967) and Munnell and Getty (1968) found a similar relationship between the deposition of lipofuscin in the canine cardiac muscle and age. Reichel, et al. (1968) found that the hippocampus of the rat accumulates more lipofuscin pigment than the cerebral cortex and purkinje cells of the cerebellum.

Functional relationship of lipofuscin with aging in the nerve cells

The occurrence of lipofuscin and its functional significance in aging nerve cells has been interpreted differently by various workers. Dolley (1911, 1917) regarded the presence of the pigment as a hypernormal functional product to functional depression of some duration. Altschul (1943) pointed out that lipofuscin was a waste or degenerative product. He related its presence to restricted metabolic processes or difficulty in eliminating the catabolic products of some metabolic processes. Murray and Stout (1947) supported the view of Dolley (1911, 1917) after studying sympathetic ganglionic

cells in tissue culture. The cells produced the pigment which made the cell lose its plasticity in migration with increasing pigment deposition.

Hyden and Lindstrom (1950), Hopker (1951), Ranson and Clark (1959), and Bloom and Fawcett (1967) regarded the aging pigment as of no significant metabolic importance. Sulkin (1953) subscribed that the presence of pigment was detrimental to the cell. There was loss of chromoidal substance and some cells became non-functional. In a later experiment, Sulkin and Srivanji (1960) again questioned the occurrence of lipofuscin as an age-related process. They concluded that there were various factors like stress, disease, nutritional deficiency, emotion, low oxygen, and changing environment which could initiate the deposition of lipofuscin pigment in cells. This view was contradicted by Strehler (1962), who stated that the mechanism of lipofuscin production under certain environmental conditions and aging process were two different entities. Chu (1954) regarded the pigment as a product of activity rather than aging.

Strehler, et al. (1959) studied the lipofuscin accumulation in the myocardium and stated that the pigment may interfere with efficient functioning of the heart muscle. The pigment particles may act as a binding agent between contractive elements. The magnitude of the accumulation of lipofuscin could meet the criterion of deleteriousness. They found a

linear relationship between the pigment accumulation and age.

Samorajski, et al. (1964,1965) proposed that the lipofuscin may be an insoluble end-product of cellular metabolism or a storage substance in normal cellular physiology and with the appearance of lipofuscin, significant changes in the normal cellular physiology of the organs having postmitotically fixed cellular components were likely to be initiated. The change in the cellular physiology may lead to the death of the cell.

Histogenesis of the lipofuscin pigment

Varied views regarding the origin of lipofuscin pigment have been postulated which were in many instances conflicting, inconclusive and speculative. Pilez (1895) and Obersteiner (1903) defined the pigment as lipopigment because of its stainability with dyes specific for fatty substances. Dolley (1917) thought that the pigment was a product of chromatin transformation. Sjovall (1932) reported that the pigment represented a dispersed phase of the plasma colloid which tended to decrease in its dispersion and finally flocculated. Similar views were expressed by Wunscher (1957) who regarded age-associated cytoplasmic changes as being similar to precipitation or concentration in a colloidal solution due to loss of a water-rich phase.

Bethe and Fluck (1937) found the matrix of lipofuscin to be a protein bounded to a lipid substance and a yellow pigment. Matzdorff (1948) proposed that the origin of lipofuscin may be related to the cytoplasmic matrix. He, however, did not recognize the lipophilic center as the initial site of pigment but recognized the lipid formation particles in the cytoplasm increasing in size and clumping with increasing age and occupying different sites in the cell. The sequential formation of lipofuscin in nerve cells was investigated by Hopker (1951). He regarded it as a five-stage process. The lipophilic center of the cell was considered by him as the first site of lipofuscin formation.

Gatenby and Moussa (1950, 1951) and Gatenby (1953) observed the breakdown of golgi apparatus into argentophilic parts leading to the formation of the lipofuscin pigment. This was in accordance with the earlier observations of Payne (1949, 1952) on the pineal, adrenal, and thyroid glands of fowl. The mitochondria showed alterations with increasing age, signifying the lipofuscin formation with mitochondrial degeneration. This view was further supported by Hess (1955) who regarded the swollen mitochondria as being very intimately related to lipofuscin formation. Sosa (1952) suggested that the intracellular neurofibrils condensed during the aging process and agglutinized by pigmentary granules.

Bondareff (1957, 1959) refuted the concept of the formation of lipofuscin from mitochondria. He stressed that the pigment formation was related to the golgi apparatus and appeared first in lysosomes. Duncan, et al. (1960) reported that the pigment bodies did not replace the mitochondria and suggested that lipofuscin may be formed from some other source than from degenerating mitochondria. Gosh, et al. (1962) have also subscribed to the intramitochondrial origin of the lipofuscin.

de Duve (1959) and de Duve and Wattiaux (1966) supported the above views of Bondareff (1959) and further substantiated the relation between lipofuscin formation and lysosomes. Further support was provided to this view by Essner and Novikoff (1960) and Novikoff (1961). The latter authors designated the pigment as altered lysosomes in different organs of senile human and animal subjects. Strehler and Mildvan (1962) suggested that the lipofuscin was an autoxidized cephalin product from lysosomes.

Samorajski, et al. (1965) found structural and cytochemical similarities between the lipofuscin pigment and lysosomes in aging nerve cells. They found the pigment in old age within the lysosomes. Few (1966) subscribed that the aging pigment formation occurred in five phases: (1) matrix of the lysosomes increased in density and became coarse and granular; (2) a small lipid droplet represented a vacuole was next laid

at the periphery of the lysosome; (3) the dense coarse matrix gave rise to lipoprotein leaflets represented by dense bands; (4) the vacuoles increased in size and bands became extensive; (5) the bands fused to form dense homogeneous particles which became prominent components of the pigment body in very old animals.

Munnell (1967) studied the development of lipofuscin in cardiac muscles and found that the lysosomes play an important role in the development of the pigment. The nature of the pigment granules appeared as residual bodies formed by the coalescence of altered lysosomes and other cellular organelles in varying stages of autolysis.

Sulkin and Sulkin (1967) experimentally produced the pigment in cardiac muscles and autonomic ganglionic cells. They found varied types of pigment bodies; some were swollen with dense clear bodies embedded in the center and in some the dense character of the pigment seemed to have changed into a filamentous substance.

Pallis, et al. (1967) observed the lipofuscin pigment in the area having high alkaline phosphatase activity in the central nervous system. They concluded that the pigment developed in relation with the lysosomes and represented the end-product of lipoprotein degeneration and may be associated with altered lysosomes.

Toth (1968) proposed that the lysosomes represented the ultimate source of the pigment and that the lysosomal enzyme activity could account for apparent formation of lipofuscin.

Concept of aging

The first concrete and valuable record on theory of Senescence can be credited to Weismann (1889) who propounded that aging was not an inherent property of living matter but evolved because of utility. Gompertz (1825) described aging to the progressive accumulation of metabolic product interfering with ozygen transfer and with transmission of stimuli.

Child (1915), Cowdry (1952) and Comfort (1956) came forward with the colloid theory., which was based on the findings that aggregation occurs in certain nonliving colloids with time. If this occurred also in protoplasm, it would tend tc favor the accumulation of inert or toxic catabolic products. Daniellei(1957) postulated genetic control of intracellular molecular and macromolecular metabolism. During aging some deterioration in this control may develop and useless or impaired molecules may accumulate and dilute relate normal macromolecules. Sobel and Marmorston (1956) observed that there was quantitative increase of the fibril-gel ratio of the intercellular material of various tissues during aging. This would impair the transfer of materials to and from parenchymal cells. Muhlmann (1950) contributed aging due to decrease in cell surface volume ratio occurring during growth causing starvation.

Vogt and Vogt (1946) supported the wear and tear as a cause of aging. They found the cells of inferior olivary body to involute early and the vital cells of medulla oblongata very late. Groen (1957) supported the above views and thought that the diencephalon nuclei senescence first, causing impairment of feedback mechanisms regulating food intake, metabolism and endocrine activity.

Strehler (1962) defined aging as the changes which occurred generally in the postreproductive period and resulted in a decreased survival capacity on the part of the individual organism. Whereas Comfort (1956) defined it as a deteriorative process. He further mentioned that under senescence what we measure was decreased in viability and an increase in vulnerability.

Medawar (1951) mentioned senescence as that change of the bodily facilities, sensibilities and energies which accompanied aging and which rendered the individual progressively more likely to die from accidental causes of random incidence (for all deaths were in some degree accidental). No death was wholly natural and no one died merely of the burden of years.

Strehler (1962) laid down certain criteria for defining and characterizing the age changes. These are universality, progressiveness, intrinsicality and deleteriousness. The above criteria implied that any age change would be found accountable in all older members of the species, any change to

be called as age changes be progressive during the lifetime of the individuals in the species, age changes should be due to intrinsic and not extrinsic factors and should show decline in the functional capacity of the individuals in aging.

MATERIALS AND METHODS

The study was designed to study the extrinsic and intrinsic blood supply to the brain, age changes in the cerebral arteries and certain brain areas of the dog and pig. Two sets of materials were taken to encompass different segments of the above study.

In order to study the blood supply to the brain of the dog and pig fifteen specimens of each species were included. The study was conducted by injecting the arteria carotis communis with latex or India ink and dissecting or making different segments of the injected brains transparent subsequently.

The animals were anesthetized and the arteriae carotis communes of both sides were exposed. The venae jugulares were similarly exposed. The arteriae carotis communes were cannulated at three points, in one of the artery two glass or metal canulae were inserted, one directed towards the head and the other towards the body whereas the other artery was cannulated only towards the head.

After completing the cannulations the animals were allowed to bleed for some time and then normal saline was perfused through the arteriae carotis communes. A slit, to allow the venous blood outflow, was made in both venae jugulares. The normal saline perfusion was continued for twenty minutes

or more depending on the size of the animal and state of the returning blood. The watery and light pinkish colored blood outflow indicated that sufficient blood was flushed out of the vessels and body and further perfusion was stopped. The next stage was variable depending upon the decapitation of the head from the rest of the body or leaving it in situ. However, in most of the cases the head was severed from the rest of the body at the level of fourth or fifth cervical vertebra.

In the cases where the subjects were not anesthetized electrocution was employed. The animals were bled through the arteria axillaris and heads decapitated at the above-mentioned level. The arteriae carotis communes were cannulated and the perfusion with normal saline was continued to flush out of the head and its arteries. The next stage of procedure was common in all cases.

The formalin solution (10% W/V) was injected through the cannulae which were previously utilized for injecting normal saline solution. The formalin solution was injected at about 100-120 mm of Hg pressure. After a few minutes of profusion with 10% formalin, the venae jugulares which were slit apart earlier were ligated to create pressure in the vessels, for fixing them in a dilated stage. Similarly vertebral arteries and spinal sinuses were blocked. The flow of formalin was continued until the tissues were observed to show signs of

fixations and hardening. The head was left for ten to fifteen minutes for furthering the effect of injected formalin solution. Taking similar routes (arteriae carotis communes) red latex was injected through both or through single arteria carotis communis though shifting alternatively, at 130-180 mm of Hg pressure. After the latex solution was observed to appear in the vessels of the gums and conjunctiva the injection was discontinued but a little quantity of latex was injected with a syringe in both arteries. Then the specimen was left in the cooler for setting and later utilized for dissection of vessels supplying the brain.

The injection procedure for the brain with India ink was different only in the respect that 0.5 - 1% Indian ink solution in formalin (10% W/V) was injected simultaneously. The procedure for making India ink injected brain transparent consisted in the following steps:

1. Two to three mm transverse sections of brain were made starting from the frontal pole backwards in a serial order.

2. Sections were then transferred to 50% ethyl alcohol, in which these were kept for twenty-four hours.

3. The sections were then transferred to 70% ethyl alcohol and kept for twenty-four hours.

4. The sections were subjected to 90% ethyl alcohol for twenty-four hours.

5. It was repeated.

6. This step consisted in shifting the sections to absolute alcohol for twenty-four hours and this was repeated.

7. Then the sections were transferred to methyle salicylate and kept for twenty-four hours by which time the sections attain transparent nature. These were stored for observations in this solution.

The nomenclature used for different arteries and their subsequent branches was followed in line with the NAV (1968) and earlier works of different authors cited elsewhere in the present study. However, new terms were also suggested and followed. The nomenclature pertaining to the brain nuclei and fiber tracts was adopted from NAV (1968), Singer (1962), Lim, et al. (1960) and Walento (1964).

Histomorphological Changes in the Cerebral Arteries with Age

For the studies relative to the gerontological aspects, included in the project, the following methods and materials were utilized.

The material consisted of dog and pig brains collected from the animals reared at Iowa State University. The dog colony was raised to study the gerontological aspects of normal aging. The dogs utilized were kept in similar environmental conditions, feed and strict care was taken to protect against disease and parasitic infections.

The dogs utilized in the research project were mostly from the colony except a few others which were from different known sources. The records on the date of birth, genetic history, breed, feed, sex, and cholesterol levels in blood were on record at the Department of Veterinary Anatomy.

The pigs used in the work were taken from the swine colony at Iowa State University Swine Nutrition farm where all the requisite information was available. In all, forty dogs and thirty pigs were used (Tables 1 and 2).

The animals were killed in the Department of Veterinary Anatomy by electrocution and were exsanguinated by cutting the arteria and vena axillaris. The collection of material was started immediately and the head was separated from the neck at the atlanto-occipital junction. After the removal of the skin, fascia, and musculature, the cranial cavity was exposed and the brain removed. The dura mater was removed and the brain was immediately transferred to a jar containing about 2,000 cc of 10% buffered neutral formalin. The brains were left for a period of a month or so and fresh 10% buffered neutral formalin solution was added to replace the previous solution completely.

Processing and staining procedures

The brains of dogs and pigs were divided into six segments to include various areas of the brain. The areas

included for localization of lipofuscin in the dog were: cortex cerebri (frontal), nucleus caudatus, putamen, globus pallidus, thalamus, nucleus rubrum, nucleus oculomotoris, gyrus hipocampus, nuclei cochleares, nuclei vestibulares, nucleus dentatus and fastigii, cortex cerebelli (Purkinje neurons), nucleus parasympatheticus n. vagi, nucleus motorius n. hypoglossi, nucleus olivaris inferior or nucleus ventralis corporis trapezoidei, nucleus cuneatus accessorius or nucleus cuneatus lateralis. The areas excluded from the above-mentioned nuclei for a similar study in the case of the pig were nucleus caudatus, putamen, globus pallidus, nucleus dentatus and fastigii. Five nuclear areas were included for the quantitative studies only in the dog. The segments were cut transversely after laying the brain on its dorsal surface. The ventral surface was taken as a guide to demarcate and cut the brain into different segments. The following guidelines were used for getting different segments:

1. Anterior part of the substantia perforans rostralis.
2. Anterior part of the optic chiasma and anterior part of lobus piriformis.
3. Posterior part of the tuber cinereum.
4. Anterior border of the pons and posterior part of interpeduncular fossa.
5. Junction of corpus trapezoideum and medulla oblongata.

6. Caudal portion of medulla oblongata.

The tissue blocks so made were processed and embedded in paraplast. These were sectioned at eight microns and stained with the following stains:

1. Haemotoxylin and eosin (AFIP, 1960).
2. Weigert's Resorcein Fuchsin Stain (AFIP, 1960).
3. Grossman's Modified Mallory's Connective Tissue Stain (AFIP, 1960).
4. Alican Blue and P.A.S. Stain (AFIP, 1960).
5. Von Kossa's Stain (AFIP, 1960).
6. Verhoeff's and Van Gieson's Stain (AFIP, 1960)

Technique for fluorescence microscopy

The slides mounted with paraplast sections were deparafinized in xylol and mounted in fluorescing immersion oil. These slides were examined under a Bausch and Lomb Dynoptic microscope using a 43x, .65 N.A. objective or 10x, .25 N.A. objective, compensated eyepiece, and an Abbe 1.30 N.A. condensor fitted with 12 mm dark field stop.

The light source consisted of a Bausch and Lomb 200-watt mercury arc lamp and filters used were a Bausch and Lomb 5-58 exciter filter, which transmits mainly to the 400 millimicron range, and a Bausch and Lomb Y-8 barrier filter which transmits above the 550 millimicron range.

Quantitative studies

For the study of finding the magnitude of lipofuscin pigment, in the different brain areas, the method employed by Chalkley (1943), Reichel (1968), and Reichel, et al. (1968) was used. Similar methods were also employed by Strehler, et al. (1959), Munnell (1967), and Munnell and Getty (1968) in finding out the rate and magnitude of the accumulation of the lipofuscin in myocardium. This consisted in using a net reticule which had 121 intersections. The net reticule was fitted in a 10x ocular. It had a total area of 5 mm^2, and each square in it was .5 mm^2.

Percentage of pigmented neurons per unit sectional area

The net reticule was focused in a random field of specific nucleus of the brain in such a way that an intersection was lying on the neuron containing pigment. The neurons containing pigment and lying at the intersections were noted. Similarly, the non-pigmented neurons still intersecting were also counted. The field and focusing was disturbed and a new field at random was again selected to repeat the process. This process was repeated ten times to find an average of the percentage of pigmented and non-pigmented cells.

Percentage of pigment per unit sectional area This process was further enlarged such that now in a particular field selected randomly the intersection was focused on the

pigment and not cells. The intersections falling on the pigment were counted. This was repeated in randomly selected ten fields and averaged. This gave a percentage of pigment per unit volume of the particular area.

Percentage of intraneuronal pigment The technique employed consisted in placing the intersections of the grid on the individual neurons of different areas of the brain. Count of the intersections on the intraneuronal pigment and as well as on the rest of the neuronal volume was noted separately. The above information was then transferred into percentage of the pigment intraneuronally in relation with the whole neuronal volume. This was repeated on ten different neurons and averaged.

OBSERVATIONS

Blood Supply to the Brain of the Dog

Arteria carotis interna

The arteria carotis interna which arose as a branch of the arteria carotis communis, in its intracranial course, reached the dorsum sallae and perforated the dura mater to traverse in the cavernous sinus. During this course in the cavernous sinus, the arteria carotis interna gave off a transverse branch from its medial aspect which joined a similar branch from the arteria carotis interna of the opposite side to form the arteria intercarotica caudalis. This branch traversed the cavernous and intercavernous sinuses behind the posterior lobe (lobus posterior) of the hypophysis cerebri. The details about its formation and branches will be mentioned later. The arteria carotis interna at this level received an anastomosing branch from the arteria ophthalmica externa called the ramus anastomoticus cum arteria carotide interna (arteria anastomotica) and from arteria meningea media, the ramus anastomoticus cum arteria carotide interna (ramus anastomoticus) representing a simple rete mirabile epidurale rostrale. The arteria carotis interna continued its course rostrally in a flexous manner after receiving the above branches. The arteria carotis interna left the cavernous sinus by perforating it. Soon

after or just before leaving the cavernous sinus, the arteria carotis interna gave off a branch which coursed medially and joined with the similar branch of the opposite side to form the arteria intercarotica rostralis, associated with it were few fine branches which will be described later. After giving the above branch, the arteria carotis interna divided into three branches, arteria communicans caudalis, arteria cerebri media and arteri cerebri rostralis. The branches given by the arteria carotis interna during above-mentioned course and at its termination were as under:

Arteria intercarotica caudalis As indicated earlier, it started as a branch of the arteria carotis interna and formed a transverse trunk with the similar artery from the opposite side (Fig. 5). The artery traversed in the cavernous and intercavernous sinus and adhered to the dura mater. From the arteria intercarotica caudalis a number of fine branches were given. These were defined as rami hypophysiales (inferiores) caudales. Then branches perforated to reach the posterior lobe (lobus posterior) of the hypophysis cerebri and supplied the infundibulum and pars intermedia adenohypophysis. In addition to the above, one or two small meningeal branches were present which distributed in the dura mater covering the hypophysis cerebri and may extend to the dura mater up to the level of the optic chiasma. The origin of this artery may be variable such that in

some cases it may arise from the ramus anastomoticus cum arteria carotide interna (branch of the arteria ophthalmica externa).

Arteria intercarotica rostralis The arteria carotis interna, near the point of its emergence from the cavernous sinus, gave off one or two small branches which coursed medially over the ventral surface of the area just in front of the hypophyseal stalk and partly on the optic chiasma and joined with a simiar branch from the opposite side to form a transverse trunk, the arteria intercarotica rostralis. From this vessel near its origin and from the arteria carotis interna one or two more branches were given off which joined with the fine branches give off by the arteria communicans caudalis. These branches as well as those from the arteria intercarotica rostralis joined to form an annular network of fine vessels around the hypophyseal stalk or infundibulum and on the ventral surface of the tuber cinereum. These branches descended into the hypophyseal stalk or infundibulum to supply the pars distalis, pars intermedia, pars infundibularis of the adenohypophysis and to a small extent to the pars nervosa. The branches perforated to supply the tuber cinereum, nucleus hypothalamicus ventromedialis, nucleus supraopticus and other associated structures.

The arteria intercarotica rostralis in addition to the above branches gave off four or six fine branches, which

coursed rostrally on the ventral aspect of the optic chiasma and optic tract. One or two branches curved dorsally in the space between the union of the optic nerves. These branches supplied the optic nerve, optic tract and optic chiasma reaching to the nucleus suprachiasmatica, nucleus supraopticus and anterior hypothalamic areas (Figs. 6, 7 and 8).

Arteria cerebri rostralis

This artery represented the rostral continuation of the arteria carotis interna. The pattern of the origin of this artery may be different such that in general both arteria cerebri rostralis and arteria cerebri media arose in common after the arteria communicans caudalis has been given off (Figs. 1, 6 and 7).

The arteria cerebri rostralis after its origin from the arteria carotis interna coursed rostrally for a short distance and bent dorsomedially towards the median plane to come in relation with the dorsal aspect of the optic chiasma and optic nerve. Then the artery continued rostrally in the midline along the longitudinal fissure (fissura longitudinalis cerebri) and ventral surface of the medial olfactory stria or tractus olfactorius medialis. It joined with the arteria cerebri rostralis of the opposite side by a side-to-side anastomosis. After forming this, each artery

separated to ascend dorsally on the medial surface of the cerebral hemisphere of its own side. The artery during this course came in relation with the gyrus rectus and formed a double curve to reach the genu corporis (Fig. 4). On reaching the genu corporis callosi it made a caudal bend to course in the sulcus corporis callosi and on the dorsal surface of the corporis callosi. It continued caudally and terminated by anastomosing with a branch of arteria cerebri caudalis (cortical branch). During its course the artery gave off a number of central and cortical branches.

Rami centrales The arteria cerebri rostralis during its initial course, before reaching the longitudinal fissure, gave off fine perforating branches which were four to five in number and supplied the area preoptic lateralis and medialis, nucleus periventricularis hypothalamicus and nucleus supraopticus.

Arteria ophthalmica interna It took origin from the ventral face of the arteria cerebri rostralis (Fig. 7). It coursed along the nervus opticus (optic nerve) dorsolaterally or dorsally. The artery left the cranial cavity through the canalis opticus (optic canal) while still in the company of the optic nerve. The artery coursed on the medial aspect of the above nerve and joined with the arteria

ophthalmica externa through a ramus anastomoticus cum arteria ophthalmica interna.

Rami striati mediales (Arteriae striati mediales) The arteria cerebri rostralis, before joining with the artery of the opposite side to form the arteria corporis callosi communis (mediane), gave off one or two branches. These branches were directed laterally and coursed on the ventral surface of the substantia perforata rostralis and trigoneum or tuberculum olfactorium. A number of fine branches may similarly leave the arteria cerebri rostralis to course on the above structures. The above branches may send anastomosing branches to the branches from the arteria cerebri media. The above-mentioned branches during their course on the ventral surface of the tuberculum olfactorium and substantia perforata rostralis gave off a number of perforating branches, rami striati mediales, which varied in number. These branches supplied the rostromedial and rostral part of the nucleus caudatus, commissura rostralis, capsula externa mainly (Figs.46 a,b and 47 a,b).

Arteria ethmoidalis interna This artery left as a ventral branch of the arteria cerebri rostralis (Figs. 1, 6 and 7). The origin of this artery was in common or slightly in front of the preceding branches. It was a slender branch which coursed along the ventral surface of the medial

olfactory stria and longitudinal fissure rostrally. It was closely associated with the dura mater. The artery reached the lamina cribrosa and medial to the olfactory bulb where it anastomosed with the ventral branch of the arteria ethmoidalis externa and arteria ethmoidalis interna of the opposite side to form the rete olfactorium (rete ethmoidalis). The rete was also contributed by fine branches from the arteria marginalis. The branches from the olfactory rete supplied the olfactory bulb and medial olfactory stria intracranially. From the rete, branches passed through the lamina cribrosa to supply the ethmoturbinates and olfactory mucosa. The branches of the arteria ethmoidalis interna continued forward to supply the posterior part of the nasal cavity and anastomosed with the branches of the arteria sphenopalatina.

Arteria corporis callosi (mediane) communis The arteria cerebri rostralis after giving the preceding branches joined the artery of the opposite side to form a common stem for the origin of the subsequent branches. The communication of the arteries was different in comparison to man and some species of the domesticated animals in which the communication was formed by means of a transverse vessel representing the arteria communicans rostralis (Figs. 6 and 7).

Arteria marginalis The artery started as a branch of the arteria corporis callosi (mediane) communis. The arteria marginalis continued along the medial olfactory tract towards

the olfactory bulb. The artery gave off a branch to the medial olfactory bulb, the arteria olfactorium medialis. The arteria marginalis continued on the rostral or frontal pole of the cerebral hemisphere to distribute on the frontal polar cortex. It may also contribute in the formation of the rete olfactorium (ethmoidalis).

Rami dorsomediales (Rami rostromediales) From the arteria cerebri rostralis directly or at the level of the union with its contralateral part, a number of fine branches were given off which were directed dorsomedially perforating the lamina terminalis and gyrus diagonalis. A strong ramus which generally started from the common stem of the arteria corporis callosi (mediane) communis coursed flexuously on the subcallosal area and reached up to the genu corporis callosi. During its course it gave off branches which were distributed, along with the above-mentioned perforating rami, to the nucleus supraoptica, area preoptica medialis, lamina terminalis, nuclei septalis medialis and lateralis, nucleus accumbens septi, column fornix, commissura rostralis, tuberculum rostrale thalami and area subcallosa. The larger ramus indicated above was generally single and gave off branches for the above areas of both the hemispheres (Figs. 4 and 47 a,b).

Arteria corporis callosi This may be regarded as the terminal continuation of the arteria cerebri rostralis. This was formed by the bifurcation of the arteria corporis

callosi (mediane) communis. The artery ascended on the gyrus proreus and reached the genu of the corpus callosum. It curved caudally to course above the corpus callosum and along the gyrus cinguli to join with the arteria cerebri caudalis. The artery in its course gave off a number of branches which were mostly cortical in distribution over the gyrus rectus, gyrus proreus, gyrus cinguli, gyrus precruciatus, gyrus postcruciatus, and corpus callosum. It may send perforating branches to the area subcallosa and septal nuclei (Fig. 4).

Arteria cerebri media

The arteria cerebri media took its origin from the arteria carotis interna. The artery was larger in caliber and had greater distribution than the arteria cerebri rostralis as well as the arteria cerebri caudalis. The arteria cerebri media after its origin coursed dorsolaterally in an ascending manner. The artery coursed along the ventral part of the gyrus diagonalis, substantia perforata rostralis and in front of the lobus piriformis (pars caudalis). It ascended to cross the tractus or stria olfactorius lateralis and reached the junction of the sulcus rhinalis lateralis pars rostralis and caudalis. It reached the sulcus sylvius at the level of which it divided into a number of cortical branches distributed to most of the lateral aspect of the

cerebral hemisphere. However, in addition to the forementioned cortical branches, the main continuation of the arteria cerebri media before reaching the sulcus rhinalis rostralis, also gave off two or three large cortical branches. These cortical branches anastomosed with similar branches of the arteria cerebri rostralis and arteria cerebri caudalis (Figs. 1, 2, 3, 6 and 7).

Arteria choroidea rostralis This artery took off as the first major branch of the arteria cerebri media. In exceptional cases, the artery may arise from the arteria carotis interna or arteria communicans caudalis. The artery left the caudal face of the arteria cerebri media. Soon after its origin the artery came to course under the lobus piriformis (pars caudalis), gyrus parahippocampalis and over the external aspect and in front of the optic tract. The artery, in its initial course, was also related to the amygdaloid (corpus amygdaloideus). The artery ascended and curved dorsomedially and rostrally after entering the ventriculus lateralis through the fissura choroidea to come in relation with the lateral geniculate body, pulvinar and parahippocampal gyrus. After entering the lateral ventricle it coursed along the stria terminalis and fimbria hippocampi in the sulcus (sulcus thalamocaudatus) separating the nucleus caudatus and thalamus. The arteria choroidea rostralis terminated in the lateral ventricle by giving off branches

to the tela choroidea for the formation of the choroid plexus of the above ventricle. A number of branches were also given off by the arteria choroidea rostralis for the formation of the choroid plexus of the third ventricle. A number of branches were given off by the arteria choroidea rostralis during its course (Figs. 7, 8, 12, 13, and 14).

Ramus ascendens Arteria choroidea rostralis during its initial course gave off a branch which coursed on the medial aspect of the lobus piriformis (pars caudalis) and ascended on the lobe to anastomose with the cortical branches from the arteria cerebri media. After giving these cortical branches the artery continued on the medial surface of the lobus piriformis where it sent branches for the amygdaloid, globus pallidus and tail of the nucleus caudatus (cauda nucleus caudati). The artery itself joined with a descending branch from the arteria cerebri caudalis. During its course it also supplied branches to the parahippocampal gyrus.

Rami perforantes A number of fine perforating rami were given off by the arteria choroidea rostralis which supplied the optic tract, crus pedunculi, nucleus endopeduncularis, fascia lenticularis, ansa lenticularis, globus pallidus, putamen, nucleus reticularis thalami, capsula interna, stria medullaris, optic radiation and nucleus caudatus. It also sent perforating rami to the corpus geniculatum lateralis.

Rami choroidei The arteria choroidea rostralis during its course gave off a number of fine branches which supplied the tela choroidea ventriculi lateralis as indicated earlier. The number of these branches and level of their origin was variable. Some were given off at the level of the cornu occipitalis and cornu temporalis of the ventriculus lateralis whereas most of them left the above artery in the cornu centralis. Generally, some of the terminal branches joined with the caudal choroidal branches from the arteria cerebri caudalis to contribute in the formation of the plexus choroideus ventriculi tertii. However, during its course in the ventriculus lateralis the arteria choroidea rostralis also received anastomosing branches from the arteria cerebri caudalis which participated in the formation of the plexus choroideus ventriculi lateralis. At the level of the foramen interventriculare the choroid plexus of the lateral ventricle curved medially and caudally in the midline to course in the ventriculus tertius to be detailed later (Figs. 12, 13, 14 51 a,b and 52 a,b).

Rami centrales Two or three rami left the arteria cerebri media after the main artery had given off the arteria choroidea rostralis. These rami perforated the lamina diagonalis to reach and supply the nucleus supraopticus, nucleus hypothalamicus lateralis and nucleus preopticus lateralis.

Rami striati laterales (Arteriae striati laterales) From the main stem of the arteria cerebri media and from its main branches given to continue as main cortical branches, a number of fine branches perforated the substania perforata rostralis and junction of the pars rostralis and pars caudalis of the lobus piriformis. Some of the branches may also perforate through the sulcus rhinalis lateralis and sulcus sylvius. The number of the above branches was variable. These branches supplied the corpus amygdaloideus, capsula externa, capsula interna, claustrum, globus pallidus, putamen, fornix, capsula extrema, nucleus reticularis thalami and lamina medullaris externa. They may also supply the nucleus caudatus, nucleus endopeduncularis, nucleus ventralis rostralis and pedunculus thalami (Figs. 47 a,b - 50 a,b).

Rami corticales The arteria cerebri media during its initial course divided and gave off two or three large cortical branches in addition to the above-mentioned central and striate branches. The site and level of the above branches, leaving the main trunk, were observed to be variable. Small cortical branches going to lobus piriformis were also observed to take origin from the arteria cerebri media. The main cortical branches may be regarded as anterior, middle, and posterior depending upon their location and supplied most of the part of the cerebral hemisphere and anastomosed with the cortical branches of the arteria cerebri rostralis and arteria cerebri media (Figs 1, 2, 3 and 6).

Arteria communicans caudalis

The arteria communicans caudalis extended between the arteria carotis interna and arteria basilaris. The artery was given off as a caudal branch of the arteria carotis interna (Figs. 1, 6, 7, 8, 9 and 10). The artery coursed on the ventral aspect of the crus cerebri before joining the arteria basilaris in front of the anterior border of the pons ventrally. The arteria communicans caudalis during its course gave off a number of branches. A major branch, the arteria cerebri caudalis left the above artery just in front of the root of the nervus oculomotorius. On the basis of the neurovascular relationship and area supplied the terminal portion of the arteria communicans caudalis may be considered as arteria mesencephalica. The arteria communicans caudalis was regarded to comprise of two segments; the proximal segment represented the proximal stem of the arteria cerebri caudalis and the distal as the arteria mesencephalica. The proximal segment corresponded with the functionally assigned arteria communicans caudalis of man (perhaps not so in the domestic animals). The distal segment corresponded with the distal part of the arteria basilaris of man but was termed presently as arteria mesencephalica.

The arteria communicans caudalis (pars proximalis arteria cerebri caudalis), before continuing as arteria

mesencephalica, gave off a number of branches, in addition to the arteria cerebri caudalis, in its course.

Rami posteriomediales (Rami caudomediales) A number of fine branches left the medial face of the arteria communicans caudalis (pars proximalis) (Figs. 6, 7, 8, 48 a,b and 49 a,b). These branches were five to eight in number and some perforated the hypothalamic floor whereas others continued towards the tuber cinereum to contribute in the formation of the circuminfundibular network with the rami (arteriae) hypophysiales (superiores) rostrales. These branches supplied the nuclei periventriculares, nucleus hypothalamicus lateralis, nucleus supraopticus, fornix, nucleus tuberomamillaris, nucleus supramamillaris, nucleus hypothalamicus dorsomedialis, nucleus hypothalamicus ventromedialis, area hypothalamica lateralis, and other associated nuclei and tracts. Their contribution to the hypophysis has already been mentioned along with the rami or arteriae hypophysiales (superiores) rostrales.

Rami postperiolaterales (Rami caudolaterales) These were given off from the arteria communicans caudalis (pars (proximalis). These branches left the above artery from its dorsal and dorsolateral aspect. These were four to six in number. Of these, one or two were quite large (Figs. 6, 7, 8,48 a,b and 49 a,b). These branches supplied the ansa lenticularis,

corpus subthalamicus and zona incerta. The larger rami coursed medially to supply the nucleus hypothalamicus dorsomedialis, nucleus paraventricularis, area hypothalamica dorsalis, mamillothalamic tracts, nucleus reunien thalami, nuclei intralaminares thalami, nucleus rostralis ventralis, nucleus rostralis mediallis, nucleus rostralis dorsalis, nucleus hypothalamicus lateralis and nucleus reticularis thalami.

Arteria cerebri caudalis

The artery took its origin just in front of the origin of the nervus oculomotorius and marked the caudal continuation of the arteria communicans caudalis as arteria mesencephalica. The artery was related to the crus cerebri dorsally and dorsolaterally and to the nervus oculomotorius ventrally. The artery after its origin coursed dorsolaterally and slightly backwards on the ventrolateral part of the crus cerebri but later coursed forwards in a slightly flexuous manner to come in deep relation with the brachium colliculus rostralis, corpus geniculatum medialis and tractus opticus. The artery was observed to ascend further to come in deep relation with the corpus geniculatum laterale, pulvinar and posterior thalamus and in superficial relation with parahippocampal gyrus and splenium of the corpus callosum. The artery left the company of the parahippocampal gyrus at splenium and

distributed on the posterio-medial cerebral cortex. It terminated by anastomosing with the cortical branches of the arteria cerebri media and arteria corporis callosi. The arteria cerebri caudalis during its course gave off a number of cortical and central branches (Figs. 1, 2, 4, 6, 7, 8 and 9).

Arteria choroidea caudalis The artery took its origin from the caudal aspect of the arteria cerebri caudalis at a variable distance. There were one or two fine branches present before the arteria choroidea caudalis was given off or directly from the latter. These rami supplied crus pedunculi, substantia nigra and medial lemniscus and may be termed as rami perforantes.

The arteria choroidea caudalis after its origin coursed in an upward or dorsalward direction on the cerebral peduncle and behind the corpus geniculatum medialis to reach the posterior part of the corpus geniculatum lateralis, pulvinar, in front of the colliculus rostralis and over its brachium. The above artery generally took origin in common with a strong caudal branch which was regarded as the ramus ad tectum mesencephali rostralis to be dealt later. The arteria choroidea caudalis during its course received anastomosing branches from the ramus ad tectum mesencephali rostralis and arteria cerebri caudalis. The arteria choroidea caudalis divided into three to four branches which curved dorsomedially towards the epiphysis and joined with the branches of the

opposite side and the terminal branches of the ramus ad tectum mesencephali rostralis forming a network around the epiphysis. One or two branches from the above artery continued rostrally in the median plane, under the stria medullaris thalami, over the dorsomedial aspect of the thalamus and along the tela choroidea ventriculi tertii. These branches joined with the choroidal branches of the arteria choroidal branches of the arteria choroidea rostralis and arteria cerebri caudalis to supply the plexus choroideus ventriculi tertii. During its course the arteria choroidea caudalis supplied perforating branches to the corpus geniculatum medialis, corpus geniculatum lateralis, brachium colliculus rostralis, brachium colliculus caudalis, commissura caudalis, pulvinar, commissura colliculum rostrallium, nucleus parataenialis, habenular complex, epiphysis, nucleus pretectalis, nuclei intralaminares, nuclei paraventriculares thalami, organum subcommissurale and subfornicale and acoustic radiation (Figs 7, 8, 10, 11, 15, 50 a,b, 51 a,b and 52 a,b).

Ramus ad tectum mesencephali rostralis This ramus arose from the arteria cerebri caudalis in common with the arteria choroidea caudalis. It curved caudalwards on the cerebral peduncle but on reaching the colliculus rostralis inclined medially to reach the dorsomedial aspect of the latter. In its course it divided into two sets of branches, the rostral branches joined with similar branches of the other

side and as well as with the branches of the arteria choroidea caudalis to continue as the rami choroidei. The caudal branches joined with the ramus ad tectum mesencephali caudalis and a small branch which may be called as the ramus ad tectum mesencephali intermedius. During its course the ramus ad tectum mesencephali rostralis sent perforating branches to the substantia nigra, nucleus tegmenti, nucleus tractur mesencephali nerve trigemini, brachium colliculus rostralis, nucleus colliculus rostralis, substantia grisea centralis, brachium colliculus caudalis, commissura colliculorum rostralium, crus cerebri, medial lemniscus and fiber tracts passing through. Some of its branches may reach to supply the oculomotor nerve nuclei and medial longitudinal fasciculus. The terminal branches of the above may continue as rami choroidae to supply the plexus choroideus ventriculi tertii (Figs. 8, 9, 10, 11, 12, 14, 53 a,b and 54 a,b).

The arteria cerebri caudalis before terminating and while in relation with the corpus geniculatum lateralis gave off branches the pattern of origin of which was variable. In most of the cases a branch left the arteria cerebri caudalis at a level between the corpus geniculatum lateralis and corpus geniculatum medialis and divided into two branches. The lateral branch coursed dorsally and rostrally on the corpus

geniculatum lateralis. It continued rostrally on the dorsolateral margin of the thalamus and sent anastomosing and contributory branches to the arteria choroidea rostralis and plexus choroideus ventriculi lateralis respectively. The above branch terminated in the area of the foramen interventriculare and contributed in the formation of the plexus choroideus ventriculi lateralis and plexus choroideus ventriculi tertii. During its course the above branch sent perforating rami to the corpus geniculatum lateralis, fornix, nucleus lateralis caudalis, nuclei rostrales thalami, nucleus dorsomedialis thalami, nucleus reticularis thalami and nucleus lateralis dorsalis. From the above branch a small branch coursed on the rostral half of the thalamus dorsally and joined the plexus choroideus ventriculi tertii in its rostral half. The medial branch from the above artery had variable origin. In most of the cases it arose as a branch from the above artery whereas in some cases it took its origin directly from the arteria cerebri caudalis. The above branch may divide into two or three rami as it coursed on the caudal aspect of the corpus geniculatum lateralis and caudomedial face of the pulvinar.

The above rami joined the plexus choroideus ventriculi tertii at variable levels and sent perforating branches which supplied the pulvinar, epiphysis cerebri, habenular complex, brachium colliculus rostralis, stria medullaris thalami and

joined with the terminal branches of the arteria choroidea caudalis and supplied the dorsomedial thalamic areas as already mentioned earlier. In view of their terminal distribution and comparative anatomy the above-mentioned branches from the arteria cerebri caudalis may be regarded as the rami choroidei caudales (Figs. 12, 13, 14, 15, 51 a,b and 52 a,b).

Rami parahippocampales The arteria cerebri caudalis during its course while in association with the parahippocampal gyrus gave off a number of branches which distributed to supply it. These branches were fine and were observed to be given off in a rake-like manner directly from the arteria cerebri caudalis. In addition to the above, it sent a descending branch which coursed in a retrograde manner along the parahippocampal gyrus to anastomose with an ascending branch of the arteria choroidea rostralis.

Rami corticales The arteria cerebri caudalis gave off a number of cortical branches before it terminated. These branches were given off during its initial course in relation with the tractus opticus, parahippocampal gyrus and after it left the company of the latter at the splenium of the corporis callosi beyond which it continued along the sulcus corporis callosi to terminate by anastomosing with the arteria corporis callosi. The cortical branches given off before reaching the splenium of the corporis callosi were distributed on the posterior and posteriomedial part of the cerebral hemisphere

including the posterior part of the lobus piriformis. The number, site of origin and distribution were observed to be variable. These branches anastomosed with similar branches from the arteria cerebri rostralis and arteria cerebri media (Figs. 2, 3 and 4).

Arteria mesencephalica

The segment of the arteria communicans caudalis extending between the origin of the arteria cerebri caudalis and termination of the arteria basilaris was regarded as the arteria mesencephalica. The artery coursed on the ventral surface of the cerebral peduncles to join with the arteria basilaris and arteria mesencephalica of the other side. During its course the arteria mesencephalica gave off a number of branches (Figs. 1, 6, 7 and 8).

Rami caudomediales (dorsomediales) These were a number of branches taking origin from the above artery and from the junction of the arteria mesencephalica and arteria basilaris . They varied in number but ranged between five to eight or more. These were directed dorsomedially. Some of these branches interanastomosed with each other at the level of the substantia perforata caudalis. These rami perforated the mesencephalic areas in a variable manner in the median plane. Some were directed obliquely caudal in addition to vertically directed ones. Some of the branches were also

directed obliquely rostral. Two or three branches which were larger than the adjoining were directed rostrally (Figs. 1, 6, 7, 8 and 27).

The rami directed caudomedially were given off just near the junction of the arteria mesencephalica and arteria basilaris. These penetrated the cerebral peduncles and the rostral part of the pons and supplied the decussation pontis, nucleus centralis superioris, nucleus reticularis tegmenti, nuclei pontis, nucleus interpeduncularis, nucleus raphe or raphe, substantia grisea centralis and associated fiber tracts (Figs. 27, 57 a,b and 58 a,b).

The rami which were directed vertically into the median plane of the mesencephalon supplied the nucleus interpeduncularis, substantia nigra, nucleus rubrum, or ruber, nuclei nervus occulomotorius, nucleus nervus trochlearis, substantia grisea centralis, ducussation tractorium rubrospinalis, fasciculus longitudinalis medialis, lemniscus medialis, decussation pedunculorum cerebellarium rostralis, raphe or nucleus raphe, fibrae nerve oculomotorius, decussation tegmenti and tractus tectospinalis (Figs. 53 a,b - 56 a,b).

The rami which were observed to be larger and were directed rostromedially perforated the interpeduncular fossa just behind and around the corpus mamillare. They penetrated the mesencephalon to supply the diencephalic areas. These rami were supplemented by fine branches from the arteria

mesencephalica near the origin of the arteria cerebri caudalis in some cases directly from the latter and perforated the caudolateral part of the corpus mamillare. These rami supplied the nucleus interpeduncularis, nucleus ruber, formatio reticularis tegmenti or nuclei tegmenti, nuclei nervus oculomotorius, nucleus nervus trochlearis, nucleus mamillaris, nucleus mamillaris medialis, corpus mamillare, nucleus dorsomedialis thalami, nucleus paracentralis, nucleus centralis medialis, nucleus ventralis caudalis, nucleus ventralis lateralis, nucleus centralis lateralis, nucleus paraventriculares thalami, centrum medianum, nucleus reticularis thalami, nucleus parafascicularis, lamina medullaris interna, substantia grisea centralis and associated subthalamic areas (Figs. 6, 18, and 50 a,b - 54 a,b).

Arteria cerebelli rostralis It was observed to be the first major branch of the arteria mesencephalica (Figs. 8, 9, 12, 20 and 24). It was directed caudalwards and dorsally over the dorsal and rostral aspect of the cerebellum. The artery crossed the dorsolateral aspect of the tectum mesencephali and crus cerebri to come in relationship with the trigeminal nerve and its ganglia. The artery coursed in the space between the cerebellum and colliculus caudalis after which it continued its terminal course. The arteria cerebelli rostralis gave off a number of branches in its course which supplied to the mesencephalon and pons in addition to

its terminal distribution on the rostrodorsal cerebellar areas of its side. An arteria cerebelli rostralis accessorius may be present. The main artery sent perforating branches to supply the crus cerebri, lemniscus lateralis, pedunculus cerebellaris rostralis and its decussation, substantia nigra, lemniscus medialis, nuclei reticularis pontis oralis or formatio reticularis, nuclei pontis and associated fiber tracts (Fig. 57 a,b).

Two or three slender branches were given off by the arteria cerebelli rostralis in its initial course while crossing the crus cerebri ventrolaterally. These took origin from caudal or ventrocaudal aspect of the arteria cerebelli rostralis. They coursed along the rostral part of the pons and brachium pontis and reached the lateral aspect of the brachium pontis. They terminated in the ventral paraflocculus. These rami in some cases may come off from a single branch arising directly from the arteria mesencephalica, representing the arteria cerebelli rostralis accessorius. These branches supplied perforating branches to lemniscus lateralis brachium pontis, brachium conjunctivum, nucleus parapeduncularis, nucleus reticularis pontis oralis, nervus trigeminalis and its associated nuclei and ventral part of the paraflocculus.

Ramus ad tectum mesencephali intermedius The arteria cerebelli rostralis during its course on the ventrolateral aspect of the crus cerebri gave off a branch which may be called as ramus ad tectum mesencephali intermedius. This ramus may arise as a single branch or as two separate rami. This ramus left the arteria cerebelli rostralis and coursed on the brachium of the colliculus caudalis to come on the tectum dorsomedially. It divided into a number of branches and distributed partly on the colliculus rostralis and colliculus caudalis. It anastomosed with the branches of rami ad tectum mesencephali rostralis and caudalis and its counterpart of the opposite side. During its course it gave off perforating branches to the crus cerebri, lemniscus medialis, substantia nigra, nucleus profundus mesencephali, nucleus tractus mesencephali, nervus trigemini, colliculus rostralis, colliculus caudalis, substantia grisea centralis, brachium colliculi caudalis, pedunculus cerebellaris rostralis, tractus rubrospinalis, nucleus reticularis pontis oralis, nuclei tegmenti, lemniscus lateralis and nucleus nervus trochlearis (Figs. 10 and 55 a,b).

Ramus lateralis The ramus lateralis may be regarded as a terminal branch of the arteria cerebelli rostralis (Fig. 24). It ascended along the anterior border of the brachium pontis to come in relation with the cerebellum where it divided into two or three branches distributed on the

parafloccculus and partly on lobus simplex. The lateral branch coursed on the parafloccculus laterally where it anastomosed with the branches of the arteria cerebelli media and rami ad pontem. It may also anastomose with ramus lateralis of the arteria cerebelli caudalis. The artery sent perforating branches to supply the parafloccculus, brachium pontis, brachium conjunctivum, nuclei vestibulares and nucleus sensibilis pontinus n. trigemini, nucleus tr. mesencephali n. trigemini and nucleus motoris n. trigemin.

Ramus ad tectum mesencephali caudalis The arteria cerebelli rostralis, after giving the above branch, continued in the space between the colliculus caudalis and cerebellum and gave off the above ramus. The origin of this ramus was variable such that it may arise in some cases, after the ramus intermedius has been given off by the arteria cerebelli rostralis. The ramus divided into a number of fine branches which distributed on the colliculus caudalis laterally, dorsally and caudally. These branches were observed to anastomose with the ramus ad tectum mesencephali intermedius as well as its counterlateral component. The ramus supplied the colliculus caudalis, its nucleus and brachium, nucleus tractus mesencephali nerve trigemini, and commissura colliculorum caudalium. In some of the cases there were two rami, which were given off from the ramus lateralis and ramus

intermedia of the arteria cerebelli rostralis, supplying the above-mentioned areas collectively (Figs. 9, 10, 11 and 56 a,b).

Ramus intermedius It generally arose after the former branch has been given off. It divided into two or three branches which ascended on the lobus simplex mostly except its medial branch which coursed in the sulcus between the above lobe and lobus vermis. These branches distributed on the above lobes and anastomosed with the rami lateralis and medialis of the arteria cerebelli rostralis and the ramus intermedius of the arteria cerebelli caudalis. The ramus supplied branches to the brachium conjunctivum, anterior medullary velum or velum medullare rostrale and nucleus dentatus (Fig. 24).

Ramus medialis This ramus was regarded as the terminal branch of the arteria cerebelli rostralis. The ramus divided generally into two branches which were mainly distributed to lobus vermis of its own side. The ramus gave off some fine descending branches which continued on to the lingula and contributed to the anterior medullary velum, choroid plexus and brachium conjunctivum. The ascending branches anastomosed with the ramus mediales of the arteria cerebelli caudalis. The ramus medialis anastomosed with its own contralateral of the other side through transverse branches and so also with ramus intermedius of its own side. In addition to the above, the

branches from the ramus medialis perforated the corpus medullare of the lobus vermis and supplied the cerebellar nuclei also (Fig. 59 a,b).

Arteria vertebralis

The arteria vertebralis started as a branch of the arteria subclavia. The artery in its terminal course reached the atlas vertebra where it entered the foramen transversium of the atlas vertebra. At this level it joined with the arteria occipitalis through the ramus anastomoticus cum arteria occipitali. The main artery then continued its course and reached the vertebral canal by way of incisure alaris and foramen vertebrale laterale. While in the vertebral canal, the artery pierced the dura mater to come on the ventral surface of the spinal cord. The arteria vertebralis (arteria cerebrospinalis) generally divided into two branches, a rostral (the main continuation) and a caudal branch. The rostral branch which was the main continuation of the arteria vertebralis (arteria cerebrospinalis) joined with a similar contralateral branch to form the arteria basilaris. The posterior branch of the arteria vertebralis (arteria cerebrospinalis) coursed backwards and joined the fellow of the opposite side and continued caudally to join and formed the arteria spinalis

ventralis. The pattern of the union of the above branches (of arteria vertebralis) was variable, however, in most of the cases an elongated and irregular quadrilateral pattern is formed between the two branches of either sides. The quadrilateral so formed had acute angles rostrally and caudally whereas the lateral angles were obtuse. The location of this quadrilateral was generally at the spinomedullary junction ventrally. From this a number of branches were given off in a variable pattern. One small branch started from the rostral branch of the arteria vertebralis, this branch ascended dorsolaterally around the spinal cord to come on its dorsolateral surface after crossing the dorsal and ventral roots of the first spinal nerve and under the cover of the spinal accessory nerve. This branch anastomosed with the ascending (dorsal) branch of the ramus spinalis of the arteria vertebralis, at the level of the second cervical vertebra to form the arteria spinalis dorsolateralis (arteria spinalis dorsalis).

A number of fine perforating branches were also given off by the posterior branch of the arteria vertebralis. These branches supplied the decussatio pyramidum, tractus spinocerebellaris ventralis and dorsalis, tractus tectospinalis, tractus cerebrospinalis, tractus spinothalamici, tractus vestibulospinalis, fasciculus cuneatus, nucleus cuneatus, fasciculus gracilis and nucleus gracilis.

Ramus medullaris From the rostral continuation of the arteria vertebralis (generally called the cerebral branch of the arteria cerebrospinalis) a ramus medullaris was given off at a variable level. This ramus may arise in common with the arteria cerebelli caudalis accessorius. The ramus was directed rostrally in its initial course on the ventral surface of the medulla oblongata and stayed in close relation with the nervus hypoglossus. The ramus coursed dorsolaterally to reach on the dorsolateral and dorsal aspect of the medulla oblongata and divided into two branches, anterior and posterior (rostral and caudal). The rostral branch anastomosed with the fine branches given off by the arteria cerebelli caudalis accessorius. The rostral branch of the ramus medullaris divides into three or five fine branches which coursed under the spinal accessory nerve root to come on the dorsal aspect of the medulla oblongata and reach the posteriolateral boundary of the fourth ventricle (its caudal one fourth). These branches supplied perforating branches to the nucleus gracilis and nucleus cuneatus and their fasciculi, nucleus tractus spinalis nervus trigemini, tractus solitorius and its nucleus, nucleus ambigus, fibrae arcuatae interna, tractus spinocerebellaris dorsalis and ventralis, tractus rubrospinalis, nucleus reticularis ventralis, tractus vestibulospinalis, nucleus parasympatheticus n. vagi (dorsal motor nucleus of vagus), tractus

spinothalamici, nucleus olivaris accessorius medialis, nucleus motorius nervus hypoglossi, area postrema and may supply fine branches to the choroid plexus of fourth ventricle (plexus choroideus ventriculi quarti).

The caudal branch of the ramus medullaris was directed dorsocaudally and curves to dorsolateral part of the medulla oblongata under the cover of spinal accessory nerve. It gave off three to four branches. Some of these branches (two or three) were directed towards the obex and dorsomedian portion of the spinomedullary junction. One branch (caudal) coursed under the spinal accessory nerve partially to continue caudally along the dorsolateral aspect of first spinal junction where it joined with the ascending branch (dorsal branch) of the arteria vertebralis and completed the formation of the arteria spinalis dorsolateralis (arteria spinalis dorsalis). The caudal branch of the ramus medullaris supplied fine branches to the area postrema, nucleus cuneatus and nucleus gracilis and their fasciculi and the tracts on the dorsolateral and ventrolateral aspect of spinomedullary junction (Figs. 16, 17, 18, 19, 20, 21, 62 a,b and 63 a,b).

Arteria cerebelli caudalis accessorius The origin and presence of the artery were variable. It was bilateral in most of the cases and arose in some cases from rostral continuation of the arteria vertebralis before the latter joined with its contralateral part to form the arteria basilaris,

whereas in some cases it arose from the arteria basilaris directly. It was also present unilaterally in some cases. The artery coursed in a flexous manner obliquely. It coursed on the ventral surface of the medulla oblongata for a short distance and ascended dorsolaterally in front of the root of the nervus hypoglossus to reach the dorsolateral aspect of the medulla oblongata. On the dorsal surface of the medulla oblongata it coursed medially to come on the ventral aspect of vermis cerebelli and terminated by continuing on the vermis cerebelli as ramus medialis arteria cerebelli caudalis of other domestic animals and man. During its course on the ventral and ventrolateral part of the medulla oblongata it sent perforating branches to the nucleus olivaris, nuclei olivares accessorii medialis and dorsalis, tractus vestibulospinalis, tractus spinothalamici, tractus rubrospinalis, tractus spinocerebellaris ventralis, fibrae arcuate externa and interna, nucleus reticularis lateralis, nucleus ambigus and root of nervus hypoglossi and nucleus tractus spinalis n. trigemini. This artery sent branches which anastomosed with the rostral branch of the ramus medullaris and branches of the arteria cerebelli caudalis. It also gave branches to choroid plexus of fourth ventricle. The perforating branches from the above artery, while on the dorsal aspect of the medulla oblongata, supplied the nucleus gracilis, nucleus cuneatus lateralis, nucleus cuneatus medialis, nucleus

parasympatheticus n. vagi, nucleus motorius n. hypoglossi, tractus and nucleus tractus solitorius, nucleus intercalatus, area porstema, nucleus tractus spinalis nervus trigemini and pedunculus cerebellaris caudalis. The main continuation which continued as the ramus medialis arteria cerebelli caudalis distributed and divided into two branches, medial and lateral. The medial branch courses on the lobus vermis and anastomosed with a similar branch from the other side, the lateral branch anastomosed with the ramus intermedius of arteria cerebelli caudalis. In some cases there may be a single branch (main continuation) and the lateral branch was supplemented by the arteria cerebelli caudalis (Figs. 16, 17, 22, 23, 25, 61 a,b and 62 a,b).

Arteria basilaris

As indicated earlier, the arteria basilaris was formed by the union or fusion of the arteria vertebralis. The artery had a flexous course along the ventral surface of the medulla oblongata, corpus trapezoideum and pons ventromedially. The artery gave off a number of branches which were distributed to the above areas including cerebellum (except its rostral and rostrodorsal portions).

Arteria cerebelli caudalis The arteria cerebelli caudalis arose from the arteria basilaris and coursed flexously to reach the dorsolateral aspect of the medulla oblongata under the cover of the spinal accessory nerve behind the

glossopharyngeal and in front of vagal nerve roots and then bent medially to come on the dorsal aspect of the medulla oblongata. In its further course the artery continued caudomedially and terminated by giving branches to the paramedian, ansiform, paraflocculus and flocculonodulus lobes. The terminal branches which distributed on the above lobes were two in number and could be named as ramus lateralis and ramus intermedius. The arteria cerebelli caudalis during its initial course, on the ventral and ventrolateral aspect of the medulla oblongata gave off a number of perforating branches supplying the root of the nervus hypoglossus, nucleus olivaris, and olivaris accessorius dorsalis, tractus spinothalamici, nucleus reticularis, fibrae arcuatae interna or profunda, tractus rubrospinalis, nucleus tractus spinalis nervus trigemini and nucleus ambigus. It also gave anastomosing branches to the arteria cerebelli media.

A number of fine perforating branches were given off from its ventral aspect while on the dorsal aspect of the medulla oblongata behind the pedunculus cerebellaris media. These branches may supply to the external arcuate fibers, nuclei vestibulares, nucleus solitorius, nucleus parasympatheticus n. vagi, nucleus intercalatus, nucleus gracilis, nucleus cuneatus lateralis and medialis and their fasciculi, nucleus tractus spinalis nervus trigemini, nucleus motorius nervus trigemini, formatio reticularis, associted fiber tracts

pedunculus cerebellaris caudalis and nucleus motorius n. hypoglossi (Figs. 16, 17, 18, 22, 23, 61 a,b and 62 a,b).

Ramus intermedius The ramus intermedius was the direct continuation of the main artery and ascended on the caudal part of the paramedian lobe and anastomosed with ramus medialis which was the continuation of the arteria cerebelli caudalis accessorius.

Ramus lateralis It was given off by the arteria cerebelli caudalis. The latter divided into two rami on reaching the inferior or ventral surface of the paramedian lobe. These branches supplied the caudolateral and inferior part of the cerebellum. These branches distributed partly to the dorsal and ventral paraflocculus lobules, flocculus, and ansiformis lobes. The branches during their course anastomosed with the ramus lateralis, arteria cerebelli rostralis and arteria cerebelli media laterally and medially with ramus intermedius of the arteria cerebelli caudalis. Few perforating branches were given off during their course to the pedunculus cerebellaris caudalis and associated structures. The arteria basilaris gave off one or two unnamed small transverse or short circumferential branches before giving off the next important vessel.

Arteria cerebelli media This arteria corresponded to the arteria cerebelli anterior inferioris of the human. The artery started as a collateral branch of the arteria basilaris

at a variable level such that on one side the artery may take off at a level behind the ventral aspect of the corpus trapezoideum and on the other side in level with the corpus trapezoideum. The artery left the arteria basilaris as a flexuous slender branch. The artery coursed forward and then ascended dorsolaterally towards the roots of the nervus facialis and nervus vestibulocochlearis. The artery crossed the root of the vestibulocochlearis nerve and then came to course between the above nerve and root of the facial nerve. Here it gave off the arteria labyrinthi and itself continued to distribute on the lateral and inferior parts of the parafloccular lobe and brachium pontis and anastomosed with the branches of the arteria cerebelli caudalis, rami ad pontem and arteria cerebelli rostralis. It supplied partly to the dorsal and ventral parafloccular lobules and flocculus lobe. It gave off a number of perforating branches during its initial and terminal course which may supply the nucleus reticularis parvicellularis, nucleus reticularis gigantocellularis, nucleus motorius nervus facialis, nucleus parasympatheticus nervus facialis, nucleus tractus spinal nervus trigemini, nucleus olivaris, nucleus dorsalis and nuclei ventrales corporis trapezoidei, tractus rubrospinalis, tractus spinothalamici and tractus vestibulospinalis. The arteria cerebelli media gave off a small branch before the main artery coursed between the facial and vestibulocochlearis nerve roots. This branch

coursed behind the latter nerve and came on dorsal aspect of the medulla oblongata and sent perforating branches and choroidal branches before anastomosing with ramus lateralis of arteria cerebelli caudalis. It supplied the nuclei cochleares and vestibulares and pedunculus cerebellaris caudalis or inferioris and other associated nuclei and tracts. (Figs. 16, 17, 18, 25, 26 and 60 a,b).

Arteria labyrinthi This artery left as a branch of the arteria cerebelli media. It arose from the parent trunk as a fine vessel and entered into the internal acoustic meatus to supply the internal ear (Fig. 26).

Rami ad pontem Generally, there were three rami which represented the rami ad pontem and so may be named as rostralis, intermedius and caudalis. These were observed to leave the arteria basilaris as transverse or lateral branches, coursing on the ventral surface of the pons. In addition to the above, small transverse branches were present which were of little consequence (Figs. 5, 16, 17 and 18).

Ramus ad pontem caudalis This was the first pontine ramus given off by the arteria basilaris. It was given off at the level of the junction of the pons with corpus trapezoideum. After a short transverse course it came in relation with the nervus abducens. It course dorsolaterally to lie in relation with the root of nervus facialis where it divided into anastomotic branches. The rostral branch joined

with the ramus ad pontem intermedius and the caudal with the arteria cerebelli media (before the latter dipped between the roots of nervus facialis and nervus vestibulocochlearis). The ramus gave off perforating branches during its course which supplied the lemniscus medialis, nuclei pontis, corpus trapezoideum, nucleus dorsalis corporis trapezoidei, nuclei ventrales corporis trapezoidei, lemniscus lateralis, tractus rubrospinalis, tractus spinothalamici, tractus spinocerebellaris ventralis, radix nervus facialis and its nucleus, tractus pyramidalis, nucleus tractus spinalis nervus trigemini, brachium pontis, nucleus motorius nervus trigemini, nucleus sensibilis pontinus nervus trigemini and other associated structures (Fig. 58 a,b).

Ramus ad pontem intermedius This ramus was given off by the arteria basilaris at a level almost in the middle of the pons ventrally. The course of this ramus was similar to the caudal ramus and anastomoses with the ramus ad pontem caudalis and ramus ad pontem rostralis. During its course it supplied branches to the radix nervus trigemini, nuclei motoris et sensibilis nervus trigemini as well as the ganglion trigeminale, pedunculus cerebellaris medius (brachium pontis) and the structure already mentioned along the caudal ramus.

Ramus ad pontem rostralis This was the most rostral branch of the arteria basilaris, before the latter joined the arteria communicans caudalis. It coursed laterally and

caudally and joined the ramus ad pontem intermedius and arteria cerebelli rostralis. This ramus supplied to the rostral part of the pons, the fibrae pontis transverse, formatio reticularis, tractus rubrospinalis, nucleus lemniscus lateralis, lemniscus medialis, nucleus reticularis tegmenti, tractus spinothalamicus, pedunculus cerebelli media, nucleus reticularis tegmenti and other associated structure mentioned along with other rami ad pontem (Fig. 57 a,b).

Rami paramediales or rami paramedianes The arteria basilaris during its course along the sulcus basilaris and fissura mediana (ventralis) gave off a number of fine branches which perforated the medulla oblongata, corpus trapezoideum and pons ventromedially and ascended to reach the floor of the fourth ventricle. They coursed perpendicularly in the brain substance. The extent of distribution and number of these branches was variable (Fig. 27).

The paramedian rami in the medullary region were twelve to eighteen in number. They supplied decussation pyramidium, pyramis,tractus tectospinalis, nucleus olivaris, raphe, nucleus parasympatheticus nervus vagi, fasciculus longitudinalis dorsalis, fasciculus longitudinalis medialis, nucleus intercalatus, nucleus tractus solitorius, decussation leminisci, nucleus roller, nucleus motorius nervus hypoglossi, lemniscus medialis. The paramedian rami of the corpus trapezoideum region supplied to the ducussation trapezoideum ,nucleus raphe,

nucleus motorius and parasympatheticus nerve dacialis, nucleus motorius nerve abducentis, tractus cerebrospinalis, tractus pyramidalis, decussation pyramidalis, tractus tegmenti centralis, fasciculus longitudinalis medialis, nuclei reticularis and associated fiber tracts. The pontine paramedian rami supplied to the nucleus tegmenti dorsalis, nuclei pontis, fibrae pontis transverse, fasciculus longitudinalis dorsalis, tractus tegmenti centralis, nucleus raphae, corpus trapezoideum, fasciculus longitudinalis medialis, fibrae corticospinales, leminiscus medialis, nuclei motorius nervus facialis and abducentis and associated fiber tracts. The above branches may also be termed as rami medianes (Figs. 58 a,b - 63 a,b).

In addition to the above branches, the basilar artery gave off a number of small lateral branches which only extended ventrolaterally for a short distance and sent perforating branches to the different segments coursed by them.

Blood Supply to the Brain of the Pig

The brain of the pig received blood supply through the arteria basilaris and arteria carotis interna. The latter vessel was observed to have undergone modifications due to the formation of the rete mirabile epidurale rostrale which was a complex formation in comparison to that in the case of the dog where it was represented by a simple anastomosis

between the branches from the arteria maxillaris and arteria carotis interna intracranially.

The arteria carotis interna which started as a branch of the arteria carotis communis entered the cranial cavity through the foramen lacerum orale. The artery perforated the dura mater after entering the cranial cavity and gave off a number of fine branches which joined with the anastomosing branches from the arteria maxillaris.

The arteria maxillaris during its course gave off a branch termed the arteria meningea media from which ramus anastomoticus or ramus ad rete mirabile epidurale rostrale left to enter the cranial cavity through the foramen ovale. The latter divided into a number of small branches and joined with retial branches of the arteria carotis interna in the cavernous sinus or sinus cavernosus. Similarly, another branch from the arteria maxillaris or arteria maxillaris interna called meningea rostralis was given off which in turn gave origin to the arteria anastomotica or ramus ad rete mirabile epidurale rostrale. The latter entered the cranial cavity through the foramen orbitorotundum to complete the formation of the rete mirabile epidurale rostrale. The retial branches from all the above-mentioned arteries converged rostromedially to reform and reinforce the arteria carotis interna. The rete so formed was almost circular in outline except in its caudal and ventral part which was

inverted cone-shaped (Fig. 28). The retes of both sides interanastomosed with each other. This interanastomosis was observed to traverse in the intercavernous sinus or sinus intercavernosi caudoventral to the hypophysis. The above interanastomosing branches joining the retes or retia of both sides represented the rami intercaroticae caudales. The arteriae hypophysiales (inferiores) caudales took origin from the rami intercaroticae caudales. These branches ascended on the caudal part of the hypophysis and perforated the lobus posterior or neurohypophysis. They also sent strong branches to the infundibulum which distributed to the pars intermedia. The above branches joined with the branches from the arteriae hypophysiales (superiores) rostrales. In addition to the above, the branches from the arteria intercaroticae caudales were also distributed to the dura mater and dorsum sallae.

Arteria carotis interna

The arteria carotis interna after leaving the cavernous sinus or sinus cavernosus gave off a caudal branch, the arteria communicans caudalis (Fig. 29). The main stem of the arteria carotis interna continued forward on the ventral surface of the optic tract or tractus opticus after which it curved in a medial direction. During the above course the artery came in relation with the dorsal surface of the optic

chiasma or chiasma opticus and nervus opticus. The rostral continuation of the arteria carotis interna in its further course gave off the arteria cerebri media before continuing as the arteria cerebri rostralis. The arteria carotis interna before giving off the above-mentioned branches gave off a number of branches.

Arteriae hypophysiales (superiores) rostrales The extradural part of the arteria carotis interna gave off one or two branches which coursed medially in front of the infundibulum. The branches may leave the above artery in common with the arteria ophthalmica interna. These branches may join with the similar branches from the contralateral arteria carotis interna forming a network on the ventral aspect of the optic chiasma (Fig. 34). The above network may be equivalent to the arteriae intercaroticae rostrales of the dog in which there was a simple anastomosis between the arteriae intercaroticae rostrales. The branches from the above joined with the rami from the arteria communicans caudalis (pars proximalis) to supply the hypothalamic floor as well as the different parts of the hypophysis, tuber cinereum, infundibulum, pars intermedia and the pars distalis (indirectly). They sent perforating branches to supply the nucleus suprachiasmatica, nucleus supraopticus, nucleus hypothalamicus rostralis, nucleus paraventricularis hypothalami and nuclei preopticae.

Arteria ophthalmica interna It left the arteria carotis interna as a small vessel and coursed on the ventral surface of the optic chiasma and ventrolateral aspect of the optic nerve (Fig. 34). In its further course it came to course on the dorsal aspect of the optic nerve and left the cranial cavity through the canalis opticus to enter the fossa orbitalis. The artery in its course in the canalis opticus anastomosed with the ramus anastomoticus cum arteria ophthalmica interna.

Arteria choroidea rostralis The arteria choroidea rostralis took its origin from the arteria carotis interna ventrolaterally. It coursed along and in front of the tractus opticus under the cover of the pars caudalis lobus piriformis or piriform lobe and ascended to come in close association with the gyrus parahippocampalis. The artery in its further course entered the lateral ventricle or ventriculus and cornu occipitale of the above ventricle. The artery coursed along the sulcus thalamocaudatus to traverse the pars centrale and reached the cornu rostrale of the ventriculus lateralis. The artery terminated near the foramen intercentriculare by giving off branches for the plexus choroideus ventriculi lateralis and plexus choroideus ventriculi tertii. The artery in its course in the lateral ventricle was related to the stria terminalis, gyrus parahippocampalis, nucleus caudatus, corpus geniculatum lateralis, and dorsolateral part

of the thalamus. During the initial course it received fine anastomosing branches from the arteria cerebri caudalis; however, at the level of the corpus geniculatum lateralis it received a strong anastomosing branch, which in some cases arose from the arteria choroidea rostralis instead and joined the arteria cerebri caudalis. The arteria choroidea rostralis gave off a number of branches in its course (Figs. 37-40).

Rami perforantes These were fine perforating branches given by the arteria choroidea rostralis. These perforating branches distributed to the optic tract, crus cerebri, nucleus caudatus, area subthalamicus, capsula interna, putamen, globus pallidus and corpus amygdaliodeum. In its course it also gave perforating branches for the nucleus reticularis thalami, corpus geniculatum lateralis, nucleus rostralis dorsalis and nucleus lateralis dorsalis.

Ramus ascendens The arteria choroidea rostralis while in relation with the deeper surface of the lobus piriformis (pars caudalis) gave off a branch which ascended by dividing into a number of branches on the caudolateral aspect of the above lobe and anastomosed with the cortical branches of the arteria cerebri media. The main branch continued on the medial aspect of the lobus piriformis (pars caudalis) and anastomosed with a descending branch from the arteria cerebri caudalis. The ramus supplied branches to the gyrus

parahippocampalis, corpus amygdaloideum, crus cerebri, optic tract and capsula interna.

Rami choroidei From the arteria choroidea rostralis a series of fine choroidal branches were given off at varying levels to supply the plexus choroideus ventriculi lateralis. The number of these branches was variable. Some of the above branches joined with the choroidal branches from the arteria cerebri caudalis. The choroidal rami given off in the terminal course of the arteria choroidea rostralis supplied the plexus choroideus ventriculi tertii (Fig. 40).

Arteria cerebri media

The origin of the arteria cerebri media and its main branches was different in comparison to the same in the case of the dog. The main stem of the artery was present which gave off subsequent main cortical branches in the dog whereas it was variable in the case of pig in which the arteria cerebri media was not represented as a single stem leaving the circulus arteriosus cerebri· instead, there were two or three branches which arose directly from the rostral continuation of the arteria carotis interna. These branches gave the impression of the arteriae cerebri mediales which actually represented its main cortical branches. These branches left the rostral continuation of the arteria carotis interna at variable levels and distributed on the ventral aspect of the

tuberculum olfactorium and substantia perforata rostralis before continuing as the cortical branches (Figs 29, 30, 31 and 34).

Rami centrales From the rostral continuation of the arteria carotis interna and its continuation as arteria cerebri media a number of branches were given off. These branches were supplemented by the fine branches from the reticulated arteria communicans rostralis mentioned later. These rami supplied the gyrus diagonalis nucleus suprachiasmatica, column fornix, nucleus supraopticus, fibrae olfactorium hypothalamicus, nucleus preopticus lateralis and medialis and nucleus periventricularis rostralis.

Rami striati laterales (arteriae striati laterales) These branches were given off by the main cortical branches of the arteria cerebri media before they reached the sulcus rhinalis lateralis. These were ten to fifteen in number and perforated the ventral surface of the tuberculum olfactorium, substantia perforata rostralis and in front of the lobus piriformis pars caudalis. These branches supplied mainly the nucleus caudatus, putamen, amygdaloid, globus pallidus, claustrum, nucleus endopeduncularis and capsula interna. These branches may be designated as the arteriae lenticulostriaticales laterales as termed by some workers in the human. Some of the above branches may also supply the capsula externa. Some of the more lateral branches may leave

The branches of the arteria cerebri media by perforating the sulcus rhinalis lateralis and sulcus sylvius (Figs. 65 a,b and 66 a,b).

Rami corticales As indicated earlier that the arteria cerebri media gave off two or three cortical branches which after traversing on the ventral aspect of the substantia perforata rostralis, tuberculum olfactorium, tractus olfactorium lateralis, sulcus rhinalis lateralis and after giving off the rami striatica laterales, distributed on the most of the lateral aspect of the cerebral hemisphere (except its rostral and caudal polar regions). During their distribution the arteries divided into a number of rami for supplying different gyri of the cerebral hemisphere. These anastomosed with the similar branches of the arteria cerebri rostralis and arteria cerebri caudalis (Figs. 30 and 31).

Two or three branches were given off by the cortical branches of the arteria cerebri media in their initial course. These branches distributed on the pars caudalis lobus piriformis and may be called as rami lobus piriformis (Fig. 30).

Arteria cerebri rostralis

The arteria cerebri rostralis was the direct continution of the arteria carotis interna after the arteria cerebri media has been given off. The arteria cerebri rostralis continued forward on the ventral surface of the tractus olfactorium medialis towards the bulbus olfactorius. The arteria

cerebri rostralis, on reaching near the caudal pole of the bulbus olfactorius, ascended in the longitudinal fissure by fusing with the artery of the opposite side to form the arteria corporis callosi (communis) mediane. This common trunk continued its ascending course on the medial aspect of the cerebral hemisphere and reached the genu of the corporis callosi. The artery continued caudalwards on the dorsal aspect of the corpus callosum as a single branch and gave off cortical branches detailed later. The arteria cerebri rostralis before forming the above trunk continued as the arteria ethmoidalis interna (Figs. 29 and 32-35).

Arteria communicans rostralis As indicated earlier the arteria communicans rostralis was formed just in front of the optic chiasma. This was formed by the fine branches from the arteria cerebri rostralis at a level at which it separated from the arteria cerebri media (Figs. 34 and 35). The communication so formed between the arteriae cerebri rostrales was reticulated or plexiform. From the above, branches were given off which perforated the dorsal aspect of the optic chiasma and associated deeper structures to supply the nucleus suprachiasmaticus, area subcallosa, nucleus supraopticus, nucleus accumbens septi and other associated structures. These rami may be termed as rami dorsomediales or rami rostromediales (Figs. 64 a,b and 65 a,b).

Rami striati mediales (arteriae striati mediales)

The arteria cerebri rostralis during its course on the ventral aspect of the tractus olfactorium medialis gave off one or two branches which traversed on the ventral aspect of the tuberculum olfactorium and continued over the tractus olfactorius lateralis and sulcus rhinalis lateralis (pars rostralis) to continue as cortical branches after giving branches to the lobus olfactorium laterally. During their course on the ventral surface of the tuberculum olfactorium they sent a number of perforating branches which supplied the rostromedial aspect of the nucleus caudatus, putamen, globus, pallidus, capsula externa and capsula interna (Fig. 64 a,b).

Arteria corporis callosi (communis) mediane The arteria cerebri rostralis of either side, after giving off the arteria ethmoidalis interna, entered into the interhemispheric space and joined to form a single trunk which ascended to reach the genu corporis callosi. It curved caudalwards to course along the gyrus cingulus and above the corpus callosum. It terminated near the caudal half of the corpus callosum by dividing into strong cortical branches distributed to the gyrus postcruciatus, gyrus cingulus, and gyrus marginalis (saggitalis) of either sides. These branches anastomosed with the branches of the arteria cerebri media and arteria cerebri caudalis. In addition to the above, a small terminal branch continued along the gyrus splenialis of its side

and above the corpus callosum to anastomose with cortical branches of the arteria cerebri caudalis near the splenium corporis callosi. During its course the arteria corporis callosi (communis) mediane gave off a number of cortical and central branches which were distributed to the area subcallosa, nuclei septales, nuclei accumbens, gyrus proreus, gyrus precruciatus and gyrus postcruciatus. Some of its branches given off in its initial course supplied to the lamina terminalis and commissura rostralis (Figs. 32-35).

Arteria ethmoidalis interna This was a comparatively larger branch of the arteria cerebri rostralis. It coursed rostrally in relation with the medial face of the bulbus olfactorius and ventral surface of the tractus olfactorium medialis to reach the lamina cribriformis at the level of which it joined with the branches of the arteria ethmoidalis externa by forming a rete ethmoidalis or rete olfactorium. The arteria ethmoidalis interna before forming the above anastomosed with the artery of the opposite side. From the above rete, number of branches penetrated to supply the bulbus olfactorius. Similar perforating branches passed through the lamina cribrosa to supply the ethmoturbinates, nasal septum and other associated structures extracranially (Figs. 34 and 35).

Ramus olfactorium medialis This started as a branch of the arteria ethmoidalis interna in most of the cases and coursed to supply the medial face of the olfactory bulb or bulbus olfactorius and possibly contributed to the formation of the rete ethmoidalis or rete olfactorium.

Arteria communicans caudalis

This artery took its origin as a direct branch of the arteria carotis interna (Fig. 29). It extended between the above artery and arteria basilaris. The artery coursed caudally on the ventral surface of the cerebral peduncles. It curved medially in front of the rostral border of the pons ventrally where it joined with the arteria basilaris and arteria communicans caudalis of the opposite side. During its course the arteria communicans caudalis gave off a number of small branches in addition to the arteria cerebri caudalis. The segment of the artery after giving off the latter may be considered as the arteria mesencephalica. This division was based on the assumption that the arteria communicans caudalis comprised two morphological and embryological segments. The proximal part of the arteria communicans caudalis represented the proximal part of the arteria cerebri caudalis which has been regarded as the arteria communicans caudalis in human in view of its physiological significance and decreased calibre. This seemed improbable in pig except for the strict homonomous acceptance in line with the condition in

the case of the human. The distal part of the arteria communicans caudalis was regarded as arteria mesencephalica because of its neurovascular relationship with mesencephalic segment of the brain. The proximal part of the arteria communicans caudalis gave off a number of branches in its course (Fig. 36).

Rami posteriomediales (caudomediales) These were given off from the medial face of the arteria communicans caudalis before it continued as the arteria mesencephalica. The number of the above rami varied from four to six. These branches were directed medially on the ventral surface of the tuber cinereum and hypothalamic floor. The branches directed towards the tuber cinereum joined with the arteriae hypophysiales (superiores) rostrales and contributed to the areas as already indicated with the description of the latter arteries. The branches going to the hypothalamic floor supplied the nucleus hypothalamicus ventromedialis, nucleus paraventricularis, nucleus supraopticus, corpus mamillare and mamillary nuclei as well as the fornix (Figs. 66 a,b).

In addition to the above from the main stem of the above artery a set of rami left its dorsal and dorsolateral face. Some of these rami perforated the crus cerebri whereas others coursed obliquely and perforated the posterior part of the hypothalamus, subthalamus and reached the thalamus. These were three to four in number and supplied nucleus reticularis

thalami, nucleus parataenialis, nucleus reunien, nucleus centralis medialis, nucleus centralis lateralis, nucleus paracentralis, nucleus rostralis ventralis, nucleus rostralis medialis, tractus mamillothalamicus, crus cerebri, nucleus venttralis rostralis, zona incerta, nucleus subthalamicus, ansa lenticularis, nucleus hypothalamicus dorsomedialis and centrum medianum (Figs. 36 and 66 a,b).

Arteria cerebri caudalis

The artery took off as a branch of the arteria communicans caudalis (at the junction of the pars proximalis and pars distalis). The artery curved dorsolaterally to ascend along the crus cerebri and under the cover of the lobus prirformis (pars caudalis). It crossed the superficial face of the corpus geniculatum medialis and deeper face of the gyrus parahippocampalis. In its further course it was related to the pulvinar and corpus geniculatum lateralis ventrally. The terminal part of the artery left the company of the splenium corporis callosi and continued for its cortical distribution by giving cortical branches distributed on the posteriomedial cortical areas above and behind the corporis callosi. It anastomosed with the branches of the arteria corporis callosi (communis) mediane and arteria cerebri media. During its course it gave off a number of branches (Figs. 36-39).

Rami perforantes The arteria cerebri caudalis during its course gave off a number of perforating branches. These were given at varied levels along its course. These branches supplied the crus cerebri, lamina medullaris externa, nucleus subthalamicus, nucleus reticularis thalami, nucleus geniculatum lateralis, nucleus geniculatum medialis caudolateral areas (Fig. 67 a,b).

Rami geniculati mediales The arteria cerebri caudalis gave off three to four perforating branches while crossing the corpus geniculatum medialis. These branches supplied the above as well as the lamina medullaris externa, radatic accousticae, brachium colliculus caudalis, nucleus lateralis caudalis and associated tracts.

Rami parahippocampales The arteria cerebri caudalis during its course along the parahippocampal gyrus gave off a number of branches from its dorsal aspect. These branches were given off at different levels. The first branch was generally given soon after the arteria cerebri caudalis came in close relation with the parahippocampal gyrus. It sent descending branches to anastomose with the ascending branch of the arteria choroidea rostralis. The other branches coming directly from the arteria cerebri caudalis distributed to the parahippocampal gyrus all along its course. These branches interanastomosed with each other. Some of these branches

even distributed on the caudoventral part of the caudal pole of the cerebral hemisphere.

The arteria cerebri caudalis, before leaving the company of the gyrus parahippocampalis, gave off two or three branches, the course of which was variable. A larger branch was generally given at the level of the corpus geniculatum lateralis which coursed rostrally on the dorsolateral aspect of the thalamus. The artery during its course gave two or three medial branches and reached the rostral part of the thalamus. The artery sent anastomosing branches to the arteria choroidea rostralis and itself contributed in the formation of the plexus choroideus ventriculi lateralis and plexus choroideus ventriculi tertii. The branches mentioned above joined with choroidal rami from the arteria choroidea caudalis. They sent perforating branches during their course to supply the nucleus rostralis ventralis, stria terminalis, nucleus rostralis medialis, lamina medullaris thalami externa, nucleus geniculatum lateralis, nucleus reticularis thalami, nucleus lateralis dorsalis, nucleus lateralis caudalis, lamina medullaris thalami interna, nucleus dorsomedialis, nucleus lateralis centralis and nucleus rostralis dorsalis. In view of their terminal distribution the above artery and its terminal branches may be termed as the rami choroidei caudales (Figs. 40, 67 a,b and 68 a,b).

The smaller branches coming directly from the arteria cerebri caudalis (mentioned already in the preceding paragraph) were given on the dorsocaudal part of the pulvinar. These branches coursed on the caudal and caudomedial part of the thalamus. These anastomosed with the choroidal branches of the arteria choroidea caudalis as well as with branches of the above-mentioned artery, described earlier. They sent perforating branches for the thalamus and contributory branches for the plexus choroideus ventriculi tertii. They supplied the nucleus pulvinaris, nucleus lateralis dorsalis, nucleus lateralis caudalis, nucleus geniculatum lateralis, brachium colliculus rostralis, epithalamus and habenular complex. These rami may also be termed as the rami choroidei caudales (Figs. 67 a,b and 68 a,b).

Rami corticales The arteria cerebri caudalis in its course along the lobus piriformis (pars caudalis) and gyrus parahippocampalis sent off a number of branches which were cortical in distribution on the caudoventral and caudomedial parts of the cerebral hemisphere. In addition to the above, the arteria cerebri caudalis gave off cortical branches after leaving the splenium of the corporis callosi. These cortical branches anastomosed with the similar branches from the arteria cerebri media and arteria rostralis (Figs. 30-33).

Arteria choroidea caudalis The artery was given off from the arteria mesencephalica directly or in common with the ramus ad tectum mesencephali rostralis. It coursed dorsolaterally around the pedunculus cerebri and behind the corpus geniculatum medialis. It bent medially to come in front of the colliculus rostralis and behind the epiphysis and pulvinar. During its course to reach the above structures it divided into two or three branches and anastomosed with the branches of the arteria cerebri caudalis and ramus ad tectum mesencephali rostralis. The above branches continued rostromedially to lie lateral to the epiphysis and on the dorsomedial aspect of the thalamus. These branches terminated by supplying the plexus choroideus ventriculi tertii. They anastomosed with the choroidal branches of the arteria cerebri caudalis and sent perforating branches to the areas traversed in their course. The areas supplied were the crus cerebri, nucleus geniculatum medialis, brachium colliculi rostralis, brachium colliculi caudalis, commissura caudalis, commissura collicullorum rostralium, fasciculus retroflex, nucleus pretectalis, nucleus parafascicularis, nucleus ventralis caudalis, nucleus rostralis dorsalis, nucleus dorsomedialis, nuclei habenulares, nucleus parataenialis, stria medullaris thalami, epithalamus, nuclei paraventriculares thalami and other associated nuclei. As indicated above, they also supplied the plexus choroideus ventriculi tertii (Figs. 37, 39 and 68 a,b).

Ramus ad tectum mesencephali rostralis The artery took its origin from the arteria mesencephalica and coursed dorsomedially to come on the dorsal and dorsomedial aspect of the colliculus rostralis. It also distributed on the dorsolateral aspect of the colliculus daudalis partly. During its course it divided into three or five branches before reaching the above structures. The above branches interanastomosed with each other and similar branches of the contralateral side as well as with branches of the arteria choroidea caudalis and ramus ad tectum mesencephali caudalis. It supplied perforating branches to the crus cerebri, brachium colliculi caudalis, tractus rubrospinalis, fasciculi tegmenti, tractus spinothalamici, fasciculus longitudinalis medialis, nuclei nervus oculomotorii, and nucleus nervus trochlearis, tractus tectospinalis, nucleus colliculus rostralis, nucleus colliculus rostralis, nucleus colliculus caudalis, nucleus tractus mesencephali nervus trigemini, lemniscus lateralis, substantia nigra, nuclei tegmenti, nucleus ruber or rubrum, lemniscus medialis, substantia grisea centralis, commissura colliculorum rostralium and caudalarium. It may also supply some contribution for the plexus choroideus ventriculi tertii. The branch of the above artery supplying the colliculus caudalis partly may arise separately as a direct branch from the arteria mesencephalica in some cases and may be regarded

as the ramus ad tectum mesencephali intermedius (Figs. 36-40 and 69 a,b).

Rami caudomediales (Rami dorsomediales) From the arteria mesencephalica, during its whole course, before it joined the arteria mesencephalica of the contralateral side and the arteria basliaris, a large number of branches were given off. These branches were directed dorsomedially towards the intercrural fossa. These branches perforated the caudomedial and caudolateral part of the corpus mamillaris and the substantia perforata caudalis. These brenches interanastomosed with each other superficially and then perforated the above areas. The size and the course of the above vessels varied depending on the area of supply. The rami were directed in a varied manner, the larger rami were directed dorsomedially and perforated the mesencephalon through the substantia perforata caudalis, nucleus interpeduncularis and tegmentum to distribute in the thalamus. Some of the above branches may come from arteria mesencephalica near its junction with the arteria cerebri caudalis and perforated the mesencephalon. The finer branches perforated through the substantia perforata caudalis and coursed dorsomedially to reach the aqueductus mesencephali. Some of the branches were directed caudomedially to perforate the rostral part of the pons medially. The above branches, collectively, supplied the crus cerebri, nucleus interpeduncularis, nucleus rubrum

or ruber, substantia nigra, fasciculus longitudinalis medialis, fasciculus longitudinalis dorsalis, tegmentum mesencephali, decussation peduncullorum cerebellarium rostralium, nucleus nervus trochlearis, nuclei nervus oculomotorii, substantia grisea centralis, formatio reticularis tegmenti, nucleus mamillaris lateralis, nucleus mamillaris medialis, nucleus supramamillaris, fornix, nucleus reunien, tractus mamillothalamicus, peduncularis mamillaris, nucleus centralis medialis, zona incerta, nucleus ventralis caudalis, corpus subthalamicus, nucleus dorsomedialis thalami, nucleus parafascicularis, lamina medullaris thalami interna, nucleus lateralis caudalis, centrum medianum and nucleus paracentralis (Figs. 36 and 67 a,b - 71 a,b).

Rami posteriolaterales (Rami caudolaterales) The arteria mesencephalica gave off a number of small lateral branches which coursed on the lateral part of the pedunculus cerebri and perforated to supply the brachium colliculi caudalis, lemniscus lateralis, substantia nigra and fiber tracts in the above areas. Some of the branches may even ascend to supply the colliculus caudalis.

Arteria cerebelli rostralis The artery took its origin from the arteria mesencephalica (Figs. 29, 36, 41 and 71 a,b). The origin of the above vessel may be variable in the same specimen such that on one side it may take origin from the

arteria mesencephalica near or at its termination. The artery, after its origin, coursed dorsolaterally around the cerebral peduncles initially and then bent medially to lie in the space between the rostral surface of the cerebellum and caudal aspect of the colliculus caudalis. The artery terminated by giving off a number of branches distributed on the rostral part of the cerebellar hemisphere of its own side. While in the above-mentioned space, the artery came in relation with the nervus trochlearis, velum medullaris rostralis and pedunculus cerebellaris rostralis. The arteria cerebelli rostralis gave off a number of branches in its course before termination. The terminal branches of the arteria cerebelli rostralis supplied most of the cerebellum except caudoventral, lateral and caudolateral aspect of the cerebellar hemisphere. In addition to the main arteria cerebelli rostralis an accessory arteria cerebelli rostralis may also be present in some of the cases and may supply the rostrolateral parts of the cerebellar hemisphere.

Rami perforantes During its initial course the above artery gave off about four to five fine perforating rami from its caudoventral aspect. These branches perforated the cerebral peduncles and pons. These branches supplied to the crus cerebri, lemniscus medialis, pedunculus cerebelli rostralis and its decussation, substantia nigra, brachium pontis

or pedunculus cerebellaris medius, pontine nuclei and fibrae pontis transversus (Fig. 71 a,b).

Ramus ad tectum mesencephali caudalis This ramus was generally given off from the arteria cerebelli rostralis while coursing dorsomedially in the space between the colliculus caudalis and cerebellum. This ramus generally divided into two branches which coursed over the lateral and dorsal aspect of colliculus caudalis and its brachium by dividing into fine rami. These rami anastomosed with the branches of the ramus ad tectum mesencephali rostralis and ramus ad tectum mesencephali caudalis of the contralateral side. The rami perforated the colliculus caudalis to supply the nucleus colliculus caudalis, commissura colliculus caudalis, substantia grisea centralis, brachium colliculus caudalis, lemniscus lateralis, pedunculus cerebellaris rostralis, fasculi tegmenti, nucleus tractus mesencephali nervus trigemini and other associated fiber tracts (Figs. 36 - 40 and 70 a,b).

Ramus lateralis The arteria cerebelli rostralis, after giving off the fore-mintioned branches, gave off a branch, the ramus lateralis. The ramus coursed along the pedunculus cerebelli media to course between the lobus paraflocculus and lobus ansiformis on which it distributed. The ramus anastomosed with the branches from the arteria cerebelli media and arteria cerebelli caudalis laterally while medially it anastomosed with the ramus intermedius of the

main artery. During its couse the ramus supplied branches to the pedunculus cerebellaris rostralis and medius and the cerebellar cortex.

Ramus intermedius This ramus was the second terminal branch of the arteria cerebelli rostralis. The ramus ascended dorsally over the lobus ansiformis, lobus simplex and partly on the lobus vermis after dividing into two or three branches. It anastomosed with the ramus lateralis and ramus medialis of the main artery as well as with ramus intermedius of the arteria cerebelli caudalis. It supplied branches to the cerebellar cortex of the lobus ansiformis, lobus simplex and lobus vermis (partly). It may also send some perforating branches to the nucleus dentatus.

Ramus medius This was a large ramus which distributed over its own half of the lobus vermis by dividing into a number of branches. It ascended on it and astomosed with the ramus medius to the contralateral side, ramus intermedius of the main artery and dorsally with the arteria cerebelli caudalis. It distributed its supply to the cerebellar cortex of the above lobe as well as to the cerebellar nuclei.

In addition to the above, the arteria cerebelli rostralis and its terminal branches gave inferior or ventral branches which descended on the cerebellar hemisphere of their own side to distribute branches for the velum medullaris rostralis, lingula as well as other inferior cerebellar cortical fields (Figs. 72 a,b).

Arteria basilaris

The arteria vertebralis while in course in the neck region reached the fossa atlantis. The artery anastomosed with the arteria occipitalis and ramus descendens. The artery passed through foramen alare and foramen vertebrale laterale into the canalis vertebralis. The arteria vertebralis (arteria cerebrospinalis) then coursed along the lateral wall of the vertebral canal at the level of the atlas vertebra. It ran a tortous course and joined with arteria condylaris and ramus spinalis to form a small rete mirabile epidurale caudalis. After forming the above, the artery continued on the ventral aspect of the junction of the medulla oblongata and spinal cord to join a similar continuation of arteria vertebralis of the opposite side to form the arteria basilaris. The arteria basilaris, after its formation, continued on the ventral surface of the medulla oblongata, corpus trapezoideum and pons in a flexous manner. The arteria basilaris decreased in its calibre rostrally in the region of pons before joining with the arteriae communicans caudales (arteriae mesencephalicae). The arteria basilaris gave off a number of branches during its course (Figs. 28 and 29).

Rami medullares These were three to five branches given from the lateral aspect of the arteria basilaris at varied levels of the medulla oblongata. These branches may

be variable in number on either side and be supplemented by the similar branches from the rostral continuation of the arteria vertebralis (arteria cerebrospinalis). These branches coursed obliquely in a flexous manner on the ventrolateral aspect of the medulla oblongata and then curved around it to come on its dorsal aspect. While curving dorsomedially, to come on the dorsal aspect of the medulla, posterior or caudal set of branches passed through the rootlets of hypoglossal nerve whereas the anterior or rostral set came in relation with the glossopharyngeal and vagus nerve roots. These arteries and their branches on the dorsal aspect of the medulla oblongata were related to the posterior part of the cerebellar hemisphere. They reached near the lateral wall of the fourth ventricle in its posterior half and the obex. The caudal ramus medullaris during its course on the dorsal aspect of the medulla oblongata gave off a caudal branch which continued caudalward dorsolaterally and was named as ramus spinalis dorsalis. It continued its backward course and joined with the segmental dorsal spinal rami from the arteria vertebralis to form arteria spinalis dorsalis. During their course on the ventral and dorsal aspect of medulla oblongata these rami interanastomosed with each other. During their course they sent perforating branches to the corpus trapezoideum, lemniscus medialis, nucleus nervus facialis,tuberculum facialis,

nucleus tractus spinalis nervus trigemini, nucleus olivaris, nucleus ambigus, nucleus and tractus solitorius, tractus vestibulospinalis, pedunculus cerebellaris caudalis, tractus olivocerebellaris, nucleus motorius nervus trigemini, nuclei and fasciculi cuneatus (lateralis) and cuneatus accessorius (medialis), nucleus and fasciculus gracilis, tractus spinocerebellaris dorsalis, nucleus vestibularis caudalis, nucleus olivaris accessorius dorsalis, plexus choroideus ventriculi quarti, nucleus fasciculi lateralis, nucleus parasympatheticus nervus vagi, nucleus intercalatus, formatio reticularis, nucleus motorius nervus hypoglossi, associated fiber tracts and area postrema (Figs. 42, 43, 71 a,b, 73 a,b - 77 a,b).

Arteria cerebelli caudalis The artery was observed to be the largest branch given off by the arteria basilaris. The origin of this artery was observed variable. The level of origin varied on either side. The artery took its origin at the junction of the corpus trapezoideum and medulla oblongata or at a variable distance on the ventral surface of the former. The artery coursed dorsolaterally and came in relation with the nervus abducens. The artery in its further course ascended dorsolaterally and obliquely to reach the dorsal aspect of the medulla oblongata in front of the root of the glossopharyngeal nerve (nervus glossopharyngeus). The artery came in relation with cerebellum and choroid plexus of

the fourth ventricle. It terminated by giving off two or three branches to the cerebellar cortex. The arteria cerebelli caudalis during its course on the ventral and ventrolateral aspect of the medulla oblongata and corpus trapezoideum aent perforating branches into the above areas. These perforating branches supplied to the corpus trapezoideum, decussatio corpus trapezoideum, nucleus motorius n. facialis, nucleus motorius n. abducentis, lemniscus medialis, tractus corticospinalis, nucleus olivaris dorsalis and nucleus olivaris accessorius medialis, nucleus tractus spinalis nervus trigemini, nucleus reticularis and formatio reticularis. It also sent anastomosing branches to the adjoining rami (Figs. 28, 29, 42, 44, 45 and 72 a,b).

Arteria cerebelli media Ther arteria cerebelli caudalis before reaching just in front of the root of glossopharyngeal nerve (nervus glossopharyngeus) sent a branch which coursed between the roots of the nervus facialis and nervus vestibulocochlearis. This branch received anastomosing branches from the rami ad pontem. The artery continued its course rostrally along the parafloccculus, flocculus, and dorsal aspect of the brachium pontis. It anastomosed with the ramus lateralis of the arteria cerebelli rostralis and sometimes with the arteria cerebelli rostralis accessorius. The artery distributed mainly on the ventral part of parafloccculus and flocculus as well as gave some perforating branches

for the pedunculi cerebellaris medius and caudalis and nuclei vestibulares and cochleares (Figs. 28, 29, 44 and 73 a,b).

Arteria labyrinthi The arteria cerebelli during its course between the roots of the nervus facialis and nervus vestibuoldochlearis gave off a fine branch which entered the internal acoustic meatus (meatus acousticus internus) to supply the inner ear.

The arteria cerebelli caudalis during its terminal course on the dorsal aspect of the medulla oblongata and under the cerebellar hemisphere gave off a number of perforating branches from its ventral aspect. These branches perforated tuberculum acusticum, the area behind the nerve root of the vestibulocochlearis nerve. In addition to that one or two fine slender branches extended caudally along the lateral margin of the roof of the fourth ventricle (ventriculus quarti) and joined with the rami medullares forming fine anastomosing chain extending towards the obex. The above slender branches along with the rami medullares supplied the pedunculus cerebellaris caudalis, nuclei vestibulares, nuclei cochleares, nucleus tractus spinalis nervus trigemini, tractus vestibulospinalis, nucleus parasympatheticus n. vagi, nucleus motorius n. hypoglossi, tuberculum acusticum, nucleus tractus solitorius, nucleus cuneatus lateralis, nucleus cuneatus accessorius or medialis, nucleus motorius nervus trigemini, nucleus intercalatus and nucleus ambigus (Figs. 74 a,b - 76 a,b).

A number of fine choroidal rami for the choroid plexus of the fourth ventricle were given by the artery at the above level. The artery cerebelli caudalis curved medially to come in relation with the ventral part of the vermis cerebelli caudally and continued as the ramus medius arteria cerebelli caudalis.

Terminal branches The arteria cerebelli caudalis generally divided into three terminal branches, ramus lateralis, ramus intermedius and ramus medius. The pattern and branching of these rami was variable (Figs. 45).

Ramus lateralis This was the first terminal branch of the above artery. It ascended over the caudal part of the flocculus and paraflocculus and anastomosed with the cortical branches of the arteria cerebelli media. The above ramus may leave the main artery in common with the ramus intermedius.

Ramus intermedius This was the second terminal branch and was comparatively larger and better distributed over the caudal and ventral part of the paramedian lobe. The lateral ramus may arise somes in common with it. The ramus intermedius anastomosed with the branches of the ramus intermedius of the arteria cerebelli rostralis as well as with adjoining rami of the arteria cerebelli caudalis.

Ramus medius This was the continuation of the arteria cerebelli caudalis and was represented by two or three branches distributed on the caudal and inferior aspect of the vermis

lobe of its side. The ramus anastomosed with the similar ramus of the other side as well as with the ramus medius of the arteria cerebelli rostralis. Some of the branches from the above ramus supplied the velum medullaris caudalis, plexus choroideus ventriculi quarti, nodulus and flocculus ventrally.

Rami ad pontem These were three or four in number and took origin from the terminal portion of the arteria basilaris. These arose as collateral branches at different levels of the pons and coursed transversely and ascended on the lateral aspect of the pons. They anastomosed with each other as well as with the arteriae cerebelli rostralis and media. These branches may be classified according to their location as rostralis, intermedius and caudalis (Figs. 29 and 30).

Ramus ad pontem caudalis This started as a single branch, generally given off at the level of the junction of the pons and corpus trapezoideum and in front of the origin of abducens nerve root. It was directed dorsolaterally and reached in front of the root of the facial nerve and anastomosed with the arteria cerebelli media and as well as with the arteria cerebelli caudalis. During its course it sent perforating branches to the caudal pontine fields, fibrae pontis transversus, fibrae corticospinalis, nuclei pontis, formatio reticularis, lemniscus lateralis and its nucleus, nucleus reticularis pontis caudalis and may also supply the nucleus

motorius nervus trigemini, nucleus sensibilis pontinus nerve trigemini and its mesencephalic tract.

Ramus ad pontem intermedius This ramus was generally smaller than the rostral as well as the caudal ramus. It was given off almost in the middle portion of pons ventrally. It was directed dorsolaterally and anastomosed with the branches of the ramus ad pontem caudalis as well as the ramus ad pontem rostralis and supplied the nerve roots of the nervus trigeminus. In addition to the above, smaller rami may also be present. During its course the ramus ad pontem intermedius gave off perforating branches which supplied the middle portion of the pons, fibrae pontis transversus, pedunculus cerebellaris medius, nuclei pontis, tractus corticospinalis, tractus corticobulbaris and tractus spinothalamici, lemniscus lateralis and its nucleus, nucleus motorius n. trigemini, nucleus sensibili pontinus n. trigemini, nucleus and tractus mesencephalicus n. trigemini and tractus spinalis n. trigemini (Fig 71 a,b).

Ramus ad pontem rostralis It was a strong and largest branch of the pontine series. It was given off near the anterior border of the pons ventrally by the arteria basilaris. It ascended dorsolaterally to come in relation with the nervus trigeminus medially, ventral part of the paraflocculus ventralis and brachium pontis. It terminated by anastomosing with the branches of the arteria

cerebelli media and arteria cerebelli rostralis. Terminally, it supplied branches to the above structures. However, while in relation with the anterior part of the pons it sent perforating branches to supply the formatio reticularis, fibrae pontis, nuclei pontis, lemniscus lateralis, radix nervus trigemini, pedunculus cerebellaris medius, pedunculus cerebellaris rostralis and nuclei nervus trigemini indicated along with ramus ad pontem intermedius.

Rami paramediales or rami paramedianes The arteria basilaris during its course along the ventral surface of the medulla oblongata, corpus trapezoideum and pons gave off a number of fine branches from its dorsomedial aspects. These branches perforated the above structures ventromedially through the fissura mediana ventralis and sulcus basilaris. These vessels varied in number in different segments but supplied the nuclear area and fibrae tracts located in the median plane. The structures supplied by these in the above segments were as under pyramis, lemniscus medialis, nucleus motorius nerve hypoglossi, fasciculus longitudinalis medialis, nucleus intercalatus, tractus tectospinalis, nucleus reticularis paramedianus, tractus tectomedullaris, nucleus raphae and raphe, nucleus olivaris, nucleus olivaris accessorius medialis and dorsalis, nucleus dorsalis corporis trapezoidei, nuclei ventralis corporis trapezoidei, nuclei reticularis, nuclei reticularis, nuclei pontis, fibrae pontis transversus,

mucleus parasympatheticus nervus vagi, nucleus roller, nucleus motoris nervus abducentis, decussation lemniscorum medialium, fasciculus longitudinalis dorsalis, substantia grisea centralis ventriculus quarti and other fiber tracts coursing in the median plane of the pons and medulla oblongata. The above branches may also be called as rami medianes (Figs. 71 a,b and 73 a,b - 77 a,b).

Age Changes in the Cerebral Arteries of the Dog

The study of age changes was extended to the cerebral arteries but it became necessary to outline the normal histology of the cerebral arteries to elucidate the changes observed. The study of the normal histological picture of the cerebral arteries was divided into three main groups, large cerebral arteries, medium and small pial arteries and intracerebral arteries.

Histology of large cerebral arteries

The large cerebral arteries include the (rostral) anterior cerebral, middle cerebral, posterior (caudal) communicating, posterior (caudal) cerebral and basilar. The basic pattern of the arteries was trilamellar, having tunica intima, tunica media and tunica adventitia.

The tunica intima, as in other arteries, formed the innermost layer of the arteries. It was further subdivided into three sublayers. These were the endothelial cell layer of

endothelium, subendothelial layer and internal elastic lamina or layer. The endothelial layer consisted of a single layer of endothelial cells arranged along the inner border of the subendothelial space. The cells were elongated with their depth increasing in the middle portion where the elongated nucleus was located. These cells were circularly arranged in a single layer. The subendothelial space or layer was observed to be a thin space between the endothelium and internal elastic lamina. The space was observed to be acellular and consisted of connective tissue ground substance. This material was fibrillar in nature. The internal elastic layer was a thick condensed elastic tissue band which marked the separation between the tunica intima and tunica media. This was a convoluted single band presenting an almost homogeneous appearance.

The tunica media formed most of the thickness of the vessel. It was comprised of a variable number of smooth muscle cell layers arranged in a circular fashion. The smooth muscle cells were surrounded by few fine elastic fibers and very little or no collagenous material under normal conditions. The thickness of the medial layer varied in different arteries. However, the number of smooth muscle cell layers varied between fifteen and twenty-one.

The tunica adventitia was comparatively thinner than the medial layer. The demarcation between the tunica media and

tunica adventitia was abrupt. However, there was always some blending of the two layers. A few elastic fibers regularly deposed near the junction of the above two layers were observed. These fibers were circularly arranged in the form of one or three interrupted elastic fibers at the inner portion of tunica adventitia. This was more evident in the basilar artery where an indistinct external lamina could be differentiated at the junction of the tunica media and tunica adventitia. The main constituent of the tunica adventitia was formed by the collagen, with few elastic fibers, fibroblasts and scanty smooth muscle cells interposed. The density of these fibers decreased towards the outer border (Figs. 86 and 87).

Structure of medium and small pial arteries

These arteries, which were the subsequent branches of the arteries described above, had characteristic features which distinguished them from the parental ones.

The tunica intima was distinguishable into three sublayers similar to the main or large cerebral arteries. This was not the case in the smaller pial arteries where only two sublayers could be easily distinguished. The endothelium was distinct and consisted of a single layer of flattened cells. The subendothelial space or layer was discernible in the medium-sized pial arteries but was indistinguishable in

smaller ones. The internal elastic lamina was evident in both categories of arteries under observation. The tunica media had similar constituents except that there were elastic fibers dispersed among smooth muscle cell layers. These fibers were coarser and slightly thicker than in the larger cerebral arteries. Their undulating nature was very evident. The other constituent in the media was a small amount of collagen. The external elastic lamina was indiscernible in these vessels also. The depth of the tunica adventitia varied with the size of the artery (Fig. 88).

Intracerebral arteries

These had a similar trilamellar arrangement of the layers. The endothelium was observed to lie directly on the wavy internal elastic lamina. The medial layer consisted of one to three layers of smooth muscle cells. There were very few collagen fibers which were present between the smooth muscle cell layers and very few elastic fibers were observed along the above connective tissue. The tunica adventitia was scanty in the form of a few irregularly arranged collagen fibers around the media. The tunica media formed the main depth of the wall.

A number of modifications in the form of valve-like structures and intimal cushions were observed in the cerebral arteries. The former were present at the site of branching

in the small pial, perforating and intracerebral arteries whereas the latter were present in the major cerebral arteries and their main branches.

The valve-like structures were present in the form of conical or cusp-like projections situated at the branching points. They arose from the collateral branch and faced into the lumen of the parent artery. Each was lined with a continuous lining of the endothelial cells continued from the collateral to the parent vessel. The main constituents of the valve-like formations were the smooth muscle cells. These were mostly arranged in a longitudinal manner or vice versa depending on the plane of section. The internal elastic lamina was present generally in the form of two bands - one under the endothelial cells and the other at the base of the valve which formed the continuity of the internal elastic lamina of the parent artery and its collateral. Few elastic fibers may be seen among the smooth muscle cells. The valve-like structures were observed to be formed by the tunica intima only (Figs. 78 - 82).

The intimal cushions had a similar configuration but were rounded at their free margin. The intimal cushions were also lined with the continuous band of endothelium. The intimal cushions were demarcated from the tunica media of the arterial wall by the internal elastic lamina. The

internal elastic lamina was laminated into a number of fine bands which continued into the collateral branch. Among the fibers smooth muscle cells were oriented in longitudinal or circular manner depending on the sectional geometry. The ground substance of the intimal cushions was rich in acid mucopolysaccharides and collagen. The general pattern of their presence was bilateral; however, single cushions were also observed. The intimal cushion may be attenuated in cases where a very small collateral was given off by a larger artery (Figs. 152, 154 and 156).

The intimal cushions observed at the age of two days in the pig were immature but were prominent and more frequent by six months of age onwards. The intimal cushions underwent changes with age. The intimal cushions and valve-like structures in the cerebral arteries, up to one year of age were musculoelastic but became fibrous, due to progressive age changes, in older arteries as described in the observations relative to the aging of cerebral arteries (Figs. 152, 174, 175, 179 and 183).

Age changes in the cerebral arteries of the dog

The specimens included in this study were divided into six age groups. These were as follows:

Group	Range of Age
1	Birth to six months
2	Six months to one year
3	One year to four years
4	Four years to eight years
5	Eight years to twelve years
6	Twelve years to sixteen years

Group 1

Six animals formed this group. These were B105, B99, E26, 068, E27, and o49 which were one day, seven weeks, two months, two and a half months, four months and five months and seven days of age respectively. The changes observed in the general picture of the cerebral arteries in this group were postnatal. These consisted in the increase in general size of the different layers, maturation and orientation of cellular components and connective tissue.

The cerebral arteries examined in the one-day old dog (B105) showed a basic trilamellar pattern similar to those of the adult dog but the endothelial cells forming the endothelium presented vesiculated or plump nuclei. There was very little cytoplasm. These cells formed a continuous layer on the luminal border of the arteries. These were laid almost directly on the internal elastic lamina. There was no evidence of the subendothelial space in any category of arteries. The

internal elastic lamina was thin and stained lightly. The layer showed a very loose wavy contour. The staining was interrupted and discontinuous. The medial layer in the main cerebral arteries was very small in depth with a thickness of about two to four smooth muscle cells. The orientation of the smooth muscle cells was basically concentric but longitudinally and obliquely placed cells were commonly seen. The nuclei were vesiculated though slightly elliptical. The medial layer showed few elastic fibers interspersed among smooth muscle cells. There were few elastic fibers at the junction of the tunica media and adventitia indicating the indistinct presence of the external elastic lamina. The tunica adventitia was poorly developed and was loosely arranged as a small collagenous layer with few elastic fibers. The collagen fibers stained lightly indicating that the collagen may be immature at this age. The pial arteries were well laid with a thin tunica intima, one to two cell layers thick media and a very thin tunica adventitia.

The tunica intima of the large cerebral arteries, at the age of about one and a half months (B99) showed differentiation from the preceding age specimen. The endothelial cells which were vesiculated now had condensed nuclei with elongated elliptical outline. The subendothelial space or layer was still undifferentiated completely and indicated signs of its initial formation. This undifferentiated thin space

appeared as a homogeneous colorless band between the endothelium and internal elastic layer. The matrix in the space was fibrillar and was thought to be elastoid in nature. The internal elastic lamina appeared as a thin band still showing weak and discontinuous staining areas along its contour.

The tunica media was better organized at this age group but still showed few vesiculated smooth cells which were not classically oriented. The number of smooth muscle cell layers increased in number, ranging between five to seven, in comparison to the medium pial arteries which had three to four cell layers at this age. The smooth muscle cells were densely packed. The elastic fibers in the tunica media were increased in number along the smooth muscle cell layers. The elastic fibers were thinner in the large cerebral arteries than in the pial arteries in which these were coarser and thicker. The collagen was laid as fine fibrillar material, the amount of which was negligible. The tunica adventitia increased in depth and also in its staining property. It was worth noting that the subendothelial layer was still obscure in the pial arteries. The pial branches of the large cerebral arteries showed elastic fibers in the tunica media which were thought to have frayed from the internal elastic lamina (Figs. 83 and 84).

At two months of age (E26), the cerebral arteries showed changes which indicated that the subendothelial space was

still very small. The internal elastic lamina stained evenly and increased in depth. The tunica media showed six to eight smooth muscle layers in the large cerebral arteries. There was further elaboration or increase of elastic fibers in the media in all types of arteries but it was comparatively greater in the small and medium cerebral arteries. In some of the pial arteries the thick elastic fibers in the medial layer seemed to be distributed as bands occupying one-fourth or one-sixth of the circumference.

At the age of four months (E27) the subendothelial space was further differentiated and was clearly demonstrable in large cerebral arteries. The subendothelial space showed a fibrillar matrix without any cells. In some places it showed staining properties specific for fibrous tissue, but this was sporadic at this stage. There was slightly increased depth of the internal elastic lamina and staining was almost homogeneous. There was an increase in the depth of the tunica media with compactly laid and circularly arranged smooth muscle cells. There was slight subintimal elaboration of collagen in some arteries. The tunic adventitia increased in thickness and also in the number of elastic fibers in it.

By the age of five and a quarter months (049), there was very light bluish tinged staining material(with Mallory triple stain) in the subendothelial space of large cerebral arteries. The internal elastic lamina showed no appreciable

change. The smooth muscle cells of the medial layer appeared in a regular and concentric form (Fig. 89). There was a slightly increased deposition of collagen in this layer. The tunica adventitia, except for an increase in thickness, showed no other demonstrable changes. The anterior cerebral artery showed a slightly interrupted internal elastic lamina accompanied by slight collagen in the subendothelial space and subintimal area. The posterior communicating artery also showed a similar condition indicated above. The basilar artery at the medullary spinal junction showed a small bead-like projection in the continuity of its luminal surface indicating proliferation of intima and media (Figs. 90 and 91). There were probably disoriented smooth muscle cells pressing against the internal elastic lamina. The internal elastic lamina was intact. The proliferation had high collagen and few clear cells, possibly the longitudinally oriented mesenchymal cells. There was increase in the thickness of the adjoining subendothelial space due to increased collagen and ground substance acid mucopolysaccharides. This formation possibly seemed to relate the initial medial changes which consisted in the shift of smooth muscle cells in the subintima which subjected pressure on the internal elastic lamina to a more elevated position than its surrounding. This pressure could

lead to the splitting of the internal elastic lamina with age. This was evident from Weigert stained section which showed the disruption of the internal elastic lamina. The presence of this structure in a number of sections of the same area indicated that it was not an artifactual representation. A small pial branch supplying the cerebellum showed intimal proliferation which was accompanied by a splitting of the internal elastic lamina and smooth muscle cell proliferation. Medial defect in the middle cerebral artery was observed (Fig. 92). The mean count of the smooth muscle cells nuclei per unit medial volume of the middle cerebral artery and basilar artery in the above age group was 49.76 and 47.45 respectively (Fig. 85, Table 3 and Graphs 1 and 2).

Group 2

In the specimens of six and a half months and eight months (B66, B48) there was a general increase of collagen in the subintimal space and outer one-fourth of tunica media. A small branch of the anterior cerebral artery of the eight-month-old brain (B48) showed a splitting of the internal elastic lamina which fragmented to spread in the underlying tunica media. A branch of the middle cerebral artery showed disrupted internal elastic lamina (Fig. 95). A slight intimal proliferation was continuous with the medial constituents which showed increased collagen. The cellular constituents of the

intimal proliferation were smooth muscle-like cells oriented in a varied manner. In an intracerebral branch from the anterior cerebral artery supplying the caudate nucleus, intimal proliferation was observed. The cellular constituents were again the smooth muscle-like cells (Fig. 93). The pial branches of the cerebral arteries indicated presence of elastic fibers in the tunica media which were comparatively more than in the main arteries (Fig. 94).

The intracerebral branch of the posterior cerebral artery supplying the lateral geniculate body had an internal elastic splitting and duplication to give a lamellar appearance. The intimal proliferation was slight with smooth muscle and modified endothelial cells oriented variably. There was also proliferation of the collagen (Fig. 96).

The basilar artery at ten months of age (B79) showed focal intimal and subintimal collagen along with the disruption of the internal elastic lamina.

The cerebral arteries at the age of eleven months (C41) revealed intracerebral branches of the cerebral artery showed intimal splitting and slight lamellar elastosis. The intracerebral branch of the middle cerebral artery supplying the caudate nucleus presented intact internal elastic layer but the cellular proliferation in it almost occluded the arteriole lumen.

The specimen at one year (B56) showed that the middle cerebral artery developed a fibromuscular intimal thickening. The internal elastic layer was fragmented at various places (Figs. 97 and 98). The proliferation was observed to be increasing progressively from one side to the other. There was collagen, acid mucopolysaccharides and elastoid tissue with longitudinally oriented smooth muscle-like cells. The collagen was also present in the subintimal area and proximal one half of the medial layer. In a branch of the middle cerebral artery there was fragmentation of the internal elastic lamina in the form of lamellae. In two intracerebral branches going to the optic radiation there was eccentric intimal proliferation of fibrous tissue. This was aggravated on one side. Similarly a branch supplying the mesencephalic nuclei (branch of the posterior communicating artery) showed internal elastic lamina splitting (Fig. 99).

Group 3

The group included the specimens ranging above one year to four years of age. The specimens were B37, B96, B80, B127, 21, 053, B68, B82, B36 and B95 which were one year two months and seven days, one year and five months, one year and seven months, two years and seventeen days, two years and seven months, two years eight months and six days, three years and two months, three years and six months and four years of age respectively.

The changes observed in this group were progressively intermediate between the preceding and subsequent groups. The subendothelium showed an increased amount of the collagenous material. The depth of the sublayer also increased. The intimal layer continued to increase in thickness. There was a tendency of slight loss of the tight serrated appearance of the internal elastic lamina. There was increased elaboration of elastic tissue in the above lamina leading to the formation of lamellae in place of a single lamella. The tunica media presented increased collagenization in a progressive manner. It was high in comparison to the preceding group (Fig. 108). The increase was especially prominent in the medium and small pial arteries. From three years onwards there was a predominant fibrosis of the medial layer. The mean of the number of the smooth muscle cell nuclei per unit medial volume of the middle cerebral artery and basilar artery was 33.9 and 32.41 respectively (Fig. 107, Table 1 and Graphs 1 and 2).

A pial branch of the anterior cerebral artery at the age of about one year and two and a half months (B37) indicated splitting of internal elastic lamina and another presented the intimal proliferation associated with splitting. Duplication of the internal elastic lamina was observed in a small perforating branch of the posterior cerebral artery. This duplication was partial (Fig. 101).

One year and five months old cerebral arteries (B96) indicated no substantial change except internal elastic lamina splitting as described in the above specimen.

At one year and seven months (B80), a pial branch of the anterior cerebral artery showed duplication of the internal elastic lamina. The basilar artery showed interruption of the internal elastic lamina whereby there was continuity of the intima and media.

The two years and seventeen days old cerebral arteries (21) presented prominent increases of the collagen in subendothelial sublayer and media and more in small pial and medium pial arteries than in the large cerebral arteries. The same was also true for the elastic tissue. In addition to the above, slight duplication of the internal elastic lamina was observed in an intracerebral branch of the anterior cerebral artery. This was accompanied by a slight deposition of collagen around the elastic lamellae (Fig. 102). This condition was also observed in three intracerebral branches of the posterior cerebral arteries supplying the mesencephalon (Fig. 103).

In two specimens of about two years and eight months of age (B68 and 053) varied types of changes were observed. In one animal, the basilar artery and a perforating branch of the posterior cerebral artery showed intimal thickenings. In the basilar artery it was characterized by fragmentation of

the internal elastic lamina and proliferation of fibrillar material in the subendothelium. The latter contained smooth muscle cells, collagen and elastoid. The collagen predominated in the subintimal area just below the splitting (Fig. 105). The picture in the perforating branch of the posterior cerebral artery was similar except that the proliferation was greater and more fibrous. There was lamellar elastosis of the intracerebral arteries, supplying the mesencephalon, in the second specimen of this age group. There were at least two lamellar bands in each of the three vessels. In a pial branch of the posterior cerebral artery (specimen C53) the above condition was exaggerated by the presence of three to four concentric layers of elastic lamellae. Some smooth muscle-like cells were observed to be entrapped in the layers (Fig. 104).

At four years of age (B95) the collagenization of inner two layers was very well established and was high (Fig. 108). It was clearly evident in medium and small pial arteries. The degree of collagenous fibrillar material in the subendothelial space was greater than in the earlier age groups. A perforating branch of the anterior cerebral artery indicated internal elastic lamina fragmentation with intimal thickening. The proliferation occluded the lumen to a very high degree. The proliferation was recognizable throughout the circumference of

the vessel though accentuated on one side (Fig. 106). There was increased acid mucopolysaccharides associated with the above.

Group 4

The animals included in this group were B118, B119, M52, B43 and B44. The age ranged between above four years to eight years.

The changes observed in this age group represented predominant presence of the collagen in the subendothelial space as a general character. This was accompanied by increased size of the subendothelial space.

The lamellar elaboration of elastic tissue in the intima observed in the preceding group was not observed. Instead fibrosis of the layer as indicated above was a prevalent feature. There was also slight reduction in the depth of the internal elastic lamina. The internal elastic lamina indicated loose undulating outline otherwise observed very tight and close in earlier age groups. The tunica media showed further increase of fibrosis accompanied by fragmentation of the already existing elastic fibers. The elastic fibers in the media of the larger cerebral arteries were generally thicker in comparison to those in the earlier age groups (Fig. 111). In general there was an increased tendency towards increase in acid mucopolysaccharides and high collagenization in all

layers. The mean number of the smooth muscle cell nuclei per unit medial volume in the middle cerebral artery and basilar was 21.93 and 20.69 respectively (Table 3 and Graphs 1 and 2).

At six years and seven months of age (B118) all the above-mentioned changes were observed which differentiated this age group from the preceding. The elastic fibers in the tunica media of the pial branches were relatively increased (Fig. 110). In addition to the above, two small branches of the anterior cerebral artery showed the splitting of the internal elastic laminae. The intimal proliferation occluded the vessels to one-half and one-fourth of their diameters (Fig. 109). Two small pial arteries, one each from the posterior cerebral and middle cerebral artery gave a similar picture but the degree of proliferation was less. An intracerebral branch of the posterior cerebral artery also indicated intimal thickening with internal elastic splitting.

There was a fibrous intimal thickening of the posterior cerebral artery at the age of six years and ten months (B119) which was characterized by increased collagen in the arterial wall and fragmentation of internal elastic lamina (Fig. 112). An intracerebral artery also presented intimal proliferation which was fibromuscular. The proliferation formed by smooth muscle cells was extensive and the internal elastic lamina was fragmented at many sites.

The specimen, M52 (seven years and six months of age), showed intimal proliferation in the branch of the posterior cerebral artery. This proliferation was accompanied with the fragmentation of the internal elastic lamina and few smooth muscle cells entrapped in it. The posterior cerebral artery showed bilateral increase in the subendothelial depth with elastoid and collagenous material which gave a picture of fibrous intimal cushions (Fig. 113). The basilar artery also revealed a similar proliferation but was more focal and had more elastoid material in comparison to the above. There was also relative increase in the acid mucopolysaccharides in the above vessels.

Group 5

The animals included in this age group were 9, M54, M53, B63, 6, M49, M42, B123, and M44 which were eight years and seven months, nine years, nine years and two months, ten years, ten years and three months, eleven years and two months, eleven years and nine months and twelve years of age respectively. They ranged between the age of eight years and twelve years.

The fibrosis of the subendothelial space was still a continuous and progressive feature. This was accompanied by the appearance of cellular constituents in the above sublayer. It was a constant feature in most of the arteries in

the above age group. The serrated appearance of the internal elastic lamina showed signs of straightening in the larger cerebral arteries. There was further increase in the fibrosis of the medial layer and there were signs of reduction in the thickness of this layer, particularly in the pial and intracerebral vessels. This was due to high fibrosis in the deeper portion of the medial layer and a subsequent ill-defined demarcation of the two layers. There was decreased density of smooth muscle cells in the medial wall. The intercellular spaces were occupied by collagen and acid mucopolysaccharides. The elastic fibers in the medial layer were almost granulated, fragmented and straight. The tunica adventitia increased in depth progressively. The mean of the number of smooth muscle cell nuclei per unit medial volume of the middle cerebral artery and basilar artery was 21.93 and 20.69 respectively (Figs. 118 and 138, Table 3 and Graphs 1 and 2).

At the age of eight years and eight months (9) two pial branches of the anterior cerebral arteries showed focal thickenings of subendothelial space with fibrosis. Internal elastic lamina splitting and focal fibrous thickening of the intima was also observed in an intracerebral branch of the middle cerebral artery. Medial defect associated with a site of branching was present in the middle cerebral artery (Fig. 114).

Two specimens representing nine years of age (M54, M53) showed the characteristic features indicated in the preceding paragraphs. There was reduction in thickness of the internal elastic lamina. A pericallosal branch of the anterior cerebral artery showed splitting of the internal elastic lamina. The intracerebral branch going to the orbital cortex indicated intimal thickening with internal elastic splitting. The intimal proliferation occluded about one-fourth of the vessel lumen. The smooth muscle cells were disoriented. A similar picture was observed in the other three intracerebral branches. The proliferation varied in degree with possible fibrosis of the internal elastic lamina. A pial branch of the middle cerebral artery presented fibrous intimal proliferation. There were signs of reduction in the tunica media thickness. This condition was also observed in small and medium cerebral branches of the posterior cerebral artery. The second specimen of this age (M53) showed fibroelastic intimal thickening in a branch of the anterior cerebral artery. The endothelium and internal elastic lamina were intact but the subendothelial space was increased in depth and contained elastoid and collagenous fibrillar material (Fig. 115). The thickening of the subendothelial space was about four to six times greater than the adjoining normal one. General subendothelial layer increase was also observed in all main

cerebral arteries (Fig. 117). An intracerebral branch of the anterior cerebral artery supplying the caudate nucleus showed intimal thickening. The smooth muscle cells occluded the lumen circumferentially (Fig. 116). The internal elastic lamina was fragmented.

The cerebral arteries of the specimen age ten years (6) showed that the vessels were heavily fibrosed in general. This fibrosis encompassed all the layers of different vessels (Figs. 124). The general increase in the subendothelial space was also associated with the fibrosis. The elastic fibers in the tunica media of the pial branches were fragmented and granulated (Fig. 123). A pial branch of the anterior cerebral artery showed intimal thickening. The endothelial layer was intact but the subendothelial space was increased due to the presence of the fibrillar material and smooth muscle-like cells (Figs. 119 and 120). A similar condition was observed in a branch of middle cerebral artery (Figs. 121 and 122). There were increased acid mucopolysaccharides in the tunica media of the cerebral arteries (Fig. 125). The cerebral arteries of ten years and three months of age (M49) indicated that the anterior and middle cerebral arteries had intimal thickening. This was in the form of fibrocellular proliferation. It showed muscle cells oriented longitudinally along with the fibrous proliferation. The other sublayers of tunica intima were intact. A pial branch of the anterior

cerebral artery indicated a change similar to the already mentioned in relation with the anterior and middle cerebral arteries. However, this was very much aggravated and presented greater amount of fibrocellular elements. The cellular elements were large and vacuolated. It occupied about one-fourth of the luminal circumference (Figs. 126-128) The internal elastic lamina was also partially fibrosed. A branch of the anterior cerebral artery showed focal duplication of internal elastic lamina with smooth muscle cells in the thickening (Fig. 129). In two intracerebral branches of the middle cerebral cerebral artery intimal proliferation was observed (Fig. 130). The basilar artery presented intimal proliferation which was fibroelastic in nature (Fig. 131). The cerebral arteries showed increased acid mucopolysaccharides in the tunica media (Fig. 132).

The large cerebral arteries at the age of eleven years and two months (M42) showed high fibrosis of the medial layer in addition to the other category of branches. There was a possible reduction in the thickness of the medial layer and the internal elastic lamina. The small pericallosal branches of the anterior cerebral artery showed intimal proliferation with a disrupted internal elastic lamina. In one case it occluded the lumen of the artery (Fig. 133). There was lamellar fibrosis of the intracerebral branch of the posterior cerebral artery. This was also accompanied by fibrosis of

the medial layer. In addition to the above, a number of pial arteries indicated intimal thickenings of varying degrees. At twelve years of age (M44) the pial branch of the anterior cerebral artery showed intimal thickening (Fig. 134). The constituents of this proliferation were smooth muscle cells and collagen. The internal elastic lamina was interrupted. The elastic fibers in the tunica media of the pial branches were fragmented (Fig. 135). The medial defect at the site of branching was observed in a branch of middle cerebral artery (Figs. 136 and 137).

Group 6

This group contained four specimens, M45, B131, M37 and M36, ranging between the ages of twelve years and sixteen years. The fibrosis of different cerebral arteries and their branches was highest of the series and higher than that of the preceding group. It covered all sizes of arteries. The subendothelial sublayer proliferation and its modified form was increased. Diffuse intimal proliferation was also a feature of this group. The internal elastic lamina decreased in thickness comparatively in contrary to the subendothelium. The undulations of the internal elastic lamina were lacking in many vessels. The elastic fibers in the medial wall were less and fragmented and collagen occupied the areas instead. The same was true about the smooth muscle cells. There was

accompanying increase in the acid mucopolysaccharides. The tunica adventitia increased in thickness particularly in the medium and small pial and intracerebral arteries. The mean of the number of the smooth muscle cell nuclei per unit medial volume of the middle cerebral artery and basilar artery was 18.95 and 18.47 respectively (Figs 144 and 148, Table 1 and Graphs 1 and 2).

The large and medium cerebral arteries at twelve years and one month of age (M45) showed a general increase in subendothelial thickening. The increased thickness of the subendothelial sublayer was filled with collagenous material. In two pial branches of the middle cerebral arteries fibromuscular proliferation of the intimal layer was evident. The internal elastic lamina was very thin and fragmented. There was partial fibrosis of the above layer. There was general fibrosis of the internal elastic lamina of two pial branches of the middle and posterior cerebral arteries. This was accompanied by its fragmentation and intimal proliferation. The proliferation was fibromuscular whereas in the other case collagen predominated. The proliferation was diffuse in both cases. The tunica media showed a high collagen content. In a pial branch along with the comparative reduction of the tunica media and its fibrosis, the internal elastic lamina was broken and fibrosed.

The cerebral arteries of the specimen age thirteen years and one month (M37) indicated that the fibrosis of the different layers of the arterial wall was the main feature accompanied by increased thickness of the intimal layer (Figs. 139 and 140). This increase was mainly due to increase in the thickness of the subendothelial space. This increase was diffuse. The media showed high collagen content with increased acid mucopolysaccharides(Fig. 141). Due to this above increase the smooth muscle cells in the media were low in density per unit area.

At the age of sixteen years in a pial branch of the cerebral artery the internal elastic lamina was fibrosed. The subendothelial space was filled with proteinous mass followed by a two- to three-cell thick layer formed by fibroblasts. The serum-like mass with blood cellular components filled the lumen (Fig. 146). In a pial branch of the posterior communicating artery an eccentric fibrous intimal thickening covering about one-half of the luminal circumference was observed (Fig. 145).

In addition to the above, total fibrosis of the different layers including the large cerebral arteries was the most predominating feature in this age group (Figs. 142 and 147). The elastic fibers in the tunica media of the different cerebral arteries were granulated and fragmented (Fig. 143).

There was an increase of acid mucopolysaccharides in the tunica media of different vessels (Fig. 149).

Age Changes in the Cerebral Arteries of Pig

The study of the age changes in the cerebral arteries of the pig was divided into five age groups as indicated below:

Group I	Birth to six months
Group II	Six months to one year
Group III	One year to four years
Group IV	Four years to eight years
Group V	Eight years to ten years

Group I

There were four specimens included in this age subgroup, 1448B, 592, 5353 and 5250 which were two days, two months and five days, two months and twenty-one days and three months and fifteen days of age respectively.

The changes observed in the arteries of various categories indicated the postnatal developmental changes similar to those observed in dog. These consisted in the organization of different layers increase in thickness of the layers, orientation and maturity of the cells forming different layers and deposition of connective tissue.

At two days of age (1448B) the large cerebral arteries were observed to have basic trilamellar pattern. The tunica

intima was observed to have two clearly marked sublayers. These were endothelial and internal elastic sublayers. The subendothelial space located between the above-mentioned sublayers was not distinct at this age. The endothelium was formed by a continuous band of endothelial cells which were slightly vesiculated. The internal elastic lamina was quite distinct. The tunica media formed the bulk of the vessel and consisted of five to seven smooth muscle cell layersoriented in varied planes. The smooth muscle cell nuclei were vesiculated. Few elastic fibers were dispersed in the tunica media. No collagen fibers were observed.

The tunica adventitia which was thin and loosely spaced around the tunica media. It was sharply separated from the tunica media. The tunica adventitia contained elastic and collagen fibers arranged circularly. There were a few vesiculated smooth muscle cells and fibroblasts. The external lamina was not evident at this age.

The major branches of these arteries indicated a similar picture with a three- to four-cell layer thick media, indistinct subendothelial space and a thin tunica adventitia.

A number of branches given off by the anterior cerebral artery and posterior communicating were observed to show slight duplication with fraying of the internal elastic lamina. The duplications affected less than half or so of the circumference of different vessels (Figs. 150 and 151).

A very small pair of intimal cushions was observed in the posterior communicating artery. The intimal cushions were muscuoelastic with almost complete endothelial lining. The smooth muscle cells in it were oriented circularly mostly in contrast to the underlying media where these were predominantly longitudinal (Fig. 152).

The cerebral arteries between the age of two to three months and fifteen days (592, 5353, 5250) showed elaboration of the subendothelial space giving the tunica intima a three sublayered structure. The internal elastic lamina was weakly stainable in various areas. The tunica media increased in thickness, having six to eight smooth muscle cell layers. The cells were still disoriented at places showing a nesting tendency. The elastic fibers in the tunica media increased slightly. This was particularly true in the pial branches in which the elastic fibers were thicker and convoluted. The tunica adventitia showed no significant change.

Two pial arteries of specimen 5353, supplying the occipital cortex showed a fraying of the internal elastic lamina and an increase of elastic fibers in the tunica media. The posterior communicating artery showed increased collagen in the outer half of the tunica media. An intracortical branch of the above artery showed internal elastic lamina disrupted

with slight intimal thickening (Fig. 153). The mean number of the smooth muscle cell nuclei per unit medial volume of the middle cerebral artery and basilar artery was 48.55 and 50.95 respectively (Table 2 and Graphs 3 and 4).

Group II

This group contained four specimens between six months and eleven months of age. These were 1292, 634, 3923 and 9442. The large cerebral arteries showed a progressive increase in the depth of the intimal layer. The subendothelial space increased in thickness as well as the internal elastic lamina. The tunica media showed compactly layered smooth muscle cells. In the tunica media fifteen to twenty cell layers were seen in this age group. The tunica media showed fine elastic fibers which were scantily distributed. The amount of the collagen in the above layer was comparatively slightly greater than in the preceding age group. The elastic fibers in the pial arteries were thicker than in the large cerebral arteries. The tunica adventitia increased in thickness slightly. The amount of elastic fibers in the above layer was greater in comparison to those in the tunica media. The tunica adventitia was minimal in the intracerebral arteries. The mean number of the smooth muscle cell nuclei per unit medial volume of the middle cerebral artery and basilar artery was 41.85 and 42.07 respectively (Table 2 and Graphs 3 and 4).

The anterior cerebral artery of a ten-month and two-week-old specimen (3923) showed the intimal cushion. The endothelial sublayer was continuous over the intimal cushion and the tunica media showed decreased depth and increased presence of collagen (Fig. 154).

In the eleven-month-old specimen (9442), the anterior cerebral arteries of both sides showed few changes. The left anterior cerebral artery exhibited bilateral intimal thickening which was comprised of the elastoid tissue, smooth muscle cells, acid mucopolysaccharides and extensive deposition of collagen. The intimal proliferation was accompanied by a frayed internal elastic lamina. There was increased collagen and acid mucopolysaccharides deposition in the subintimal area. The right anterior cerebral artery had subendothelial proliferation. The subendothelial space was filled with elastoid, collagenous material and a few mesenchymal cells. The internal elastic lamina, however, showed weak spots indicated by unstained areas in its continuity. The basilar artery also showed intimal thickening which was similar to the condition mentioned above except that all the sublayers of the tunica intima were participating in this formation. The participation of the tunica media in the above proliferation was also indicative. The cell types in the proliferation was vacuolated mesenchymal or smooth muscle-like cells (Fig. 155).

Group III

Eight animals were studied in this group. The age varied between one year to four years. These were 3430, 20215, 4491, 4512, 1790, 3195, 1362 and 4361 which were one year and two months, one year and five months, one year and eleven months, two years, two years and five months, two years and nine months, two years and eleven months and three years and ten months in age respectively.

The changes observed in the age group showed significant degrees of connective tissue proliferation in general. There was progressive increase in thickness of different layers, especially of the subendothelial and tunica media. The subendothelial space indicated the deposition of a slight amount of collagenous material which became prominent from two years of age onwards. The tendency for this substance elaboration was observed progressively from one year onwards becoming distinct at two years of age. The cerebral arteries showed increased acid mucopolysaccharides in their walls, particularly in the intimal layer. The above increase predominated in arteries with associated intimal involvement.

The tunica media started to show signs of progressive increase in the elaboration of collagen. The increase was significant from two years of age onwards. The tendency of this substance elaboration was observed progressively from

one year onwards becoming distinct at the above-mentioned age. The pial and intracerebral arteries showed signs of elastosis and increased collagen in the tunica media earlier and to a greater degree than in the major cerebral arteries and their branches. The mean number of the smooth muscle cell nuclei per unit medial volume of the middle cerebral artery and basilar artery was 29.2 and 28.59 respectively (Table 2 and Graphs 3 and 4).

The anterior cerebral artery of the one-year-and-two-month-old specimen (3430S) showed intimal thickening. This intimal thickening (cushion) was bilateral (Fig. 157). The proliferation was characterized by the presence of acid mucopolysaccharides, collagen, smooth muscle cells and fraying of the internal elastic lamina. Two intracerebral branches of the posterior cerebral artery, supplying the mesencephalic nuclei, showed an internal elastic lamina splitting with elaboration of collagen in the media (Fig. 158). The elastic fibers in the media were relatively thicker than those observed in the main cerebral arteries. The basilar artery showed fibrous intimal thickening. This consisted of an extensive fibrosis with smooth muscle cells oriented circularly. The internal elastic lamina showed slight fraying. The tunica media also indicated increased collagen with focal changes in the organization of the smooth muscle cells, unrelated to any branching area as observed from all other

sections from this area (Fig. 159).

At the age of one year and five months (2021S) a branch of the anterior cerebral artery supplying the callosal area showed subendothelial proliferation. The subendothelial space contained collagen and a few smooth muscle cells which were longitudinally cut and looked vesiculated. The internal elastic lamina was discontinuous at places. At another site in the vicinity the internal elastic lamina was completely dissolved and the tunica media was continuous with the tunica intima. There was fibrosis of the latter layer.

A branch of the middle cerebral artery showed duplication of the internal elastic lamina. A slight intimal thickening of the basilar artery was noted. The thickening was diffuse in extent and gave a varied picture at different levels. This was associated with fragmentation of the internal elastic lamina. The thickening was diffuse and low. It comprised collagen and acid mucopolysaccharides deposition with slight amount of the elastoid material which was present near the internal elastic lamina. A few cells oriented in a variable manner were also observed in the matrix.

The cerebral arteries of the specimens two years and two years and five months of age (4512, 1790) showed an increased but light collagenization of the tunica intima and tunica media. This was observed to increase slowly and

progressively in the preceding specimens. It was a sporadic feature in the earlier age group. The tunica media appeared to show increased tendency of collagenization such that at places nests of collagen could be observed. The tunica media thickened slightly. The tunica adventitia showed well formed elastic fibers, circularly disposed, among the collagen fibers. Elastic fibers were larger and thicker than those in the tunica media. There were no clear cut external elastic lamina. The small pial and intracerebral arteries showed signs of increased fibrosis of the tunica media.

The cerebral arteries at the age of two years and nine months (3195), the only morphological change observed was in the basilar artery which showed focal dissolution or absence of the internal elastic lamina with smooth muscle-like cells in the low intimal proliferation.

The anterior cerebral artery, at the age of two years and eleven months (1362), was noted to have a large intimal thickening occupying about half of its circumference. This proliferation exhibited extensive fibrous tissue, smooth muscle cells and elastoid. The proliferation occupied about four-fifths of the lumen. The internal elastic lamina was broken at two main points. The smooth muscle cells were observed to be located at the junction of the tunica media and tunica intima, indicating the elaboration and shifting from the former. The fibrous tissue was more towards the luminal border of the

thickening than near the junction with the tunica media. The increased fibrous tissue was also slightly greater at the levels where the internal elastic lamina was intact between the broken points. The smooth muscle cells were variably oriented. There was also an increase in acid mucopolysaccharides deposition (Figs.160-162). In a medium-sized cortical branch of the anterior cerebral artery a slight focal fibromuscular intimal thickening was observed. The internal elastic lamina and endothelium were intact.

A major branch of the middle cerebral artery was observed to have an intimal thickening. This thickening was fibromuscular. The section had been obliquely cut and the degree of proliferation was not easy to ascertain but the proliferation was relatively large (Fig. 163). Similarly in an adjoining branch there also was an intimal thickening with internal elastic splitting. The above proliferations were fibromuscular with increased acid mucopolysaccharide deposition.

An intracerebral artery supplying the putamen showed that the internal elastic lamina was duplicated partially with intimal proliferation. The proliferation was fibrous with increased elaboration of the collagen and a few smooth muscle-like cells were oriented circularly and longitudinally. The proliferation covered almost one-half of the circumference of the luminal surface of the vessel. There was

associated fibrosis of the tunica media (Figs. 164 and 165). A branch of the posterior communicating artery showed focal fibrosus intimal thickening (Fig. 166).

The cerebral arteries at three years and nine months of age (4361) showed varied types of intimal thickenings with increased collagen and acid mucopolysaccharides. The changes occurring were characteristic of the whole age group. Two small branches of the anterior cerebral arteries showed intimal proliferation. This was characterized by the intimal thickness caused by the smooth muscle cells and collagen increase. The internal elastic lamina was broken at two or three places. The proliferation occluded the lumen partially Another cortical branch showed similar changes but was fibrosed to a greater degree. In another small branch there was intimal thickening. This was seen to cover the luminal border circumferentially. This was elaboration of collagen and acid mucopolysaccharides in the subendothelial space causing its increased thickness. The internal lamina was observed to be slightly interrupted. The endothelial lining was intact.

The middle cerebral artery and most of its branches near the optic chiasma were involved (Fig. 167). The large middle cerebral artery branches showed slight fibrosis of the intima without the involvement of the internal elastic lamina. The proliferated subendothelial space indicated the presence of collagen, elastoid and smooth

muscle cells oriented in an irregular manner which was in contrast to the situation in the intimal cushions. The endothelial lining was interrupted at places. These cells were relatively enlarged and could be observed in the proliferated matrix. Collagen was predominated. A branch of the middle cerebral artery showed eccentric intimal proliferation whereas in another it was concentric (Figs. 168, 169 and 170). The connective tissue matrix was observed around endothelial cells and smooth muscle cells. The internal elastic lamina was disrupted. The tunica media showed increased collagen.

In two small arteries in addition to the intimal thickenings fibrosis of the internal elastic lamina was observed. Two other branches showed intimal thickening involving complete circumference occluding the lumen to one-half. The proliferation comprised the collagen, smooth muscle cells and elastoid elements. An intracerebral artery supplying the corpus striatum also showed intimal proliferation. This was accompanied by slight duplication of the internal elastic lamina. The thickening was characterized by a collagenous matrix with smooth muscle cells.

The posterior cerebral artery at the level of the mesencephalon showed splitting of the internal elastic lamina with intimal thickening. The tunica media was highly fibrosed.

A branch of the posterior cerebral artery showed focal intimal thickening. There was slight disruption of the internal elastic lamina. The thickening was fibromuscular in nature (Fig. 171). Three cortical branches of the posterior cerebral artery showed intimal proliferation with the fibrosis of the tunica intima and media. The internal elastic lamina was duplicated and fibrosed in two vessels. The intimal proliferation was characterized by the mesenchymal cells entrapped in the collagenous matrix. Similarly, another set of two pial branches of posterior cerebral artery showed circumferential intimal proliferation. The proliferation consisted of three to four muscle cell layers oriented in a variable manner. The thickening was fibrosed. A branch of the posterior cerebral artery in the vicinity of the rostral colliculus showed a very large and crescentric shaped intimal thickening (Figs. 172 and 173). This proliferation was fibromuscular in morphology. The thickening was larger than the thickness of the tunica media. The internal elastic lamina was broken at various points. The constituents of the proliferation were smooth muscle cells and collagen fibers. The smooth muscle cells were oriented concentrically as well as longitudinally. However, in general the orientation of the cells was variable. The collagen and acid mucopolysaccharides predominated.

The branches of basilar artery of this specimen showed varying degree of eccentric intimal proliferations. The nature of the thickenings was fibromuscular accompanied by internal elastic lamina splits. A branch of the basilar artery was observed to show two intimal cushions. One intimal cushion was more fibrous than the other (Figs. 174 and 175). Smooth muscle cell density in the tunica media of the basilar artery was progressively decreased (Fig. 176).

Group IV

This group contained animals of four years to eight years of age comprising ten specimens: 190-10, 3654, 1350, 930-259, 221, 312, 119-259, 26-258, Fletcher and 1816-260.

The general changes occurring with age in this age group showed that there was progressive increase in the general thickness of subendothelial space. There was increased elaboration of the collagen by the smooth muscle cells of the media along with disintegration of the elastic fibers. There was progressive increase in the fibrosis of the tunica media of the arteries in this age group. The mean of the number of the smooth muscle cell nuclei per unit medial volume of the middle cerebral artery and basilar artery was 23.81 and 24.21 respectively (Figs. 185, 186 and 205, Table 2 and Graphs 3 and 4).

The middle cerebral arteries at the age of four years and six months (1910-10), showed fibrous intimal proliferation. This consisted in the predominance of collagen in the intimal thickening. The internal elastic lamina was discontinuous and a few smooth muscle cells were present in the fibrous matrix. A pial branch showed a similar change which indicated the hyperplasia of the subendothelial layer with few mesenchymal cells in the fibrous and elastoid material. The internal elastic lamina was broken at places. There was accompanying increase in the acid mucopolysaccharides contents. Intimal proliferation simulating the above, although enlarged in size, was observed in branches of the posterior communicating artery and middle cerebral artery. These were fibromuscular in nature. The basilar artery had a subendothelial fibrous proliferation located focally. The cerebral arteries at this age showed increased collagen in the subendothelial space and tunica media.

The middle cerebral artery of the pig, five years and two months of age (3654) indicated a fibrous intimal thickening with increased acid mucopolysaccharides in the thickening and tunica media (Fig. 177). In a branch of basilar artery there were three intimal cushions (fibrosed) and in another there was only one (Figs 178 and 179). The basilar artery was observed to have an eccentric intimal thickening (Fig. 180).

A pial branch of the anterior cerebral artery at the age of six years and two months (1350) showed internal elastic lamina splitting with fibrous proliferation. There were two pial branches of the middle cerebral arteries which showed similar formations (Figs. 181 and 182). A number of intimal cushions were observed in the branches of the middle cerebral and basilar arteries. The general picture indicated fibrosis of all categories of arteries (small, medium and large).

At the age of six years and three months (930-259), a branch of the anterior cerebral artery showed focal intimal thickening. There was a break in the internal elastic lamina. The proliferation was not even but was prominent only at one side of the vessel lumen. In a branch of the posterior communicating artery two intimal cushions of unequal size were observed (Figs. 183 and 184). The intimal cushions were fibrosed. One intimal cushion was comparatively larger than the other. The endothelial lining on the cushion was almost complete. A pial branch of the posterior cerebral artery showed eccentric intimal thickening. There was fraying of the elastic lamina and the thickening was fibrosed. In both cases, it was accompanied by an accumulation of acid mucopolysaccharides.

The cerebral arteries of specimen 312, age six years and nine months concurred the earlier observations regarding

the fibrosis of the intimal and medial layers. The posterior communicating artery indicated a focal fibrous proliferation of the intima (Figs. 187 and 188). The internal elastica lamina seemed intact but there was proliferation of the rest of the intimal layer with the result that the fibrosed proliferation with very few smooth muscle cells could be seen. The endothelial cell layer was almost absent. A similar picture was observed in the basilar artery but the proliferated intima was slightly detached from the rest of the wall and hung in the lumen. There was an increase in the acid mucopolysaccharides in the intima and inner part of the tunica media in most of the vessels.

A number of arteries, in the pig 119-259, age seven years, were observed to show intimal thickenings. In a branch of the middle cerebral artery, the intimal thickening was covering about half of the luminal circumference. It occluded about one third of the luminal diameter of the vessel (Fig. 189). The intimal thickening was crescentic in outline and was fibromuscular in nature. The muscular elements were nearer the luminal border than at the base which was almost fibrous. The thickening was equal or slightly greater than the total thickness of the tunica media and tunica adventitia. It was observed that the part of the tunica media just under the intimal thickening had fewer smooth muscle cells than the part of the tunica media

devoid of the intimal thickening. The middle cerebral artery which had been obliquely sectioned showed extensive intimal thickening occluding the luminal diameter (Figs. 190 and 191). The thickening was present almost all around the luminal circumference and was fibromuscular in its constituents. A perforating branch of the middle cerebral artery showed slight intimal thickening which was crescentic in outline (Fig. 192).

Specimen 26-258, age seven years and three months, showed a number of changes in the different cerebral arteries and their branches. The pial branches of the anterior cerebral arteries showed slight intimal thickenings (Figs. 193-195). These thickenings were restricted to the subendothelial sublayer and endothelium because of the intact nature of the internal elastic lamina. The thickening was fibromuscular in nature with increased acid mucopolysaccharides content. The endothelium was interrupted at places. The thickening was caused by proliferation of the fibrous tissue with a few smooth muscle cells entrapped in this matrix. The extent of proliferation was all around the luminal border in one case whereas in another branch it was restricted to about one-fourth of the luminal circumference. A similar condition was also observed in a pial branch of the middle cerebral artery but the thickening was fibrous. The middle cerebral artery branches perforating

the hypothalamic areas around the optic chiasma showed a number of changes (Figs. 196-198). Two small perforating arteries were occluded partially due to intimal proliferation. This was characterized by internal elastic lamina fraying. There was extensive proliferation of fibrous tissue in the matrix of which a few smooth muscle cells oriented in a variable pattern were seen. The proliferation was extensive on one side. The endothelium was totally disrupted. The narrowing of luminal diameter was one-tenth or one-twelfth in one case whereas in the other artery the intimal thickening covered only one-fourth or one-sixth of the lumen. In two other arterioles fibrosis of the internal elastic lamina with slight intimal proliferation and disrupted endothelium was the chief feature. The nature of the proliferation was fibromuscular and circumferential in varying degree. The posterior communicating artery and one of its major branches also showed intimal thickenings which occupied about three-fourths of the vessel's luminal border (Figs. 199 and 200). This was very prominent on two sides in one case whereas eccentric in the other. There was fraying of the internal elastic lamina with discontinuity at various points. The thickening contained collagen, acid mucopolysaccharides and elastoid tissue with smooth muscle cells.

Two branches of the posterior cerebral artery, one medium and one small, indicated intimal thickenings. The smaller vessel showed a duplicated internal elastic lamina with proliferation of fibromuscular tissue occupying half of the luminal circumference. In the medium-sized branch the proliferation was almost all around.

A perforating branch of the basilar artery showed a similar eccentric thickening extending to three-fourths of its luminal border. There was fibrosis of internal elastic lamina and medial layer as observed in most of the arteries described above. The basilar branches given near the junction of medulla oblongata and spinal cord indicated intimal proliferation of varied types and extent in nine or ten arteries. The intimal thickenings were eccentric or focal or concentric in nature varying from one cell thick to almost equal to the medial layer thickness of the vessel affected (Figs. 201-204). The thickenings were divided into three categories based upon the degree of involvement. In the first category the intimal thickening consisted of a single smooth muscle cell layer in most of the area. The amount of collagen was minimal. This was observed in three arteries. Under the second category two vessels were included in which there was duplication of the fibrosed internal elastic layer with one to three cells layer thick intimal proliferation.

The main constituents of the thickenings were smooth muscle cells. The third category included the vessels which had a frayed and fibrosed internal elastic lamina with varied number of smooth muscle layer and extensive fibrous matrix. The collagen and acid mucopolysaccharides predominated. The thickenings were concentric and occluded the lumen varying between one-half to one-fourth approximately.

Group V

This age group included four specimens, D1287-260, 9090, 254 and Merrick, which were eight years and three months, nine years and one month, nine years and three months and ten years of age respectively.

Two small branches of the anterior cerebral artery, in the pig D1287-260, age eight years and three months, showed slight fibromuscular intimal thickenings (Fig. 206). Similar but enlarged intimal thickenings were observed in a number of branches of the middle cerebral artery. These thickenings were focal or concentric in outline. In a cortical branch of the above artery a concentric intimal thickening was observed (Figs. 207 and 208). It covered the whole of the luminal border of the artery. The internal elastic lamina was interrupted at a number of places. The height of the thickening was about half the total thickness of the rest of the vascular wall. Two main branches of the middle cerebral

artery, at the level of the optic chiasma, also had intimal thickenings which were comparatively very extensive (Fig. 209). The thickened intima occluded about half of the arterial lumen. The thickening was about twice as thick as the underlying tunica media and tunica adventitia. A perforating branch supplying the hypothalamic floor had a concentric intimal thickening (Fig. 210). This thickening was almost equal to the thickness of the arterial wall and occluded about half of the arterial diameter. A small branch of the middle cerebral artery also showed a small concentric intimal thickening (Fig. 211) and in another a focal intimal thickening was present (Fig. 212).

In the specimen, age nine years and one month (9090), a cortical branch of the anterior cerebral artery had an intimal thickening which was present along the luminal border. The intimal thickening was accentuated at one segment whereas low in the rest. The thickening was fibrous with a few smooth muscle-like cells as its constituents. The middle cerebral artery showed a focal intimal thickening protruding in its lumen. The thickening was fibromuscular and was about half the thickness of the vessel wall. Two cortical branches of the above artery also showed low focal intimal thickenings.

In the specimen 254 age nine years and three months, the anterior cerebral artery showed focal fibromuscular intimal

thickening. A small branch of the above artery showed a concentric thickening occluding the vessel lumen. In a branch of the posterior communicating artery, the intimal thickening was located in a manner such that it divided the lumen into almost two halves (Figs. 213 and 214). The smooth muscle cells were present in the collagenous matrix of the intimal thickening. The internal elastic lamina was interrupted at places. A focal intimal thickening was observed in another branch of the posterior communicating artery (Fig. 215). Two branches of the basilar artery were also observed to have low intimal thickenings (Fig. 216).

In the pig Merrick age ten years, there was significant intimal proliferation in three branches of the anterior cerebral artery. The main arterial branch showed circumferential fibrosed intimal proliferation. This was greater in thickness on one side. There were smooth muscle cells entrapped in the above thickening. The other pial branches had focal intimal thickening of varying degrees (Fig. 218). Similarly, branches of the posterior communicating artery and basilar artery had low intimal thickenings which were fibrosed.

The mean of the number of the smooth muscle cell nuclei per unit medial volume of the middle cerebral artery and basilar artery in the above age group, was 17.70 and 19.82 respectively (Fig. 219).

Lipofucsin Pigment in the Brain of the Dog

The segment of the present study pertaining to the age pigment in the different brain areas of the dog and pig was extended to include fifteen areas in the dog and twelve areas in the case of the pig. Five nuclear areas of the brain stem of the dog were included to estimate the quantitative distribution of the lipofuscin pigment per unit area, percent of the neurons pigmented and percent of its intraneuronal distribution with aging.

Nucleus olivaris inferioris

The lipofuscin pigment granules were observed to be present in the inferior olivary nucleus at the age of eleven months. It was observed that there were present in the form of loose deposition in the perinuclear areas of the neurons. The percentage of the neurons with the lipofuscin pigment was very low but increased from one year of age onwards. The pattern of the distribution of the pigment was mostly polar and perinuclear. The granules were compact around the nucleus or near the axonal hillock. The percentage of the neurons with the pigment increased to about 35 percent at one year and five months. The mean percentage of the neurons with pigment was 49.11 in the third age group.

In the fourth group which contained animals ranging between four years and eight years of age, showed that the mean percent of the neurons with lipofuscin pigment increased steadily, 81.57. The magnitude of the pigment also increased significantly.

In the fifth and sixth age group, the changes in the percentage of the lipofuscin laden neurons increased to their highest percentage in the latter age group in which about 92 percent of the cells were pigmented. The relative increase in the percentage volume of intracellular lipofuscin to the cell volume increased progressively reaching maximum in the sixth age group (Figs. 220-223, Tables 5 and 7 and Graphs 5, 10, 15, 20, 21 and 22).

Nucleus Hypoglossus or Nucleus motorius n. hypoglossi

The lipofuscin in the neurons was first observed at the age of eleven months where it was very loosely distributed in the form of fine granules but became loosely focal by the four years of age. About 56 percent of the neurons were pigmented at four years of age. The pattern of the accumulation was bipolar or polar. The pigmentation increased in the fourth age group in which the pigment was moderately distributed. This increase was not only associated with the amount of the lipofuscin but also in the number of the neurons involved. The pigmentation again

increased in the fifth and sixth group whereby almost 75-87 percent of the cells were having lipofuscin pigmentation. The amount of the intracellular pigmentation increased steadily with increasing age so that neurons with one-fourth to one-fifth of their volume filled with pigment were frequently observed in the last two age groups (Figs. 224-226, Tables 5 and 8 and Graphs 6, 11, 16, 20, 21 and 22).

Dorsal motor nucleus of vagus nerve or nucleus parasympatheticus n. vagi

The pigmentation appeared very late in this nucleus. There were signs of loose granular arrangement of the lipofuscin was observed at the age of four years. The rate of the pigmentation seems to increase with the age in the fourth group where focal deposition in the form of polar and perinuclear accumulation was observed in 36 percent of neurons. The other neurons showed the loose granular deposition. The pigmentation in the fifth group, in the above nucleus was heavy. The focal accumulation of the granules was signigicantly heavy in most of the neurons. At places the perinuclear was also observed.

In the sixth age group the increase in the deposition was very high such that by the end of this age group the neurons were laden with the pigment. There was heavy pig-

mentation which was almost completely masking the nucleus and cytoplasm whereas in others the granulation covered one-half or more of the cytoplasmic volume of the neurons. About 79 percent of the neurons were pigmented by the sixteenth year of age (Figs. 227-229, Tables 5 and 9 and Graphs 7, 12, 17, 20, 21 and 22).

Nucleus cuneatus accessories or nucleus cuneatus lateralis

The accumulation of the pigment in the cell bodies of the above nucleus was observed in the form of loosely packed polar formations. The pigment appeared as a loose granular formed at two years and seventeen days of age beyond which it took the loose focal form. The pigment was small in amount at this stage but increased in amount and frequency at four years of age.

In the fourth age group the accumulation increased further in which about 70-80 percent of the cell bodies indicated the presence of the above pigment, in the polar or bipolar forms. This increasing trend was also evident in the fifth and sixth age groups where the pigmentation occupied more and more cytoplasmic volume of the neurons as well as the number of the neurons having the pigment increased. The sixth group specimens indicated that about 79 to 92 percent of the cells were affected with the pigment and cell bodies of the above nuclei contained the

pigment almost throughout their cytoplasmic volume in many cases (Figs. 230-232 and Table 7).

Nuclei vestibulares

The first signs of the appearance of the pigment were observed at one year of age when the pigment granules were present in the form of disseminated sandy granules, forming loose polar and bipolar masses.

The rate of the accumulation increased in the third age group appreciably. In this age group the depostion was axonal and bipolar sometimes filling one-sixth or one-tenth of the cytoplasmic volume of the neurons. About 36 percent of the neurons were pigmented.

The age group four revealed further increase whereby about one fourth or one sixth of the cytoplasmic volume of the neurons were filled with the pigment in some cases. About 70 percent of the neurons were pigmented in this age group.

The observations in the group five and six indicated that the increased deposition was perinuclear, bipolar and polar pattern of distribution. The frequency of neurons involved was considerably high, about 90 percent of the neuronal population. The cytoplasmic volume of many neurons was filled with pigment, almost completely in some cases (Figs. 233-235, Tables 5 and 10 and Graphs 8, 13, 18, 20, 21 and 22).

Nuclei cochleares

The nuclei showed that the disseminated granular distribution was present at the age of one year and seven months, where it was scantily distributed in the form of few granules in very small percentage of cells. The pigment increased in its distribution beyond one year and seven months of age and occupied the perinuclear location in the cytoplasm. About 25 percent of the neurons were pigmented in the third age group. The deposition became focal in the form of loose foci. This was appreciable by the four years of age in which about 58 percent of the neurons had pigmentation of varying amount.

The pigmentation increased in frequency and amount in the fourth age group. The deposition was focal but still discrete fine granules could be seen in the neuronal cytoplasm. The pattern of distribution was perinuclear and sometimes polar.

By the end of the fifth age group and in the sixth age group the accumulation increased considerably to appear as polar and perinuclear. About 82 percent of the cells were having the pigment by sixteen years of age (Figs. 236-238, Tables 5 and 11 and Graphs 9, 14, 19, 20, 21 and 22).

Cerebellar nuclei

The dentate and fastigial nuclei were considered under the above. The pigmentation was loose and dispersed in the cytoplasm of the neurons of both nuclei in the third group.

The pigment showed the tendency of focal accumulation by four years of age but was still loosely packed. The granules were perinuclear and polar in location. The above was true for the dentate nucleus. The pigment increase in the fastigial nucleus was very slow and was loose granular even by the middle of the fourth age group, whereas the pigmentation in the dentate was comparatively greater and focal.

The pigmentation continued to increase slightly with age in the fifth age group whereas in the sixth age group there seened to be a rapid increase both in amount and frequency of neurons with the pigment. This was very distinct in both nuclei at the age of sixteen years (Figs. 239-242 and Table 5).

Cerebellar cortex or cortex cerebelli

No substantial intraneuronal pigmentation was observed in the Purkinje cells of the cerebellum of the dog at any age group; however, pigment accumulations was discernible

in areas surrounding the Purkinje cells beyond four years of age. This accumulation increased steadily with age.

Red nucleus or nucleus rubrum

The presence of the lipofuscin pigment in the above nucleus was present in the second age group (11 months of age). This was present in the form of loose focal (perinuclear and axonal) accumulation. The magnitude of the deposition was small.

The increase in the lipofuscin pigment was observed in the third age group. The number of the neurons with the above pigment also increased. The clumping of the pigment was distinct and compact by four years of age though in some neurons disseminated granules were also present. About fifty-five percent of the neurons were pigmented by four years of age.

The accumulation increased from the above age group to the fourth age group significantly. It was considerably increased in a greater number of the cells of this nucleus, about seventy-five percent of the neuronal population. The pigment was showing tendency to form perinuclear and axonal deposition. The clumping of the pigment was loose particularly in the perinuclear areas.

The pigment occupied axonal, perinuclear and bipolar sites which in some cases masked the nucleus. The

pigmentation was considerably heavy and occurred in about ninety to ninety-five percent of the neurons in the sixth age group (Figs. 243-245 and Table 5).

Oculomotor nucleus or nucleus oculomotorius

The pigment was observed at about two years of age in the form of loosely disseminated granules. It appeared to occur in the perinuclear and polar areas of the neurons in the third age group speciment. The pattern of this distribution continued in this age group but it was observed that the pigmented granules were always loosely distributed in the neurons of above age group except in the last specimen (B95) of the third age group in which focal accumulation could be appreciated in some cells.

The progressive increase was observed in the fifth age group, which indicated the location of the pigment was axonal or perinuclear but rarely bipolar. The cells were heavily pigmented by twelve years of age. The pigmentation revealed dense focal accumulations in about 60 to 70 percent of the neurons. This progression continued in the sixth age group where the pigmentation was very heavy and almost all the cells showed varying degree of accumulation; however, it was heavy in most of the cells. The pigmentation was axonal in most of the cases whereas in addition to that granules were also distributed in the

cytoplasm at various locations giving it a perinuclear or bipolar appearance (Figs. 241-248 and Table 7).

Thalamic area

Under this, the posterio-ventral, ventro-medial, and posteriolateral thalamic areas were considered collectively. The accumulation was observed to be slight and the number of the neurons having it were few in number at the age of one year and seven months. The accumulation axonal or perinuclear was very light and loosely packed.

The accumulation of the pigment increased very slowly and showed significant increase in the third age group where the frequency of the neurons involved increased. The location of the pigment was generally axonal or perinuclear but never bipolar. About thirty-five percent of the neurons were pigmented in the above age group.

The pigmentation of the thalamic nuclei in the fourth age group increased in respect to the neuronal involvement and amount of deposition. This increase was observed to be about forty to fifty percent of the neurons.

The fifth age group showed increased trend for the neuronal percentage rather than any significant increase in the magnitude of the pigment deposition. The latter was observed to be the case in the sixth age group where about seventy to eighty percent of the neurons were having

pigment. The deposition was increased but was still polar and perinuclear (Figs. 249, 250 and Table 5).

Hippocampal gyrus or gyrus hippocampus

The pigmentation of the hippocampal neurons was observed to occur in the form of a few disseminated granules, in very few numbers and very sporadic in the third age group (four years of age).

The neurons in the fourth age group (six years and seven months onwards) indicated slight increase in the accumulation in relatively greater numbers. The progression of the deposition and cell involvement was very slow and still was loose granular in nature. About thirty to forty percent of the neurons were observed to contain loosely focal pigmentation by the age of seven years and six months.

The pigment became slightly focal in small masses in the perinuclear and axonal areas of a greater number of neurons in the fifth age group. About seventy or eighty percent of the neurons were pigmented by twelve years of age. The amount of the pigment increased from the preceding age group.

The pigmentation in the hippocampal gyrus was widespread in almost ninety percent of the neurons by the sixth age group. The amount of the deposition was variable such

that in addition to the axonal and perinuclear compact accumulation there will still some neurons which indicated loose spread out of pigment granules in the cytoplasm (Figs. 251 and 252 and Table 5).

Cortex cerebri (frontal)

The localization of the lipofuscin pigment was observed in the area precentralis giganto-pyramidalis (Motor cortex corresponding to the area four of human cerebral cortex).

The first evidence about the appearance of the pigment was observed in the giant pyramidal cells of the fifth layer of the above cortex. The pigment was present in the form of fine granular material spread in the cell at the age of ten months but became localized in the form of small focal deposition by the end of the second age group by the age of one year. This accumulation was scanty earlier but it increased to appear as perinuclear and polar by one year of age. The above increase indicated that the number of the Betz cells having the pigment increased similarly.

The presence of the lipofuscin in the pyramidal neurons in the third cortical layer of above area was evident by the age of two years and seven months. This again was diffuse and non-focal. The Betz cells by this age showed

further clumping of the pigment and at places were seen to mask the nucleus. The common pattern was perinuclear and axonal.

At the age of four years, increased pigmentation of the Betz cells and pyramidal cells of third layers was evident. The latter showed clumpings of the pigment in contrast to the earlier age period.

The changes in the lipofuscin deposition in the fourth age group (four years to eight years) indicated that it was heavy in the Betz cells; in some cases about one-third or one-half of the neuronal cytoplasmic volume was occupied by the pigment. The accumulation became denser with reference to the accumulation in the pyramidal cells of the third layer. In this age period, it was observed that the pigmentation was heavier than the preceding age group but was comparatively lesser than in the Betz cells. The pattern of its distribution was polar (axonal) and perinuclear.

The Betz cells in the fifth age group indicated further increase in the magnitude of the deposition as well as increase in the number of cells involved. At places the accumulation was occupying about one-half to three-fourths of the cell cytoplasm. An increasing trend in the deposition and cell involvement with pigmentation was observed in the pyramidal cells of the third layer also.

In the sixth age group it was observed that almost all the Betz cells in the fifth cortical layer were very heavily pigmented whereas the pigmentation in the third layer pyramidal cells was lesser in magnitude as well as the number of the neurons involved, in comparison to Betz cells of the fifth layer (Fig. 253 and Table 5).

Nucleus caudatus

The presence of the pigment was observed to be present in the form of small polar and perinuclear loose clumps by the age of four years. The slight granular deposition was, however, observed to be present after three years of age. This was only present in some neurons of the caudate nucleus, about twenty-five to thirty percent of the neurons.

The pigmentation increased from the third group to the fourth group steadily so that more neurons were having the pigment in their cytoplasm but the accumulation was not high and was in loose clumps.

The changes in the distribution of the lipofuscin pigment in the fifth age group indicated that there was increase in the amount of the pigment as well as in the number of the neurons having it, about fifty-five to sixty-five percent of the neurons. This was significantly high when compared to the preceding age group but was low when

compared with the putamen and globus pallidus. The basic pattern of loose focal distribution, however, did not change significantly.

By the age of sixteen years, the increase in the number of neurons with the pigment along with the slight increase in the amount such that at places focal and perinuclear distribution could be observed. About eighty to ninety percent of the neurons were observed to have the pigment by this age (Table 5).

Putamen and globus pallidus

The observations on the above set of nuclear areas indicated that the deposition was present at the age of two years and seven months. The distribution of the pigment was small loosely packed polar in both of the areas. Accumulation was better in globus pallidus than in the putamen, which became significant only by four year years of age. At this age, however, again the pigmentation was higher in the globus pallidus than the putamen. This trend continued progressively up to the fourth age group.

The increase in the pigmentation and the number of neuronal involvement was more in globus pallidus designating that the rate of pigment deposition was at a higher rate in the above area. Abour forty to fifty percent of the neurons were pigmented by twelve years of age in the

globus pallidus. The pigmentation became more focal such that one can find polar and perinuclear accumulation in most of the nurons. It was observed that in some neurons of globus pallidus one-fifth to one-fourth of the cytoplasmic volume was occupied by the lipofuscin.

The observations in the sixth age group, on the lipofuscin in the above-mentioned nuclei revealed that by sixteen years of age about seventy to eighty percent of the neurons in the globus pallidus were loaded with pigmentation, whereas about fotry to fifty percent of the neurons represented the above condition in the putamen. The pigment was more coherent and focal in the globus pallidus than in the putamen in which loosely placed granules could be observed still (Table 5).

Lipofuscin Pigment in the Brain of the Pig

Nucleus olivaris inferior

The above nucleus in the pig was observed to have the pigment at the age of two years in the form of loose focal accumulation. It was also present sporadic and in granular form in the pig as young as one year and two months and was considered as trace.

The pigment was in the polar and perinuclear form and increased with age. The rate of accumulation and amount of

pigmentation at different age groups indicated that this nuclear area had higher tendency to the accumulation. The neurons at the age of three years and nine months contained loose focal accumulation in the perinuclear and polar areas. This was observed to be present in about forty to fifty percent of the cell population of the above nucleus.

The magnitude of the intracellular pigmentation and the number of the neurons with pigmentation increased so that by eight years and ten years of age about ninety to ninety-five percent of the neurons were pigmented heavily. The pattern of distribution remained polar and perinuclear (Figs. 254 and 255 and Table 6).

Nucleus hypoglossus or nucleus motorius n. hypoglossi

The pigment in the hypoglossal nucleus was recognized in loose granular form at the age of one year and five months. This was distributed in a few cells. The pigment was loosely focal at the age of two year and occupied polar position in the neurons. The observations indicated that with age there was increased frequency of the neuronal involvement. About sixty to seventy percent of the neurons contained pigment in the form of polar (axonal) and bipolar and perinuclear formations by the age of three years and nine months. The pigmentation was focal and compact. The

hypoglossal nucleus at the age of eight years and ten years of age showed that the percentage of neurons with pigment increased considerably to range between eighty-five and ninety-five percent. The pigment occupied about one-third or one-fourth of the cytoplasmic volume in axonal and bipolar formations (Figs. 256 and 257 and Table 6).

Dorsal motor nucleus of vagus or nucleus parasympatheticus n. vagi

The lipofuscin pigment in the above nucleus appeared as disseminated granular form at the age of two years and five months. The pigment was loosely focal at the age of three years and nine months. The pattern of distribution was perinuclear and polar in most of the neurons. About thirty-five to forty percent were pigmented in the above specimen.

The pigmentation increased with age progressively so that fifty to sixty percent of the neurons were pigmented at seven years and three months. The amount of the pigment increased but some loosely arranged granules could still be seen in some of the neurons. The percentage of neurons pigmented increased to seventy or eighty at the age of eight years and ten months. The pigmentation was perinuclear and polar in distribution (Figs. 258 and 259 and Table 6).

Nucleus cuneatus accessorius or nucleus cuneatus lateralis

The pigmentation was observed to be present in traces at the age of two years and nine months. The distribution of the pigment was sporadic and in the form of loosely arranged granules. The pigment increased in the third and fourth group occurring as loose focal formation at the perinuclear or polar part of the neurons. The pigment increased with age but was comparatively low when compared with that of the dog. The pigment was present in about seventy to eighty percent of the neurons by the age of eight years and ten years but still its loose focal formation could be seen in some of the neurons (Table 6).

Nuclei vestibulares

The pigment in the above nuclei was first observed in sporadic form at the age of one year and five months. The granules were loosely arranged in the perinuclear areas of the neurons. The granules became focally accumulated by the age of two years and showed perinuclear and axonal forms. By the age of two years and eleven months the focal accumulation was very conspicuous in many neurons. About thirty to forty percent of the neurons were pigmented at the above age group.

The pigment was present in substantial amounts at the age of three years and nine months at which age about forty-five to fifty-five percent of the neurons were indicating polar and bipolar distribution of the pigment. It was also perinuclear in some cases.

The neurons were heavily laden with the pigment by the age of seven years and three months. The pigmented neurons in the above nucleus ranged between seventy-five to eighty-five percent by ten years of age (Fig. 260 and Table 6).

Nuclei cochleares

The pigmentation in the above nuclei was not evident till the age of two years and five months. The pigmentation was slight and was present in very low percentage of cells by two years and eleven months but became significant by the age of three years and nine months. The pigmentation was crescentic perinuclear but loosely focal in distribution characteristically. The pigmentation increased with advancing age retaining its characteristic manner of distribution. The pigment did not increase substantially in its amount at a rate comparable to other nuclear areas like vagal, inferior olivary, hypoglossal, vestibular, oculomotor and red nucleus, etc. About seventy-five to eighty percent of the cells were pigmented by ten years of age (Fig. 261 and Table 6).

Cortex cerebelli

The pigment was contained in the Purkinje cells of the cerebellar cortex at two years of age. This was observed to be in the form of small granular accumulation in the polar part of the above neurons. The pigment was present in very few neurons. The number of the pigment-containing neurons increased steadily so that by the end of the third age group (three years and nine months) about forty to forty-five percent of the neurons were pigmented. The rate of increase of pigment was, however, slower with advancing age which was evident in the older age groups in which the pigment though increased was very low when compared with neurons of other nuclear areas. About eighty to ninety percent of the neurons were pigmented by the age of ten years. The pattern of distribution was polar and, in some cases, perinuclear (Figs. 262 and 263 and Table 6).

Nucleus rubrum or red nucleus

The pigment in the nucleus rubrum was present in traces by the age of two years. The granules were distributed loosely in the perinuclear areas. The distribution was perinuclear and axonal by the age of two years and eleven months. It involved about forty to fifty percent of the neurons. The pigmentation was heavy in the fourth age group where most of the neurons contained bipolar,

perinuclear and axonal accumulation of the pigment. About sixty-five to seventy percent of the cells were involved at the age of seven years and three months. The neurons were heavily pigmented. Many neurons with disseminated pigment were also present.

At the age of ten years the nucleus showed that almost all the neurons were heavily loaded with the pigment; the pattern was mostly bipolar or polar and sometimes perinuclear (Fig. 264 and Table 6).

Nucleus oculomotorius

The localization of the pigment in the oculomotor nucleus revealed that the pigment was present in the form of disseminated granules at the age of two years of age. The pigment took the form of loose focal accumulation at the age of two years and eleven months. The pattern of accumulation was in axonal and perinuclear form.

The rate of increase was moderately high so that the subject in the fourth age group showed high axonal and perinuclear distribution of the pigment in most of the cells. The pigment increased further with age in the fifth age group but there were very few neurons which still showed diffuse accumulations (Table 6).

Thalamus

The pigment in the thalamic areas of the pig was not evident until the age of two years and nine months; however, the pigment granules could be seen in the two years and five months old specimen but the distribution was in the form of fine granulation in very few neurons. The pigment increased in the third age period to appear in the form of small accumulations in the perinuclear and polar locations in the neurons. It was present in about fifty to sixty percent of the neurons at the age of three years and nine months. The pigmentation increased with age in the subsequent age groups to indicate that about seventy-five to eighty-five percent of the neurons were pigmented by the end of the fourth age group (at the age of eight years of age). The amount of pigment increased with age but the increase was comparatively lesser than most of the nuclear areas being studied concurrently, with an exception to the cochlear nuclei and to some degree comparable with the cerebellar cortex (Purkinje cells). The pigment was present in almost all neurons by the age of ten years (Fig. 265 and Table 6).

Hippocampal gyrus or gyrus hippocampus

The pigment was present in the fine granular form at the age of four years and six months. The pigment was

distributed in about forty to forty-five percent of the neurons and was low in fluorescence. The pigment became loosely focal at the polar and perinuclear form by the age of seven years and three months. The amount of the pigment also increased simultaneously. It was present in about sixty to seventy percent of the neurons.

The pigment was still in the loose focal accumulations at the age of ten years. About ninety to ninety-five percent of the cells were observed to have it in the perinuclear, polar and axonal areas of the neurons (Fig. 266 and Table 6).

Cortex cerebri

The pigment in the large pyramidal cells at the fifth cortical layer of the precentral cortex of the pig was seen in the form of the loose focal granulation at the age of one year and eleven months of age. The pigment became focal and compact by the age of two years and nine months. The pattern of the distribution of the pigment was axonal and perinuclear.

The pigment increased in amount and more neurons were involved with increasing age; however, the rate of increase and amount of intraneuronal pigment was comparatively lesser than in the case of the dog. In the fourth and fifth group

many of the giant pyramidal cells of the fifth layer of the above cortex showed the pigmentation in moderate amounts, distributed axonal or perinuclear (Table 6).

DISCUSSION

Blood Supply to the Brain of the Dog and the Pig

From the results based on the dissected specimens and injected transparent sections of the brains of dogs and pigs it was observed that the blood supply to the brain of both species differed due to some modifications undergone, discussed in subsequent paragraphs.

The blood supply to the brain of the dog has been investigated by Tandler (1899), Hofmann (1900), Bruckner (1909), Jenke (1919), de Vriese (1905), Zietzschmann (1943), Jewell (1952), de la Torre (1959), de la Torre and Netsky (1960), de la Torre, et al. (1962) and Luginbuhl (1966). The blood supply to the brain has also been mentioned in different textbooks on veterinary anatomy relative to the dog, Montane, et al. (1953, 1964), Bradley and Grahame (1959), Miller (1948) and Miller, et al. (1964). Mention about the above has also been made in textbooks like Chaveau and Arloing (1905), Ellenberger and Baum (1943), Sisson and Grossman (1953), Bruni and Zimmerl (1951), Koch (1965), Schwarze and Schroder (1965) and Dobberstein and Hoffmann (1964).

The blood supply to the brain of the dog was observed to be supplied by the arteria carotis interna as well as

from the arteria vertebralis. The arteria carotis interna received anastomosing branches from the arteria maxillaris interna (arteria maxillaris, NAV, 1968). The above artery gave off a branch termed as the arteria meningea media from which a branch, ramus anastomoticus was given which coursed in the cavernous sinus and joined the arteria anastomotica, the latter being a branch of the arteria meningea rostralis (branch of the arteria ophthalamica externa). The arteria anastomotica then joined with the arteria carotis interna. The above formation has been recognized by a number of workers cited above but different terminology was used for the contributing branches. NAV (1968) termed the ramus anastomoticus as the ramus anastomoticus cum arteria carotide interna, a branch of the arteria meningea media and arteria anastomotica as the ramus anastomoticus cum arteria carotide interna, a branch of the arteria meningea rostralis (branch of arteria ophthalamica externa). The latter ramus as a homologue of the primitive arteria stapedia was suggested by Daniel, et al. (1953) but de la Toore and Netsky (1960) thought that the proximal part of the above ramus was related to the primitive arteria maxillaris and only the origin of its distal part was homologous to vividian and stapedial systems. Similarily, the ramus anastomoticus cum arteria carotide interna (branch of the arteria meningea media) was homologous with the proximal part of the primitive arteria maxillaris.

The above formation was recognized as a rete mirabile by Tandler (1899) and Ask-Upmark (1935) and a rudimentary carotid rete by Daniel, et al. (1953) in the dog. A similar but complex condition has been observed in the pig by Tandler (1899), Hofmann (1900), Tandler (1906), Diwo and Roth (1913), Jenke (1919), and Daniel, et al. (1953), Becker (1960), Nickle and Schwarz (1963) and Flechsig and Zintzsch (1969). The presence of the above rete in the pig has been mentioned by Chauveau and Arloing (1905), Ellenberger and Baum (1943), Sisson and Grossman (1953), Bruni and Zimmerl (1951), Montane, et al. (1964), Koch (1965) and Dobberstein and Hoffmann (1964).

The rete mirabile epidurale rostrale in the pig was formed by the ramus anastomoticus, a branch of the arteria meningea media and the arteria anastomotica, a branch of the arteria meningea rostralis (branch of the arteria ophthalamica externa), contributed on one hand whereas the arteria carotis interna on the other. The above rete was recognized as the carotid rete or rete mirabile by earlier workers whereas Becker (1960) termed it as the rete mirabile epidurale. NAV (1968), however, termed it as the rete mirabile epidurale rostrale to differentiate it from a caudal rete. The ramus anastomoticus was termed by the NAV (1968) as the ramus ad rete mirabile epidurale rostrale, a branch of the arteria meningea media and arteria anastomotica as the

ramus ad rete mirabile epidurale rostrale, a branch of the arteria meningea rostralis, which may be accepted in view of the comparative anatomy and homology.

Taking into consideration the simple anastomosis and a complex rete formation in the dog and pig respectively, the only difference other than the sites of origin of the contributory branches from the arteria maxillaris interna (arteria maxillaris, NAV, 1968) was the presence of a complex network formed by the interanastomosing branches from the above vessels and the arteria carotis interna in the pig in comparison to the dog. Studies of Tandler (1899, 1906), Diwo and Roth (1913), Jenke (1919), Daniel, et al. (1953), and Becker (1960) indicated that the arteria carotis interna in the pig underwent atrophic changes during its late prenatal and early postnatal stages. The studies of the above workers in the pig and Balankura (1954) in the sheep, indicated that the formation of the rete was initiated in response to the progressive occlusion of the arteria carotis interna in the above species. Muller (1904) has indicated that the reticulated networks in the course of the blood vessels was due to haemodynamic responses. It seemed that the occlusion of the above artery led to a search for a nearer and adequate source of blood supply to the developing brain. In the view of the present worker, it may be presumed that the formation of the rete may be

due to a number of factors; first, the tendency of the arteria carotis interna to regress; second, simultaneous increased demand of blood supply to the developing brain; and third, search for an alternate blood source to supplement during the latter parts of the life.

The contribution by the arteria maxillaris through the anastomotic rami has been regarded to be the homologous of the persistent primitive arteria maxillaris, arteria vividan in the earlier stages of the development in the dog. These regions were supplied by arteria maxillaris during latter stages but the above connections remained patent in comparison to the condition in man. As already indicated, the anastomotic rami were considered by Daniel, et al. (1953) as persisting remnants of the mandibular branch of the arteria stapedia in domestic animals. Similar homologues of the anastomotic rami may be true in the pig also.

The presence of the rete in cavernous sinus has been assigned a number of functions in addition to be just an alternate and additional source of blood for the brain. Daniel, et al. (1953) regarded that the carotid rete was of some haemodynamic significance in relation to the cerebral circulation. They mentioned that its presence in the venous lake was a feature of interest which might have physiological significance. Ask-Upmark (1935) regarded that

the role of the rete mirabile was probably related with the hydrodynamic effect which could keep the pressure in the cerebral arteries at a convenient and fairly constant level. Earlier, Willis (1664) asserted that the importance of the rete was to regulate against too sudden changes of the blood supply to the brain. Abdelbaki (1964) regarded that the direct contact of the wall of the retial arteries and venous blood in the cavernous sinus had some other functional significance. He believed that the cerebral rete mirabile represented a most efficient heat exchange system. Many workers have found that wherever arteries and veins were in close proximity, the venous blood returning from the surface of the body had a cooling effect on the arterial blood flowing towards the periphery. Hovarth, et al. (1950) believed that cooling of the arterial blood could be due to heat transfer to the venous blood coursing in the nearby arterial vessels.

Recent studies by Magilton and Swift (1967, 1968) indicated that there were two heat exchange areas in the dog, one in the nose and other in the cavernous sinus which played to modify the brain temperature. Similar studies carried on by Baker and Hayward (1967, 1968) on cat and sheep brought conclusions supporting the former workers. They observed that the heat exchange between the central arterial blood in the carotid rete and the cranial venous

blood in the cavernous sinus was a factor regulating the cerebral blood and brain temperature.

It seems that the presence of the interanastomosing small retial branches and their obvious intimate contact with the venous blood in the cavernous sinus exposes the formers to offer more surface area for the temperature regulation and as well as formed a flow regulatory mechanism.

The presence of the arteria intercarotica caudalis has been recognized previously but was termed differently by a number of workers. Dandy and Goetsch (1911) described the blood supply to the hypophysis cerebri of the dog through the branches from the above anastomosis without assigning any name to it. Basir (1932) and Jewell and Verney (1957) defined the above vessel as the posterior lobar artery. Green (1951) named it as arteria hypophysial inferioris whereas de la Torre, et al. (1959) and de la Torre and Netsky (1960) called it as the arteria hypophysial posterior. Miller, et al. (1964), however, recognized it as arteria intercarotica caudalis from which arteriae hypophysiales (inferiores) caudales took their origin. Jenke (1919) and Bruni and Zimmerl (1951) mentioned an intercarotid anastomosis in the dog. NAV (1968) recognized the arteria intercarotica caudalis in the dog and horse. In view of the present worker, the term arteria intercarotica caudalis

be recognized in line with Miller, et al. (1964) and NAV (1968) but also in view of its topographical location and formation. Its contribution to the hypophysis was through its subsequent branches termed as the arteriae hypophysiales (inferiores) caudales.

The arteria intercarotica caudalis took its origin from the arteria carotis interna during its course at the level of the posterior pole of the hypophysis cerebri and joined its fellow of the opposite side to complete the anastomosis in the intercavernous sinus. Regarding the blood supply from the arteria intercarotica caudalis in the dog, Dandy and Goetsch (1911), Basir (1932) and Miller, et al. (1964) observed that the branches from the above artery supplied the pars nervosa of the hypophysis mainly, but also to the infundibulum and pars intermedia partly as observed in the present study.

In the pig the arteria intercarotica caudalis or its homologue has not been recognized so far in the available literature, but the anastomosis between the rete mirabile epidurale rostrale of either side represented a formation homologous to the arteria intercarotica caudalis in the species (canine and equine) and may be termed as the rami intercaroticae caudales. The reticulated anastomosis in the pig instead of a transverse tubular anastomosing vessel as seen in the dog and horse, was due to the reflection of

the modifications undergone by the intracavernous segment of the arteria carotis interna in those species which possessed a rete mirabile epidurale rostrale or rete mirabile epidurale rostrale or rete mirabile epidurale. Mention about the anastomosis between the above structures has been recognized by a number of workers including Daniel, et al. (1953) and Becker (1960) in the pig but no mention regarding its homologous nature with the arteria intercarotica caudalis has been put forth by any earlier worker. Flechsig and Zintzsch(1969) recognized that the rete mirabile epidurale of either side joined in the pig and formed the plexus intercaroticus.

The arteria intercarotica rostralis was present in the case of the dog. The artery took origin as a branch of the arteria carotis interna directly and traversed medially to join the contralateral branch to form a transverse trunk between two arteriae carotis internae. Its branches and supply have been mentioned in the observations. The arteria intercarotica rostralis has been recognized to be present in the dog by Miller, et al. (1964), NAV (1968) and as well as in the present work. This was recognized by Jewell and Verney (1957) as intercarotid anastomosis.

From the arteria carotis interna a number of small branches arose along with the forementioned artery. Some of these branches joined with the branches of the arteria

intercarotica rostralis to form a circumferential anastomosis around the infundibular stalk and tuber cinereum, in conjunction with the caudomedial branches of the arteria communicans caudalis. These branches have been defined as the arteriae hypophysiales (superiores) rostrales.

A similar anastomosis between the arteria carotis interna of either side was observed to be present in the pig. The above plexiform anastomosis has not been recognized by any earlier workers known to the present worker. The same was true also for NAV (1968).

The termination of the arteria carotis interna in the dog and pig has been described differently by a number of workers. Hofmann (1900) recognized that the arteria carotis interna terminated by giving off a ramus cranialis and a ramus caudalis. Jenke (1919) and Popesko (1960) recognized the divisions as the ramus nasalis and ramus communicans caudalis. However, Ellenberger and Baum (1943), Bruni and Zimmerl (1951), Koch (1965), Schwarze and Schroder (1965), Dobberstein and Hoffmann(1964), Schmaltz (1928) and Martin (1923) regarded the rostral ramus of arteria carotis interna as ramus communicans rostralis and the caudal ramus as ramus communicans caudalis. Bradley and Grahame (1959), Miller (1948), Miller, et al. (1964) and Sisson and Grossman (1953) did not term the rostral division but mentioned about its subsequent branches. The latter workers, however,

termed the arteria communicans caudalis for the ramus caudalis or ramus communicans caudalis of other workers. The nomenclature put forth by NAV (1968) recognized in line with the latter workers. The arteria carotis interna in the dog almost trifurcated to give off arteria cerebri rostralis, arteria cerebri media and arteria communicans caudalis (comprising pars proximalis arteria cerebri caudalis and arteria mesencephalica). However, in the case of the pig the arteria carotis interna bifurcated to give off a stem for the origin of the arteria cerebri media and arteria cerebri rostralis rostrally contrary to the condition in the dog. The above stem may be taken as a rostral continuation of the arteria carotis interna which reduced in the ascending scale of vertebrates till it was totally absent as observed in the case of man. Besides the above, phylogenic development and factors like shape and development of different parts of the brain in different species, level of the emergence of the arteria carotis interna from the sinus cavernosus in relation to the base of the brain, may also be a few of the factors relating to the absence or presence of the rostral stem of the arteria carotis interna for the origin of the arteria cerebri media and arteria cerebri rostralis.

The arteria choroidea rostralis in the dog took its origin from the arteria cerebri media whereas in the pig

from the rostral continuation of the arteria carotis interna. The present findings were in accord with the observations of Hofmann (1900), Jenke (1919), Ellenberger and Baum (1943), Bradley and Grahame (1959), Miller (1948), Miller, et al. (1964), de la Torre and Netsky (1960), Koch (1965), Dobberstein and Hoffmann (1964), Schwarze and Schroder (1965) and Flechsig and Zintzsch (1969). However, NAV (1968) regarded the origin of the above artery from the circulus arteriosus cerebri as has been accepted for man by NA (1961). Kaplan and Ford (1966) observed that the arteria choroidea rostralis in man took off mostly from the arteria carotis interna, proximal to the origin of the arteria cerebri rostralis and arteria cerebri media except in some cases where it originated either from arteria cerebri media or even from the proximal part of the arteria cerebri caudalis (arteria communicans caudalis of other authors in the human). The origin of the arteria choroidea rostralis corresponded to the above views in the case of the pig whereas in the case of the dog the artery distinctly took off from the arteria cerebri media. Bertan and Wilson (1966) studied the above artery in the dog and also found to arise from arteria cerebri media.

The arteria choroidea rostralis has been observed to be represented in lower vertebrates like reptiles in which a vessel arising most caudal, in the group of lateral

striate arteries, passed dorsally and then inside the forebrain to reach the primordial amygdaloid where it divided into a number of branches. This has been observed by Abbie (1934), Dendy (1909), Hofmann (1900), and Gillilan (1967) in different reptiles. Hofmann(1900) called this artery as the arteria choroidea rostralis in snakes. Abbie (1934) suggested that the arteria cerebri inferioris of lower vertebrates was the forerunner of that portion of the arteria choroidea rostralis which supplied to the amygdaloid complex of higher forms and acquired choroidal and hippocampal branches from the arteria cerebri caudalis. Regarding the distribution of the arteria choroidea rostralis, it formed an important source of blood supply to the amygdaloid complex, optic tract (tractus opticus), internal capsule (capsula interna), caudal part of the caudate nucleus (pars cauda nucleus caudati), putamen, globus pallidus, and associated thalamic areas as well as the plexuses choroideae ventriculi laterales and tertii. The artery formed anastomosis with the arteria cerebri caudalis at variable levels, along para-hippocampal gyrus and corpus geniculatum lateralis to which it supplied partly. Abbie (1934) recognized the latter anastomosis in the sheep.

The arteria cerebri media arose as a single stem in the case of the dog and pig. However, in the case of the pig the artery was also represented by two or three

branches taking off directly from the rostral continuation of the arteria carotis interna in some cases. The former has been well recognized by most of the workers mentioned earlier in relation with the blood supply to the brain of the dog. In the pig, Jenke (1919) recognized that the origin of the arteria cerebri media was through two or three stems of origin from the ramus nasalis of the arteria carotis interna. Luginbuhl (1966) also observed a similar situation in his specimens. The presence of more than one branch simulating two or three individual stems of origin of the arteria cerebri media was regarded by the present workers as representing the subsequent cortical branches of the arteria cerebri media of other animals and man. The presence of multiple branches represented earlier split to cause multiplicity of origin from the main trunk.

NAV (1968) mentioned about the rami striati as branches from the arteria cerebri media in all domestic animals. The presence of such branches have only been recognized in the case of the sheep by Abbie (1934). In present studies, rami striati were differentiated as done in man. These rami were equivalent of the rami striati laterales or arteriale striati laterales of different workers in man, depending upon the site of origin and topographical areas of supply. These rami were termed as rami striati laterales and formed blood supply for the lateral and caudal parts of

the corpus striatum and associated structures. From the comparative point of view the above branches have been observed to be present in all the vertebrates. In lower forms like fishes, amphibians, and reptiles they arose from the arteria olfactorium lateralis or its homologue, the arteria cerebri media, Abbie (1934), Shellshear (1920), Kappers (1933), Dendy (1909) and Gillilan (1967). According to Elliot Smith (1919) the corpus striatum started evolving from the fishes and the primordial striatal vessels entered through the length of the endorhinal fissure to supply it, however, a specific arteria striatica lateralis was observed to come off from the arteria olfactorium lateralis. The above worker studied the development of the corpus striatum from reptile to man and related it to go along with the evolution of the arteriae striati. Shellshear (1920), however, differed with the interpretation regarding arteriae striati laterales put forth by the former. Gillilan (1967) observed that the single arteria striati lateralis of the amphibians multiplied in reptiles to have four to six branches and to a similar number in birds. Abbie (1934) observed that the striatal branches in reptiles could be traced in three groups, one which entered through the lobus piriformis, second group through the endorhinal fissure and the third which entered through the palaeo-olfactorium ventral to the endorhinal sulcus. He observed

similar groups in submammalian specimens where the arteria cerebri media have shifted more lateral and away from the palaeo-olfactorium and the branches at the level of the endorhinal fissure were taken over by the arteria cerebri rostralis such that the above branch took over the supply for some of the lateral parts of the palaeo-olfactorium. From the anastomotic channels around and over the palaeo-olfactorium a large single artery, the artery of Heuber was formed from the arteria cerebri rostralis. However, other striatal arteries were retained by arteria cerebri media in higher mammals. Whereas in lower mammals, like the dog and pig, it seemed, in view of the present work, the arteria cerebri media did not show substantial changes from the condition observed in reptiles and lower mammals by Abbie (1934).

Arteria cerebri rostralis has been observed as the continuation of the arteria carotis interna. The arteria ophthalamica interna was observed to start from the arteria cerebri cerebri rostralis in the case of the dog, whereas, from the rostral continuation of the arteria carotis interna in the case of the pig. Tandler (1899) and Hofmann (1900) defined this artery as the arteria ophthalamica whereas Jenke (1919), Schmaltz (1928), Zietzschmann (1943), Ellenberger and Baum (1943), Miller (1948), Bruni and Zimmerl (1951), Daniel, et al. (1953), Jewell (1952), Becker

(1960), Nickle and Schwarze(1963), de la Torre and Netsky (1960) Miller, et al. (1964), Koch (1965) Schwarze and Schroder (1965) and Dobberstein and Hoffmann (1964) and NAV (1968) termed it as arteria ophthalamica interna in various animals. According to various workers in the human, Johnston, et al. (1958), Brash (1953), Peele (1961), Crosby, et al. (1962), Kaplan and Ford (1966) and NA (1961) an arteria ophthalamica was present originating directly from the arteria carotis interna. It coursed along the optic nerve to traverse through the optic canal and reached the orbit where it divided into a number of branches. Daniel, et al. (1953) contended that the arteria ophthalamica of man has a peripheral distribution which has been taken over by the arteria ophthalamica externa of the domestic animals and the primitive arteria ophthalamica persisted in the adult as arteria ophthalamica interna in the above animals. Padget (1948) observed that the arteria ophthalamica of man was a later formation during the embryogenesis than the arteria ophthalamica interna and the former took over the peripheral distribution and replaced the arteria ophthalamica externa.

de la Torre and Netsky (1960), however, regarded that the difference in the origin of the above-mentioned artery in man and the dog could be explained in light of the migration of vessels occurring in the embryogenesis but were not certain about its complete homologue. It may be

mentioned that the arteria ophthalamica interna arising from the ramus rostralis of the arteria carotis interna has been recognized in the fowl by Westfpahl (1961).

The arteriae striati mediales or rami striati mediales arose from the arteria cerebri rostralis in both species. These have not been recognized previously by any earlier workers in the species under discussion. Their area of supply corresponded with other species worked out by other workers. The branches perforated the tuberculum olfactorium and substantia perforata rostralis (pars rostralis of the lobus piriformis). The trunks which gave off the above branches were varying from one to two in numbers. According to Abbie (1934) these branches were first represented in reptiles as fine networks and supplied the medial and rostral part of the palaeostriatum. Their homologues in mammals supplied the ventromedial part of the nucleus caudatum, putamen, and rostral and medial two-thirds of the globus pallidus. The above artery in higher mammals was regarded as the artery of the Heuber by Critchley (1930), Shellshear (1930), and other earlier workers; however, Abbie (1934) suggested the term arteria striatica medialis. It was thought that the general nomenclature put forth by NAV (1968) for the above branches as rami striati arising from the arterior cerebri rostralis and arteria cerebri media be adopted, however, they may be differentiated as

laterales and mediales depending on their origin and areas supplied.

The arteria ethmoidalis interna has been observed to be present in both species studied presently. The artery participated in the formation of an ethmoidal rete or rete ethmoidalis with the branches of the arteria ethmoidalis externa. This formed a rich blood supply to the olfactory bulb and meningeal layer around it. The above artery has been observed to be present in the dog and pig by Hofmann (1900) as ramus ethmoidalis, whereas, Jenke (1919), Diwo and Roth (1913), Zietzschmann (1943), Ellenberger and Baum (1943), de la Torre and Netsky (1960), Bradley and Grahame (1959), Miller (1948), Miller, et al. (1964), Koch (1965), Nickle and Schwarz (1963), Schwarz and Schroder (1965), Dobberstein and Hoffman (1964), Popesko (1960), Becker (1960), Flechsig and Zintzsch (1969) and NAV (1968) termed it as arteria ethmoidalis interna. The arteria ethmoidalis interna was comparatively larger in the case of the pig and gave the impression of the rostral continuation of the arteria cerebri rostralis; however, from the comparative point of view it represented only a branch.

The true arteria communicans rostralis was observed to be present in the case of the pig. The term arteria communicans rostralis has also been applied to a side-to-side anastomosis between the arteriae cerebri rostrales of the

dog by most of the authors. Miller, et al. (1964) indicated that only a transverse communicating trunk between the above arteries be regarded as arteria communicans rostralis, a situation homologous to the case in man. Longo (1905a, b) observed that the arteria cerebri rostralis of either sides joined to form a single trunk and divided into two branches before reaching the genu corporis collosi in the case of the dog as observed presently and mentioned by various workers. He found similar conditions in other species including the pig.

Watts (1934) observed that in various primates there was side-to-side fusion of the arteriae cerebri rostrales. Windle (1887) and Shellshear (1927) found similar but anomalous condition in 34 of the cases in man and mentioned that it was common in lower mammals. Bapista (1964) also found such condition in man. Shellshear (1930) studied the blood supply to the brain of chimpanzees and encountered a similar fusion of the two arteriae cerebri rostrales and remarked that it was not the true arteria communicans rostralis. de Vriese (1905) indicated that such formations were present in some reptiles, marsupials, lemurs, rodents, chiropter, pinnides, pressiodactyles and carnivores included in his study. He also observed that there was no such anastomosis in most of the amphibians, fishes and birds. Brown (1966, 1968) has used the term arteria cerebri

rostralis azygos for the above union in the rat and mink. But, Haines, et al. (1969) proposed, in specific relation to the condition in the dog, that the term arteria cerebri rostralis proximalis be applied when referring to the portion of the arteria cerebri rostralis between the arteria carotis interna and common trunk and the term arteria cerebri rostralis distalis then be applied to those portions of the vessel distal to the bifurcation of the common trunk. In the opinion of the present worker, the term arteria corporis callosi (communis) mediane be applied to the common trunk between the two arteriae cerebri rostrales as they form a single trunk by their fusion and furthermore gave off the arteria corporis callosi for each of the cerebral hemisphere medially, the above artery being a continuation of the arteria cerebri rostralis of either side.

A similar situation was observed to be present in the case of the pig in which, in addition to the arteria communicans rostralis, a single trunk formed by the fusion of the interhemispheric continuation of the arteriae cerebri rostrales was present. The unpaired artery represented the complete fusion of the arteriae corporis callosi of either side and so was termed as the arteria corporis callosi (communis) mediane. The above unpaired artery, formed by the union of the arteriae cerebri rostrales, has been recognized by Hofmann (1900), Jenke (1919), Becker (1960), and

Flechsig and Zintzsch (1969), Ellenberger and Baum (1943) and Dobberstein and Hoffmann (1964) but no terminology was applied.

From the phylogenetic point the fusion of the arteriae cerebri rostrales was observed to be present in the lower mammals, subprimates and in some lemurs by de Vriese (1905) as indicated earlier. She termed the above artery as arteria corporis callosi mediana (mediane) as it coursed as a single vessel in the interhemispheric space of the brain and distributed by giving branches for the medial face of the cerebral hemispheres rostral and dorsal to the corpus callosum. She observed that a similar artery was present in the case of man but was attenuated and arose from the arteria communicans rostralis. However, she noted that in some cases (human) the artery may be represented in the form described in the former cases. This pattern she labelled as type "D" in man. She advanced the hypothesis that originally, during early stages of the embryonic life, either one or three arteriae cerebri rostrales would exist.

Van Der Eecken (1959) observed the above-mentioned condition in one case in man. The presence of a similar condition was observed in a number of cases in man by Godinov (1929). He compared the above with similar formations in other primates. The above patterns were comparable with

the condition in the pig and dog. He recognized the artery as the arteria corporis callosi mediana (mediane).

From the embryological point of view the studies of Padget (1948) and Kaplan and Ford (1966) showed that arteria corporis callosi media (mediane) was always present during the embryogenesis of the cerebral arteries in the human embryo and the newborn. This was present as a fine vessel and was given off from the arteria communicans rostralis. Padget (1948) regarded that the above vessel was absent in the adult but was a well developed branch in the embryonic stages going to the commissural plate. de Vriese (1905) found that in man the above artery was present, as indicated earlier and mentioned that the artery may become larger and as an unpaired source for the areas otherwise supplied by the arteria cerebri rostralis of either sides. This was associated with the lack of the development of the paired arteriae cerebri rostrales which in turn led to the development of the arteria corporis callosi mediane. She observed that the unpaired nature of the arteria corporis callosi mediane as well as its greater development was a more common feature in a majority of the reptiles and submammals normally.

It may be remarked that from the studies available in different lower vertebrates, reptiles, and mammals three types of the circulus arteriosus cerebri were predominating;

one, which was open type as there was no substantial communication between the two arteriae cerebri rostrales; second, which was closed type as there was fusion between the arteriae cerebri rostrales to form a single trunk; third, which was also a closed type but the communication between the arteriae cerebri rostrales was through a transverse vessel, termed as the arteria communicans rostralis. The first type was prevalent in the lower vertebrates and some birds, the second in most of the reptiles and some mammals, whereas the third was featured in some primates and lower mammals. The typication was made based on the generalities as there were changes in the pattern even in same classes of the animals. To correlate what morphological changes in the brain phylogeny led to the above patterns in different classes of animals may be due to multiple factors associated with evolution of the brain. Some of these may be the absence of the longitudinal fissure, absence of the corpus callosum and greater development of the corpus striatum and olfactory brain in the lower vertebrates, the constant reduction of the olfactory cortex and associated areas with their backward displacement, constant reduction in corpus striatum and development of the isocortex in the frontal polar cortex in the ascending scale of the evolution.

In the view of the present worker, the common stem of origin of the arteria corporis callosi in the dog and unpaired nature of the same in the pig may be termed, preferably, as the arteria corporis callosi (communis) mediane, the degree of their unpairedness being a species difference.

Arteria communicans caudalis was regarded to be present in the domestic species and extended between the arteria basilaris, NAV (1968). In primates, especially in man and monkey, the segment of the circulus arteriosus cerebri between the arteria carotis interna and arteria cerebri caudalis has been recognized as the arteria communicans caudalis, Brash (1953), Peele (1961), Netter (1953), de la Torre and Netsky (1960), Johnston, et al. (1958) and others. This artery was smaller in calibre and formed a connection between two sources of blood supply to the brain (carotis interna and vertebral). With special reference to domestic animals the arteria communicans caudalis has been regarded to continue caudally to join the arteria basilaris without any appreciable decrease in calibre. Moreover, from the phylogenetic point of view the arteria communicans caudalis or ramus caudalis (lower vertebrates) was present between the arteria carotis interna and arteria basilaris irrespective of the source of the blood. From the embryological standpoint, Padget (1948), Kaplan and Ford (1966), the arteria carotis interna in man supplied the blood to the

arteria basilaris and its branches in early embryonic stages which was taken over by the arteria vertebralis partly in the later stages. It seems that in the domestic animals, depending upon the species, the arteria vertebralis contributed to the arteria basilaris in varying degrees. The extent of the contribution by the arteria vertebralis reached to terminal branches of the arteria basilaris (arteriae cerebri caudales) in man. However, in the dog and pig this was probably not so and was speculative at this stage.

Kramer (1912) observed that the internal carotid blood in the dog distributed whole of the cerebral cortex except the caudal part which rested on the tentorium. The areas supplied also included the crus pedunculi and subthalamus. Whereas, the vertebral blood distributed to the medulla, pons, cerebellum, caudal two-thirds of the crus pedunculi, pulvinar, optic thalamus and corpus mamillare, etc. However, de la Torre, et al. (1962) observed filling of the arteria communicans caudalis in one case out of about one hundred carotid angiograms but found the consistent filling of the above artery with vertebral angiography. Jewell and Verney (1957) found variable patterns of distribution of the dyes injected through arteria carotis interna and arteria vertebralis. de la Torre, et al. (1959), de la Torre and Netsky (1960) and de la Torre, et al. (1962) regarded

the arteria communicans caudalis as the direct backward continuation of arteria carotis interna in accord with NAV (1968) and the present work, the only difference in the above and the present interpretation was that in the former, proximal segment was not recognized as the pars proximalis of the arteria cerebri caudalis whereas in the present work its recognition was stressed.

The arteria communicans caudalis as recognized by NAV (1968) may be divided into two segments, a proximal segment corresponding to arteria communicans caudalis of the various workers in human or proximal segment of the arteria cerebri caudalis of Williams (1937), Kaplan (1956), and Kaplan and Ford (1966), Moffat (1961), and Van den Berg and Van der Eecken (1968), and a distal segment corresponding to the arteria mesencephalica of Kaplan (1956), Kaplan and Ford (1966) and Van den Berg and Van der Eecken (1968). It may be mentioned that the recognition of the arteria communicans caudalis in man is arbitray based only on the source of blood, the proximal stem being supplied by arteria carotis interna and the distal from the arteria vertebralis or arteria basilaris, but morphologically, phylogenetically and embryologically, it represented the proximal stem of the arteria cerebri caudalis, the distal stem of which has been overtaken by the vertebral source due to the expansion of the cerebral hemisphere. This was based on the fact that

the above segment was the proximal stem of the arteria cerebri caudalis which occupied the above position because of the caudal expansion and backward shift of the cerebral hemisphere as the phylogenetic scale was ascended. The above has been recognized even in man by Williams (1937), Kaplan (1956), Kaplan and Ford (1966), Moffat (1961), and Van den Berg and Van der Eecken (1968) anatomically, morphologically and embryologically. The shifting of the arteria cerebri caudalis in a backward direction from lower vertebrates to higher was first suggested by Hofmann (1900).

Van den Berg and Van der Eecken (1968) suggested that the above may be adopted in man in line with the views of the forementioned workers. Williams (1937) traced the carotid plexus branches continued along the arteria cerebri caudalis. Padget (1948) and Kaplan and Ford (1966) described the mesencephalic segments of the circulus arteriosus cerebri in the development stages of the cerebral arteries of man. The above segment supplied mostly the mesencephalic and adjoining segments of the brain. This was also recognized by Kaplan (1956), Kaplan and Ford (1966) and Van den Berg and Van der Eecken (1968). In view of the above suggestions the arteria communicans caudalis was divided into two segments in the case of the dog and pig.

The proximal segment of the arteria communicans caudalis in the dog and pig gave off a number of branches which

supplied to the hypothalamic floor and adjoining areas mentioned in the observations. These rami (rami caudomediales) have not been described in detail elsewhere in domestic animals. These rami have been recognized in human by various workers. The same was true for the rami caudolaterales recognized presently in the dog and pig. Jewell and Verney (1957) recognized a thalamic branch from the arteria communicans caudalis which perhaps corresponded with the larger caudolateral ramus mentioned presently.

The arteria cerebri caudalis in the dog and pig has been regarded as a branch of arteria basilaris by Jenke (1919), Ellenberger and Baum (1943) and Koch (1965) whereas Hofmann (1900), Schwarze and Schroder (1965) and Bruni and Zimmerl (1951) regarded it as a branch of the arteria communicans caudalis in the pig.

Bradley and Grahame (1959), Miller (1948) and Miller, et al. (1964) regarded the arteria cerebri caudalis as a branch of the arteria basilaris whereas according to de la Torre and Netsky (1960) and de la Torre, et al. (1962) it was a branch from the arteria communicans caudalis. The latter view has been accepted by NAV (1968) for all domestic species.

The present work indicated that the arteria cerebri caudalis in the dog and pig supplied the caudal part of the cerebral hemisphere, parahippocampal gyrus, part of the

pedunculus cerebri, corpus geniculatum lateralis, corpus geniculatum medialis, thalamus, epithalamus and plexuses choroideus ventriculi lateralis and tertii. In the dog it gave off a ramus ad tectum mesencephali rostralis which arose from arteria mesencephalica in the pig. A number of choroidal branches were observed to come off from the arteria cerebri caudalis in both species. These branches distributed to the thalamic areas in their course but terminally contributed in the formation of the plexuses choroideus ventriculi lateralis and ventriculi tertii. Similar branches have been observed to be present in the human by a number of workers, Foix and Hillemand (1925), Peele (1961), Galloway and Greitz (1960) and Johnston (1958). Choroidal branches from the arteria cerebri caudalis were recognized in the sheep by Abbie (1933) and Nilges (1944) in the dog.

According to present observations, the arteria cerebri caudalis, during its initial course gave off a large branch, arteria choroidea caudalis which gave branches to the pedunculus cerebri and associated thalamic fields mentioned in the observations. The artery in its terminal course came on the dorsomedial aspect of the thalamus and lateral to epithalamus and gave off choroidal branches for the plexus choroideus ventriculi tertii. Similarly, a lateral set of

choroidal branches left the arteria cerebri caudalis before leaving the splenium corporis callosi to distribute terminally to the plexuses choroideus ventriculi lateralis and ventriculi tertii. Similar branches branches in the human have been recognized as rami choroidei caudales by NA (1961), however, different terminology have been used by some workers like Foix and Hillemand (1925), Peele (1961), who termed them as thalamogeniculate arteries, Rauber and Kopsch (1950) described arteria choroidea lateralis and a number of lateral thalamic arteries supplying the corpus geniculatum lateralis and pulvinar. In view of their terminal distribution and homonomy the above arteries be recognized as rami choroidei caudales and their contribution to the different areas of the thalamus be recognized, as done presently. The arrangement of the above was similar in both species except that the arteria choroidea caudalis arose from the arteria mesencephalica in the pig as mentioned earlier.

The arteria mesencephalica was observed to give off a number of rami before joining with its contralateral as well as the arteria basilaris. The caudomedial rami or posteriomedial rami have been recognized by most of the workers in human, These rami perforated so as to reach the caudal hypothalamus and thalamus through their larger perforating components. The smaller rami reached to supply the mesencephalic

areas. The above rami have been termed thalamoperforating by Foix and Hillemand (1925), Crosby, et al. (1962), Kaplan (1956), and Kaplan and Ford (1966) in human. The above rami could be termed as rami paramedianes but Gillilan (1964) called them as posterior perforating arteries whereas most of the other workers named tham as caudomedial (posteriomedial) rami in man, in relation to the position of their origin from circulus arteriosus cerebri. The above rami were studied by Hara and Fujino (1966) in man and divided their course into cisternal, parenchymal and terminal segments. The areas supplied by the above rami in human, dog and pig showed a lot of similarities except that in pig ventral source for the supply to the thalamus was comparatively less predominant than in the dog and man which was compensated by the dorsal sources in the former (pig).

Ramus ad tectum mesencephali rostralis was recognized in both species. The above ramus arose in common with the arteria choridea caudalis in dog and directly from the arteria mesencephalica in the case of the pig. The ramus distributed on the colliculus rostralis and sent perforating branches to the laterally and dorsally located fiber tracts and nuclear areas except the ventral and ventromedial fields which were supplied by the posteriomedial or caudomedial rami. No details about the distribution of the above ramus have been worked out by earlier workers, known to present

worker, in domestic animals. In view of the obvious clinical and anatomical importance the above ramus should be recognized. The extent of distribution of the above ramus was comparatively greater in the pig due to the greater development of the colliculus rostralis in comparison to that in the dog. The origin of the branches was variable such that one or two small branches may arise individually from the arteria mesencephalica giving the impression of multiple branches for the colliculus rostralis.

Arteria cerebelli rostralis which was homologous of the arteria cerebelli superioris of man was observed to leave the arteria mesencephalica (pars distalis arteria communicans caudalis) in the case of the dog. The origin of the above artery was variable in the case of the pig such that it may start at the junction of the arteria mesencephalica and arteria basilaris or from the arteria mesencephalica. The arteria cerebelli rostralis has been recognized in domestic animals but in particular reference to the dog and pig; Hofmann (1900) showed it to come off from the ramus caudalis in the dog and terminal part of the arteria basilaris in the pig. Jenke (1919) mentioned its origin from the terminal part of the arteria basilaris in the dog and pig, he mentioned a number of variations. Ellenberger and Baum (1943) regarded its origin from the arteria cerebri caudalis in the dog and from arteria basilaris in

the pig. With particular reference to the dog, de la Torre and Netsky (1960) and de la Torre, et al. (1962) regarded the arteria cerebelli rostralis to take off from the arteria communicans caudalis, whereas Miller (1948) and Miller, et al. (1964) regarded the arteria cerebelli rostralis as a branch of the arteria cerebri caudalis, Bradley and Grahame (1959), however, regarded it to be a branch of the arteria basilaris. According to Becker (1960) the arteria cerebelli (nasalis) rostralis in the pig was given off at the junction of the arteria communicans caudalis (ramus communicans aboralis) and arteria basilaris. It may arise from the arteria basilaris. He also mentioned that the origin of this artery was very variable due to extreme variations in its course and its branches. The discrepancies in the literature regarding the origin of the arteria cerebelli rostralis stemmed from the fact that some workers recognized the arteria communicans caudalis to extend between the arteria carotis interna and arteria cerebri caudalis. The presence of the arteria cerebelli rostralis accessorius was also recognized in agreement with Jenke (1919) and Becker (1960).

The arteria cerebelli rostralis supplied the rostrodorsal aspect of the cerebellar hemisphere of its own side but also gave fine collateral branches which perforated to supplying the associated structures in its course. It

supplied the colliculus caudalis through one or two rami which may be regarded as rami ad tectum mesencephali intermedius and caudalis. The perforating rami from the terminal portion of the arteria cerebelli rostralis entered through the corpus medullare and pedunculus cerebellaris rostralis to supply the cerebellar nuclei, in agreement with the observations of Goetzen (1964) in the dog, calf, and sheep.

The arteria basilaris was formed by the union of the cerebral branch of the arteria cerebrospinalis of either sides on the ventral surface of the spinomedullary junction in the dog and pig, Hofmann (1900), de Vriese (1905), Tandler (1899), Jenke (1919), Zietschmann (1943), Ellenberger and Baum (1943), Luginbuhl (1966), Bruni and Zimmerl (1951), Sisson and Grossman (1953), Koch (1965), Dobberstein and Hoffmann (1964) and Schwarze and Schroder (1965). Similar views were given for the dog by Bruckner (1909), Miller (1948), Miller, et al. (1964), Bradley and Grahame (1959) and in the pig by Montane, et al. (1964), and Becker (1960). However, NAV (1968) contended that the arteria cerebrospinalis be regarded as a continuation of the arteria vertebralis and the former term may be discontinued. Their concept has been based on the fact that the ramus descendens which was regarded as a branch of arteria occipitalis earlier, may be taken as a branch of arteria vertebralis in view of the

comparative anatomy in different animals. According to NAV (1968) the arteria vertebralis in the pig may be considered to continue through the fossa atlantis after anastomosing with the arteria occipitalis. The artery then passed through the foramen alare and foramen vertebrale laterale into the canalis vertebralis where it joined with the rete mirabile epidurale caudale and continued to form the arteria basilaris by uniting with the artery of the opposite side. According to NAV (1968), in the dog, the arteria vertebralis passed through the foramen transversarium atlantis, gave off a ramus anastomoticus cum arteria occipitalis and turned dorsally through incisura alaris and entered the foramen vertebrale laterale. The right and left arteriae vertebrales joined to form the arteria basilaris. NAV (1968) contended that in man the arteria basilaris was the direct continuation of arteria vertebralis. In this connection it may be mentioned that Streeter (1918) observed that it was the arteria vertebralis which joined and became continuous with the arteria basilaris in the developmental stages in the pig. Similar situations have been observed by Padget (1948) and Kaplan and Ford (1966) in the human.

Jenke (1919) and Becker (1960), however, regarded that in the pig the ramus descendens of the arteria occipitalis contributed, by joining the vertebral branch, in the formation of the arteria cerebrospinalis. Jenke (1919), Sisson

and Grossman (1953), Bradley and Grahame (1959), Miller (1948), and Miller, et al. (1964) regarded that the arteria cerebrospinalis was formed by the anastomosis between the ramus descendus of arteria occipitalis and arteria vertebralis and the latter continued to form the above artery in the dog. The difference in the opinion about the course and branches of the arteria vertebralis and occipitalis was due to difference in the interpretation regarding the terminal arterial segment (atlantal and spinal canal segment) formed by the anastomosis of the arteria occipitalis and arteria vertebralis which has been regarded by a number of earlier workers as arteria cerebrospinalis.

From the comparative standpoint the arteria occipitalis in most of the vertebrates had its major distribution to the muscles around the base of the skull and anterior part of the neck region. The arteria vertebralis supplied the cervical segment of the spinal cord and also the caudal segments of the brain in varying degree, usually in an ascending order of the mammalian evolution. In man, the arteria vertebralis supplied almost all of posterior or caudal half of the brain whereas in domestic animals like the dog, pig, horse, goat, sheep and cat, the contribution was variable and the arteria vertebralis may show varying degree of

influence. However, from the point of view of homonomy, area of supply and topographical course, the above arterial segment formed after the anastomosis of the arteria vertebralis with the arteria occipitalis may be considered as the atlantal and spinal continuation of the arteria verte bralis.

The arteria basilaris in the dog and pig contributed a number of branches which distributed to supply the medulla oblongata, pons and cerebellum detailed in the observations. Rami medullares have been recognized in the dog and pig presently. These rami have been referred to as short circumferential arteries by Foix and Hillemand (1925) and Hassler (1967), as transverse arteries by Stopford (1916a,b) and lateral arteries by Duret (1874).

The most caudal ramus medullaris gave off a branch on the dorsolateral aspect of the medullospinal junction. This ramus may be defined as ramus spinalis dorsalis. It has been regarded as posterior spinal ramus by Peele (1961), Gillilan (1964), Crosby, et al. (1962) and other workers in man. The above ramus joined with the ramus spinalis dorsalis of the arteria vertebralis in the second cervical segment of the spinal cord to form the arteria spinalis dorsalis.

The arteria cerebelli caudalis was observed to be present in the form of two separate arterial branches, one arising at the junction of the arteria vertebralis

or cerebral segment of the arteria cerebrospinalis with the arteria basilaris or directly from the former and the other from the arteria basilaris, in the case of the dog. The presence of these arteries was variable: in most of the cases there were two on either side; however, only one branch may be represented on one side in some cases.

The site of the origin similarly showed variations. Jenke (1919) mentioned that the arteria cerebelli caudalis had two or three roots of origin in the case of the dog. Fazzari (1929) recognized a vertebro-cerebellar artery in the dog and man. The distribution of both arteries have been described in the observations. The above arteries when present in the form of single branch distributed the areas covered by both arteries.

The arteria cerebelli media was observed to be present in the dog and represented the homologue of arteria cerebelli inferior anterior of man. The above artery has not been recognized in domestic animals but instead has been termed as arteria labyrinthi or auditiva interna by most of the workers: Jenke (1919), Ellenberger and Baum (1943), Sisson and Grossman (1953), Bruni and Zimmerl (1951), Miller, et al. (1964), Koch (1965), Bradley and Grahame(1959), and others. According to the latter workers the arteria auditiva interna was a direct branch from arteris basilaris as was thought earlier in the case of man. However, in view of

the distribution and topography, the main arterial stem may be regarded as arteria cerebelli media from which arteria labyrinthi was given off. The arteria cerebelli media in the dog was listed as arteria cerebelli inferioris anterior by de la Torre and Netsky (1959) which was contrary to the postural topography in the domestic animals.

Rami ad pontem were varying from one to four in number. These have been termed as the short lateral arteries by Gillilan (1964) and short circumferential arteries by Foix and Hillemand (1925). These branches supplied most of the pons and inter-anastomosed with each other as well as with adjoining branches. Thexe branches have been recognized to be present in most of the domestic animals by a number of workers: Jenke (1919), Zietschmann (1943), Ellenberger and Baum (1943), Bradley and Grahame (1959), Miller (1948), Miller, et al. (1964), Sisson and Grossman (1953), Bruni and Zimmerl (1951) and Koch (1965).

The rami paramedianes were given off by the arteria basilaris while in course on the ventral aspect of the medulla oblongata, corpus trapezoideum, and pons in the sulcus basilaris and fissura mediana ventralis. No mention of the above rami in domestic animals has been made earlier. These rami formed an important supply to the nuclear areas and fiber tracts in the median plane of the above-mentioned segments of the brain. In addition to the above, short

circumferential arteries were found to be present, at variable levels, between the origin of the above-mentioned major arteries supplying the cerebellum. These supplied the ventrolateral and dorsolateral nuclear areas and fibre tracts of the medulla oblongata, pons and corpus trapezoideum by sending perforating branches along their course.

The arteria basilaris in the pig had course similar to that in the dog. The arteria basilaris was less tortous than in the dog. It may be noticed that the arteria basilaris, in the pig, which coursed rostrally on the ventral aspect of the medulla oblongata, corpus trapezoideum and pons, decreased in its calibre as it reached the pons (near the junction of the corpus trapezoideum and caudal half of the pons) but again increased in calibre before joining the arteria e mesencephalicae. This gave the impression that the two sources of blood, vertebral and carotid met somewhere in the pontine segment of the arteria basilaris. The arteria basilaris gave off a number of rami medullares. These were generally three to five in number and arose from arteria basilaris except the caudal one. The increase in the number of the above rami was credited to more rostral origin of the arteria cerebelli caudalis in the pig. These were significant in the pig as they formed major contribution to almost whole of the medulla oblongata, except medial part which was supplied by rami paramedianes or rami

medianes. The rami medullares anastomosed with each other on the ventrolateral and dorsolateral part of the medulla oblongata. On the latter part they formed an inter-anastomosing trunk which converged to meet its fellow of the opposite side at the obex and continued caudally as a plexiform vessel on the spinal cord. The caudal ramus medullare gave off a ramus caudalis spinalis similar to that in the dog. The arteria cerebelli caudalis has been recognized in agreement with the views of Hofmann (1900), Jenke (1919), Ellenberger and Baum (1943), Montane, et al. (1964), Koch (1965), Becker (1960), and Popesko (1960). The arteria cerebelli media arose as a branch of the arteria cerebelli caudalis and gave off the arteria labyrinthi. Similarly, rami ad pontem were recognized in accordance with similar branches in the dog. The intrinsic distribution of the above arteries have been detailed in the observation in view of the lacking information in both species.

Histomorphological Age Changes in the Cerebral Arteries of the Dog and Pig

The study of the age changes in the cerebral arteries of the dog and pig was undertaken on the dogs raised in the Department of Veterinary Anatomy and pigs at the farm managed by the Department of Animal Sciences of Iowa State University. Animals of each species were kept under similar

environmental conditions and had similar diets. The subjects included comprised a segment of the population specially reared to investigate gerontological studies in different tissues and organs of the dog and hog underway in the Department of Veterinary Anatomy for over twelve years.

The present study was oriented to study the normal morphological changes in aging cerebral arteries. The changes studied included connective tissue changes, ground substance acid mucopolysaccharides, intimal proliferations, changes in the different layers and medial defects.

The arterial wall showed microscopic alteration in its architecture with aging. The results indicated a remarkable and unusually constant relationship to the chronological age of the subjects under study in almost all individuals.

A number of factors have been associated with the changes in the morphology of the arterial wall during aging and experimental atherosclerosis.

Aschoff (1939) and Duguid (1926) stated that the mechanical factors may be primary in inducing the proliferative changes in the arterial wall. Texon (1957) postulated it to be the haemodynamic suction pressure and lifting action of the blood flow on the intima at bends and curves and over the plaques in the arterial wall. According to Texon (1967), McDonald (1960), and Stehbens (1959, 1960, 1965) the tunica intima was exposed to the possibility of

mechanical injuries due to pulsatile movements, hypertension, shear vibrations and turbulent flow of the blood.

French (1966) indicated that due to lack of blood and lymphatic supply the intima was exposed to mechanical injuries, formation of surface deposits or accumulation of material infiltrating from the lumen. The intima resisted any alterations but with increasing age the intima succumbed and lost its integrity leading to the formation of intimal thickenings.

According to McDonald (1960) the arterial wall was exposed to longitudinal and radial movements as a result of the passage of pulse wave. The outside of the wall was attached to the connective tissue, which under the effect of viscous drag created a longitudinal shearing strain between inside and outside of the wall.

Schwartz and Mitchell (1962) and Gofman and Young (1963) regarded that there was significant correlation between the blood pressure levels and atherosclerosis. According to Lindsay and Chaikoff (1963) greater pulse rate caused the internal elastic lamina fragmentation, intimal proliferations and other connective tissue changes in the blood vessels.

Dahme (1965a) stressed that the sclerotic changes in blood vessels were polyaetiological in origin, haemodynamic, aging, disturbance of endothelial permeability,nutrition of the blood vessels, metabolic and enzymatic disorders.

Biochemical studies on the arteries of the different ages studied by Kirk (1959) and Zemplenyi (1962) revealed that there was a decline in the enzymatic activity in the middle zone of the tunica media with aging. This was related to the anoxic or hypoxic effect on the metabolism of the smooth muscle cells and may be an indication of the ischaemic atrophy.

Aetiological factors like phylogeny, hereditary, domestication, arterial structure, composition and metabolism of diet, physical activity, environment and sex have also been propounded by various workers reviewed by Detweiler and Luginbuhl (1967).

A number of theories about atherosclerotic lesions in the arterial wall have been put from time to time; these theories were filtration, lipophage, migration, lipid synthesis, capillary haemorrhage, encrustation, and thrombogenic theories. Similarly, the role of the hormones has also been stressed. The above theories have their merits and demerits which are well discussed by Constantinides (1965).

Age as related to the morphological changes in the components of the arterial wall have already been reviewed elsewhere.

Cerebral arteries in the dog and pig

Current textbooks on histology mentioned about the elastic and muscular arteries in general but do not indicate any

differences in the arteries of specific regions or organs. The cerebral arteries in the dog and pig studied presently showed certain differences of interest from other muscular arteries of the body. Basically, the histologic picture showed a trilamellar arrangement of the layers, the tunica intima, tunica media and tunica adventitia. The tunica intima has been divided into three sublayers, endothelium, subendothelium, and internal elastic lamina. The tunica intima in the newborn dog and pig consisted of only two sublayers as the sub-endothelial sublayer differentiated by six months of age in the dog and pig. The internal elastic layer appeared as a very thick wavy layer. The internal elastic layer appeared to be thicker in the cerebral arteries than in other muscular arteries. It seemed that more of the elastic tissue of the cerebral arteries was concentrated in this layer than in any other layer, such as the tunica media and tunica adventitia. The latter two layers contained a few fine elastic fibers. The thickness of the internal elastic layer varied but its thickness in relation to that of muscle layer was in general greater in cerebral arteries than in any other artery of the body. Triepel (1902) observed the transition of structure from the usual extracranial arteries to that of the intracranial arteries. He noted that during this transition the aggregation of the elastic tissue into the internal elastic lamina assumed a greater thickness as the arteries entered the skull. There

was also disappearance of the irregularly grouped elastic fibers from the medial layer. The reduction of the adventitia and especially the longitudinally oriented elastic fibers seemed to be sufficiently strong as they have to meet the pressure requirements only from within. The intramural stretch imposed by the blood was very well taken care of by the very strong internal elastic lamina.

According to Obersteiner (1884) the internal elastic lamina was a delicate membrane which disappeared as the caliber of the artery diminished. The tunica media was composed of spindleshaped muscle fibers which encircled the inner layer of the blood vessel. He described the adventitia as a delicate layer of connective tissue which was not attached to the muscle layer. Binswanger and Schaxel (1917) studied the normal histology of the cerebral arteries and inferred that the small cerebral arteries differed from the larger ones by having less elastic tissue in their media.

Hackel (1928) observed that there was no external elastic lamina, the adventitia was small but the internal elastic lamina was thicker than the other systemic arteries. Benninghoff (1930) described the internal elastic lamina as the fenestrated membrane. Ranke (1915) believed that the internal elastic lamina was not a layer but a mesenchymal network which was continuous from the subendothelium to the adventitia.

The present observations indicated that the tunica media was similar to other muscular arteries except that it was devoid of a large number of elastic fibers as indicated above. The tunica media was comprised of circularly arranged smooth muscle cells. The elastic fibers in the extracerebral (pial) arteries were conspicuous and thicker than those in the tunica media of the main cerebral arteries. Fine collagen fibers were also present in the tunica media. In contrast to other muscular arteries, the cerebral arteries did not have an external elastic lamina as such. This band was present only in the form of a few elastic fibers at the junction of the tunica media and tunica adventitia but was not a discrete layer. The poorly developed external elastic lamina was represented by a few circularly arranged elastic fibers located in the inner part of the tunica adventitia or at the junction of the tunica media and tunica adventitia. This was more developed in the basilar artery as well as in the anterior and middle cerebral arteries. The absence of a discrete and thick external elastic layer was reported by Triepel (1896), Hackel (1928), Glynn (1940), Duff (1954) and Baker and Iannone (1959a). Hassler and Larsson (1962) observed the presence of the external elastic lamina in children up to two years of age. They further mentioned that the layer is well developed in the internal carotid artery and basilar artery. However,

the present study which included the basilar artery and cerebral portion of the internal carotid artery did show a poorly developed and interrupted external elastic layer.

The tunica adventitia represented the outermost layer of the cerebral arteries and contained longitudinally arranged collagen fibers with interspersed elastic fibers arranged circularly. These latter were predominant near the junction of tunica media and adventitia as indicated above. A number of smooth muscle cells and fibroblast were also seen in this layer but no longitudinally oriented elastic fibers were observed.

The electron microscopic studies on the cerebral arteries have been investigated by Dahl and Nelson (1964), Flora and Nelson (1965), and Flora, et al. (1967) in human subjects and Pease and Paule (1960), Pease and Molinari (1960), Pallie and Pease (1958) and Prosser, et al. (1960) in the cat, pig and monkey. The results of these studies correspond with the basic histologic picture of the light microscopy as described in the present study. The significant results of the earlier studies (electron microscopic) showed that the endothelial cells were seen to have occasional lysosome-like structure in their cytoplasm. Between the endothelial cells and the inner part of internal elastic lamina, there was a dense substance which was fibrillar or floccular in nature. The ground substance was in close apposition

with the endothelium. The fenestrations were regularly observed and were completely or partially filled with the unelasticized matrix. The penetration by smooth muscle cells was particularly obvious in conditions which stimulated the development of the subendothelium, but even in the normal arteries the fenestrations often contained extrusions of smooth muscle cell cytoplasm. The internal elastic membrane was not a solid sheet of elastin but was composed of fibers. In the tunica intima elastic and collagen fibers and collagen fibers and some smooth muscle-like cells were seen occasionally.

The presence of the valve-like structures in the small cerebral arteries were noted by Legait (1947, 1949) in various vertebrates. He also observed the intimal cushions which he referred to as sphincters. He attributed these formations to the functions of complete or incomplete closure of the arterial lumen at the site of branches and so regulating the cerebral blood flow. Moffat (1959) observed valvular formations in the rat and called them polypoid cushions. He noted that these were rich in metachromasia and each smooth muscle cell was surrounded by the reticular fiber network, more so than in the medial cells. He attributed the function of these structures to the blood flow regulation into the collateral branch. He suggested that the longitudinally oriented smooth muscle cells contract resulting in

swelling which caused an increase in their bulk so diminishing the lumen of the collateral branch.

Shanklin and Azzam (1963a,b) also observed the valves in the cerebral arteries of the brain in rats and they too suggested the possible functional relationship of these structures to the cerebral blood flow.

Fourman and Moffat (1961) studied the regulatory mechanism of the polypoid intra-arterial cushions or valves and found that these structures served to regulate the blood flow into the collateral vessels by a sphincter-like action. They observed that the larger cushions projecting into the lumen produced cell skimming, whereas the smaller overproduced plasma skimming.

Murphy and Webster (1966) and Taggart and Rapp (1969) confirmed the findings of Shanklin and Azzam (1963a,b) and suggested that the action of the valve-like structures was sphincter-like. Rosen (1967) agreed with the above findings. According to him, the smooth muscle cells were not the main components of the valves. He found that the fibroblast-like cells with dense granular cytoplasmic matrix formed the valve and differed from the smooth muscle cells of the tunica media. In the view of the present worker, it seemed that these were smooth muscle cells which may look like fibroblast because of their high functional activity.

In view of the present findings, the valve-like structures observed in the small cerebral arteries were not only present in the area around the optic chiasma or ventral aspect of the hypothalamus, but were distributed to the small pial, small perforating and small intracerebral arteries also. It seemed that these formations were related to the usual morphological changes in the branching pattern and may play an important role in the regulation of the blood flow into the collateral branches. The action of the valve-like structures may be due to their sphincter-like action by the contraction of the smooth muscle cell constituents which may reduce the lumen. This may further be supported by the fact that the contraction of the smooth muscle cells in the tunica media will cause a compensatory effect in helping the above mechanism. This was supported by the fact, as observed in the present work, that these modifications were almost concentric at and around the orifice of the main and collateral branches.

Regarding the large intimal cushions observed in the large cerebral arteries, it was observed that these were not polypoid or conical but were crescentric and semicircular. They were located at the branching site and reached a maximum height mostly at the orifice of the collateral branch beyond which they receded. The present investigation revealed that these were bilateral in most cases; however,

single intimal cushions were also observed. The constituents of the intimal cushions revealed that these resembled those in the valve-like structures. The elastic fibers were more widely distributed and the collagen was associated with their distribution in varying degrees with age. These intimal cushions may also serve to play a role like a sphincter by the contraction of their smooth muscle cell constituents which shortens and makes the cushion protrude more in the lumen around the orifice and so regulates the flow of the blood. The medial smooth muscle cells may also contract to narrow the orifice and supplement the intimal cushion in a pattern similar to the condition described in the valve-like structures. The intimal cushions do not occur diffusely at the site of branching but appeared as separate pads or cushions at these specific anatomic sites. These have been regarded as integral part of the atherosclerosis by Wilens (1951), Prior and Jones (1952), Levene (1956) and Moon (1957) and as prospective sites of atherosclerosis by a number of workers.

The presence of intimal cushions has been regarded to be physiological and normal components of the artery because they occurred during the period of active growth, Ophuls (1933), Hassler (1961, 1962a,b,c) and Robertson (1960a,b). Rodbard (1954, 1956, 1959) and Texon (1957, 1967) attributed their presence to a suction effect because of a local

decrease in static pressure at the branching sites. Stehbens (1960, 1965) recognized the locations of the intimal pads and suggested that they were related to hemodynamic factors. Conti (1951) observed the cushions in the coronary arteries of man and defined them as regulatory structures controlling the blood flow for collateral branches.

The presence of the cushions caused turbulence at the area distal to them and may cause aneurysm (Hassler, 1961); however, in the present study no concrete evidence could be collected to recognize the aneurysm except that in some cases the tunica media distal to the cushion was appreciably reduced (discussed elsewhere in the text).

The presence of intimal cushions in fetal and infant cerebral arteries have been reported by a number of workers. Hassler (1961), Stehbens (1960), and Hassler (1962c) noticed that in the cerebral arteries of neonates intimal cushions were of smaller volume than in the adult of the second decade. This corresponded to the present findings in which the intimal cushions were observed to be well laid by the second age group, ranging from six months to one year and onwards. The absence of the intimal cushions at certain sites and variations in the size may be due to differences in the function and the part of the brain supplied, Hassler (1962a). Texon (1957, 1967) was of the view that the branching sites were seats of predilection for the development of atherosclerosis

due to the suction effect upon the vessel wall. The intima was subjected to lifting or pulling effect upon the endothelial cell layer and superficial cells represented the initial changes. The subsequent changes represented the thickenings at these sites projecting into the lumen and causing reduction in the lumen size. These cushions were observed to be present in the fetuses and young ones by Tuthill (1931), Hackel (1928) and Benke (1931) also. Hackel (1928) and Robertson (1960a,b) observed that these cushions remained unchanged in their morphology until twenty years of age. Benke (1931) and Robertson (1960a,b) observed their presence as due to pulse forces and stresses, the latter, similar to the views of other workers, regarded that these formations constituted a physiologically efficient method of compensating for the rise in blood pressure. By the above formations, not only the muscular bulk of the wall was increased but also tended to reduce the tension in the wall. The splitting of the internal elastic lamina, at the site of the branching and associated with cushion formation, was accomplished by smooth muscle cells. Jores (1904), Robertson (1960b), Gross, et al. (1934), Altschul (1950) and many recent light and electron microscopic studies indicated that the smooth muscle cells penetrated through the fenestra of the internal elastic lamina or through the splits.

According to the present observations it seemed that the prevalence of the cushions was greater in the anterior cerebral, middle cerebral, and posterior cerebral arteries and least in the basilar artery and its branches. The size of the intimal cushion changed with age. There was a definite increase in the connective tissue components also. The intimal cushions in the earlier age group were more of a musculoelastic type whereas with increasing age there was increased deposition of collagen leading ultimately in old age to formation of fibrous intimal cushions. It may be worth mentioning that the rate at which the fibrosis of the intimal cushion took place indicated its greater and earlier involvement than the rest of the cerebral arterial wall. This in turn again indicated that the metabolic and dynamic activity occurring at the site of branching were comparatively higher than in the rest of the cerebral arterial wall. The changes so undergone were not pathological but were physiological aging in nature.

The physiological nature of the intimal cushions has been recognized by various authors: Hackel (1928), Glynn (1940), Rotter, et al. (1955), Hassler (1961, 1962a) Stehbens (1960, 1963), Legait (1947, 1949), Robertson (1960a,b), Serban and Ovuia (1961), Elias and Pauly (1966), and Jaffe, et al. (1968). Most of the above authors agreed that the intimal cushion work as arterial sphincters and regulator of

blood flow. Hassler (1962a) and Serban and Ovuia (1961) also observed the nerve supply to the intimal cushions. The nerve fibers enter through the adventitia and media to innervate cushions. Nerve fibers were derived from periarterial plexuses. Hackel (1928) and Glynn (1940) observed that the localized elastic hyperplasia developed through a process of work hypertrophy and may be assumed to indicate a local condition of strain. Glynn (1940) found that the intimal hyperplasia may be due to greater pressure that was exerted on the wall that was in line with the blood stream. This pressure difference has been recognized by most of the above workers. He mentioned that the intimal thickenings at branchings may also be due to the eddy current occurring at those sites.

A high amount of elastic fibers at this site of the intimal cushion can be related to its functions as the elastic fibers were very easily stretched and produced elastic tension, without the expenditure of excessive biochemical energy, to resist the distending force of the blood pressure, Burton (1965). According to him elastic fibers, particularly in the elastic intima, appeared histologically to be folded, and when this folded spring was compressed, the elastic intima resisted compression as well as extension when the vessels were distended under excessive blood tension. The elastic fibers worked in collaboration with collagen

fibers which resist stretching much more than do the elastic fibers. So, it seemed that the functions of the elastic and collagen at the site of branching helps in maintaining a steady tension to hold the wall in equilibrium against transmural pressure exerted by blood pressure in the vessels.

The function of the vascular smooth muscle cells was rather to produce active tension by contraction under physiological control and so change the diameter of the lumen, Burton (1962). In view of the above, it seemed that the presence of the longitudinally placed smooth muscle cells in the intimal cushions and a few in the underlying media supplemented the active tension by their contraction under physiological conditions to change the lumen size whereas the presence of elastic fibers resisted overstretching and helped in the narrowing or closure of the lumen of the vessel at the site of branching. The elastic fibers may also modify the pulsations from the heart and caused suction at the site of branching (Hassler, 1962a).

The structure of the valves and intimal cushions showed certain structural similarities with valves of the veins. They all had a continuous endothelial cell lining, continued from the main artery to the collateral through the branching site. In all the above cases in the area below the endothelium there was a network of elastic fibers continued with elastic tissue of the intima. There were

smooth muscle cells present among these fibers.

The study of the nature of the valvogenesis in veins, lymphatic vessels and heart indicated that the formation of the above structures followed the patterns of flow as suggested by Bremer (1928), Kampmeier and Birch (1927), Chung (1932) and Rodbard (1953, 1954, 1956, 1958, 1959).

According to the above workers, the valves developed at the site of hydraulic stress. Their analysis of the mode of the valve formations in the lymph vessels, veins, and heart suggested that hydrodynamic forces actually contributed to the selection of the site of valvogenesis. Studies of Kampmeier (1928) and Kampmeier and Birch (1927) have demonstrated that during development of heart clearly formed intimal cushions served as the first cardiac valves of the embryo and so also in the valves of the veins and lymphatics.

According to Kampmeier and Birch (1927), the first sign of its presence was represented by the endothelial thickening, followed by the subsequent growth due to invasion of the subjacent mesenchyme. Rodbard (1953, 1954, 1956) studied the changes in the structure of the vessel wall. These were produced by modification of flow patterns. He suggested that the valve and cushion-like formations could be produced by the decreased lateral pressure, markedly diminished at the branching sites which released the

local atrophic influence. The lining cells could no longer be compressed and inhibited from growth and instead they could round up and begin to proliferate forming a hillock or cushion. This was true at branching sites in the arterial channels where, at the area just around the branching points, the lateral pressure decreased. Texon (1957, 1967) mentioned that there was decreased lateral pressure at the curvature, bifurcation or branching of the arterial vessels. The intima at these sites was exposed to a lifting or pulling effect upon the endothelial cells and superficial cells which represented the initial change. The local reaction consisted of a reparative process, a thickening dur to proliferation of the endothelial cells and fibroblasts from the subjacent layers. According to Chung (1932) the thickenings were due to the proliferation of the subendothelial tissue which was composed of mesenchymal cells.

Rodbard (1956, 1958, 1959) based cn his earlier and above studies, again stressed that when the pressure was reduced at low valves on a segment of the vessel, the lining cells released from the pressure, proliferated to form cushions. The development of small cushions tended to increase the likelihood of further growth. This was due to the fact that the cushion deviated and accelerated the stream lines of the blood flow, to the local increased velocity which was further associated with the reduction in the local pressure.

Functions of different components of the cerebral arterial wall

Endothelium of the arterial wall was generally assigned the functions of exchange of water, electrolytes and other substances in the blood stream. However, the endothelial cells can close the capillaries particularly due to swelling of the endothelial cell nuclei which round up into the lumen. The endothelial cells were also resistant to the stretch forces to a considerable extent. This rounding up of the endothelial cells and change in shape was important in closure of the lumen of small blood vessels.

According to Benninghoff (1930) the structure of the cerebral arteries placed the greatest strength in its inner layers. He regarded this as an adaptation to the obvious requirement for resistance to the blood pressure within the lumen and to the absence of any need for protection of the cerebral arteries against external stresses because of their relative immobility and shielded position within the cranial cavity. Glynn (1940) regarded that the thick internal elastic lamina of the cerebral arteries, alone and without support of the layers external to it could withstand very high intra-arterial pressure. Triepel (1902) pointed out that the modulus of elasticity of the smooth muscle cells was much smaller than that of the elastic tissue such that the

amount of stretch to a given load in the case of smooth muscle fiber may be as much as thirty times greater than that of elastic tissue which indicated that the elastic tissue was more rigid as compared with smooth muscle fibers and added rigidity to the tubular vascular system. This rigidity may be less if elastic tissue were spread throughout the media and adventitia and vice versa. However, according to Burton (1965), the elastic fibers were very easily stretched and were quite remarkable in that they can be extended many times their unstretched length before reaching an elastic limit. The function of the elastic fibers was to produce an elastic tension and resist the distending force of the blood pressure.

The collagen fibers have their young modulus of electricity about hundred times greater than elastic fibers so a relatively small number of collagen fibers in the wall of the artery can give it a high degree of resistance to distension. The collagen fibers were so arranged in the arterial wall that they do not exert their tension until there has been some degree of stretching of the wall. The function of the smooth muscle cells was, rather, to produce active tension by contraction under physiological control and so change the diameter of the lumen of the vessel. The smooth muscle cells had their greatest manifestation of control over the size of the lumen in the arterioles where it

was in abundance. The arterioles, because of their small lumen size can also increase the total resistance to the flow much more than would the constriction of larger vessels (Burton, 1965).

According to Burton (1954), the total tension of the arterial wall necessary to counteract the distending tendency of blood pressure is due to collagen and elastin.

Wolinsky and Glagov (1964) observed that the circumferentially aligned collagen fibers bore most of the stress forces at physiological blood pressure while the elastic tissue uniformly distributed the stress involved.

Age changes in the connective tissue components of the cerebral arteries

Collagen The cerebral arteries of the dog and pig showed variable picture of the collagen deposition of the different layers depending upon the size of the vessel. The observations showed that the collagen started appearing in the subendothelial space of the cerebral arteries beginning from the second age group onwards in the present study and was a consistent feature from the third age group onwards. It was very conspicuous in the medium and small cerebral arteries in the early specimens but was consistently present also in large cerebral arteries in the older specimens.

The collagen increase in the tunica media of the cerebral arteries was especially very variable. The first increase of medial collagen was observed in the medium and small extracerebral arteries in a progressive manner from the beginning of the third age group; however, there were sporadic signs of medial collagen increase even before one year of age.

The manner of collagenization was observed to be due to the increased elaboration of collagen by the smooth muscle cells to some extent and proliferation of collagen from the adventitia. The increase in the adventitial layer of small intracerebral arteries was observed to increase with age such that in some cases the adventitia was observed to be thicker than the media and intima collectively. The increase of collagen fibers squeezed the smooth muscle cells around which they were present. Heavy collagen deposition was the common observation in the oldest animals. The apparent decrease in the medial thickness was a constant feature in old specimens.

The small and medium extracerebral arteries showed that the development and deposition of collagen with age was more interstitial than focal. The increased collagen constituents were focal in the early age groups, from third age group, but became diffuse by the fourth age group onwards.

The manner of the increased deposition was thought to be due to the proliferative activity of the smooth muscle cells; however, signs of collagenous increase from the tunica adventitia was also observed, such that particularly in the medium and small extracerebral arteries the tunica adventitia was equal to or about twice the size of the rest of the wall in the above arteries respectively. This was also true of the main cerebral arteries but in a lesser degree. This could be well appreciated above eight years of age particularly. The above condition in the small intracerebral arteries could be seen much earlier.

The increased collagen deposition in the large cerebral arteries revealed that these arteries were affected to a lesser degree than the others. The first signs of the focal collagen increase were seen in the subintimal zone of the media but in the latter age groups the proximal one-third of the medial layer was involved. The diffuse involvement of the medial layer was only observable above eight years but this fibrosis was far less than what was observed in the medium and small cerebral arteries.

In general, on the basis of the above changes in the cerebral arteries of the dog and pig, it was observed that the amount of fibrosis in the dog was higher in all vascular layers than in the pig.

Obersteiner (1884), Triepel (1896), and Hackel (1928) noted that the collagen increased in the cerebral arteries of man. Binswanger and Schaxel (1917) observed that the increased collagen in the small cerebral arteries was at the expense of the smooth muscle cells and elastic fibers.

Baker (1937) and Baker and Iannone (1959a,b,c) found a similarity in all categories of the cerebral arteries in the human. They observed that with aging, the increased collagen deposition varied in an ascending order from large cerebral arteries to small intracerebral arteries. These observations corresponded to the present studies in the dog and pig. The above authors found that there was hyalinization of the collagen in the small cerebral arteries after the fifth or sixth decade in the human.

Staemmler (1923) noted that in the muscular arteries of the human, in general there was an increased amount of collagen deposition by the third decade. The media of these arteries in the fourth decade showed rough collagenous bundles interlacing, leading to an abnormal arrangement of the smooth muscle cells. In the sixth decade the smooth muscle cells were scarce and their places were filled by collagen. Abramson and Turman (1961) discussed the changes in the tunica media of the muscular arteries and agreed with Staemmler (1923) and Baker and Iannone (1959a). The present study revealed similar changes regarding the abnormal

orientation of the smooth muscle cells in the normally aging media, their decrease per unit area and interstitial increase of collagen and acid mucopolysaccharides ground substance with age.

The present work indicated that collagen was scanty in the first age group. Whereafter, it started increasing with age. This has been observed by Troitzkaja-Andreewa (1931) in muscular arteries in general and by various studies on cerebral arteries in the human, Baker (1937), Baker and Iannone (1959a,b,c), Blumenthal et al. (1954), Klassen, et al. (1968) and many others.

According to Troitzkaja-Andreewa (1931) the accumulation of the collagen in the large muscular and elastic arteries was not focal but was present in small areas near the junction of the media and adventitia. Such a pattern was observed in the cerebral arteries of the dog and pig but in the earlier age groups accumulation of collagen at subintimal areas was also focal. The latter age groups showed that the collagen was, however, diffuse.

Studies on the cerebral arteries of the dog and pig done with particular reference to atherosclerotic changes by many workers did not mention the accompanying age changes in the medial layer. The exception to the above were the studies carried out by Braunmuhl (1956) and Dahme (1957, 1962, 1964, 1965 a,b). According to these workers the meningeal

and cerebral arteries of old dogs underwent degenerative changes which led to the loss of contractibility. Fankhauser, et al. (1965) indicated that fibrosis of the intima, media, and adventitia individually or combined was common in cerebrospinal arteries of old dogs, in agreement with the present findings.

Boueck (1959) observed that the vascular wall changes. He included collagen deposition in the intima and media and related them to the changes resulting from age involved connective tissues of the vessels.

Deposition of collagen in the normal vascular wall of the human with age was stressed by Levene and Poole (1962). They found that in normal aorta collagen deposition in the intima appeared by the second decade. They felt that this increase was related to the physiological rather than a pathological process. According to them this deposition occurred in response to aging to alter the mechanical and physiological behavior of the aorta. Similar deposition in the normal intima has been observed in the cerebral arteries of the dog and pig from third age group onwards in the present work. The present worker agreed with the above views and regarded that the production of collagen with aging was in response to the factors affecting the vessel wall and its constituents. The production of collagen in normally aging arteries may be in response to the mechanical, enzymic or metabolic insults.

The above production may be reparative to the above physiological disturbance.

According to Sinex (1968) during aging the smooth muscle cells of the media and elastin were exposed more to the chemical and mechanical factors than was collagen. The media under these conditions thickened and put most of the stress on collagen. Due to the presence of increased collagen and other inelastic substances, resistance was offered to the increased pulse pressure which apparently stimulated the intimal proliferation with more fibrosis and mucopolysaccharides which led to deposition of more collagen. He further stated that collagen may not be held responsible for the initiation of the above changes but was in response to the failure of normal functional activity of smooth muscle cells and elastin. He agreed that in later stages the deposition of excessive collagen led to the new structural and functional failures.

Solomon (1967) studied the effect of increased collagen in the different layers of the arterial wall with aging. He found that this increase resulted in increased rigidity, greater than the smooth muscle cells and elastic fibers. It provided a limiting factor to the extensibility of the vascular wall. The collagen of the media was arranged in such a

manner that it provided a protection against the tension in all direction.

Lowther (1963) and Sobel (1967, 1968) found that the increase in collagen content resulted in an increase in the diameter of existing fibers and formation of the new collagen. They observed that the production of the new collagen was not only chronological but also due to changes in the environment in which the fibroblasts or smooth muscle cells were present. This agreed with the views of Hall (1968 a,b) who postulated that the fibroblast could produce elastin or pseudoelastin or collagen depending upon the environmental conditions.

The production of collagen with aging in the different tissues of the body has been correlated with the activities of fibroblasts by numerous workers in the field of connective tissue research. However, in view of the facts, to be mentioned later along with the discussion on the elastic tissue and smooth muscle cell changes in the vascular wall, it will be appropriate to assume that the smooth muscle cells in response to the various intra- and extramural factors produced the collagen similar to the manner of release by the fibroblasts.

Sinex (1968) related that with aging of collagen fibers there was an increase in cross linkage. The collagen was

tanned with the metabolic products and ingested materials which were potentially capable of inducing cross linkages. This view agreed with that of Milch (1963, 1965) and Hall (1968a).

Elastic tissue The present study based on the cerebral arteries of the dog and pig indicated that the elastic tissue of arterial wall was mostly accentuated in the internal elastic lamina. This lamina was thick in comparison to other muscular arteries of the body. The elastic elements of the media were very few. The elastic fibers were also distributed in the tunica adventitia. The distribution of these fibers was not similar to other muscular arteries. These fibers were present circularly mostly in the junctional portion of the tunica adventitia with the tunica media. They appeared to be present in the form of one to three interrupted bands. These fibers were more predominant in the basilar, anterior and middle cerebral arteries, especially in the young and adult specimens. At places the arrangement of the elastic fibers simulated similar to the external elastic lamina of other muscular arteries.

The histomorphological age changes in the cerebral arteries of the above species revealed that the changes in the elastic tissue formed basis and initial age changes. These changes consisted of splitting, reduplication and

fraying, but were comparatively lesser in frequency in comparison to coronary arteries or aorta as reported by other authors.

The above changes in the arterial wall were assigned as wear-and-tear changes: Marchand (1904), Hueck (1920), Thoma (1923), and Aschoff (1939). Wolkoff (1923, 1929) and Jores (1904, 1924) recognized the splitting of the elastic lamina as the primary visible change in arteries with age. Moon (1959) designated the fracture, fragmentation and fraying of the internal elastic lamina as an initial change in the arterial wall. Ophulus (1907) regarded that the progressive deterioration of the elastic fibers was the most important change caused by aging. The above changes have also been noted by various workers in aortas, coronary, and uterine arteries: Skold and Getty (1961), Getty (1965, 1966), Gross, et al. (1934), Movat, et al. (1958). Luginbuhl (1966), Luginbuhl and Jones (1965), Detweiler and Luginbuhl (1967), Bal (1966, 1969) and many other workers.

In particular reference to the cerebral arteries in man as well as in the dog and pig, the splitting, fraying, and reduplication was observed by many workers. Principal among these were Triepel (1896), Tuthill (1930), Baker (1937), Baker and Iannone (1959a,b,c) Stehbens (1960), Zugbie (1961), Zugbie and Brown (1960, 1961), in man; and

Braunmuhl (1956), Dahme (1957, 1962, 1965a,b), Getty (1965, 1966), Luginbuhl (1965, 1966), Luginbuhl and Jones (1965a,b), Fankhauser, et al. (1965) and Detweiler and Luginbuhl (1967) in the dog and pig.

In addition to the above changes in the internal elastic lamina it was observed that with aging there was a change in the elastic tissue stain affinity represented mostly in the small extracerebral and intracerebral arteries which was generally observed from the fourth age group onwards in the present study. However, the loss of stain affinity for elastic tissue was also observed in medium-sized arteries and focally in large cerebral arteries of older animals. This condition was also observed by Baker (1937), Baker and Iannone (1959a) and Smith, et al. (1951) in aorta.

The internal elastic lamina of the cerebral arteries was thrown into tight indulations stimulating a beading-like pattern up to the four years of age in the present study; beyond this age the internal elastic lamina was observed to lose this pattern and assume a straighter form progressively, being present as a straight band below the endothelium and subendothelium in older specimens. This condition was also observed by Blumenthal, et al. (1954) beyond forty years of age in human cerebral arteries and in aorta after the fifth decade by Ahmad (1967). Solomon (1967)

observed that with aging, the elastic elements show lessening of recoils and they underwent hyperplastic and regressive changes. These elements became thickened and frayed. They lose their stain affinity and may even undergo calcification.

The changes in the elastic fibers in the tunica media and tunica adventitia observed in the present investigation, revealed that the elastic fibers increased with age up to the fourth group beyond which there was conspicuous deterioration evidenced by their fragmentation and granulation in the above layers. These fibers were surrounded by an increased amount of collagen and ground substance acid mucopolysaccharides.

Relative decrease and degeneration of the elastic tissue elements in the above layers of the cerebral arteries in man has been observed to occur with age by Binswanger and Schaxel (1917), who observed that in the individuals above fifty years of age there was decrease in elastic elements of the media. They noted that the elastic tissue increased only up to the above-mentioned age followed by deterioriation. This was also observed by Baker and Iannone (1959a) and Triepel (1896) in the cerebral arteries. According to Revault (1928, 1929), Myers and Lang (1946), and Blumenthal, et al. (1954) the elastic fibers fragmented and frayed with

aging leading to the loss of the elasticity of the arterial wall. Many workers, including the workers cited above, related the fragmentation of internal elastic lamina to excessive intra-arterial pressure greater than the tensile strength of the elastic tissue, which worked as an initiating factor.

A number of workers like Moon and Rinehart (1952), Bunting and Bunting (1953), Taylor (1953), Bertelsen (1963), and Bertelsen and Jensen (1960) believed that the fragmentation of the internal elastic lamina and elastic fibers was closely associated with the metabolism processes mediated through the intercellular ground substance and any imbalance could relate forementioned changes. They always found increased sulphated mucopolysaccharides around the degenerating elastic fibers. Moon and Rinehart (1952) stated that the fragmentation of the internal elastic lamina was due to intra-arterial tension. It was likely that the maintenance of elastic tissue and collagen by metabolic processes mediated through the intercellular ground substance was involved. The alterations in this mechanism secondary to nutritional or hormonal imbalance would produce quantitative and qualitative changes in the intercellular ground substance, collagen and elastic fibers.

In view of the present studies it was thought that the shifting of the smooth muscle cells and their disorientation in the subintimal area due to some atrophic changes which produced acid mucopolysaccharieds and collagen may lead to the pressure atrophy of the internal elastic lamina. This was in agreement with the observations of Murray, et al. (1966, 1968).

Schultz (1922) observed that the arteries working under high tension such as the aorta showed an increase of total elastic elements whereas in vessels in which pressure was low there was an actual decrease with aging. Gray, et al. (1953) suggested that increased tension served as a stimulus to the formation of elastic tissue. The above may be true in regard to the increased production of the rough and larger elastic fibers observed in small extracerebral and intracerebral arteries and may also be true for the lamellar elastosis working under high tension as observed in the present study.

Lansing, et al. (1950) mentioned that the changes with age in the elastin content may not be due only to decrease in elastin contents but may also be due to changes in the nature of the elastic tissue. In his subsequent studies in 1959, Lansing again related aging as a factor for the

deterioration of the elastin lamellae evidenced by fraying and fragmentation.

Hall (1964) studied the elastin contents of the aortic wall and found that there was an initial rise from birth to maturity in the elastin content followed by a marked decrease with aging.

A number of quantitative studies on the elastin content changes with age were made by Kraemer and Miller (1953), Scarselli (1961), Scarselli and Rappetto (1961) and Scarselli, et al (1960). They showed that there was an initial increase in the elastin content from 19-50 percent during the first twenty years followed by a definite decrease, being 26.2 percent at 63-88 years of age in the human. Bertolin (1958) agreed with the above findings and observed a decrease in elastin content of the aged human arterial wall. The apparent increase of the elastic fibers in the media may be due to the fact that elastic fibers which frayed or fractured or fragmented from the internal elastic lamina occupied new locations in the media.

Milch (1963) mentioned that the characteristic age changes in the native connective tissue appeared to be the loss of the water contents associated with the fragmentation and calcification of elastic tissue.

A number of studies regarding the process of elastolysis has been done since the past two decades. It was observed that elastase enzyme activity and its inhibitors were responsible for the above process (Balo and Banga 1953). Later Banga and Balo (1954) found that disturbance in acid base balance towards the acid side led to the gradual disappearance of the elastase inhibitors which freed the elastase to act on the elastic tissue of the arterial wall.

Studies of Lansing, et al. (1953), Balo and Banga (1953) and Lansing (1959) revealed that the elastase was produced in the pancreas. The amount of elastase decreased in old age thus depriving the elastic fibers from elastase activity. This was very important for the metabolism of the intact elastic fibers and so resulted in their destruction.

Balo (1963) observed that the loss of elastic fibers or tissue in the organism with age may be explained in two ways: one, with partial or total disappearance of inhibitors the elastase became predominant and may destroy elastic tissue; second, the pancreas ceased to secrete elastase with increasing age and for want of it the elastic tissue could not be renewed. Saxl (1957) also gave a similar view after observing marked reduction in the elastase inhibitor activity in middle and old age subjects. He related this to the elastolysis. In accordance with the above findings of

various workers it was inferred that the initial increase in the elastic tissue in the arterial wall may be due to changes in the elastase activity which decreased particularly in old age and could be responsible for the destruction and degradation of elastic elements in later life.

Hall (1968a,b) while agreeing with the various workers about the age changes in the connective tissue elements proposed that these changes were extracellular in fact, and assembling the products of fibroblasts in the extracellular space into original collagen subunits or cross linked hydroxyproline free units depended upon the time passed since its original synthesis. These fragments were reassembled by fibroblasts depending upon the nature and on the normal physiological changes in the environment. Also these changes determined whether relatively an inextensible or highly extensible substance was required such that synthesis of collagen or elastin or even pseudoelastin took place.

The above observations of Hall (1968a,b) can very well be correlated in view of the recent findings that the smooth muscle cells are the only main cellular components of the arterial wall. These elements have been assigned multifunctional properties by Buck (1963), Wissler (1967, 1968), Haust and More (1963), Geer and Guidry (1965), Luginbuhl (1965, 1966), and Luginbuhl and Jones (1965a,b). These cells were

observed to be responsible for production of connective tissue elements in addition to other potencies. As a parallel to the observations of Hall (1968 a,b) on fibroblasts, smooth muscle cells may also respond to produce collagen, elastin or pseudoelastin depending on time dependence, physiological needs and extracellular environment in the arterial wall.

Regarding the changing role of the elastic tissue Hass (1954), Lansing (1959) and Sobel (1968) considered that the elastic lamellae of the arteries were involved in more than mechanical support. They served as relatively impermeable barriers to the movement of materials between the media and intima in young subjects. Accordingly with age-related fraying and granulation of these fibers major changes may result in the manner of movement of the materials between the above two layers and also loss of elasticity.

Hass (1954) mentioned that the internal elastic lamina underwent degenerative changes. These changes in the internal elastic lamina affected its structural and chemical integrity and led to the structural modification in the overlying intima and subjacent media. The usual changes in the intima were proliferative whereas in the media these were degenerative. According to him these changes were age related and he mentioned that reduction in the tensile strength

was due to the transverse fracture of the elastic network. These discontinuities in aged elastic tissue decreased the effective amount of elastic tissue.

Ayer (1964) observed that the essential role of the elastic tissue was to allow in combination with the collagen, mucopolysaccharides and muscle a damping mechanism for contraction and stretch. Carton, et al. (1962) attributed loss of elasticity of the aging aorta to the loss of elastin which was substituted by collagen. Yu and Blumenthal (1958) observed that elastic fibers, in the young, were highly resistant materials with a primary function of returning distended structure to the original state. The changes with age in them included structural changes as mentioned earlier. The above age-related changes were responsible for loss of resiliency and increased rigidity. Similar studies on the aging of cerebral arteries, iliac arteries and aortas, with respect to the mechanical functional changes with aging, conducted by Burton (1954), Roach and Burton (1957, 1959) and Busby and Burton (1965) indicated that the elastic tissue underwent degeneration with aging which resulted in an increased of slackness in older arteries.

In view of the above findings and observations of different workers the splitting, fraying, duplication of the internal elastic lamina and initial increase in the elastic

elements of the vascular layers and their subsequent fraying, granulation and decrease was age related. These changes affected metabolic and mechanical functional integrity of the cerebral arteries with aging.

Lamellar elastosis The cerebral arteries of the dog and pig showed lamellar elastosis. This was represented as two or three annular bands of the elastic tissue at the junction of the intima and media. Frequently, a few smooth muscle cells were also observed to be trapped in the lamellar formations. The presence of lamellar elastosis may be due to hyperplasia of the elastic tissue. The presence of the lamellar elastosis was observed frequently in the dog and pig in the small extracerebral arteries up to four years of age.

The occurrence of lamellar elastosis, besides the degeneration of the elastic fibers was also often observed by Balo (1963). The hyperplasia of the elastic tissue was observed to be in various forms, lamellar elastosis being one those forms. This was generally observed in the small arteries and have been observed in the small arteries of kidneys by Lorincz and Goracz (1955). He observed that in mild cases there may be doubling or tripling of the internal elastic layer resulting into the narrowing of the lumen. Balo (1963) mentioned that this was also observed in the pancreas, liver, spleen, and seldom even in the brain. He attributed this as a response to hypertension and may occur in the cases of

atherscleroSis. He mentioned that in the small arteries the elastic tissue greatly increases with hypertension.

Baker and Iannone (1959b) observed that the internal elastic lamina of small intracerebral arteries occasionally showed the appearance of being in two to three layers. Klassen, et al. (1968) also observed the addition of elastic bands in the intima of the cerebral arteeies which were present in large arteries, but increased in frequency in small arteries in aging. There were not lamellar but were focal reduplication, which were different from the lamellar elastosis being referred above. The lamellar formation will correspond with the proliferative activity of the smooth muscle cells under stress in small cerebral arteries prone to increased hypertension in aging, reflected by the formation of elastic lamellae in lamellar form. The views of Balo (1963) seem appropriate regarding the increase of the elastic tissue in small arteries and correspond with the present observations which indicated that elastic fibers were more and thicker in the media of the medium and small extracerebral arteries and increased with age, up to four years, whereafter there was a decrease with their replacement by collagen.

Boyd (1961) mentioned that the lamellar elastosis was more marked in large arterioles, medium-sized arteries and to some degree in the smallest vessels. The internal

elastic plastic lamina was split into many layers. He mentioned that muscular-type arteries were converted into elastic-type so as to withstand greater strain and so were little more than passive conducting tubes.

Benninghoff (1930) also observed the lamellar elastosis and found to be present in specimens of middle age in humans. In view of the above findings, it seems that the small cerebral arteries respond to hypertension by having more elastic elaboration. This seems to be true also in relation to the present findings that in small cerebral arteries more elastic elaboration. This seems to be true also in relation to the present findings that in small cerebral arteries more elastic fibers were observed.

Smooth muscle cells According to Burton (1965) the smooth muscle cells of the media have the function to produce active tension by contraction under physiological control and so change the diameter of the lumen of the vessel. The way in which the smooth muscle cells were attached to the associated element wall offered mechanical advantage such that by the contraction of the smooth muscle cells the associated structures were pulled in causing the inner as well as the outer diameters to decrease. The smooth muscle cells in the small arteries have more resistance to blood flow than would the larger vessels. This was observed to be due to their

control on the lumen size. In the present study the smooth muscle cells in the early age group had vesiculated nuclei and were broader in comparison to the latter age groups in which they were elongated and narrower. It was observed that beyond the second age group the vascular smooth muscle cells were associated with more fibrous elements than in the earlier age group in which the collagen was almost absent. The smooth muscle cells in the arterial walls from birth to six months were very compactly arranged. However, with aging there was progressive loss of compactness such that the cells were widely apart in old age, evident by the nuclear count per unit area of the media in different age groups in both species. This was due to the increase in the connective tissue and ground substance around them with age. It was also observed that the above may also be due to a decrease in size of the smooth muscle cells which in old age were sometimes vacuolated. This was based on the preliminary studies carried out by observing the percentage of nuclei of the smooth muscle cells of the arterial wall per unit area in the middle cerebral and basilar artery of the dog and pig. These observations were restricted only to the larger cerebral arteries. The above observations confirmed the views expressed by Smith, et al. (1951), Ahmad (1967) and Sell and Scully (1965).

De faria (1965, 1968) observed that the smooth muscle cells were loosely placed in the tunica media of the coronary arteries in aged specimens and there was a lower percentage of smooth muscle cell volume in older specimens as compared to the younger specimens. According to him the decrease in volume was about 14 percent. The vessel thickness (medial) increased to approximately one year of age at a very rapid rate which led to the belief that the smooth muscle cells underwent proliferation. The smooth muscle cells forming the media in a one-day-old dog and a two-day-old pig was arranged in two to four layers in the dog and five to seven in the pig. The smooth muscle cell layers increased progressively reaching fifteen and twenty in the tunica media of the large cerebral arteries by one year of age in both species in the present study.

The changes in the outlay of the smooth muscle cells indicated many features occurring with aging in the present study. The smooth muscle cells in the vascular wall were observed to penetrate into the subendothelial layer at the frayed and fragmented internal elastic lamina in a number of cerebral arteries. The orientation of the smooth muscle cells varied at the site of branching as mentioned elsewhere. In addition to the above in older specimens as well as those showing intimal proliferation there was focal disorientation of the smooth muscle cells in the underlying media of the vessels.

Morehead and Little (1945) observed that the medial changes in the aortas of older dogs were due to focal loss of the elastic tissue with grouping and hyperplasia of the smooth muscle cells. Lindsay, et al. (1952a) observed that the smooth muscle cells were irregularly grouped in the media in aged dogs and related it to the edema. They also found that this was due to their hyperplastic nature and due to focal proliferation of the smooth muscle cells. All the above changes were related to aging in view of no detected disease in young dogs. Staemmler (1923) observed that the smooth muscle cells of the media showed abnormal arrangement in the fourth decade and were replaced by collagen in the fifth decade. Rottino (1939) observed that there was focal smooth muscle cell loss in the media of the human aorta which was replaced by mucoid substance and elastic lamellae came closer and he related it to age and focal ischaemia. According to Sell and Scully (1965) nuclear size and the number of vascular smooth muscle cells decreased with aging.

Movat, et al. (1958) stated that atrophy of the smooth muscle cells and loss of functional capacity of the elastic fibers along with increased collagen in the media and intima with aging predisposed focal arteriosclerotic lesions.

The present studies indicated that with aging the density of smooth muscle cells decreased, due to the increased

production of the ground substance and collagen around them progressively. This production was assigned to the smooth muscle cells themselves in response to some mechanical or metabolic changes causing a constant stress and so may undergo atrophy and take up different forms and orientations.

Evidence that the smooth muscle cells can undergo the mitotic process has been provided by Clark and Clark (1940) and Karrer (1960) who studied the development of the medial cells in the regenerating arteries of the rat and chick aorta. They found that the cells increased in number by undergoing mitosis of the existing cells. Karrer (1960) found that the smooth muscle cells developed from the fibroblast-like cells of the earlier embryonic stages, into typical smooth muscle cells.

Evidence has been put forth by a number of workers that the smooth muscle cells in the vascular wall were multifunctional. Evidence that these were the only cell components in the arterial media has been put forth by Pease and Paule (1960), Pease and Molinari (1960), and Buck (1963). The smooth muscle cells were assigned a number of functions by Wissler (1967, 1968). According to his view and in support of the earlier observations on which his hypothesis was based (Haust and More,1963; Haust, et al. 1960, 1965; Buck, 1961, 1963; Parker, 1960; Parker and Odland, 1966; McGill, et al.,1963; Wissler, 1965; Wolinsky and Glagov, 1964;

Constandinides, 1965; and French, 1966) he proposed that the smooth muscle cells were multipotent by producing collagen, elastin, mucopolysaccharides and basement membrane and could migrate in subendothelial space in addition to their contracting ability. The smooth muscle cells have been also thought to transform into macrophages and foam cells. Wissler (1967, 1965, 1968) defined arterial smooth muscle cells as multifunctional medial mesenchymal cells. According to Ross (1968) and Ross and Klenbanoff (1967) the smooth muscle cells which were mesenchymal may have a latent ability to synthesis under appropriate conditions.

Murray, et al. (1966, 1968) studied the behavior of the smooth muscle cells after different grades of injury and found that the smooth muscle cells became metabolically very active at least in terms of respiration and protein synthesis after a slight injury. The cells produced collagen fibrils and replaced the non-functioning smooth muscle cells. They found that smooth muscle cells behaved like fibroblasts. The smooth muscle cells may not recover, may become necrosed or may undergo metabolic and morphologic changes with the result that the cell membranes immediately after injury became swollen, the mitochondria altered and production of fat vesicles were seen so that it may become fat cell. According to them the arterial smooth muscle cells distant to the injured cells, may become active smooth muscle cells and

participated in healing. They postulated that in the development of atherosclerosis the medial cells were injured, became fat laden and migrated through the broken internal elastic lamina into the intima where they lost their polarity, became globose and with time accumulated increasing number of lipid inclusions.

The above corresponded with the views of Wissler (1965, 1967, 1968) and others which indicated that the sequence of changes observed in the atherosclerotic lesions could be similar. The smooth muscle cells in the media might be subjected to constant but slight insults with aging, due to metabolic disturbance, nutrition, imbalance in anabolic and catabolic processes and possibly may behave in a manner described by Murray, et al. (1966, 1968).

Similar results have been inferred by Knieriem (1967), Knieriem, et al. (1968) and Wissler (1968) who observed the behavior of smooth muscle cells in the aging aorta of bovine. According to them the smooth muscle cells played an important role in the morphogenesis of intimal proliferation. They observed the smooth muscle cells to be related in the elaboration of collagen, elastin, ground substance and acid mucopolysaccharides. The smooth muscle cells proliferated and migrated in subendothelial space to form the intimal thickenings. They credited the lipids formed in the smooth muscle cells as due to hypoxia. This has been further supported by

Garbarsch, et al. (1969) stated that the intimal changes might be secondary to the medial lesions as the media was more sensitive than the intima to the damages caused by systemic hypoxia. This was more relevant to the vulnerability of the middle part of the medial layer which was sensitive to slight systemic changes. Scott, et al. (1969) showed that in preproliferative stages of diet induced atherosclerosis in swine there was increased respiration of the smooth muscle cells which was related to more ATP synthesis induced by cholesterol feeding. It may be stressed that the behavior of the vascular smooth muscle cells underwent alterations due to the hypoxia, ischiaemia, and other mural changes like hypertension stress and so led to the excessive laydown of connective tissue, fat, acid mucopolysaccharides and even resulted in intimal thickenings associated with the presence of foam cells.

Intimal thickenings The intimal thickenings associated with medial changes have been categorized as atherosclerotic changes. It was always associated with the lipid deposition in the intima. Different interpretations of the terms relative to intimal thickenings have been reviewed.

A number of studies have been conducted on the occurrence of the initial thickenings on human and animal aortas and coronary arteries from time to time. A few of these studies have been mentioned elsewhere in the present text.

The present studies on the cerebral arteries of the dog and pig showed that the aging cerebral arteries were related to a number of different types of intimal thickenings. These were diffuse intimal thickenings and focal intimal thickenings; the latter were differentiated if they were on the branching site or on the rest of the circumference of the arterial intima.

Diffuse intimal thickenings (Subendothelial thickenings) The tunica intima of the cerebral arteries just after birth showed that the endothelial cell layer lay directly on the internal elastic lamina. This was observed to be the case until six months of age. Beyond this period the subendothelial space, which was undifferentiated earlier, started showing its appearance. This continued to increase in thickness from second age group onwards in a steady and progressive manner. The increase in this thickness was mainly due to the progressive increase in the thickness of the subendothelial space. This space was observed to be a fibrous zone of uniform width at different ages and increasing with age. The occurrence of this layer was a regular and constant feature throughout the vessel circumference. This diffuse thickening varied from similar thickenings in the aortas, coronary, iliac and femoral arteries of man as reported by different workers - Jores (1904), Gross, et al. (1934), Sappington and Horneff (1941), Wilens (1951 and Movat, et al.

(1958), who found that smooth muscle cells were always present in this type of thickening. They also found that the collagen and elastic elements were also present. On the contrary, studies on the aortas of rat, rabbit, cat, and ferret by Buck (1958), showed that there were only a few collagen fibers in the diffuse intimal thickening. Keech (1960) similarly observed the increase of collagen in the subendothelial space with aging in the rat aorta. The absence of the cellular elements in the normal subendothelial space of aortas and coronary arteries of the rabbit and rat were also observed by Pease and Paule (1960) and Parker (1960).

The absence of a very well developed diffused intimal thickening of the cerebral arteries under normal physiological conditions and unassociated with any change in the internal elastic lamina indicated that the occurrence of the large diffused intimal thickening associated with the smooth muscle cells in the arteries reported by earlier workers may be due to the susceptibility of the vessels in different regions of the body. However, a progressive and constant increase in intimal thickening (subendothelial) of the cerebral arteries, unassociated with internal elastic splitting, was related to an aging process in the present work. Balo (1963) mentioned that diffuse thickening of the arterial intima

occurred as associated with growth of arteries and hence with age. This increase continued until the third decade of life. Whereafter, the elastic tissue decreased and collagen increased with atrophy of smooth muscle fibers.

The diffuse intimal thickening has been assigned as aging due to its regularity and uniformity by Jores (1924), corresponding to the present findings. It may be pertinent to add that the above findings about the diffuse subendothelial or intimal thickenings were observed in arteries without any visible changes in the internal elastic lamina and was unrelated with the branching sites. The diffuse intimal thickenings could occur without involvement of the split in the internal elastic lamina or shift of the smooth muscle cells into the subendothelium as a normal age change; this was evident in the present findings on the cerebral arteries. There was increased collagen deposition as the thickenings increased from the second age group onwards in the dog and pig. The increased subendothelial space during aging may be due to the increased filtration and permeability with time. Klassen, et al. (1968) also observed that the subendothelial space in the cerebral arteries of man was an acellular homogeneous band having eosinophilic material. This band became prominent after four years of age and was visible in all arteries after ten years of age in man. They observed a definite trend towards its gradual thickening with

increasing age reaching a maximum at the fourth or fifth decade in man, in agreement with the present findings. However, diffused intimal thickening with a few mesenchymal or smooth muscle cells was present in the cerebral arteries of the dog from the age of ten years onwards in a number of cases.

Focal intimal thickenings The focal intimal thickenings in the aortas and coronary arteries of man and animals. These focal intimal thickenings when associated with lipid deposition have been defined as atherosclerotic thickenings. The intimal thickenings have been associated with aging by a number of workers reviewed earlier. The view that intimal thickenings were initiated by the splitting of the internal elastic lamina have been put forth by a number of workers like Ophuls (1907), Wolkoff (1923, 1929), Jores (1903, 1924), Hackel (1928), Wilens (1951), Gross, et al. (1934), Duff and McMillan (1951), Lindsay and Chaikoff (1963, 1966), Getty (1965, 1966), Davies and Reinert (1965), Luginbuhl (1965), and Detweiler and Luginbuhl (1967). According to them the internal elastic lamina split and fraying and duplication occurred as an early change related to age. The subsequent changes in the intima resulted in the formation of intimal thickenings which increased with age not only in frequency but also in the extent of the involvement.

According to Wilens (1951) the alterations in the elastic elements were associated with smooth muscle cell atrophy along with an increase of collagenous tissue which predisposed the development of atherosclerotis changes. Solomon (1967) mentioned that the intima thickened by splitting as well as by hypertrophy of the internal elastic lamina producing extension which entered into the intima. This layer proliferated and thickened. According to him the changes were more visible in the intima which involved focal laydown of the mucopolysaccharides, fat, smooth muscle cells and elastic fibers. These were age changes and not pathological.

Different views about the cell constituents of the intimal proliferation or thickening have been attributed by various workers. Altschul (1950) mentioned that the smooth muscle cells which were observed in the thickenings were derived from the endothelial cells. However, recent findings of the various workers cited with the discussion on the smooth muscle cells have indicated that the smooth muscle cells of the media entered through the fenestrated or split internal elastic lamina into the subendothelial space and transformed themselves into fibroblast, macrophages, foam cells or even retained their entities. This observation was further supported by experimental studies of Murray, et al. (1966, 1968). The participation of the endothelial cells

in the intimal thickenings and proliferating in the musculo-elastic thickenings were doubtful.

Smooth muscle cells entering the subendothelial space through the split internal elastic membrane has been well documented by Pease and Paul (1960), Buck (1961, 1963), French, et al. (1963), Murray, et al. (1966, 1968) and has been observed in the present work. The behavior of the muscle cells in the atherosclerotic plaque formations have been investigated by Parker (1960), Buck (1961), 1962), Haust, et al. (1960, 1965), Ross and Klenbanoff(1967), Parker and Odland (1966), Murray, et al. (1966, 1968), and Wissler (1967, 1968). Their observations indicated that the smooth muscle cells, during plaque formation, showed changes in the cytoplasm by having rough endoplasmic reticulum and golgi apparatus associated with increased production of the collagen, elastin, acid mucopolysaccharides, etc. These studies offered evidence to support the above view because there were no fibroblasts to account for the production of the increased connective tissue in the atherosclerotic plaques. Since the smooth muscle cells were mesemchymal, they may have the latent potencies to synthesize the connective tissue elements under appropriate conditions. The present observations indicated that the intimal proliferation in the cerebral arteries was more frequent and higher in degree in the case of the pig than in the dog. These increased with age.

The present findings in the cerebral arteries of the dog and pig indicated that the intimal proliferation was a constant feature in and after the second age group in the case of the pig. Whereas in the case of the dog intimal proliferation was present in a manner similar to the above but was not very pronounced. The dog showed more fibrosis of all the layers than the pig. The intimal thickenings with splitting of the internal elastic lamina were present in all age groups but frequency and severity increased with age represented by high fibrosis especially after three years of age. The intimal thickenings in contrast to the dog were well pronounced. The intimal thickenings were mostly associated with the internal elastic splitting. The smooth muscle constituents formed very large thickenings protruding and occluding the lumen of the vessels to a greater degree.

The observations showed that these thickenings were distributed in variable patterns: eccentric, concentric and focal. These involved the large cerebral arteries, their branches and even the perforating branches to the hypothalamus, thalamus, brain stem, cerebral peduncles and corpus striatum. The majority of the thickenings were observed to be associated with the anterior cerebral, middle cerebral, basilar, posterior communicating and basilar arteries in order of their involvements. The intimal proliferation

increased with age in frequency and degree especially after three years of age onwards. The intimal thickening became more fibrous and less cellular as age advanced.

The intimal thickenings in the dog and pig observed in the present study indicated that the smooth muscle cells were mostly involved and probably shifted through the internal elastic lamina split or fenestra and proliferated. They arranged themselves in different patterns in the intimal proliferation as well as in the underlying media indicating the shift was from the media which may be due to many factors occurring in the latter layer. The smooth muscles in the intimal thickenings elaborated collagen and ground substance acid mucopolysaccharides. The difference in the early intimal thickenings from the older one was due to heavy collagen deposition with possible atrophy of the smooth muscle cells in the latter. No attempts were made in the present study to localize fat in the intimal thickenings of the cerebral arteries. However, with special reference to the cerebral arteries of the pig, studies carried out by Getty (1965, 1966), Luginbuhl and Jones (1965a,b), Luginbuhl, et al. (1965), Fankhauser, et al. (1965), Luginbuhl (1966, 1965), and Detweiler and Luginbuhl (1967), showed that lipid deposition was associated with intimal thickenings in the pigs whereas in the dog the presence of

lipid was either absent or minimal. So, it was assumed that the intimal thickenings observed presently may be atherosclerotic at least in the pig.

The functional relationship of the intimal smooth muscle cells has been investigated and it was found that the intimal smooth muscle cells were capable of the formation of elastin and collagen by Buck (1961, 1962, 1963), French, et al. (1963), Haust, et al. (1960), and Haust and More (1963). The smooth muscle cells of the intimal thickenings have inclusions and have been reported by Geer, et al. (1961), Haust and More (1963), McGill and Geer (1963), Geer and Guidry (1964), Geer (1965), Getty (1965, 1966), Luginbuhl and Jones (1965a,b), Luginbuhl, et al. (1965), Luginbuhl (1965, 1966), Detweiler and Luginbuhl, (1967) and many others. The manner in which the intimal smooth muscle cells accumulate lipid has been debated among different workers in the field.

The observations of the workers already reviewed on the cerebral arteries of man, dog and pig indicated that the cerebral arteries showed intimal thickening comparatively later in the life of the subject. However, this was not the case as far as the pig was concerned as reported by Luginbuhl and his associates (cited earlier). They observed that the intimal thickenings in the cerebral arteries

were more frequently and were more severely affected than the coronary arteries in the aged pig.

The present studies which were restricted to cerebral arteries only tend to agree with the above in view of frequency and severity.

That intimal thickenings of the cerebral arteries are age related has been the view of various workers cited earlier. Baker (1937) and Baker and Iannone (1959a,b,c) observed that the atherosclerotic lesions in larger cerebral arteries appeared as early as second decade and its severity and frequency increased with age. In later studies, Flora, et al. (1968) mentioned that there was hardly any doubt that the cerebral atherosclerosis gradually increased with age but suggested that the age was an important accompanying factor.

Giertson (1964) studied the interrelationship of atherosclerosis of the aorta, coronary and cerebral arteries by chemical techniques and found that chemically atherosclerosis increased progressively and nearly linerally with age until the eighth decade. His correlation of atherosclerosis with age was very strong with occasional individual variations. Similar relationships were drawn by Moosy (1959) based on histological findings.

Winter, et al. (1950) graded the different degrees of atherosclerotic involvement of the cerebral arteries in the

human and observed that the grade of involvment increased steadily with age. The increase was more rapid beyong the fourth decade. The middle cerebral artery was more severely involved than the anterior cerebral or the internal carotid arteries. Klassen, et al. (1968) observed the cerebral arteries of man and found that the intimal thickenings were observed to occur more frequently and more extensively as age advanced. A similar trend was observed in the present work.

Blumenthal, et al. (1954) observed atherosclerotic changes in the cerebral arteries of man and found that these thickenings were age related, in response to mechanical and haemodynamic factors. Getty (1965, 1966) observed the atherosclerotic changes in aging cerebral arteries of the pig. Similar relationship has been drawn in the dog and pig by Braunmuhl (1956), Dahme (1962, 1957), French, et al. (1963), Jennings, et al. (1961), Luginbuhl, et al. (1965), Luginbuhl (1966, 1965), Luginbuhl and Jones (1965 a,b), Fankhauser, et al. (1965), and Detweiler and Luginbuhl (1967).

Dahme (1965a) mentioned that there was no doubt that intimal sclerosis and stiffening of the arterial wall was a normal aging process and termed uncomplicated aging process as physiosclerosis. He observed that in the case of the dog small meningeal arteries and cerebral arteries the changes were restricted to medial changes which caused loss of contractability conforming with the present findings.

The focal intimal thickenings at the site of branching, observed in the present study have been assigned different names and functions as described in discussion on branching sites of high physiological activity and were subjected to hemodynamic stresses.

The age changes in the focal intimal thickenings have been reported by various workers, Stehbens (1959, 1960, 1965), Jennings, et al. (1961) and Hassler (1961, 1962a,b,c) in the cerebral arteries of man and animals and Klassen, et al. (1968) in man. These focal intimal thickenings were observed by them to be located at the site of branching. Their findings indicated that these were sites of predilection for atherosclerotic changes. They observed that changes observed in the focal intimal thickenings at branching sites were more frequent and earlier than the focal intimal thickenings elsewhere on the arterial wall. Their size increased similarily. Lipid deposition was observed by them. According to Hassler (1962a,b,c), the structural composition of the intimal cushions varied with age. He found that the intimal cushions of the young and infant cerebral arteries had more smooth muscle cells, more elastic fibers and minimal collagen whereas with age the smooth muscles and elastic fibers decreased but collagen increased. He found that the muscular thickening under the cushions decreased with age, De faria (1961) observed the musculoelastic cushions and

commented on the unsettled nature of their presence, normal change or arteriosclerotic change. He found that the cushion size increased with age.

According to Hassler (1962a) there was confusion prevailing concerning the normal physiological and atheromatous intimal thickenings of cerebral arteries. Hackel (1928) and Glynn (1940) emphasized the differences and mentioned that no fat was observed in physiological intimal thickenings. Robertson (1960 a,b) and Blumenthal, et al. (1954) observed that the cushions underwent fibrosis and lipid deposition with increasing age. These changes were similar to the changes observed at non-branching areas but were early. The present work was in agreement with the above views. The changes observed in and beyond the third age group of present study indicated that the changes were well evident. The changes observed in the intimal cushions in the present study indicated that with advancing age in addition to the increase in size there was loss of elastic tissue also. There was increased collagen deposition with atrophy of the smooth muscle cells. The preliminary work on localization of fat in the intimal cushions showed that there was extracellular lipid deposition present in old age.

Acid mucopolysaccharides The present studies on the cerebral arteries of the dog and pig indicated that acid mucopolysaccharides in the arterial wall increased with age.

The increase was diffuse in the arterial media, mostly the inner half, but was also focal at the sites of branching, intimal proliferations and intimal cushions. The increase was significant in the latter two as the intimal proliferations and intimal cushions underwent fibrosis more rapidly with aging. The initial signs of the increase with age were subintimal which became diffuse in the medial layer later as it underwent fibrosis. The intimal cushions in the first and second age groups showed low acid mucopolysaccharides content as compared to the latter age groups (tinctorially).

The changes in acid mucopolysaccharides in the arterial wall with aging have been the subject of various studies: Wislocki, et al. (1947), Bunting (1950), Bunting and Bunting (1953), Taylor (1953), Moon (1957), Moon and Rinehart (1952), Berenson (1961), Movat, et al. (1958), Moore and Schoenberg (1959), and Bertelsen (1961, 1963) on the aorta and coronary arteries of man. The above workers regarded that the deposition of the acid mucopolysaccharides was related to the oxygen tension in the vessel wall. The deposition increased when the oxygen content of the arterial wall decreased, which was particularly the case in the proximal half of the tunica media which was devoid of vasa vasorum.

The increased deposition with increasing age was also related to the fragmentation of the elastic fibers and lamina in the tunica intima and media by most of the above-mentioned

workers. They also observed that the increased deposition was constant or decreased after four or five decades, also agreed by Bertelsen and Jensen (1960), Bertelsen (1963), Kaplan and Meyer (1960), Taylor (1953), and Buddeck (1962). A similar increase in the chondrotin sulphate with age was observed by Ahmad (1967) and Kumar, et al. (1967 a,b) in the aorta up to the sixth decade beyond which there was a decrease in the aortas and coronary arteries of man.

Studies of Taylor (1953) indicated that the ground substance condensed in the focal areas of the arterial wall with advancing age. He always observed the association of degeneration of the elastic elements with the above increase in acid mucopolysaccharides. He inferred that this deposition was secondary to the alterations in the elastic elements. Whereas, Zugbie (1962a,b; 1963a,b) and Zugbie and Brown (1959, 1960, 1961) observed that the increased acid mucopolysaccharides in the aortas, coronary arteries, and cerebral arteries of man was associated with collagen. They found that the increase was progressive with advancing age. They observed that the increase was present in areas which were devoid of elastic tissue. They associated this increase with the coarse collagen. The increase was conspicuous in old age at the sites or reduplication of the internal elastic lamina and intimal proliferation. They confirmed the same in their repeated studies and supported the views of Kaplan and

Meyer (1960). According to the latter, there was consistent association between chondrition sulphate B and collagen to strengthen the arterial wall with increasing age, at the site of fragmentation of the internal elastic lamina.

Bertelsen and Jensen (1960) and Bertelsen (1963) recognized that the acid mucopolysaccharides were present normally in the arterial wall throughout the life to some degrees. Balo (1963) agreed with the above and noted that the increase may be due to destruction of the elastic and collagen fibers because acid mucopolysaccharides were constituents of the above fibers as suggested earlier by Hall, et al. (1952, 1955). De faria (1965, 1968), however, believed that the increase was a reparative process due to decrease in the elastic elements and smooth muscle cells. During the present study it was observed that there was decreased density of smooth muscle cells per unit area with a consequent increase in the acid mucopolysaccharides ground substance and other fibrous elements with aging of cerebral arteries. This corresponded with the above views.

Flora, et al. (1967) observed that there was an increase in the ground substance in aging cerebral arteries of man both in the intima and media. They accounted this increase was due to smooth muscle cell functions. They suggested that the increased ground substance with aging played a primary role in intimal thickenings. The increased ground substance was observed by them to be present in the intimal

thickenings without or with very little fatty deposition which suggested that the increased ground substance preceded or perhaps predisposed the development of lipid deposition.

Increase in the sulphated acid mucopolysaccharides has been observed in the aorta, coronary arteries and basilar arteries by Curran and Crane (1962) and Genda (1966). The latter found this increase with age in arteries relatively free from atherosclerotic changes. He again stressed the views of the other workers that this increase in acid mucopolysaccharides may play a prominent role in subsequent atheroma formation. Knieriem (1967) and Knieriem et al. (1968) observed the increased acid mucopolysaccharides and ground substance with aging in the bovine aorta. They a agreed with the above views. Wissler (1967, 1968) and other workers, mentioned elsewhere, believed in the pluropotential nature of the smooth muscle cells and regarded that these cells were capable of producing the increased ground substance and acid mucopolysaccharides.

Bertelsen and Jensen (1960) and Bertelsen (1963) stated, in agreement with most of the workers, that the ground substance increased progressively with age and will cause the medial cellular and fibrous elements to separate with aging as was also observed in present work. The increased ground substance not only affected the elastic fibers which have straightened and fragmented but also impeded the metabolic

processes. Muir (1964) and Likar, et al. (1968) agreed with the above and stated that the physio-chemical changes in the ground substances will produce changes in the permeability, diffusion, sedimentation and loosening of water binding system in the tissue which may cause metabolic disorders.

Lehninger (1959) stressed the changes in the extracellular composition of the tunica media was concerned with transport by diffusion of O_2, CO_2, foodstuffs and waste products to and from the intima and vasa vasorum. Any change in the surrounding will not only modify the physical properties of the wall elasticity but in permeability and rate of transport as agreed by Kirk (1959).

Garbarsch, et al. (1969) in their study on arteriosclerosis and hypoxia observed that the changes were exclusively in the tunica intima and tunica media (inner half). The changes observed were in the intercellular substance which was focal and diffuse. This increased ground substance resulted in changes such as increased distance between the elastic lamellae and fibers, disintegration and splitting of the above fibers. According to them, these changes were reparative in response to hypertension and hypoxia.

Sobel and Marmortson (1965) and Sobel (1967, 1968) agreed that increased connective tissue (fibrous and amorphous) around the cells with aging impeded the nourishment of the

cells. He stressed that the changes in the microenvironments of cells contributed directly or indirectly in the genesis of cellular age changes by decreasing the rate of transfer of molecules to and from the cells. He agreed with Casarett (1964) that increased ground substance and collagen accumulation reduced the capillary filtration and impaired the diffusion due to the above increase in histohematic barrier. The ground substance became apparently less permeable in old age so causing decreased nutrition.

Similar views have been put forth by Schallok (1962) who regarded that all the substances needed by the smooth muscle cells of the media should penetrate the ground substance to the cells where they were metabolized. The increased viscosity of the gel occurring due to changes in the composition will decrease the oxygen permeability and so the smooth muscle cells will be deprived of the necessary oxygen for their metabolism. He stressed that the change in the vicinity of the ground substance formed a most important principle governing atherosclerosis. He supported the views of Hauss and Jung-Hulsing (1961) and Hauss, et al. (1962) who observed that there were changes in the subendothelial and intramedial layers of ground substance in the rabbits fed on atherogenic diet before fat deposits were discernible. He regarded that the development of the atheroma like

formation of new connective tissue, was preceded by processes which impeded the passage of metabolites.

Medial defects The medial defect observed in the present study on the cerebral arteries of the dog and pig showed that these were related to the sites of branching. These were observed frequently in the large and medium cerebral arteries. The medial defects varied in degree in different arteries.

The presence of these defects was reported by Forbus (1930), Glynn (1940) and Carmichael (1945, 1950) in the cerebral arteries of man. According to Forbus (1930) these were congenital in origin. But, according to Glynn (1940) the defects were acquired in infancy and their frequency increased with age. He further observed that there was a difference in the frequency of the aneurysms occurring in the cerebral arteries than the other arteries. This was related to the elastic tissue. The elastic tissue in the intima of the cerebral arteries was very strong in comparison to other arteries (muscular). Whereas, in the latter, the elastic tissue was distributed more in the media and adventitia than in the cerebral arteries. He proposed that the arteries with lesser elastic tissue in the media and adventitia were more prone to aneurysms.

Bremer (1943 suggested that the medial defects were not weak points in the continuity of the arterial wall. These

were rather reinforced and strong to counteract any mechanical or hemodynamic factors. He suggested that the intrusion of the mass of the adventitial tissue was a reinforcement like the stem of the boat which otherwise would give way under the force of the oncoming streams.

Stehbens(1957) observed the medial defects in the cerebral arteries of the dog, horse, and sheep at the branching sites. In his further studies in 1959 and 1963, he observed the medial defects opposite the intimal cushions. He agreed that these were not congenital and were more in aged cerebral arteries. He regarded that the medial defects were due to degenerative processes secondary to some mechanical factors. He found that the adventitia sometimes lay almost against the internal elastic lamina. Similar defects were observed in the present work. The collagen wedged between the defects in the medial layer and the fibers were longitudinally oriented as opposed to the normal circular arrangement. Jennings, et al. (1961) observed the presence of the medial defects in the cerebral arteries of the pig and explained their presence in a manner described by Stehbens (1957, 1959, 1963).

Blumenthal, et al. (1954) observed that there were structurally weaker areas in the arterial tube but the tension at these (branching) points was greater and may introduce muscle defects at the branching sites. Since the branches were generally smaller than the main artery, their operating tension,

therefore, was also smaller. It was possible that the effective tension at the mouth of bifurcations was that of the parental artery while the structures on which it acted were weaker (branch). Forbus (1930) also cane to the same conclusion and postulated that the pressure within the branchings and bifurcations was not exerted equally but was greatest at the point opposite the long axis. Hassler (1961) observed medial defects in the arteries of the circle of Willis in human, dogs, cows, horse, and rabbit. He quoted Koppen (1927) and Ask-Upmark and Ingvar (1950) who observed aneurysms in the basilar artery of the colt and llama. Hassler (1961) found that the medial defects in the dog were present mostly in the internal carotid, posterior cerebral, basilar and vertebral arteries. The defects were related to branching points and some were covered by intimal cushions. He explained that the junction of the main trunk and branch was more exposed to the streaming blood. The hemodynamic strain then might not only be responsible for the development of medial defects but also the aneurysms. The smaller defects below the intimal cushions may be due to pressure atrophy or bursting of a congenitally weak seam between the main trunk and branch.

Glynn (1940) who observed the medial defects, subjected the cerebral arteries to raised internal pressure, but found

that the defects did not yield to this, indicating that these were not weak points.

It seemed that the medial defects were very much related to the formation of the intimal cushions and branching site as their occurrence was generally related to the above. The presence of these cushions which were formed due to the hemodynamic response perhaps caused the shift of the medial cells to the new locations at the site of branching. The defects or gaps so formed were repaired or occupied by adventitial tissue (collagen) to reinforce this. It seemed that the intimal cushions which were more prone to age changes were responsive for increased frequency of the defects, such that it seems probable that the intimal cushion formations and their subsequent changes with age under continuous physiological stress, go hand in hand with the medial defects in degree and frequency.

The contention that these were responsible for aneurysms and were the sites of predilection for the above seemed to be contrary to the fact that the gaps so filled by the collagen were rather strong and resistant to normal or abnormal forces until some atrophic factors may play a part in it. However, the degree of the medial defect locally may increase with age due to subsequent smooth muscle cell atrophy and fibrosis of the media.

The relative absence of the aneurysm in the cerebral arteries in animals in comparison to other muscular arteries may be attributed to relatively thicker and stronger internal elastic lamina in the intima of the cerebral arteries.

Effect of aging on the cerebral arteries in the dog and and pig The various degrees of intimal proliferations in the cerebral arteries will affect the blood flow to the dependent regions of the supply. This will affect the changes in the parenchymatous tissue because of a decreased amount of the nutrients otherwise supplied in the mormal conditions in young and adult animals. Aside from this the connective tissue changes (elastic and collagen) in the cerebral arteries will multiply the above-mentioned sequlae. During aging, unassociated with intimal proliferations, the cerebral arterial wall showed that there was increased deposition of the collagen in all layers.

According to Burton (1954) the elastic tissue was effective over normal blood pressure range whereas the inextensible collagen acted as a supportive beyond the normal range of blood pressure. This was contradicted by Wolinsky and Glagov (1964) who observed that the circumferentially aligned collagen fibers bore most of the stressing forces at physiologically normal blood pressures. According to the above, the elastic tissue helped in uniformly distributing the stresses involved. But with aging the tensile strength which depended on the

collagen increased whereas the ability to uniformly distribute the stress was comparatively decreased.

The normal blood vessel was observed to have three times more circumferential elasticity than the longitudinal, Roach and Burton (1959). During aging, according to the above authors, the longitudinal as well as circumferential elasticity of the blood vessel decreases. This was assigned by them to the increased collagen proportion and their physiochemical stability with age.

Busby and Burton (1965) found that the longitudinal extensibility decreased markedly after thirty years of age in the cerebral arteries of man. This was attributed to greater stiffness of the arteries beyond the above age group. They found that with increasing age the major cerebral arteries became less distensible. These changes were attributed to the progressive failure of the vessel wall to retract due to the loss of recoiling of the elastic fibers with age. That the arterial wall appeared to become stiffer with age was also suggested by Banga and Balo (1961).

The present findings revealed that the small and medium cerebral arteries showed heavier collagen deposition in comparison to the large sized cerebral arteries. This occurred much earlier in the former than in the latter category of arteries. According to Casarett (1964) the smallest blood vessels with their thin wall and narrow lumen were more important

in the fundamental age changes than were the larger vessels. The increased fibrosis of such small arteries and arterioles was associated with the functional effectiveness of the blood circulation. The progressive increase in the degree of these processes with increasing age eventually reached a point at which the functional inadequacy was involved in terms of support of the dependent parenchymal cells, leading to the gradual loss of these cells at varying degrees and rates in different tissues. Their resultant fibrosis, narrowed lumen and increased wall thickness increased the histohematic barrier progressively leading to the decreased functional effectiveness of the above barrier in terms of selective diffusion, transport of nutrients and waste products across the barrier. According to him aging was due to the increased histohematic barrier between the vascular wall and the dependent parenchymal cells through which O_2, CO_2, nutrients and wastes must pass. The increase in the histohematic barrier was due to the increased fibrillar density and in the collagenous fibers with a relative increase of ground substance leading to fibrosis. According to present worker the same seemed true about the arterial wall which itself represented an organ receiving nutritions through distant sources and could be affected by increased histohematic barriers due to progressive increase in the interstitial connective tissue elements around the smooth muscle cells which reflected its effect on the latter.

Sobel (1968) stated that increased fibrous elements and ground substance around the cells impeded its normal nutritional and excretory processes which formed the basis for the cellular aging. Cowdry (1933, 1952) also speculated that the increased fibers may obstruct the flow of fluid when densely packed.

Hass (1954) supported the above views and mentioned that the aging process as a factor for arteriosclerosis was self-evident. The fundamental age changes occurring in the fibro-elastic framework of arterial wall were distinct because of their remote blood supply and nutrient transfer. The maintenance of this framework and the enclosed cells depended upon acquiring necessary nutrients and elimination of metabolites by diffusion over relatively long distances. The changes in the supporting connective tissue limited the process of diffusion and caused medial change.

Lipofuscin Pigment in the Brain of the Dog and Pig

The neurons of the mammalian nervous system have been categorized as postmitotic cells. These cells reached their final state of differentiation during early postnatal life. They rarely under further differentiation, cell renewal or cell division. These characteristics were in contrast to other organs and tissue whose cells continuously underwent cell differentiation, cell renewal and cell division to replenish the

cell loss. The cardiac muscle cells have also been recognized as postmitotic cells.

A number of workers, cited in the review, observed that the postmitotic cells underwent certain changes during their lifetime which was depicted by what was defined as wear-and-tear pigment, lipopigment or lipofuscin.

Bondareff (1957, 1959, 1964), Strehler, et al. (1959), Strehler (1962), Whiteford (1964), Whiteford and Getty (1966), Few (1966) and Few and Getty (1967) concluded that in the postmitotic cells, the most consistent morphologic observations was the accumulation of the lipofuscin pigment with increasing age.

It has been estimated by Brody (1955) that in some areas of the brain more than 20 percent of the neurons may be lost by the seventh decade of life in man. This presumingly indicated that the considerable loss of cells may be one of the leading features of biological aging leading to a functional impairment associated with cell loss from the brain as well as from other tissues in which cell division did not occur as suggested by Strehler (1967). Similar views were also exhibited by Samorajski, et al. (1964, 1965) who mentioned that the accumulation of the pigment may affect all aspects of cellular physiology and possibly result in the loss of neurons.

From the review cited it will be clear that since over a decade attempts have been made to study the localization,

distribution, origin and significance of the presence of the lipofuscin pigment, repeatedly. The present study was conducted on the fifteen nuclear areas of the brain in the dog and twelve nuclear nuclear areas of the brain in the pig. The subjects included were reared under similar normal environmental conditions with feed and genetic history known. The animals were raised for gerontological studies.

It was observed that the pigment increased with advancing age in different nuclei. The pigment was observed to appear first in a fine granular form in the perinuclear areas of the neurons which was then seen to appear in the form of focal accumulation, either in perinuclear, polar or bipolar or axonal part of the neurons. The latter was polar in location but was present at the axonal hillock of the neurons.

The sequence of the presence of the pigment in the different nuclear areas of the brains in the dog and pig showed that the lipofuscin appeared earlier in some and late in the others. Similarly, the variations in the amount of the pigment per unit sectional area and intracellular pigment were also observed which will be discussed subsequently.

A number of hypotheses regarding the origin of the pigment granules have been put forth by a number of workers. Payne (1949, 1952) revealed that the mitochondria of pituitary gland, adrenal gland and throid gland of old fowl underwent significant alterations with age. The correlation of such

changes with increased age pigment accumulation resulted in the suggestion by the above worker, that mitochondrial alterations or degenerations resulted in pigment formation.

The lipofuscin pigment derived from the altered mitochondria was further supported by the works of Hess (1955), Duncan, et al. (1960) and Gosh et al. (1962). The mitochondrial origin of the pigment was refuted by Bondareff (1957) who suggested that the pigment associated vacuoles were delimited by a single membrane and not by the double membrane of mitochondria. The single layer enclosed nature of the pigment was further supported by a number of workers.

The origin of lipofuscin pigment was also related to the endoplasmic reticulum. This was suggested by Strehler (1964) and Kimamoto and Bourne (1963) but was speculative only and did not receive much attention. The morphologic changes in the golgi apparatus led to the formation of pigment was propounded by Gatenby and Moussa (1950) and Gatenby (1953). They suggested that the golgi apparatus tends to fragment with increasing age and was transformed into pigment which occupied different locations in the neuronal cytoplasm.

The introduction of the lysosomes into the problem of lipofuscin genesis received considerable attention following the works of de Duve (1959), de Duve and Wattiaux (1966), Novikoff, et al. (1956), Novikoff (1961), Essner and Novikoff (1960). They suggested that the pigment granules were altered

lysosomes. Studies of Samorajski , et al. (1964, 1965) and Brandes (1966) regarding the enzymic activity of the lysosomes and lipofuscin pigment showed that the altered lysosomes had similarities with the pigment.

Few (1966), Few and Getty (1967), Munnell (1967), and Munnell and Getty (1968) supported the view that the pigment granules appeared to be formed by the coalescence of altered lysosomes and other cellular organelles in varying degrees of autolysis. They suggested that the lysosomal enzymes were responsible for the autolysis seen in these organelles.

Few (1966) observed that the normal lysosomes were less frequently observed in old age indicating the decreased normal lysosomic activity which could have an adverse effect on the functional activity of the cell. This was in accord with the views of Samorajski, et al. (1964). The above workers as well as Munnell (1967) supported the view that lysosome played a definite role in the genesis of the pigment.

Friede (1962) observed that the nerve cells with strong succinic dehydrogenase and DPN-diaphorase activity in their cytoplasm contained more lipofuscin than nerve cells characterized by little enzyme activity. He observed the experimental manipulations resulting in marked decrease of DPN-diaphorase activity were accompanied by the decreased presence of lipofuscin. He observed that there was cross correlation between functional activity, oxidative enzymatic activity and

deposition of lipofuscin. He regarded the lipofuscin formation, whatever the origin, to be a reaction byproduct of cells possessing strong oxidative enzymatic activity. This appeared to be the situation in cardiac and neural tissue, Toth (1968). He mentioned that the evidence presented thus far showed that the lysosomes represented the ultimate source of lipofuscin and that lysosomal enzyme activity can account for the apparent formation of lipofuscin from all other cell organelles. The above view corresponded with the earlier observations of de Duve (1959), Samorjaski, et al. (1964, 1965, 1968), Few (1966) and Munnell (1967).

Significance of lipofuscin

Dolley (1911,1917) regarded the presence of the pigment as due to the functional depression of nerve cells. Altschul (1938) suggested that it was equally logical to assume that the lipofuscin was a physiologically important material which accumulated as a result of decreased cellular activity. He attributed its appearance as the result and not the cause of cellular disfunction.

Altschul (1943) further pointed out that the presence of the lipofuscin pigment in the neurons represented some changes in the metabolism of cells, difficulty in eliminating waste products of normal metabolism or replacement of some inactive or absent constituents of the cell cytoplasm by an auxiliary

material. He regarded the presence of pigment as a sign of a weak cell. Ellis (1920), while studying the aging of human cerebellum, observed that there was appreciable decrease in the purkinje cells and there was no pigmentation even in the oldest specimens. He found that on the contrary, the cells of the dentate nucleus were disintegrating to a lesser degree but had pigmentation developed. A number of supporting and contradictory views regarding the significance of the presence of the lipofuscin pigment have been put forth. Murray and Stout (1947) stated that the pigment in the neurons could interfere with the plasticity of the cells and so could be detrimental to their normal functions. Sulkin (1955) observed that the lipofuscin granules seemed to be more widespread in efferent than the afferent neurons. This was also agreed by Few (1966) and Few and Getty (1967). They found that the autonomic cells were most resistant to pigmentation and efferent ventral horn cells of the spinal cord were less resistant. These differences were progressively reduced as the animal increased in age.

Wilcox (1956, 1959) has suggested that the highly active cells tend to accumulate less pigment than the less active ones. He reported that the earliest pigmentation occurred in the mesencephalic nucleus of the trigeminal nerve, the activity of which was only slightly less than that of the somatic brachiomeric motor nuclei. He also observed that the

exteroceptive sensory nuclei which were more or less continuously fired were quite slow to accumulate lipofuscin. He found that in the cochlear nuclei, dorsal motor nucleus of vagus nerve and perhaps in the nucleus of Edinger-Westphal there was no pigment accumulation even in the oldest specimens. This was contrary to the findings of Whiteford (1964), Whiteford and Getty (1966) and present findings. The latter studies showed that the pigment accumulation was definitely present in the above nuclei both in the dog and pig.

Strehler, et al. (1959) suggested that the pigment particles may act as binding agents between the contractile elements of the cardiac muscle which could be detrimental. Bjorkund (1964), however, mentioned that biochemically the increase in the pigment concentration with age, the partial solubility in the lipid solvents and the resistance to acid hydrolysis indicated that the pigment may be only an accumulation of inert waste products. However, Samorjaski, et al. (1968) assumed that the progressive accumulation of the intraneuronal pigment may result in some significant consequences for the cellular metabolism and neuronal physiology. Studies of Friede (1962) also exhibited similar views cited earlier.

Strehler, et al. (1959) proposed three alternate possibilities to elaborate the effect of accumulation of lipofuscin pigment in the cardiac muscle: one, the pigment interfered with the efficient working of heart muscle; second, the

inclusion represented some advantages functional unit developed to compensate for some other loss; third, these bodies did not affect the function appreciably either positively or negatively. They considered the first as the most likely whereas Munnell (1967) and Munnell and Getty (1968) were in favor of the second alternative. They regarded that this by-product or endproduct was essential to maintain these cells in the undividing state over long periods.

Reichel, et al. (1968) indicated that it was difficult to define what represented greater physiological activity of a given cell in vivo. They mentioned that any speculation about the relationship between the activity level and pigment accumulation would be premature. According to them a complete survey of central nervous system would be essential before valid generalizations about the pattern of pigmentation could be made. This might answer whether the area involved was primarily motor or sensory, or associative or vegetative and whether the pigmentation was related to metabolic variations.

The present investigations revealed that the resistance of the different nuclear masses in the brain of dog and pig may be diminished progressively with increasing age. This can be well evident if the increasing trend of the pigment per unit sectional area, percentage of pigmented neurons and intraneuronal pigment was taken into consideration similar

views were exhibited by Andrew (1956), Sulkin (1958) and Few (1966).

In regard to the above the changes in the blood vessels supplying the different nuclear masses should be taken into consideration. The present study in which the age changes in the extra- and intracerebral arteries were studied simultaneously, revealed that the cerebral arteries showed significant age changes which directly affected the blood supply to the different areas of the brain. The blood vessels showed connective tissue changes and intimal thickenings occurring progressively with age, so impeding nutrient blood supply to the target areas.

Casarett (1964) postulated that the progressive age changes in the small blood vessels led to the functional inadequacy in term of the support to the dependent parenchymal cells and subsequently to the gradual loss of the cells at varying degrees and rates in different tissues. No attempts were made to study the eventual neuronal loss with age in the present work. However, Andrew (1952) and Brody (1955) reported the neuronal loss with age. It was assumed that the progressive increase in the lipofuscin, per unit cross sectional area, percent of neurons involved and percent of the intraneuronal lipofuscin pigment may be partly resulting from the aging cerebral arteries, an added effect to the neuronal aging.

The views of Casarett (1964) and Getty (1966) that the resultant fibrosis, narrowed lumen and increased wall thickness of the vascular wall increased the histohaematic barrier progressively which in turn resulted in the decreased functional effectiveness of the above barrier in terms of the transport of the nutrients and waste products may be true for the nuclear masses in the central nervous system because of their dependence on the above barrier for their normal functions.

In view of the present worker, the presence of the lipofuscin in the different nuclear areas of the brain of the dog and pig appeared progressively in an increasing order with age. This signified that the expression of aging by the neurons was displayed by its presence and subsequent increase. The pigmentation was consistent and was the only main change observed in the nuclear areas studied. The presence of the pigment in the neurons of the older specimens where it occupied a major portion of the cellular volume may be detrimental to the normal cellular metabolism even if it may be a byproduct or endproduct of the cellular metabolism. The pigment occupying the major segment of the cell volume certainly reduced the metabolic activity and physiological functions due to organelle loss of the cell and also due to the fact that it left lesser cell volume for the above functions. The presence of the pigment in the axonal and perinuclear area

could affect the impulse relay and cell functions. The above views may be speculative at this but definitely require further probing and consideration.

Qualitative and quantitative studies

The qualitative studies were conducted on fifteen cell masses of the brain in the dog and pig whereas quantitative studies were restricted to only five areas in the case of the dog only.

Brody (1960) observed that the pigment was present in the pyramidal neurons of the precentral cerebral cortex of human. The pigment was mostly restricted to the fifth and third layer neurons of the above cortex. The percentage of the neurons containing pigment increased with age. Reichel, et al. (1968) obtained similar results. The present study revealed that the Betz cells of the precentral cortex in the dog showed pigment at the age of eight months and increased progressively with age. The pyramidal neurons of the third layer of the above cortical area showed the pigment at the age of two years and seven months which became loosely focal by the age of four years. In the case of the pig the Betz cells showed pigment at the age of three years and nine months and showed increasing trend with age.

The pigmentation in the basal ganglia of man was studied by Altschul (1943) who found that all nuclear areas included

in the basal ganglia contained pigmentation. He found that the pigmentation was perinuclear in globus pallidus inagreement with the present findings in which high pigmentation was observed in the globus pallidus and putamen whereas the pigment in the caudate nucleus was comparatively less.

Stevenson (1959) observed that the thalamic nuclear areas showed early pigmentation and suggested it to be a possible factor for emotional state of the aged. The thalamic nuclear areas included in the present study showed the pigmentation in both species. The pigmentation increased from the third age group onwards in the dog but was slow in its progression. The pigmentation of the thalamic nuclei was observed from two years and seven months onwards in the case of the pig.

Nucleus olivaris inferioris of the dog and pig was studied by Whiteford (1964) and Whiteford and Getty (1966). They found the accumulation of pigment from the age of four years onwards. They observed that the pigmented granules may even be present at the age of six or eight months in both species. The present study showed that the pigment was present at the age of eleven months in the dog and one year and five months in the pig.

Nucleus hypoglossus in the dog and pig was included by Whiteford (1964) and Whiteford and Getty (1966). They found the pigment at the age of two years and a half in the dog and at the age of three years and four months, in significant

amounts, in the pig, however, with fluorescence microscopic technique they could localize it at one year of age in both species. In the present study the pigment was observed to be present in loose granular form at the age of eleven months in the dog and at the age of one year and five months in the case of the pig.

The dorsal motor nucleus of vagus nerve showed the presence of the lipofuscin from four years of age onwards in the dog whereas in the pig slight pigmentation was discernible from two years and five months of age onwards. The pigmentation was loosely granular focal in the above ages but increased to show focal localization in the latter age periods.

The lipofuscin pigment was present in the accessory cuneate nucleus or nucleus cuneatus medialis of the dog at one year and seven months of age in the disseminated granular form which was well established by the age of two years and seven months. It was present at the age of two years in traces and increased later in the case of the pig.

The occurrence of the pigment in the cochlear nuclei, vestibular nuclei red nucleus, oculomotor nucleus indicated that these nuclei developed the aging pigment at different periods of age in the dog and pig. The earliest pigmentation was present in the red nucleus and vestibular nuclei, by the age of eleven months in the case of the dog. The nucleus oculomotorius and cochlear nuclei indicated the granulated

form of pigmentation by about two years and one year and seven months respectively in the case of the dog. Regarding the distribution in the pig, vestibula nuclei were pigmented at one year and five months, nucleus rubrum or red nucleus at one year and eleven months, nucleus oculomotrius at two years and nuclei cochleares at two years and nine months of age. The above findings corresponded with the results obtained by Whiteford (1964) and Whiteford and Getty (1966) in the dog and pig.

The fastigal and dentate nuclei in the dog showed granular pigmentation at the age of four years. Ellis (1920) also observed that the dentate nucleus of the cerebellum of man developed pigmentation with age. He found that the cells of the dentate nucleus disintegrated and disappeared in a much less extent than the purkinje cells do. According to him the pigmentation should be regarded as a product of metabolism and the failure to eliminate it was an indication of defective function in the nerve cells. He drew a parallelism between the actual disintegration of the purkinje cells and occurrence of the pigmentation of the dentate nucleus neurons.

The pigmentation in the hippocampal gyrus has been studied by Reichel, et al. (1968) in the case of the rat. They found the intracellular pigment as 7 to 9 percent between the ages of twenty-six months and twenty-nine months. The present investigation indicated its presence at four years in the dog and four years and six months in the case of the pig. No attempts were made to count its magnitude intracellularly.

The pigment was present in purkinje cells of the pig at the age of three years and nine months. Similar studies in the case of the dog produced negative results. However, there was lipofuscin-like material present extracellularly. Ellis (1920) observed that the pigmentation in the purkinje cells was rarely seen. He related the absence of the pigment in the purkinje cells to their tendency to disintegrate with age. This was based on his findings that with age there was considerable loss of the purkinje cells of human which in turn affected the motor strength and skill. Similar studies to indicate loss of purkinje cells with age have been carried out by Harms (1924) and Inukai (1928). Sulkin (1955) observed the presence of lipofuscin in the granular cells of the cerebellum but not frequently in the purkinje cells of the cerebellum of the dog. Friede (1962) mentioned that the lipofuscin can be removed from the purkinje cells by glial cells. However, there seemed to be a conflict in the interpretation with that of Issidorides and Shanklin (1961) and Shanklin, et al. (1957) who ascribed such pigment formation to a neurosecretory function in purkinje cells since they found abundant extracellular lipofuscin granules in synaptic fields.

SUMMARY AND CONCLUSIONS

An investigation was conducted to study the extrinsic and intrinsic blood supply to the brain, histomorphological age associated changes in the cerebral arteries and age associated changes in the cortices and nuclei of the brain of the dog and pig. The study was a segment of the gerontological project being pursued in the Department of Veterinary Anatomy at Iowa State University.

For the study of the extrinsic and intrinsic blood supply to the brain of the dog and pig, fifteen brains were studied in each species. The study was conducted by injecting the cerebral arteries with latex and India ink. The specimens used for the intrinsic study were made transparent whereas dissections were conducted for the extrinsic blood supply.

The arrangement of the blood vessels that contributed in the cerebral circulation varied in the dog and pig. The arteria carotis interna and arteria vertebralis were the main contributors. The arteria maxillaris contributed insignificantly by forming a simple anastomosis through its branches with the arteria carotis interna in the case of dog. In the pig, the arteria maxillaris contributed to a greater degree and formed through its branches and arteria carotis interna the rete mirabile epidurale rostrale. This was a complex network in comparison to a simple anastomosis in the case of dog.

The arteria carotis interna gave off the arteria intercarotica caudalis and arteria intercarotica rostralis during its course, before dividing into the main cerebral arteries, in the case of dog. But in the pig the arteria intercarotica caudalis was not represented as a simple tubular branch. The above vessel was in the form of plexiform vessels extending and connecting the caudal part of rete mirabile epidurale rostrale. These branches were regarded as the rami intercaroticae caudales.

The arteria carotis interna divided to give off arteria communicans caudalis, arteria cerebri media and arteria cerebri rostralis soon after its emergence from the sinus cavernosus in the case of dog whereas in the pig the artery gave off the arteria communicans caudalis but itself continued rostrally for a short distance before giving off the arteria cerebri media and arteria cerebri rostralis.

The arteria choroidea rostralis took its origin from the arteria cerebri media and participated in the supply to the plexus choroideus ventriculi lateralis and tertius. The above artery, however, took its origin from the rostral continuation of the arteria carotis interna in the case of pig.

The arteria cerebri media, in the dog and pig, gave off a number of rami striati laterales (arteriae striati laterales) to supply the lateral and caudal part of the corpus striatum mainly. The above vessels were not recognized by

earlier authors; however, their presence was speculated by them in the above species.

The arteria cerebri rostralis was observed to have a similar set of branches termed as rami striati mediales (arteriae striati mediales) in both species.

The arteria ophthalmica interna was a branch of the arteria cerebri rostralis whereas it took its origin from the rostral continuation of the arteria carotis interna in the case of pig. The arteria ethmoidalis interna was comparatively well developed in the case of pig.

The arteria communicans rostralis was not present in the dog but in the pig a plexiform communication between the arteriae cerebri rostrales represented the above.

The arteria cerebri rostralis of either sides fused with each other to form a single, common or median trunk. This trunk was termed the arteria corporis callosi (communis) mediane. In the dog, the trunk divided into two branches to course as the arteria corporis callosi for each cerebral hemisphere. The condition in the pig, however, was different because the trunk did not divide but gave off collateral branches for distribution on the medial surface of both cerebral hemispheres.

The central branches from the arteria cerebri media, arteria cerebri rostralis and arteria carotis interna were traced to supply the hypothalamic areas, septal nuclei, area

subcallosa and anterior commisures principally. The arteriae hypophysiales caudales (inferiores) and rostrales (superiores) supplied the hypophysis and related hypothalamic fields in both species.

The arteria communicans caudalis, in both species, was regarded to extend between the arteria carotis interna and arteria basilaris. The above artery was divided into two segments, a proximal and a distal. The proximal segment corresponded to the arteria communicans caudalis of the human. This has also been regarded as the proximal part of the arteria cerebri caudalis by a number of authors in the human. The distal segment was termed as the arteria mesencephalica because of its neurovascular relationship and topographical distribution to the above segment of the brain. A number of branches from the above segments supplied the choroid plexuses, diencephalon and mesencephalon and were detailed. The species differences with regard to the origin of their branches and the areas supplied were discussed.

The arteria cerebelli rostralis arose from the arteria mesencephalica in the case of the dog. Its origin in the pig was variable;however, in most cases it arose as a branch from the terminal part of the arteria mesencephalica.

The arteria basilaris in the dog and pig showed certain principal differences. The above artery in the dog gave off

a single ramus medullaris in comparison to the pig in which there were three to five rami medullares.

There were two arteriae cerebelli caudales in the case of dog but in the pig one vessel represented the above. The latter arose as a single branch near the junction of the corpus trapezoideum and medulla oblongata.

The arteria cerebelli media took its origin from the arteria basilaris directly, whereas in the case of pig it was a branch from the arteria cerebelli caudalis. In both cases the arteria labyrinthi was a branch of the arteria cerebelli media. The rami ad pontem were recognized in both species.

The arteria basilaris in the pig tapered in the pontine region before joining the arteriae mesencephalicae. A number of rami paramedianes or medianes were observed to leave the dorsal face of the arteria basilaris in both species.

The study on the intrinsic blood supply indicated that most of the medulla oblongata and caudal part of the cerebellum was supplied by the arteriae cerebelli caudales in the dog, but in the case of pig rami medullares supplied most of the former but the caudal aspect of the cerebellum was supplied by the cortical (terminal) branches of the arteria cerebelli caudalis.

The corpus trapezoideum and pons were supplied by the rami ad pontem and arteria cerebelli media in the case of the

dog. It differed in the pig in which the arteria cerebelli caudalis (in its proximal course) supplied the corpus trapezoideum.

The part of the study relative to the age-associated changes in the cerebral arteries of the dog and pig was carried on in forty dogs and thirty pigs. The dogs ranged in age from one day to sixteen years and from two days to ten years of age in the case of pig. The animals were from the environment common to the species. The birth records, feed records and the complete past history of the animals were known.

The animals were killed in the Department by electrocution. The brains with the vessels were removed as soon as possible and were fixed in 10 percent buffered neutral formalin. The brains were cut into a number of thin transverse segments with the help of the brain knife and were embedded in the paraplast.

The blocks were sectioned at eight microns and were stained with different connective tissue stains.

In order to study the age changes it was felt necessary to study the normal histology of the cerebral arteries to ascertain the differences between the histology of the above arteries and other major arteries of the body in both species.

It was observed that the internal elastic lamina was comparatively thicker, elastic fibers in the tunica media were scanty and a distinct external elastica lamina was lacking.

These formed the major distinctive features of the cerebral arteries from the other arteries of the body.

A number of valve-like structures and intimal cushions were observed. Their possible functional significance and age-related changes were discussed.

The cerebral arteries of the dog and pig underwent histomorphological changes during aging. The changes were progressive in the ascending order of age.

The cerebral arteries showed age-related changes in the connective tissue components of the different vascular layers. The tunica intima increased in its thickness with age. The increase was due to the uniform increase in the subendothelial space caused by the laydown of the ground substance with age. This increase was progressive. The subendothelium developed early fibrosis followed by fibromuscular thickenings of the tunica intima by ten years of age in the case of dog, whereas the latter was much earlier in the case of the pig from third age group (one year to four years of age) onwards.

The tunica media showed decrease in the smooth muscle density along with the increase in the ground substance with age in both species.

The collagenization of the tunica media with age was very pronounced in the case of dog in which the increase was at a rapid rate from four years of age onwards; however, the

progression was at a comparatively slower rate in the case of pig.

The elastic fibers in the tunica media were fine and scanty in the first three age groups (up to four years of age) beyond which there was an apparent increase which may be due to the splitting and fragmentation of the already existing elastic fibers. The fibers were rough and showed affinity for collagen stains. The tunica adventitia increased in its thickness progressively with age.

The internal elastic lamina split, fragmentation and duplication was consistently observed in the cerebral arteries of the animals studied.

The intimal thickenings of the cerebral arteries were more pronounced and were greater in frequency, severity and appeared much earlier in the pig than in the case of dog.

The intimal thickenings were occluding the vessel lumen in varying degrees in the pig whereas in the dog these were low and small but the fibrosis of the vessel layers was more pronounced than in the pig.

The intimal thickenings were observed to be associated with fibromuscular proliferation which became more fibrous in the cerebral arteries between four years and eight years and onwards.

The role of the mesenchymal cells, collagen, ground substance and elastic tissue in causing the fibrosis and intimal thickening with aging of the vascular wall was discussed.

The presence of the medial defects in the cerebral arteries of both species was observed. Their occurrence and relationship with the aneurysms was discussed.

The material utilized for the segment of the study on the age-associated changes in the nuclei and cortices of the brain in the dog and pig was collected in a manner described earlier for the study on the histomorphological age changes in the cerebral arteries of the above species.

The sections were stained with Alican blue and P.A.S. in the dog whereas unstained sections were studied with the help of the fluorescence microscopy.

For the quantitative studies a net reticule of five mm square was placed in the eyepiece of the microscope and percentage of the lipofuscin pigment per unit area, percentage of the intraneuronal pigment and percentage of the neurons in a number of nuclei were ascertained.

The qualitative studies on the lipofuscin pigment indicated that the pigment was P.A.S. positive and exhibited yellow-orange autofluorescence with the ultraviolet light under fluorescence microscopy.

The distribution of the pigment was variable in its pattern of distribution. It was dispersed around the nucleus or focal in the neurons. The latter was polar or axonal, bipolar or perinuclear. The dispersed form was present in the neurons

of younger animals before the pigment formed focal or cluster formations in the aged specimens.

The pigment was present in the nuclei and cortices studied; however, the percentage of the intraneuronal pigment, percentage of the pigmented neurons and pigment per unit area varied depending on the nucleus or cortex under study and had linear relationship with age.

The quantitative and qualitative studies conducted revealed that the pigmentation increased progressively with age; however, the rate and amount of pigmentation varied in the different nuclei and cortices studies.

It was observed that the motor nuclei and large pyramidal neurons of the motor cortex developed pigment at an earlier age and the increase with age was rapid in comparison to the sensory and associative nuclei. The nuclei related with the autonomic functions developed the pigment comparatively late.

It was concluded that there was relationship between the functional status of the nuclei and cortices to the pigmentation.

In view of the absence of the lipofuscin pigment in the clinically healthy young dogs and pigs but its presence in the older specimens of the above species, it was concluded that the pigment was a product of the cell metabolism and was

the only consistent and basic cellular change in the neurons with aging.

In light of the criteria of aging, universality, time dependence, innateness and deletoriousness, the lipofuscin pigment, which met the above criteria, formed the basic age change in the neurons.

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APPENDIX A

Table 1. Age, breed and sex of the dogs included in the study (Age changes)

Serial No.	Dog No.	Years	Months	Days	Breed	Sex
1	B105	-	-	1	Beagle	Female
2	B99	-	1	19	Beagle	Female
3	E26	-	2	-	Beagle	Male
4	068	-	2	15	Beagle	Male
5	E27	-	4	-	Beagle	Male
6	049	-	5	7	Beagle	Female
7	B66	-	6	15	Beagle	Female
8	B48	-	8	-	Beagle	Female
9	B79	-	10	-	Beagle	Female
10	C41	-	11	-	Beagle	Female
11	B56	1	-	-	Beagle	Male
12	B37	1	2	11	Beagle	Male
13	B96	1	5	-	Beagle	Female
14	B80	1	7	-	Beagle	Male
15	B127	2	-	-	Beagle	Female
16	21	2	-	17	Beagle	Male
17	053	2	7	-	Beagle	Female
18	B68	2	8	6	Beagle	Female
19	B82	3	3	-	Beagle	Female
20	B36	3	6	-	Beagle	Male
21	B95	4	-	-	Beagle	Male

Table 1 (Continued)

Serial No.	Dog No.	Years	Months	Days	Breed	Sex
22	B118	6	7	-	Beagle	Female
23	B119	6	10	18	Beagle	Female
24	M52	7	6	-	Basenji	Male
25	B43	7	7	-	Beagle	Female
26	B44	7	9	-	Beagle	Female
27	9	8	8	-	Beagle	Male
28	B42	8	7	-	Beagle	Female
29	M54	9	-	-	Gold Retriever	Female
30	B63	9	2	-	Beagle	Male
31	M53	9	-	-	Gold Retriever	Female
32	6	10	-	-	Beagle	Male
33	M49	10	3	-	Lab Retriever	Female
34	M42	11	2	-	Fox Terrier	Female
35	B123	11	9	-	Beagle	Female
36	M44	12	-	-	Corgi	Female
37	M45	12	1	-	Fox Terrier	Female
38	B131	12	9	-	Beagle	Female
39	M37	13	1	-	Gold Retriever	Female
40	M36	16	-	-	Cocker Spaniel	Female

Table 2. Age, breed and sex of the pigs included in the study (Age changes)

Serial No.	Pig No.	Years	Age Months	Days	Breed	Sex
1	1448B	-	-	2	Y-LR[a]	Male
2	592	-	2	5	PC-Y-LR[b]	Female
3	5353	-	2	21	PC-Y-LR	Female
4	5250	-	3	15	PC-Y-LR	Female
5	1292	-	6	7	PC-Y-LR	Female
6	634	-	8	5	PC-Y-LR	Female
7	3923	-	10	15	Yorkshire	Female
8	9442	-	11	-	Y-LR	Female
9	3430S	1	2	-	Y-LR	Female
10	2021S	1	5	-	Y-LR	Female
11	4491	1	11	-	Y-LR	Female
12	4512	2	-	-	PC-Y-LR	Female
13	1790	2	5	-	Y-LR	Female
14	3195	2	9	-	Y-LR	Female
15	1362	2	11	-	Y-LR	Female
16	4631	3	10	-	Pol. China[c]	Male
17	190-10	4	6	-	Yorkshire	Female

[a] Yorkshire-Landrace

[b] Poland China-Yorkshire-Landrace

[c] Poland China

Table 2 (Continued)

Serial No.	Pig No.	Years	Age Months	Days	Breed	Sex
18	3654	5	2	-	Pol. China	Male
19	930-259	6	2	-	Landrace	Female
20	1350	6	3	3	Hampshire	Male
21	221	6	5	-	Landrace	Male
22	312	6	10	-	Y-LR	Female
23	119-259	7	-	-	Duroc	Female
24	26-258	7	3	-	Hampshire	Female
25	Fletcher	8	-	-	Landrace	Female
26	1816-260	8	-	-	Duroc	Female
27	D1287-260	8	3	-	Duroc	Female
28	9090	9	1	-	Duroc	Female
29	254	9	3	-	Duroc	Female
30	Merrick	10	-	-	Yorkshire	Female

Table 3. Showing the smooth muscle cell nuclei per unit area in the tunica media of the arteria cerebri media and arteria basilaris of the dog at different ages

Serial No.	Dog No.	Age Years	Age Months	Age Days	Count of smooth muscle cell nuclei in arteria cerebri media	Count of smooth muscle cell nuclei in arteria basilaris
1	B105	-	-	1	53.0	55.2
2	B99	-	1	19	50.2	46.8
3	E26	-	2	-	51.0	53.2
4	068	-	2	15	49.9	50.7
5	E27	-	4	-	46.5	41.8
6	049	-	5	7	48.0	37.0
7	B66	-	6	15	44.2	49.3
8	B48	-	8	-	38.8	41.4
9	B79	-	10	-	42.1	43.0
10	C41	-	11	-	38.5	36.9
11	B56	1	-	-	36.4	37.2
12	B37	1	2	11	38.0	34.0
13	B96	1	5	-	34.2	36.2

Table 3 (Continued)

Serial No.	Dog No.	Age Years	Age Months	Age Days	Count of smooth muscle cell nuclei in arteria cerebri media	Count of smooth muscle cell nuclei in arteria basilaris
14	B80	1	7	-	40.1	31.8
15	B127	2	-	-	33.4	32.0
16	21	2	-	17	39.3	36.2
17	053	2	7	-	32.2	30.1
18	B68	2	8	6	34.5	36.8
19	B82	3	2	-	28.6	26.0
20	B36	3	6	-	32.8	34.0
21	B95	4	-	-	26.1	26.9
22	B118	6	7	-	23.3	28.2
23	B119	6	10	-	30.4	26.4
24	M52	7	6	-	25.2	27.0
25	B43	7	7	-	28.9	24.1
26	B44	7	9	-	25.6	28.3
27	B42	8	7	-	24.6	20.7
28	9	8	8	-	22.0	19.6

Table 3 (Continued)

Serial No.	Dog No.	Age Years	Age Months	Age Days	Count of smooth muscle cell nuclei in arteria cerebri media	Count of smooth muscle cell nuclei in arteria basilaris
29	M54	9	-	-	19.3	21.8
30	M53	9	-	-	24.0	23.3
31	B63	9	2	-	22.4	19.9
32	6	10	-	-	24.5	17.2
33	M49	10	3	-	20.3	21.6
34	M42	11	2	-	23.3	19.0
35	B123	11	9	-	18.8	21.4
36	M44	12	-	-	20.1	22.4
37	M45	12	1	-	17.5	21.8
38	B131	12	9	-	20.7	17.0
39	M37	13	1	-	19.0	18.2
40	M36	16	-	-	18.6	16.9

Table 4. Showing the smooth muscle cell nuclei per unit area in the tunica media of the arteria cerebri media and arteria basilaris of the pig at different ages

Serial No.	Pig No.	Age Years	Age Months	Age Days	Count of smooth muscle cell nuclei in arteria cerebri media	Count of smooth muscle cell nuclei in arteria basilaris
1	1448B	-	-	2	51.6	54.0
2	592	-	2	5	49.6	52.7
3	5353	-	2	21	48.8	47.6
4	5250	-	3	15	44.2	46.5
5	1292	-	6	7	41.2	44.3
6	634	-	8	5	42.8	46.0
7	3923	-	10	15	38.8	39.6
8	9442	-	11	-	44.6	38.4
9	3430	1	2	-	38.0	36.8
10	2021S	1	5	-	37.0	33.5
11	4491	1	11	-	32.0	34.7
12	4512	2	-	-	36.8	33.3
13	1790	2	5	-	29.2	27.7
14	3195	2	9	-	36.6	32.0

Table 4 (Continued)

Serial No.	Pig No.	Age Years	Age Months	Age Days	Count of smooth muscle cell nuclei in arteria cerebri media	Count of smooth muscle cell nuclei in arteria basilaris
15	1362	9	11	-	29.4	32.8
16	4631	3	10	-	28.8	27.2
17	190-10	4	6	-	26.6	28.8
18	3654	5	2	-	27.4	25.0
19	1350	6	2	-	23.6	29.4
20	930-259	6	3	3	25.6	19.7
21	221	6	5	-	19.4	22.3
22	312	6	10	-	21.2	24.8
23	119-259	7	-	-	23.7	23.0
24	26-258	7	3	-	22.8	26.2
25	Fletcher	8	-	-	19.0	24.0
26	1816-260	8	-	-	21.3	18.9
27	D1287-260	8	3	-	18.6	20.4
28	9090	9	1	-	17.4	21.3
29	254	9	3	-	18.0	19.4
30	Merrick	10	-	-	16.8	18.2

Table 5. Showing the presence of lipofuscin pigment in different areas[a] of the brain in the dog

Serial No.	Dog No.	Years	Age Months	Days	1	2	3	4
1	B105	-	-	1	-	-	-	-
2	B99	-	1	19	-	-	-	-
3	E26	-	2	-	-	-	-	-
4	068	-	2	15	-	-	-	-
5	E27	-	4	-	-	-	-	-
6	C49	-	5	7	-	-	-	-
7	B66	-	6	15	-	-	-	-
8	B48	-	8	-	-	-	-	-
9	B79	-	10	-	-	-	-	-
10	C41	-	11	-	Traces	Traces	-	-
11	B56	1	-	-	+	Traces	-	-
12	B37	1	2	11	-	-	-	-
13	B96	1	5	-	+	+	-	-

[a] 1 = Nucleus olivaris inferioris; 2 = Nucleus hypoglossus; 3 = Dorsal motor nucleus of vagus; 4 = Nucleus cuneatus accessorius; 5 = Nuclei vestibulares; 6 = Nuclei cochleares; 7 = Nuclei cerebelli; 8 = Cortex cerebelli; 9 = Nucleus rubrum; 10 = Nucleus oculomotorius; 11 = Thalamus; 12 = Gyrus hippocampus; 13 = Cortex cerebri; 14 = Nucleus caudatus; 15 = Globus pallidus and putamen.

5	6	7	8	9	10	11	12	13	14	15
-	-	-	-	-	-	-	-	-	-	-
-	-	-	-	-	-	-	-	-	-	-
-	-	-	-	-	-	-	-	-	-	-
-	-	-	-	-	-	-	-	-	-	-
-	-	-	-	-	-	-	-	-	-	-
-	-	-	-	-	-	-	-	-	-	-
-	-	-	-	-	-	-	-	-	-	-
-	-	-	-	-	-	-	-	Traces	-	-
-	-	-	-	Traces	-	-	-	+	-	-
-	-	-	-	+	-	-	-	+	-	-
Traces	-	-	-	-	-	-	-	+	-	-
-	-	-	-	+	-	-	-	+	-	-
+	-	-	-	+	-	-	-	+	-	-

Table 5 (Continued)

Serial No.	Dog No.	Years	Age - Months	Days	1	2	3	4
14	B80	1	7	-	+	+	-	Traces
15	B127	2	-	-	+	+	-	Traces
16	21	2	-	17	+	+	-	+
17	053	2	7	-	+	+	-	+
18	B68	2	8	6	+	+	-	+
19	B82	3	2	-	+	+	-	+
20	B36	3	6	-	+	+	-	+
21	B95	4	-	-	+	+	Traces	+
22	B118	6	7	-	+	+	+	+
23	B119	6	10	-	+	+	+	+
24	M52	7	6	-	+	+	+	+
25	B43	7	7	-	+	+	+	+
26	B44	7	9	-	+	+	+	+
27	B42	8	7	-	+	+	+	+
28	9	8	8	-	+	+	+	+
29	M54	9	-	-	+	+	+	+
30	M53	9	-	-	+	+	+	+
31	B63	9	2	-	+	+	+	+
32	6	10	-	-	+	+	+	+
33	M49	10	3	-	+	+	+	+

5	6	7	8	9	10	11	12	13	14	15
+	Traces	-	-	+	-	-	-	+	-	-
+	+	-	-	+	-	+	-	+	-	-
+	+	-	-	+	Traces	+	-	+	-	-
+	+	-	-	+	+	+	Traces	+	-	+
+	+	-	-	+	+	+	-	+	-	+
+	+	-	-	+	+	+	Traces	+	-	+
+	+	-	-	+	+	+	Traces	+	+	+
+	+	+	-	+	+	+	+	+	+	+
+	+	+	-	+	+	+	+	+	+	+
+	+	+	-	+	+	+	+	+	+	+
+	+	+	-	+	+	+	+	+	+	+
+	+	+	-	+	+	+	+	+	+	+
+	+	+	-	+	+	+	+	+	+	+
+	+	+	-	+	+	+	+	+	+	+
+	+	+	-	+	+	+	+	+	+	+
+	+	+	-	+	+	+	+	+	+	+
+	+	+	-	+	+	+	+	+	+	+
+	+	+	-	+	+	+	+	+	+	+
+	+	+	-	+	+	+	+	+	+	+
+	+	+	-	+	+	+	+	+	+	+

Table 5 (Continued)

Serial No.	Dog No.	Years	Age Months	Days	1	2	3	4
34	M42	11	2	-	+	+	+	+
35	B123	11	9	-	+	+	+	+
36	M44	12	-	-	+	+	+	+
37	M45	12	1	-	+	+	+	+
38	B131	12	9	-	+	+	+	+
39	M37	13	1	-	+	+	+	+
40	M36	16	-	-	+	+	+	+

5	6	7	8	9	10	11	12	13	14	15
+	+	+	-	+	+	+	+	+	+	+
+	+	+	-	+	+	+	+	+	+	+
+	+	+	-	+	+	+	+	+	+	+
+	+	+	-	+	+	+	+	+	+	+
+	+	+	-	+	+	+	+	+	+	+
+	+	+	-	+	+	+	+	+	+	+
+	+	+	-	+	+	+	+	+	+	+

Table 6. Showing the presence of lipofuscin pigment in different areas[a] of the brain in the pig

Serial No.	Pig No.	Age Years	Age Months	Days	1	2	3	4
1	1448B	-	-	2	-	-	-	-
2	592	-	2	5	-	-	-	-
3	5353	-	2	21	-	-	-	-
4	5250	-	3	15	-	-	-	-
5	1292	-	6	7	-	-	-	-
6	634	-	8	5	-	-	-	-
7	3923	-	10	15	-	-	-	-
8	9442	-	11	-	-	-	-	-
9	3430S	1	2	-	-	-	-	-
10	2021S	1	5	-	Traces	Traces	-	-
11	4491	1	11	-	+	-	-	-
12	4512	2	-	-	+	+	Traces	Traces
13	1790	2	5	-	+	+	+	-
14	3195	2	9	-	+	+	+	+

[a] 1 = Nucleus olivaris inferioris; 2 = Nucleus hypoglossus; 3 = Dorsal motor nucleus of vagus; 4 = Nucleus cuneatus accessorius; 5 = Nuclei vestibulares; 6 = Nuclei cochleares; 7 = Cortex cerebelli; 8 = Cortex cerebri; 9 = Nucleus ruber; 10 = Nucleus oculomotorius; 11 = Thalamus; 12 = Gyrus hippocampus.

5	6	7	8	9	10	11	12
-	-	-	-	-	-	-	-
-	-	-	-	-	-	-	-
-	-	-	-	-	-	-	-
-	-	-	-	-	-	-	-
-	-	-	-	-	-	-	-
-	-	-	-	-	-	-	-
-	-	-	-	-	-	-	-
-	-	-	-	-	-	-	-
-	-	-	-	-	-	-	-
Traces	-	-	-	-	-	-	-
Traces	-	-	Traces	Traces	-	-	-
+	-	+	+	+	Traces	Traces	-
+	-	+	+	+	+	+	-
+	Traces	+	+	+	+	+	-

Table 6 (Continued)

Serial No.	Pig No.	Age Years	Age Months	Days	1	2	3	4
15	1362	2	11	-	+	+	+	+
16	4631	3	9	-	+	+	+	+
17	190-10	4	6	-	+	+		+
18	3654	5	2	-	+	+	+	+
19	1350	6	2	-	+	+	+	+
20	930-259	6	3	3	+	+	+	+
21	221	6	5	-	+	+	+	+
22	312	6	10	-	+	+	+	+
23	119-259	7	-	-	+	+	+	+
24	26-258	7	3	-	+	+	+	+
25	Fletcher	8	-	-	+	+	+	+
26	1816-260	8	-	-	+	+	+	+
27	D1287-260	8	3	-	+	+	+	+
28	9090	9	1	-	+	+	+	+
29	254	9	3	-	+	+	+	+
30	Merrick	10	-	-	+	+	+	+

5	6	7	8	9	10	11	12
+	Traces	+	+	+	+	+	+
+	+	+	+	+	+	+	Traces
+	+	+	+	+	+	+	Traces
+	+	+	+	+	+	+	+
+	+	+	+	+	+	+	+
+	+	+	+	+	+	+	+
+	+	+	+	+	+	+	+
+	+	+	+	+	+	+	+
+	+	+	+	+	+	+	+
+	+	+	+	+	+	+	+
+	+	+	+	+	+	+	+
+	+	+	+	+	+	+	+
+	+	+	+	+	+	+	+
+	+	+	+	+	+	+	+
+	+	+	+	+	+	+	+
+	+	+	+	+	+	+	+
+	+	+	+	+	+	+	+

Table 7. Quantitative lipofuscin distribution in the nucleus olivaris inferioris of the dog with age

Serial No.	Dog No.	Age Years	Age Months	Age Days	Percentage of pigment per unit sectional volume	Percentage of pigmented neurons per sectional area	Percentage of intraneuronal pigment volume per neuronal volume
1	B105	-	-	1	-	-	-
2	B99	-	1	19	-	-	-
3	E26	-	2	-	-	-	-
4	068	-	2	15	-	-	-
5	E27	-	4	-	-	-	-
6	049	-	5	7	-	-	-
7	B66	-	6	15	-	-	-
8	B48	-	8	-	-	-	-
9	B79	-	10	-	-	-	-
10	C41	-	11	-	Traces	Traces	Traces
11	B56	1	-	-	Traces	Traces	Traces
12	B37	1	2	11	-	-	-
13	B96	1	5	-	.6	34.83	8.33

Table 7 (Continued)

Serial No.	Dog No.	Years	Age Months	Days	Percentage of pigment per unit sectional volume	Percentage of pigmented neurons per sectional area	Percentage of intraneuronal pigment volume per neuronal volume
14	B80	1	7	-	1.1	44.90	10.90
15	B127	2	-	-	.8	39.20	8.90
16	21	2	-	17	1.3	56.00	13.84
17	053	2	7	-	1.6	61.43	19.24
18	B68	2	8	6	1.4	58.42	16.72
19	B82	3	2	-	1.6	67.50	21.11
20	B36	3	6	-	1.7	55.30	18.10
21	B95	4	-	-	1.9	73.60	26.06
22	B118	6	7	-	2.5	80.95	26.32
23	B119	6	10	-	2.8	82.72	28.08
24	M52	7	6	-	3.0	87.50	29.13
25	B43	7	7	-	2.8	76.40	25.03
26	B44	7	9	-	3.1	80.30	27.60
27	B42	8	7	-	2.7	84.70	31.40

Table 7 (Continued)

Serial No.	Dog No.	Years	Age Months	Days	Percentage of pigment per unit sectional volume	Percentage of pigmented neurons per sectional area	Percentage of intraneuronal pigment volume per neuronal volume
28	9	8	8	-	2.5	85.18	32.19
29	M54	9	-	-	2.6	90.00	33.76
30	M53	9	-	-	3.1	86.19	34.73
31	B63	9	2	3.3	90.80	37.60	
32	6	10	-	-	3.4	91.66	35.87
33	M49	10	3	-	3.0	90.56	38.64
34	M42	11	2	-	3.2	82.35	35.84
35	B123	11	9	-	3.6	86.30	42.08
36	M44	12	-	-	3.0	91.99	47.90
37	M45	12	1	-	3.4	92.90	45.88
38	B131	12	9	-	3.7	95.00	47.10
39	M37	13	1	-	3.2	86.00	43.31
40	M36	16	-	-	3.9	94.00	48.60

Table 8. Quantitative lipofuscin distribution in the nucleus hypoglossus of the hog with age

Serial No.	Dog No.	Years	Age Months	Days	Percentage of pigment per unit sectional volume	Percentage of pigmented neurons per sectional area	Percentage of intraneuronal pigment volume per neuronal volume
1	B105	-	-	1	-	-	-
2	B99	-	1	19	-	-	-
3	E26	-	2	-	-	-	-
4	068	-	2	15	-	-	-
5	E27	-	4	-	-	-	-
6	049	-	5	7	-	-	-
7	B66	-	6	15	-	-	-
8	B48	-	8	-	-	-	
9	B79	-	10	-	-	-	-
10	C41	-	11	-	Traces	Traces	Traces
11	B56	1	-	-	Traces	Traces	Traces
12	B37	1	2	11	-	-	-
13	B96	1	5	-	Traces	Traces	Traces

Table 8 (Continued)

Serial No.	Dog No.	Years	Age Months	Days	Percentage of pigment per unit sectional volume	Percentage of pigmented neurons per sectional area	Percentage of intraneuronal pigment volume per neuronal volume
14	B80	1	7	-	Traces	Traces	Traces
15	B127	2	-	-	.7	36.29	8.10
16	21	2	-	17	.5	22.35	5.53
17	053	2	7	-	1.3	51.80	9.47
18	B68	2	8	6	.9	32.06	7.63
19	B82	3	2	-	1.6	40.36	12.07
20	B36	3	6	-	1.2	38.10	9.25
21	B95	4	-	-	1.3	56.39	11.96
22	B118	6	7	-	1.8	58.97	13.03
23	B119	6	10	-	1.9	65.90	14.78
24	M52	7	6	-	2.2	71.18	15.69
25	B43	7	7	-	2.0	62.70	17.30
26	B44	7	9	-	2.4	73.20	13.82
27	B42	8	7	-	2.1	76.00	14.36

Table 8 (Continued)

Serial No.	Dog No.	Years	Age Months	Days	Percentage of pigment per unit sectional volume	Percentage of pigmented neurons per sectional area	Percentage of intraneuronal pigment volume per neuronal volume
28	9	8	8	-	1.8	68.47	13.16
29	M54	9	-	-	2.5	73.75	16.37
30	M53	9	-	-	2.3	72.85	18.15
31	B63	9	2	-	1.9	67.30	15.90
32	6	10	-	-	3.0	79.23	19.46
33	M49	10	3	-	2.6	80.61	20.94
34	M42	11	2	-	2.8	71.40	19.75
35	B123	11	9	-	2.9	89.9	18.30
36	M44	12	-	-	3.2	75.00	19.68
37	M45	12	1	-	3.4	79.72	20.95
38	B131	12	9	-	3.1	86.30	21.03
39	M37	13	1	-	3.8	88.68	21.91
40	M36	16	-	-	4.7	92.46	23.21

Table 9. Quantitative lipofuscin distribution in the dorsal motor nucleus of vagus of the dog with age

Serial No.	Dog No.	Years	Age Months	Days	Percentage of pigment per unit sectional volume	Percentage of pigmented neurons per sectional area	Percentage of intraneuronal pigment volume per neuronal volume
1	B105	-	-	1	-	-	-
2	B99	-	1	19	-	-	-
3	E26	-	2	-	-	-	-
4	068	-	2	15	-	-	-
5	E27	-	4	-	-	-	-
6	049	-	5	7	-	-	-
7	B66	-	6	15	-	-	-
8	B48	-	8	-	-	-	-
9	B79	-	10	-	-	-	-
10	C41	-	11	-	-	-	-
11	B56	1	-	-	-	-	-
12	B37	1	2	11	-	-	-
13	B96	1	5	-	-	-	-

Table 9 (Continued)

Serial No.	Dog No.	Years	Age Months	Days	Percentage of pigment per unit sectional volume	Percentage of pigmented neurons per sectional area	Percentage of intraneuronal pigment volume per neuronal volume
14	B80	1	7	-	-	-	-
15	B127	2	-	-	-	-	-
16	21	2	-	17	-	-	-
17	053	2	7	-	-	-	-
18	B68	2	8	6	-	-	-
19	B82	3	2	-	-	-	-
20	B36	3	6	-	-	-	-
21	B95	4	-	-	Traces	Traces	Traces
22	B118	6	7	-	.6	24.00	10.33
23	B119	6	10	-	.9	41.28	22.95
24	M52	7	6	-	1.1	33.43	17.39
25	B43	7	7	-	.8	39.20	24.30
26	B44	7	9	-	1.0	43.50	20.30
27	B42	8	7	-	1.5	49.30	24.52

Table 9 (Continued)

Serial No.	Dog No.	Years	Age Months	Days	Percentage of pigment per unit sectional volume	Percentage of pigmented neurons per sectional area	Percentage of intraneuronal pigment volume per neuronal volume
28	9	8	8	-	2.1	50.02	22.80
29	M54	9	-	-	1.2	44.50	27.45
30	M53	9	-	-	2.2	53.54	20.00
31	B63	9	2	-	2.6	57.06	30.40
32	6	10	-	-	3.3	62.70	31.15
33	M49	10	3	-	3.1	73.92	36.63
34	M42	11	2	-	2.7	64.04	37.92
35	B123	11	9	-	2.9	71.90	35.20
36	M44	12	-	-	2.6	65.00	35.82
37	M45	12	1	-	3.4	69.11	41.07
38	B131	12	9	-	3.7	83.20	43.20
39	M37	13	1	-	3.3	76.79	37.93
40	M36	16	-	-	4.3	88.67	53.22

Table 10. Quantitative lipofuscin distribution in the nuclei vestibulares of the dog with age

Serial No.	Dog No.	Age Years	Age Months	Days	Percentage of pigment per unit sectional volume	Percentage of pigmented neurons per sectional area	Percentage of intraneuronal pigment volume per neuronal volume
1	B105	-	-	1	-	-	-
2	B99	-	1	19	-	-	-
3	E26	-	2	-	-	-	-
4	068	-	2	15	-	-	-
5	E27	-	4	-	-	-	-
6	049	-	5	7	-	-	-
7	B66	-	6	15	-	-	-
8	B48	-	8	-	-	-	-
9	B79	-	10	-	-	-	-
10	C41	-	11	-	Traces	Traces	Traces
11	B56	1	-	-	Traces	Traces	Traces
12	B37	1	2	11	-	-	-
13	B96	1	5	-	Traces	Traces	Traces
14	B80	1	7	-	.6	36.65	9.29

Table 10 (Continued)

Serial No.	Dog No.	Years	Age Months	Days	Percentage of pigment per unit sectional volume	Percentage of pigmented neurons per sectional area	Percentage of intraneuronal pigment volume per neuronal volume
15	B127	2	-	-	.4	33.30	7.20
16	21	2	-	17	0.7	42.54	8.73
17	053	2	7	-	1.0	38.84	5.78
18	B68	2	8	6	1.3	47.60	16.28
19	B82	3	2	-	0.09	52.29	13.65
20	B36	3	6	-	1.2	49.60	14.90
21	B95	4	-	-	1.0	54.70	16.87
22	B118	6	7	-	1.4	59.80	18.31
23	B119	6	10	-	1.2	50.79	18.76
24	M52	7	6	-	1.8	61.87	19.33
25	B43	7	7	-	1.5	74.30	20.01
26	B44	7	9	-	1.9	64.80	17.93
27	B42	8	7	-	2.2	78.61	22.30
28	9	8	8	-	1.8	76.92	21.20

Table 10 (Continued)

Serial No.	Dog No.	Years	Age Months	Days	Percentage of pigment per unit sectional volume	Percentage of pigmented neurons per sectional area	Percentage of intraneutronal pigment volume per neuronal volume
29	M54	9	-	-	2.0	69.22	20.79
30	M53	9	-	-	1.7	70.00	21.36
31	B63	9	2	-	1.5	72.30	19.80
32	6	10	-	-	2.2	82.90	22.39
33	M49	10	3	-	2.4	81.00	21.15
34	M42	11	2	-	1.9	81.88	21.79
35	B123	11	9	-	2.1	78.70	23.60
36	M44	12	-	-	1.9	80.00	20.30
37	M45	12	1	-	2.5	90.79	22.60
38	B131	12	9	-	2.8	92.30	25.03
39	M37	13	1	-	2.6	88.80	24.00
40	M36	16	-	-	2.3	91.66	24.60

Table 11. Quantitative lipofuscin distribution in the nuclei cochleares of the dog with age

Serial No.	Dog No.	Years	Age Months	Days	Percentage of pigment per unit sectional volume	Percentage of pigmented neurons per sectional area	Percentage of intraneuronal pigment volume per neuronal volume
1	B105	-	-	1	-	-	-
2	B99	-	1	19	-	-	-
3	E26	-	2	-	-	-	-
4	068	-	2	15	-	-	-
5	E27	-	4	-	-	-	-
6	049	-	5	7	-	-	-
7	B66	-	6	15	-	-	-
8	B48	-	8	-	-	-	-
9	B79	-	10	-	-	-	-
10	C41	-	11	-	-	-	-
11	B56	1	-	-	-	-	-
12	B37	1	2	11	-	-	-
13	B96	1	5	-	-	-	-
14	B80	1	7	-	Traces	Traces	Traces

Table 11 (Continued)

Serial No.	Dog No.	Years	Age Months	Days	Percentage of pigment per unit sectional volume	Percentage of pigmented neurons per sectional area	Percentage of intraneuronal pigment volume per neuronal volume
15	B127	2	-	-	Traces	Traces	Traces
16	21	2	-	17	.3	27.91	6.92
17	053	2	7	-	.5	38.29	4.61
18	B68	2	8	6	.5	32.43	7.43
19	B82	3	2	-	.9	55.0	6.97
20	B36	3	6	-	.7	47.30	5.32
21	B95	4	-	-	1.2	57.69	8.24
22	B118	6	7	-	1.3	46.31	9.15
23	B119	6	10	-	1.6	67.92	13.03
24	M52	7	6	-	1.2	56.66	10.21
25	B43	7	7	-	1.6	59.02	11.30
26	B44	7	9	-	1.7	62.24	12.82
27	B42	8	7	-	2.1	60.70	12.96
28	9	8	8	-	1.6	64.00	10.21

Table 11 (Continued)

Serial No.	Dog No.	Years	Age Months	Days	Percentage of pigment per unit sectional volume	Percentage of pigmented neurons per sectional area	Percentage of intraneuronal pigment volume per neuronal volume
29	M54	9	-	-	1.9	54.50	14.53
30	M53	9	-	-	1.7	66.67	12.20
31	B63	9	2	-	2.0	68.00	15.47
32	6	10	-	-	1.8	79.07	16.27
33	M49	10	3	-	1.9	80.79	18.94
34	M42	11	2	-	2.1	73.38	20.25
35	B123	11	9	-	1.8	79.30	16.92
36	M44	12	-	-	2.0	77.14	19.47
37	M45	12	1	-	2.3	82.61	27.68
38	B131	12	9	-	2.6	85.30	25.30
39	M37	13	1	-	2.5	78.70	22.50
40	M36	16	-	-	2.8	81.25	21.33

APPENDIX B

Graph 1. Age group distribution and mean of the smooth muscle cell nuclei number per unit medial volume of the arteria cerebri media of the dog

Serial no.	Age group	Number of dogs	Mean number of smooth muscle cell nuclei per unit medial volume of	Range of values
1	Birth to 6 months	6	49.76	53.0 - 46.5
2	6 months to 1 year	5	40.00	44.2 - 36.4
3	1 year to 4 years	10	33.90	40.1 - 26.1
4	4 years to 8 years	5	26.80	30.4 - 25.2
5	8 years to 12 years	10	21.93	24.6 - 18.8
6	12 years to 16 years	4	18.95	20.7 - 17.5

Number of smooth muscle cells per unit medial volume
0
10
20
30
40
50
60
70
80
90
100
Age groups
1
2
3
4
5
6

Graph 2. Age group distribution and mean of the smooth muscle cell nuclei number per unit medial volume of the arteria basilaris of the dog

Serial no.	Age group	Number of dogs	Mean number of smooth muscle cell nuclei per unit medial volume of	Range of values
1	Birth to 6 months	6	47.45	55.2 - 37.0
2	6 months to 1 year	5	41.56	49.3 - 36.9
3	1 year to 4 years	10	32.41	36.8 - 26.0
4	4 years to 8 years	5	26.80	28.3 - 24.1
5	8 years to 12 years	10	20.69	23.3 - 17.2
6	12 years to 16 years	4	18.49	21.8 - 16.9

Number of smooth muscle cells per unit medial volume
0
10
20
30
40
50
60
70
80
90
100
Age groups
1
2
3
4
5
6

Graph 3. Age group distribution and mean of the smooth muscle cell nuclei number per unit medial volume of the arteria cerebri media of the pig

Serial no.	Age group	Number of pigs	Mean number of smooth muscle cell nuclei per unit medial volume of	Range of values
1	Birth to 6 months	4	48.55	51.6 - 44.2
2	6 months to 1 year	4	41.85	44.6 - 38.8
3	1 year to 4 years	8	33.45	38.0 - 28.8
4	4 years to 8 years	10	23.81	28.8 - 19.0
5	8 years to 10 years	4	17.70	18.6 - 16.8

Number of smooth muscle cells per unit medial volume
10
20
30
40
50
60
70
80
90
100
0
1
2
3
4
5
Age groups

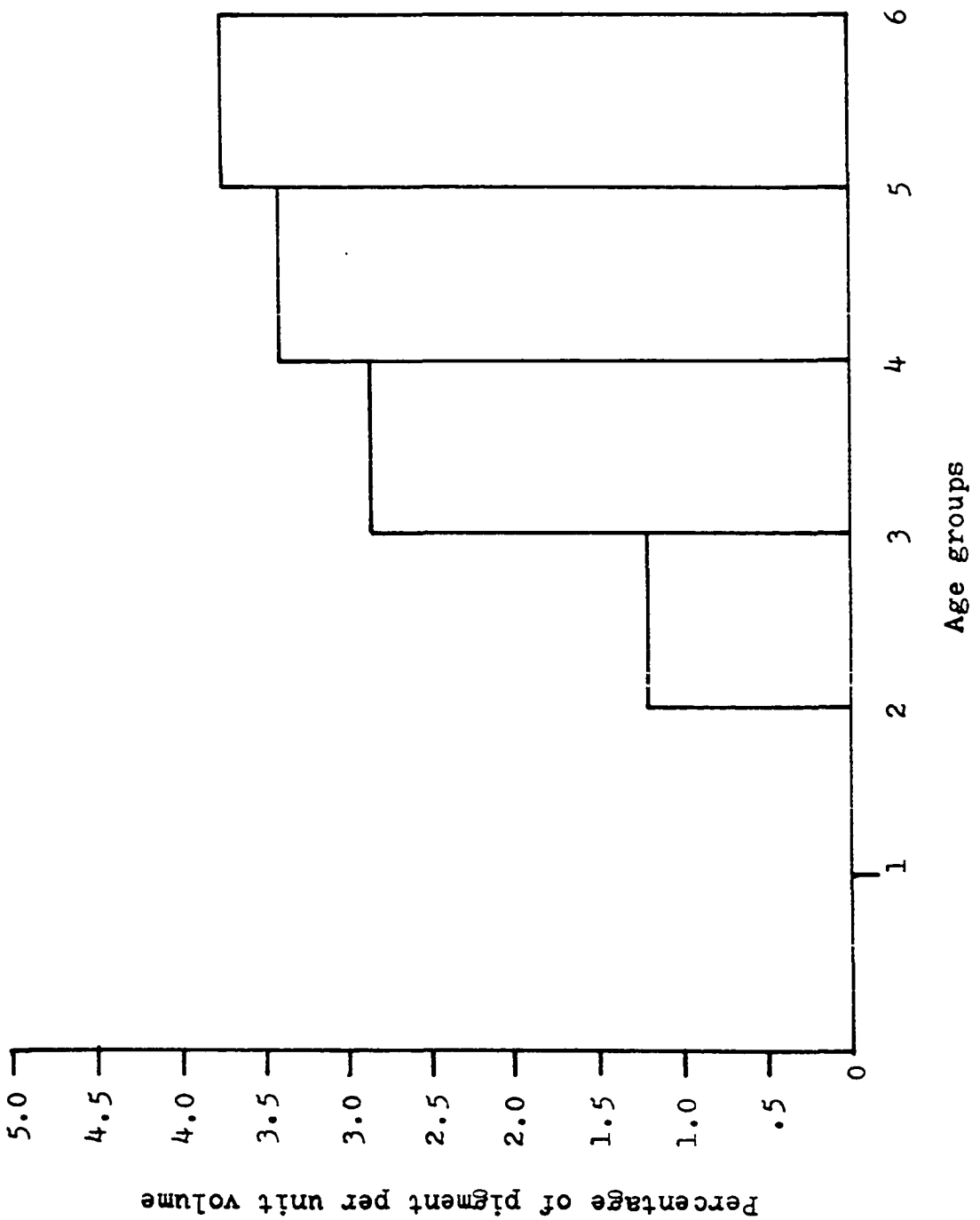
Graph 4. Age group distribution and mean of the smooth muscle cell nuclei number per unit medial volume of the arteria basilaris of the pig

Serial no.	Age group	Number of pigs	Mean number of smooth muscle cell nuclei per unit medial volume of	Range of values
1	Birth to 6 months	4	50.95	57.0 - 46.5
2	6 months to 1 year	4	42.07	46.0 - 38.4
3	1 year to 4 years	8	33.50	36.8 - 27.2
4	4 years to 8 years	10	24.21	29.4 - 19.7
5	8 years to 10 years	4	19.82	21.3 - 18.2

Number of smooth muscle cells per unit medial volume
0
10
20
30
40
50
60
70
80
90
100
Age groups
1
2
3
4
5

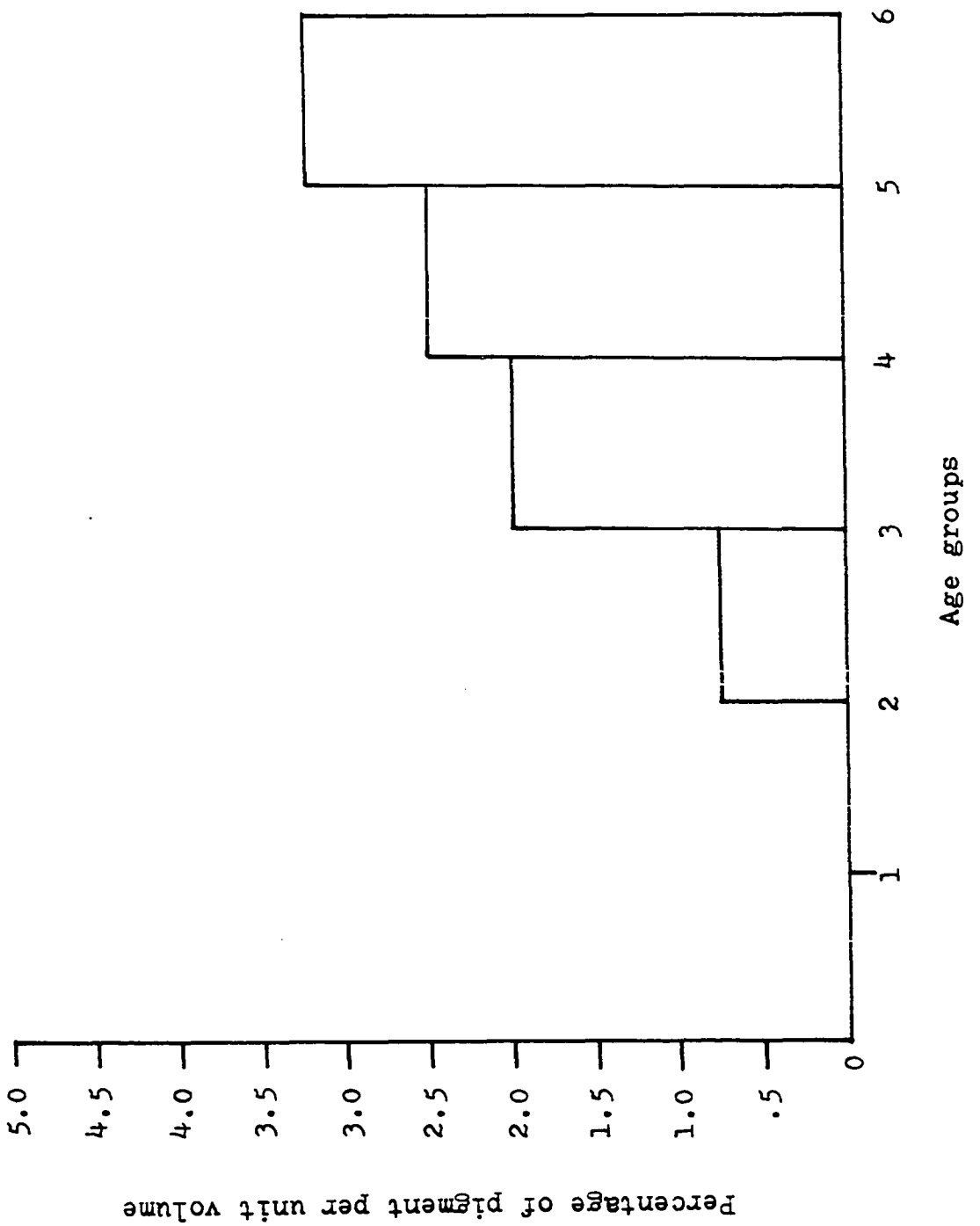
Graph 5. Age group distribution and mean percentage of the lipofuscin pigment per unit sectional volume of the nucleus olivaris inferioris of the dog

Serial no.	Age group	Number of dogs			Mean percentage of pigment per unit sectional volume	Range of values
		Negative	Trace pigment	Measurable pigment		
1	Birth to 6 months	6	-	-	-	-
2	6 months to 1 year	3	2	-	-	-
3	1 year to 4 years	1	-	9	1.20	0.0 - 1.9
4	4 years to 8 years	-	-	5	2.84	2.5 - 3.1
5	8 years to 12 years	-	-	10	3.40	2.5 - 3.6
6	12 years to 16 years	-	-	4	3.72	3.2 - 3.9


Percentage of pigment per unit volume
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
.5
0
1
2
3
4
5
6
Age groups

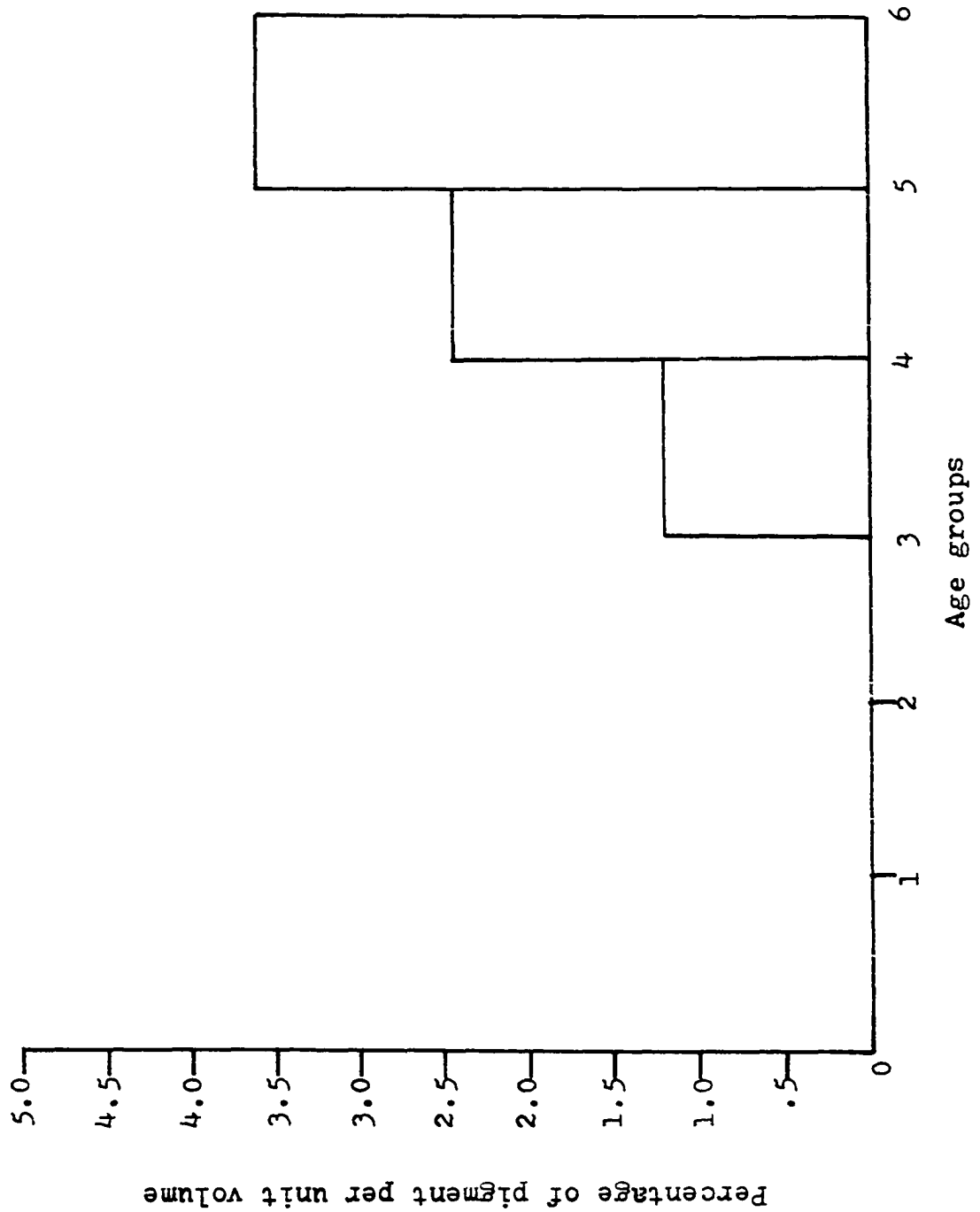
Graph 6. Age group distribution and mean percentage of the lipofuscin pigment per unit sectional volume of the nucleus hypoglossus of the dog

Serial no.	Age group	Number of dogs			Mean percentage of pigment per unit sectional volume of	Range of values
		Negative	Trace pigment	Measurable pigment		
1	Birth to 6 months	6	-	-	-	-
2	6 months to 1 year	3	2	-	-	-
3	1 year to 4 years	1	2	7	0.75	0.0 - 1.6
4	4 years to 8 years	-	-	5	2.06	1.8 - 2.4
5	8 years to 12 years	-	-	10	2.50	1.8 - 3.2
6	12 years to 16 years	-	-	4	3.75	3.1 - 4.7


Percentage of pigment per unit volume
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
.5
0
1
2
3
4
5
6
Age groups

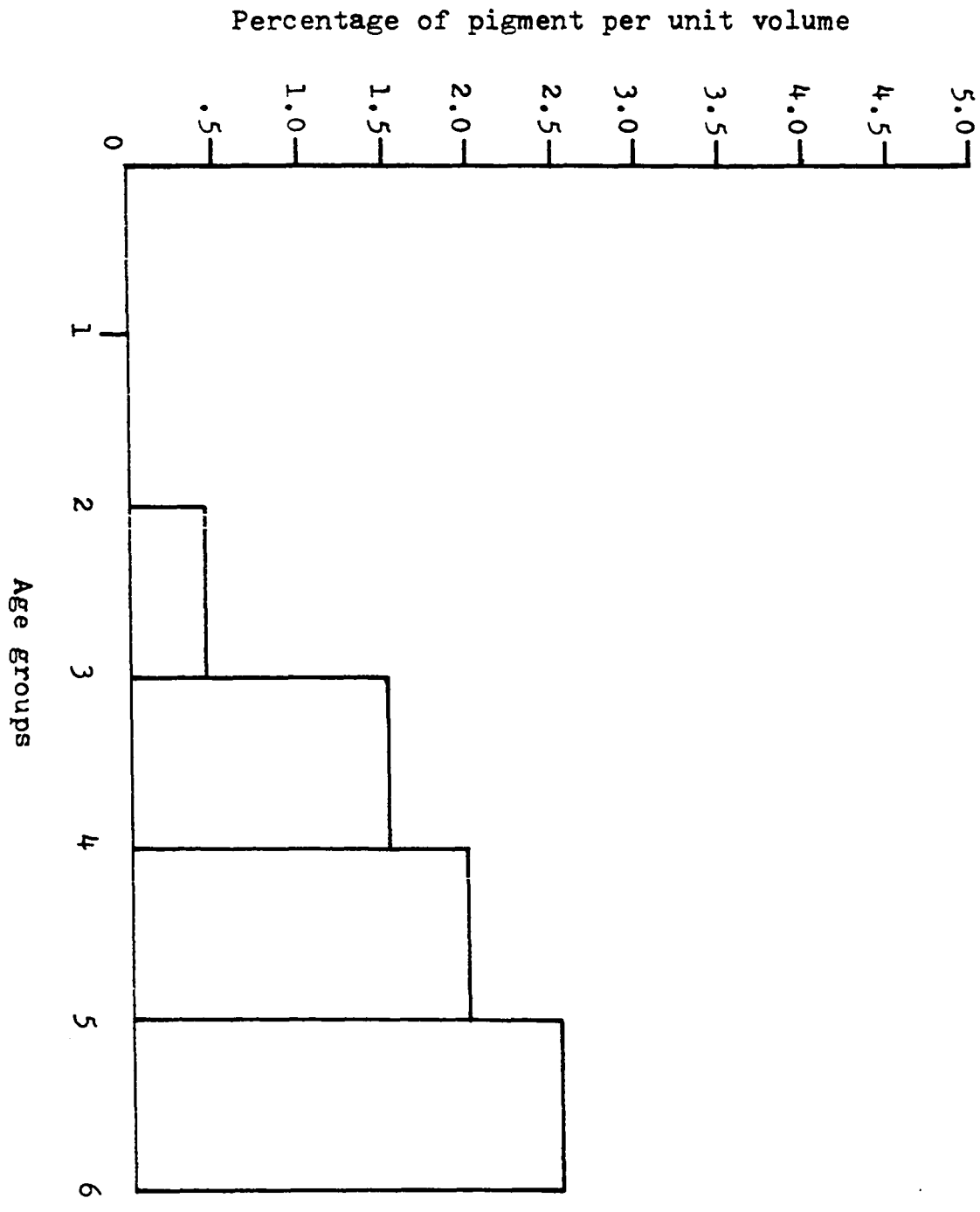
Graph 7. Age group distribution and mean percentage of the lipofuscin pigment per unit sectional volume of the dorsal motor nucleus of vagus of the dog

Serial no.	Age group	Number of dogs			Mean percentage of pigment per unit sectional volume of	Range of values
		Negative	Trace pigment	Measurable pigment		
1	Birth to 6 months	6	-	-	-	-
2	6 months to 1 year	5	-	-	-	-
3	1 year to 4 years	9	1	-	-	-
4	4 years to 8 years	-	-	5	1.18	0.6 - 1.5
5	8 years to 12 years	-	-	10	2.42	1.2 - 3.3
6	12 years to 16 years	-	-	4	3.67	3.4 - 4.3


Percentage of pigment per unit volume
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
.5
0
1
2
3
4
5
6
Age groups

Graph 8. Age group distribution and mean percentage of the lipofuscin pigment per unit sectional volume of the nuclei vestibulares of the dog

Serial no.	Age group	Number of dogs: Negative	Trace pigment	Measurable pigment	Mean percentage of pigment per unit sectional volume of	Range of values
1	Birth to 6 months	6	-	-	-	-
2	6 months to 1 year	3	2	-	-	-
3	1 year to 4 years	1	1	8	0.71	0.0 - 1.3
4	4 years to 8 years	-	-	5	1.56	1.2 - 1.9
5	8 years to 12 years	-	-	10	1.97	1.5 - 2.4
6	12 years to 16 years	-	-	4	2.55	2.3 - 2.8


Percentage of pigment per unit volume
0
.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
Age groups
1
2
3
4
5
6

Graph 9. Age group distribution and mean percentage of lipofuscin pigment per unit sectional volume of the nuclei cochleares of the dog

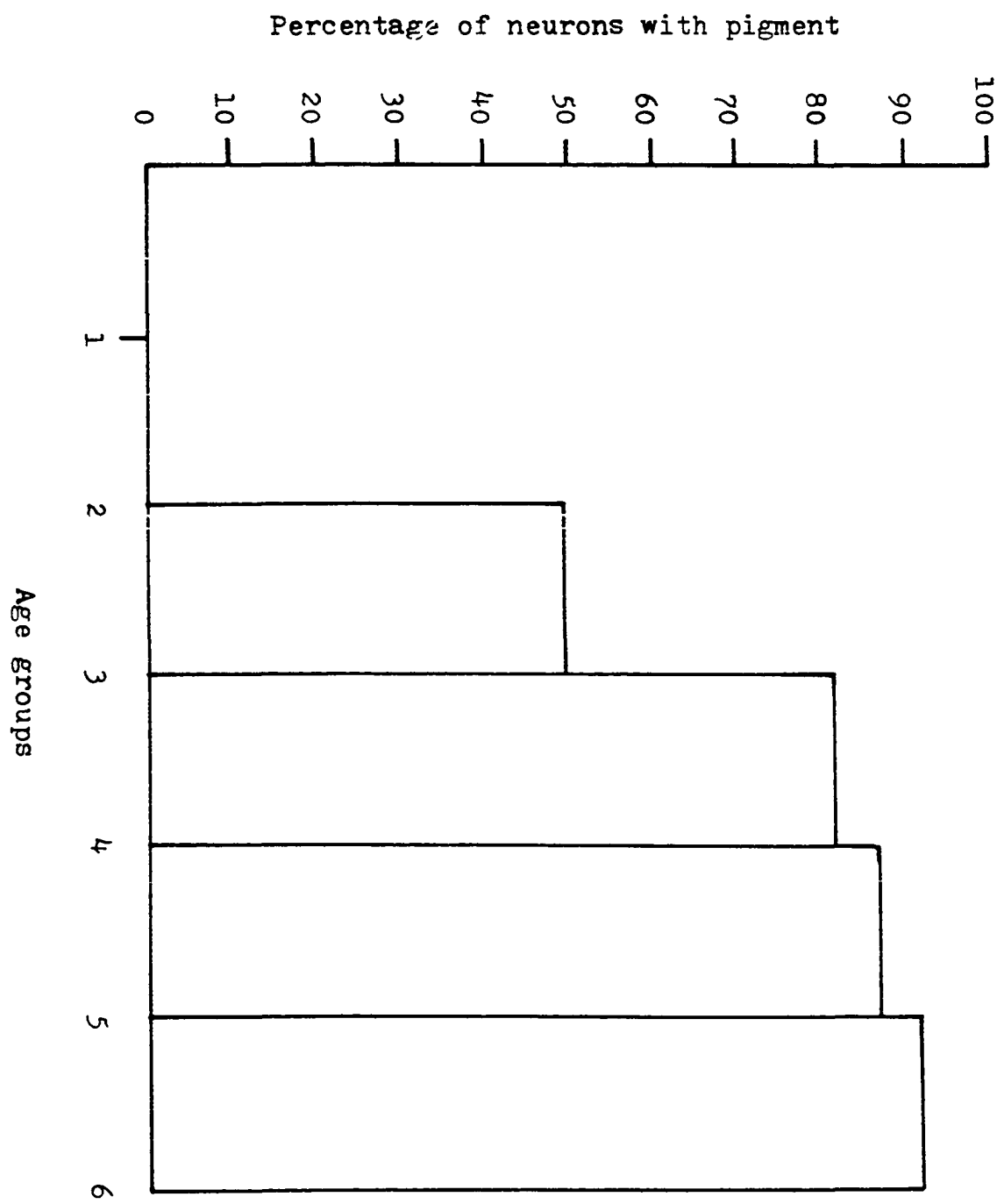
Serial no.	Age group	Number of Dogs: Negative	Trace pigment	Measurable pigment	Mean percentage of pigment per unit sectional volume of	Range of values
1	Birth to 6 months	6	-	-	-	-
2	6 months to 1 year	5	-	-	-	-
3	1 year to 4 years	2	2	6	0.41	0.0 - 1.2
4	4 years to 8 years	-	-	5	1.44	1.2 - 1.7
5	8 years to 12 years	-	-	10	1.67	1.3 - 1.9
6	12 years to 16 years	-	-	4	1.95	1.8 - 2.1

Percentage of pigment per unit volume
0
.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
Age groups
1
2
3
4
5
6

Percentage of pigment per unit volume
0
.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
Age groups
1
2
3
4
5
6

Graph 10. Age group distribution and mean percentage of the neurons with lipofuscin pigment per unit sectional volume of the nucleus olivaris inferioris of the dog

Serial no.	Age group	Number of dogs: Negative	Trace pigment	Measurable pigment	Mean percentage of pigmented neurons per sectional area (measurable)	Range of values
1	Birth to 6 months	6	-	-	-	-
2	6 months to 1 year	3	2	-	-	-
3	1 year to 4 years	1	-	9	49.11	0.0 - 73.60
4	4 years to 8 years	-	-	5	81.57	76.40 - 87.50
5	8 years to 12 years	-	-	10	86.96	82.35 - 91.99
6	12 years to 16 years	-	-	4	91.97	86.00 - 95.00


Percentage of neurons with pigment
0
10
20
30
40
50
60
70
80
90
100
Age groups
1
2
3
4
5
6

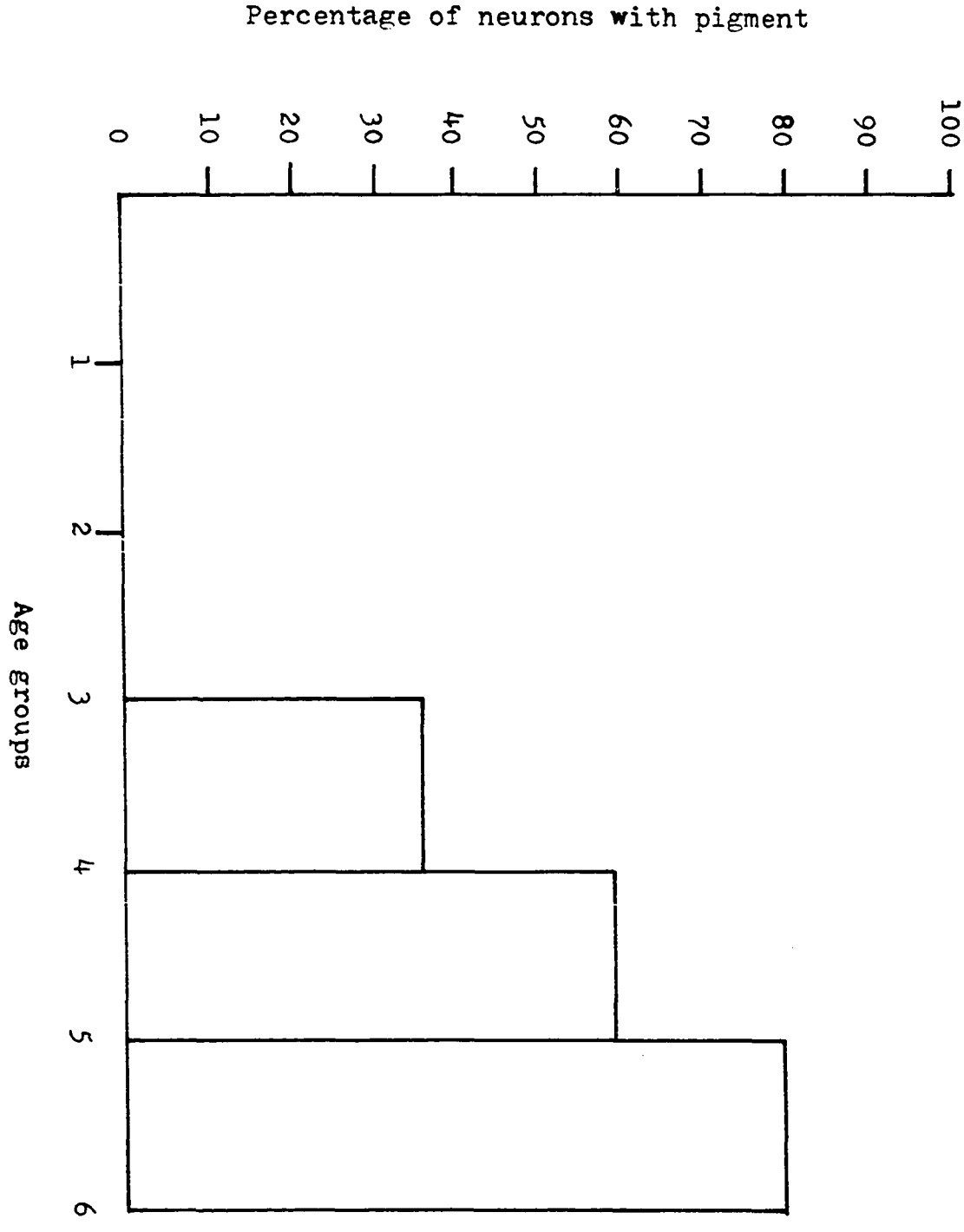
Graph 11. Age group distribution and mean percentage of the neurons with lipofuscin pigment per unit sectional volume of the nucleus hypoglossus of the dog

Serial no.	Age group	Number of dogs: Negative	Trace pigment	Measurable pigment	Mean percentage of pigmented neurons per sectional area (measurable)	Range of values
1	Birth to 6 months	6	-	-	-	-
2	6 months to 1 year	3	2	-	-	-
3	1 year to 4 years	1	2	7	27.73	0.0 - 56.39
4	4years to 8 years	-	-	5	66.39	58.97 - 73.20
5	8 years to 12 years	-	-	10	75.40	67.30 - 89.40
6	12 years to 16 years	-	-	4	86.79	79.72 - 92.46

Percentage of neurons with pigment
0
10
20
30
40
50
60
70
80
90
100
Age groups
1
2
3
4
5
6

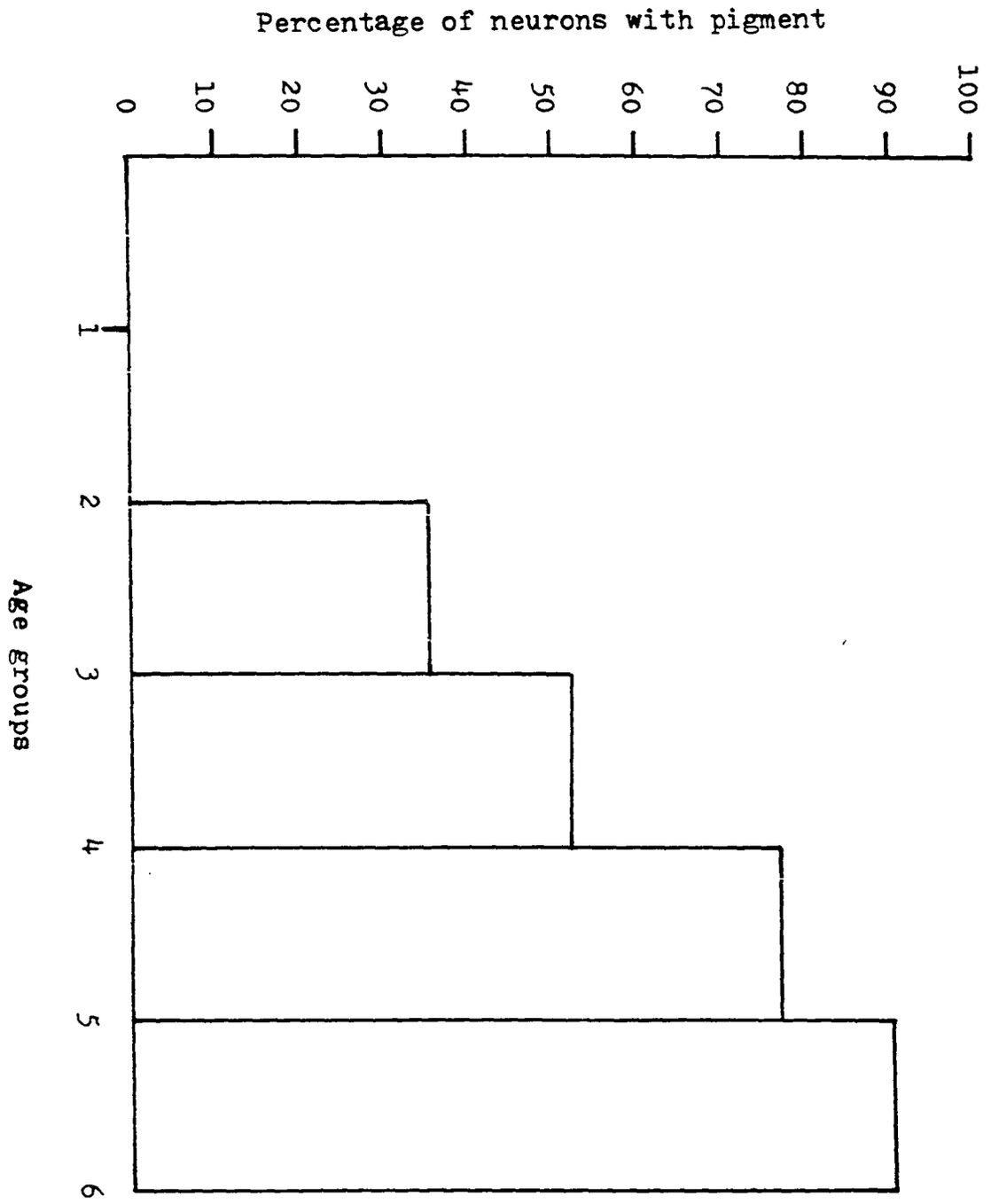
Graph 12. Age group distribution and mean percentage of the neurons with lipofuscin pigment per unit sectional volume of the dorsal motor nucleus of vagus of the dog

Serial no.	Age group	Number of dogs			Mean percentage of pigmented neurons per sectional area (measurable)	Range of values
		Negative	Trace pigment	Measurable pigment		
1	Birth to 6 months	6	-	-	-	-
2	6 months to 1 year	5	-	-	-	-
3	1 year to 4 years	9	1	-	-	-
4	4 years to 8 years	-	-	5	36.08	24.00 - 43.50
5	8 years to 12 years	-	-	10	59.19	49.30 - 73.92
6	12 years to 16 years	-	-	4	79.44	69.11 - 88.67


Percentage of neurons with pigment
0
10
20
30
40
50
60
70
80
90
100
Age groups
1
2
3
4
5
6

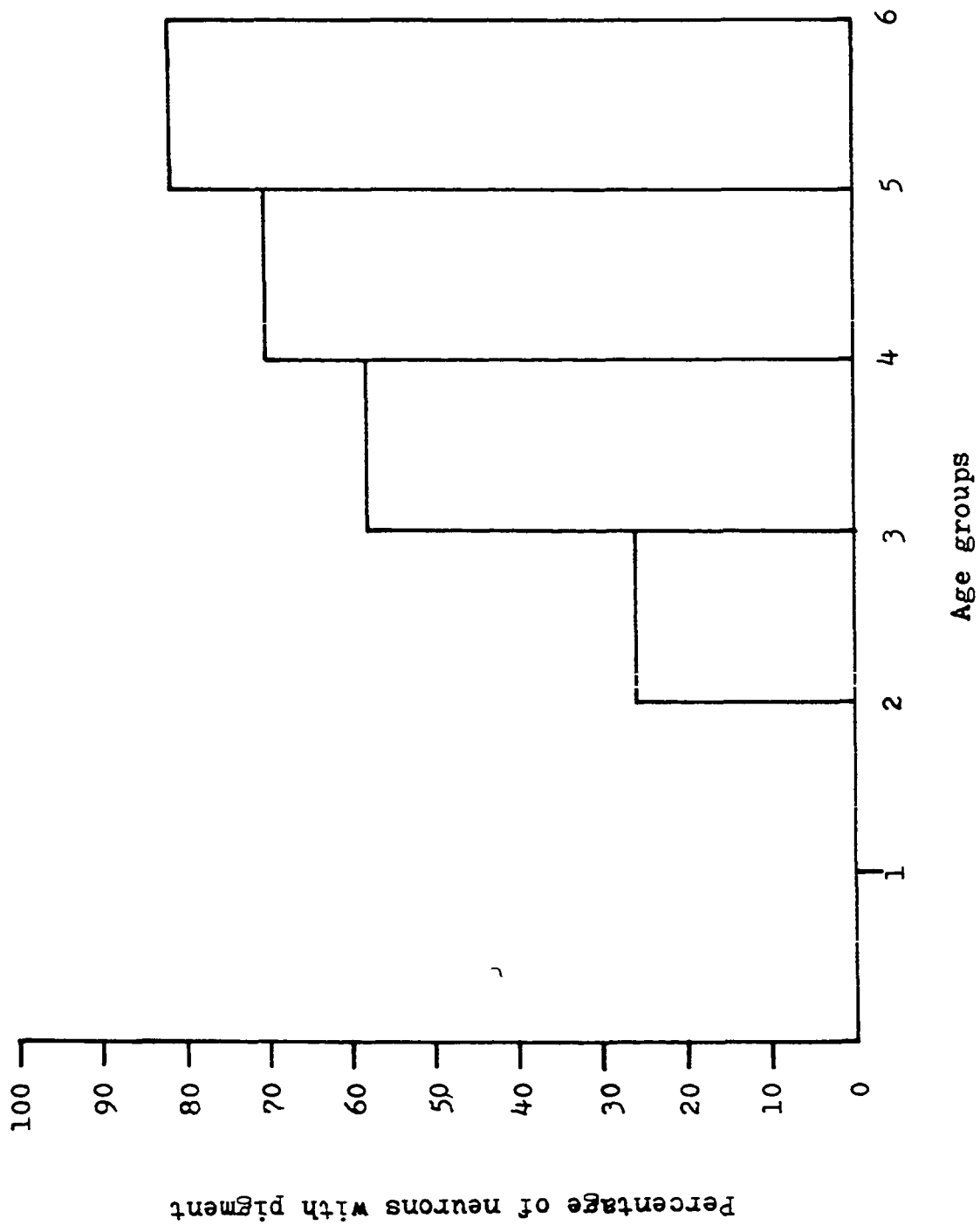
Graph 13. Age group distribution and mean percentage of the neurons with lipofuscin pigment per unit sectional volume of the nuclei vestibulares of the dog

Serial no.	Age group	Number of dogs			Mean percentage of pigmented neurons per sectional area (measurable)	Range of values
		Negative	Trace pigment	Measurable pigment		
1	Birth to 6 months	6	-	-	-	-
2	6 months to 1 year	5	-	-	-	-
3	1 year to 4 years	1	1	8	35.55	0.0 - 54.70
4	4 years to 8 years	-	-	5	62.31	50.79 - 74.30
5	8 years to 12 years	-	-	10	77.21	69.22 - 82,90
6	12 years to 16 years	-	-	4	90.88	88.80 - 91.66


Percentage of neurons with pigment
0
10
20
30
40
50
60
70
80
90
100
Age groups
1
2
3
4
5
6

Graph 14. Age group distribution and mean percentage of the neurons with lipofuscin pigment per unit sectional volume of the nuclei cochleares of the dog

Serial no.	Age group	Number of dogs			Mean percentage of pigmented neurons per sectional area (measurable)	Range of values
		Negative	Trace pigment	Measurable pigment		
1	Birth to 6 months	6	-	-	-	-
2	6 months to 1 year	5	-	-	-	-
3	1 year to 4 years	2	2	6	25.80	0.0 - 57.69
4	4 years to 8 years	-	-	3	58.43	46.31 - 67.92
5	8 years to 12 years	-	-	10	70.35	54.50 - 80.79
6	12 years to 16 years	-	-	4	81.96	78.70 - 85.30


Percentage of neurons with pigment
0
10
20
30
40
50
60
70
80
90
100
1
2
3
4
5
6
Age groups

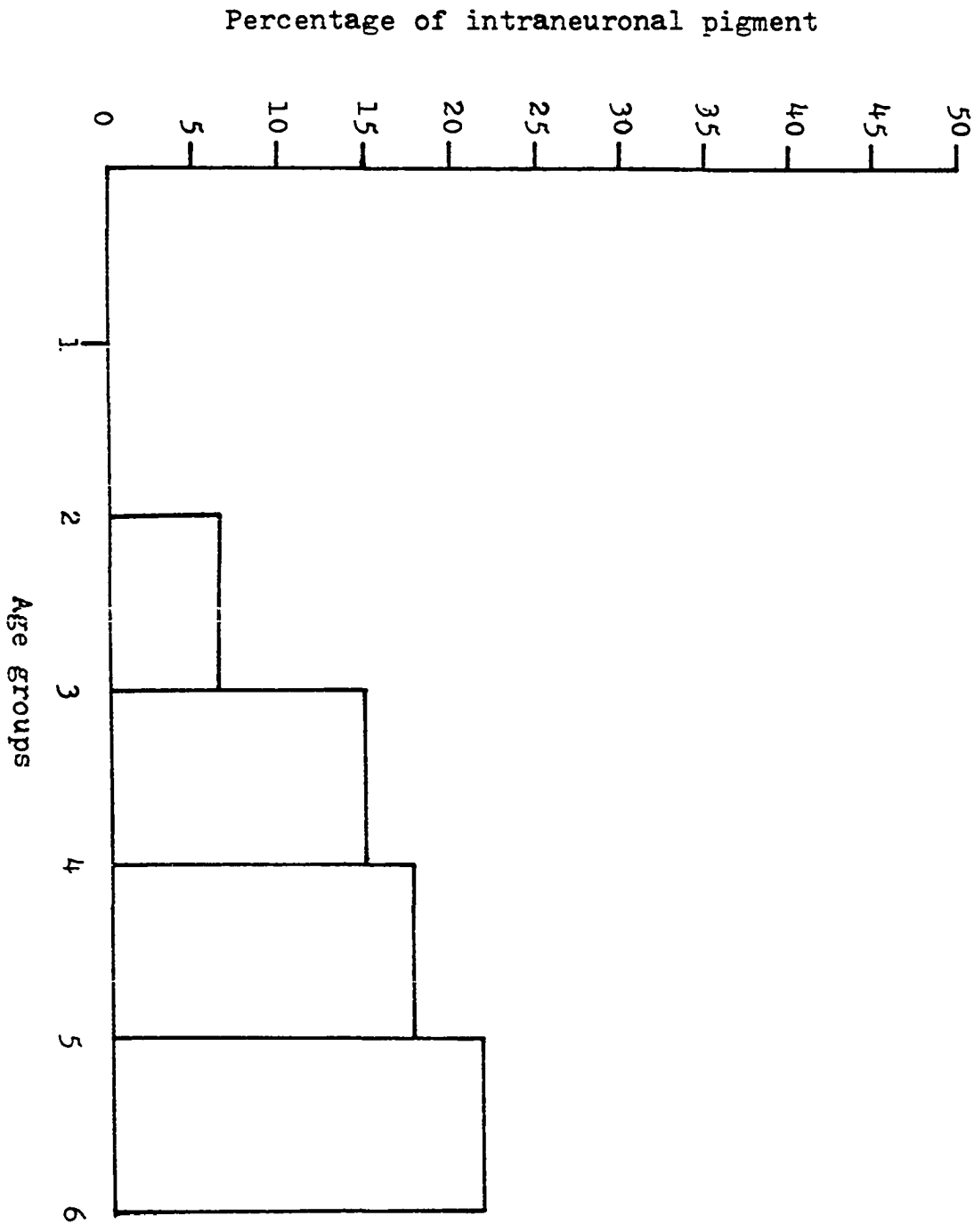
Graph 15. Age group distribution and mean percentage of the intraneuronal lipofuscin pigment per neuronal volume of the nucleus olivaris inferioris of the dog

Serial no.	Age group	Number of dogs			Mean percentage of pigmented neurons per sectional area (measurable)	Range of values
		Negative	Trace pigment	Measurable pigment		
1	Birth to 6 months	6	-	-	-	-
2	6 months to 1 year	3	2	-	-	-
3	1 year to 4 years	1	-	9	14.32	0.0 - 26.06
4	4 years to 8 years	-	-	5	27.28	25.03 - 28.08
5	8 years to 12 years	-	-	10	37.00	31.4 - 47.90
6	12 years to 16 years	-	-	4	46.22	43.31 - 48.60

Percentage of intraneuronal pigment
0
5
10
15
20
25
30
35
40
45
50
Age groups
1
2
3
4
5
6

Graph 16. Age group distribution and mean percentage of the intraneuronal lipofuscin pigment per neuronal volume of the nucleus hypoglossus of the dog

Serial no.	Age group	Number of dogs			Mean percentage of intraneuronal pigment per neuronal volume (measurable)	Range of values
		Negative	Trace pigment	Measurable pigment		
1	Birth to 6 months	6	-	-	-	-
2	6 months to 1 year	3	2	-	-	-
3	1 year to 4 years	1	2	7	6.40	0.0 - 12.07
4	4 years to 8 years	-	-	5	14.92	13.03 - 17.30
5	8 years to 12 years	-	-	10	17.60	13.16 - 20.94
6	12 years to 16 years	-	-	4	21.77	20.95 - 23.21


Percentage of intraneuronal pigment
0
5
10
15
20
25
30
35
40
45
50
Age groups
1
2
3
4
5
6

Graph 17. Age group distribution and mean percentage of the intraneuronal lipofuscin pigment per neuronal volume of the dorsal motor nucleus of vagus of the dog

Serial no.	Age group	Number of dogs			Mean percentage of intraneuronal pigment per neuronal volume (measurable)	Range of values
		Negative	Trace pigment	Measurable pigment		
1	Birth to 6 months	6	-	-	-	-
2	6 months to 1 year	5	-	-	-	-
3	1 year to 4 years	9	1	-	-	-
4	4 years to 8 years	-	-	5	19.05	10.33 - 24.30
5	8 years to 12 years	-	-	10	30.18	20.00 - 37.92
6	12 years to 16 years	-	-	4	35.08	37.93 - 53.22

Percentage of intraneuronal pigment
0
5
10
15
20
25
30
35
40
45
50
Age groups
1
2
3
4
5
6

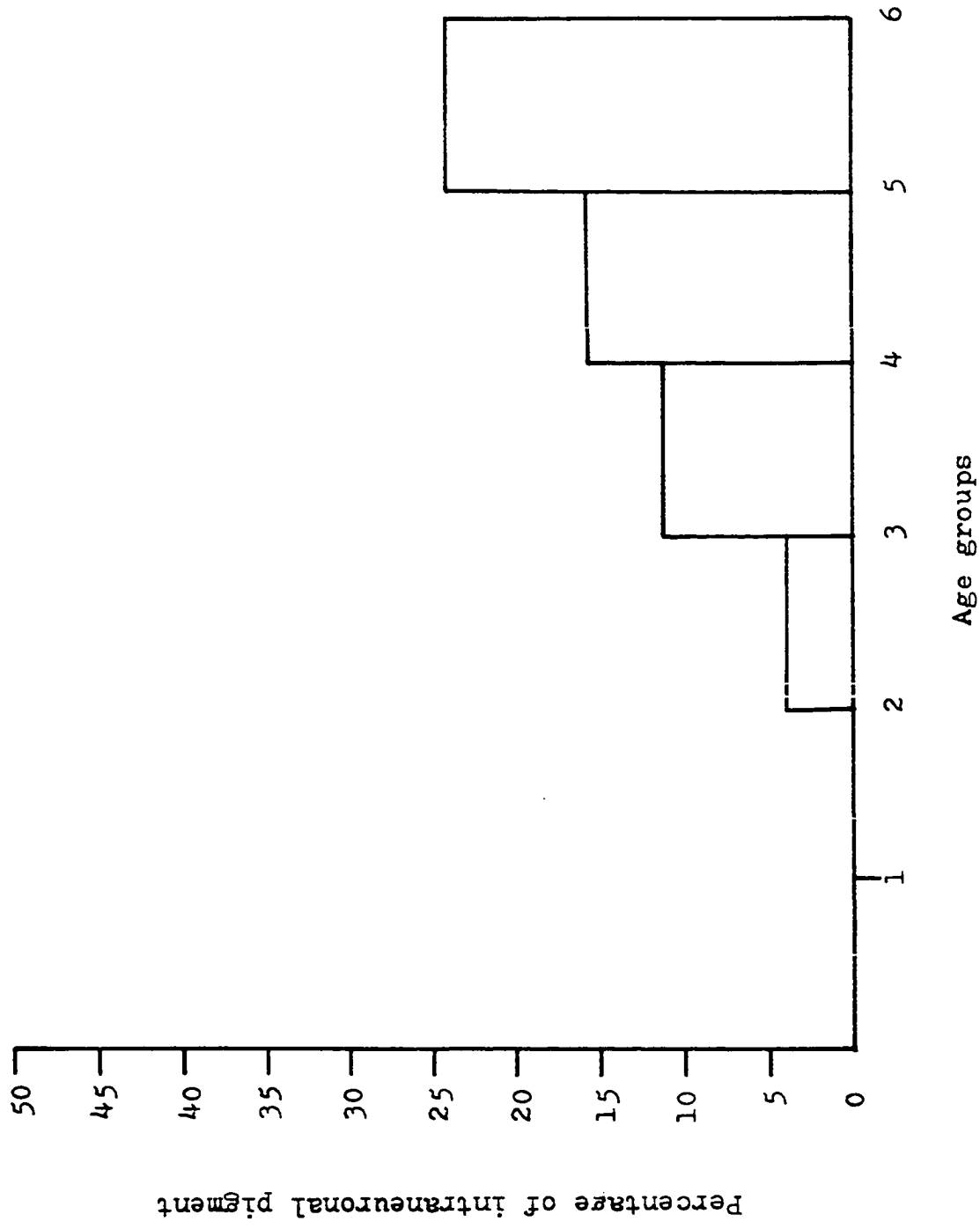
Graph 18. Age group distribution and mean percentage of the intraneuronal lipofuscin pigment per neuronal volume of the nuclei vestibulares of the dog

Serial no.	Age group	Number of dogs: Negative	Trace pigment	Measurable pigment	Mean percentage of intraneuronal pigment per neuronal volume (measurable)	Range of values
1	Birth to 6 months	6	-	-	-	-
2	6 months to 1 year	3	2	-	-	-
3	1 year to 4 years	1	1	8	9.37	0.0 - 16.80
4	4 years to 8 years	-	-	5	18.86	17.93 - 20.01
5	8 years to 12 years	-	-	10	21.48	19.80 - 23.80
6	12 years to 16 years	-	-	4	24.05	22.60 - 25.03

Percentage of intraneuronal pigment
0
5
10
15
20
25
30
35
40
45
50
Age groups
1
2
3
4
5
6

Graph 19. Age group distribution and mean percentage of the intraneuronal lipofuscin pigment per neuronal volume of the nuclei cochleares of the dog

Serial no.	Age group	Number of dogs: Negative	Trace pigment	Measurable pigment	Mean percentage of intraneuronal pigment per neuronal volume (measurable)	Range of values
1	Birth to 6 months	6	-	-	-	-
2	6 months to 1 year	5	-	-	-	-
3	1 year to 4 years	2	2	6	3.94	0.0 - 8.24
4	4 years to 8 years	-	-	5	11.30	10.21 - 13.03
5	8 years to 12 years	-	-	10	15.72	10.20 - 20.25
6	12 years to 16 years	-	-	4	24.20	21.33 - 27.68


Percentage of intraneuronal pigment
0
5
10
15
20
25
30
35
40
45
50
1
2
3
4
5
6
Age groups

Graph 20. Composite of the Graphs 5 to 9 showing the percentage of pigment per unit volume of the nuclei in different age groups

1. Nucleus olivaris inferioris
2. Dorsal motor nucleus of vagus
3. Nucleus hypoglossus
4. Nuclei vestibulares
5. Nuclei cochleares

Percentage of pigment per unit volume
0
.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
Age groups
1
2
3
4
5
6

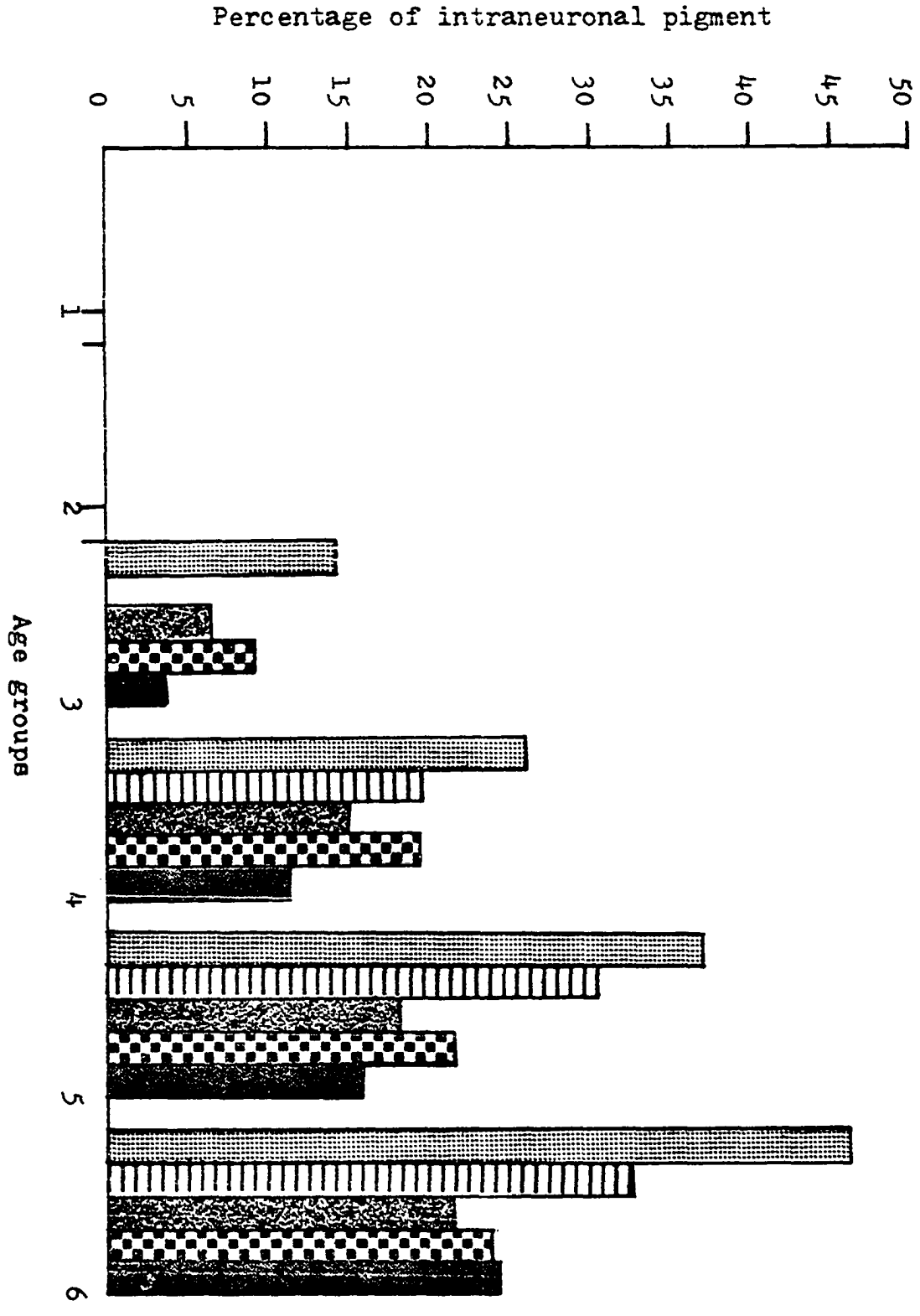
Graph 21. Composite of the Graphs 10 to 14 showing the percentage of pigmented neurons per unit volume of the nuclei in different age groups

1. Nucleus olivaris inferioris
2. Dorsal motor nucleus of vagus
3. Nucleus hypoglossus
4. Nuclei vestibulares
5. Nuclei cochleares

Percentage of neurons with pigment
0
10
20
30
40
50
60
70
80
90
100
Age groups
1
2
3
4
5
6

Graph 22. Composite of the Graphs 15 to 19 showing the percentage of the intra-neuronal pigment in the nuclei in different age groups

1. Nucleus olivaris inferioris
2. Dorsal motor nucleus of vagus
3. Nucleus hypoglossus
4. Nuclei vestibulares
5. Nuclei cochleares


Percentage of intraneuronal pigment
0
5
10
15
20
25
30
35
40
45
50
Age groups
1
2
3
4
5
6

APPENDIX C

Figure 1.
Ventral view of the brain of the dog showing the major cerebral arteries.
1. Arteria ethmoidalis interna. 2. Arteria carotis interna. 3. Arteria cerebri media. 4. Arteria communicans caudalis. 5. Arteria cerebelli rostralis. 6. Arteria basilaris. 7. Arteria cerebelli media.
8. Arteria cerebelli caudalis.

Figure 2.
Lateral view of the brain of the dog showing the cerebral arteries.
1. Rami corticales of arteria cerebri media. 2. Rami corticales of arteria cerebri rostralis. 3. Rami corticales of arteria cerebelli caudalis.

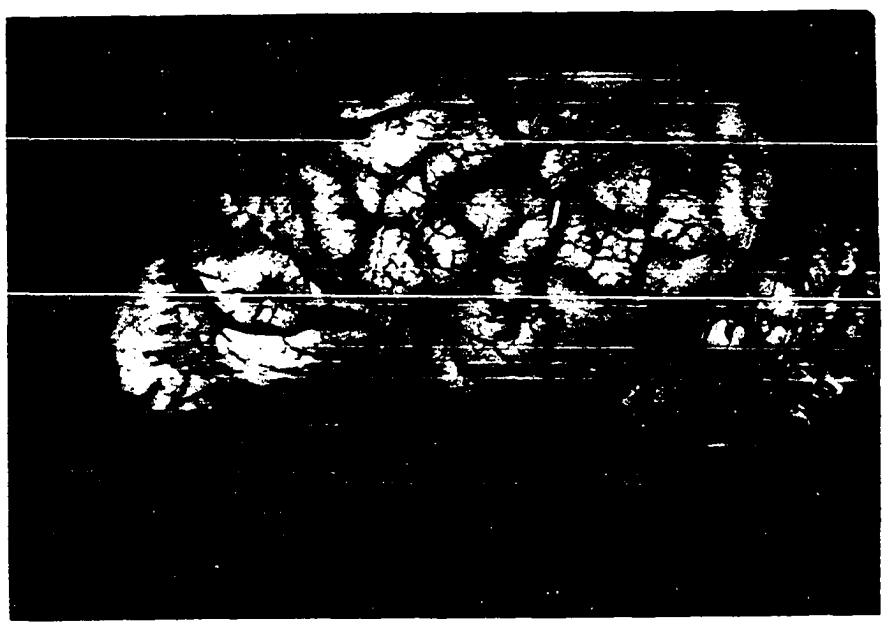
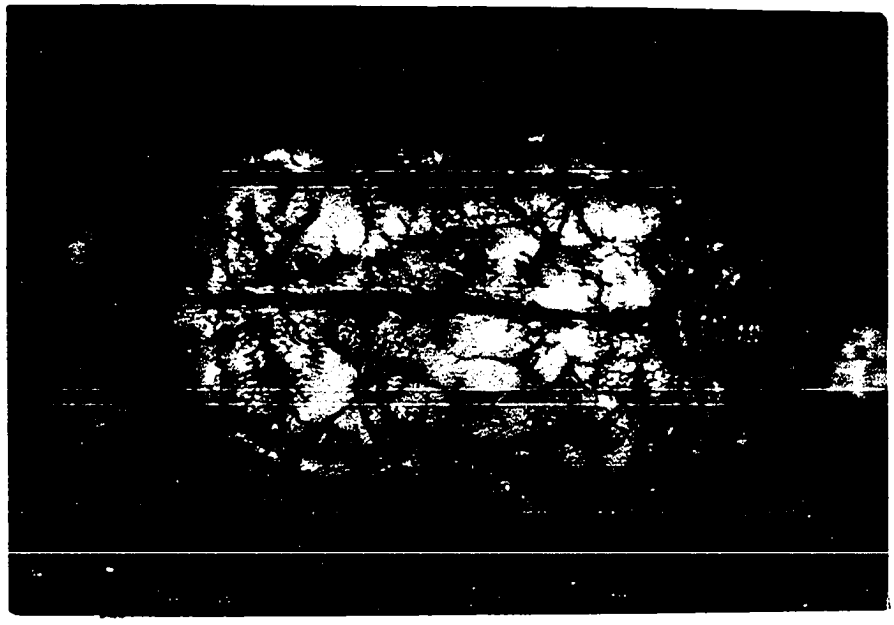


Figure 3.
Dorsal view of the brain of the dog showing cortical distribution of the major cerebral arteries. 1. Rami corticales of arteria cerebri media. 2. Rami corticales of the arteria cerebri rostralis. 3. Rami corticales of the arteria cerebri caudalis.

Figure 4.
Midsagittal section of the brain of the dog. 1. Arteria corporis callosi (mediane) communis. 2. Arteria corporis callosi. 3. Rami corticales of the arteria cerebri rostralis and arteria corporis callosi. 4. Rami corticales of the arteria cerebri caudalis. 5. Rami paramedianes of the arteria basilaris.



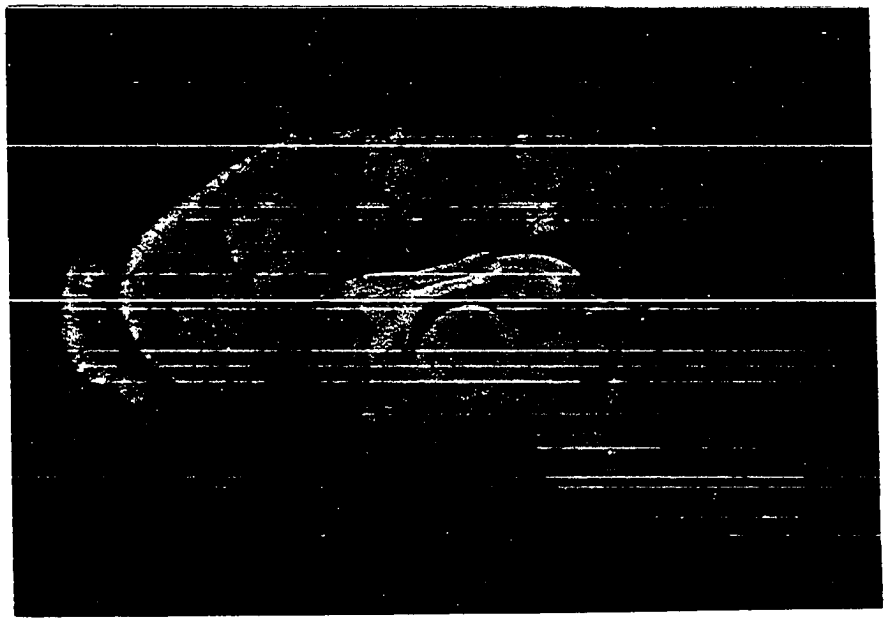


Figure 5.
Ventral view of the brain of the dog. 1. Arteria intercarotica caudalis. 2. Arteria carotis interna. 3. Arteria basilaris. 4. Hypophysis.

Figure 6.
Ventral view of the brain of the dog showing the arterial branches. 1. Arteria ethmoidalis interna. 2. Arteria corporis callosi (mediane) communis. 3. Arteria carotis interna. 4. Arteria cerebri media. 5. Arteria communicans caudalis (pars proximalis). 6. Arteria communicans caudalis (pars distalis). 7. Arteria cerebri caudalis. 8. Arteria cerebelli rostralis. 9. Arteria intercarotica rostralis. 10. Rami dorsomedialis or caudomediales of arteria communicans caudalis (pars distalis).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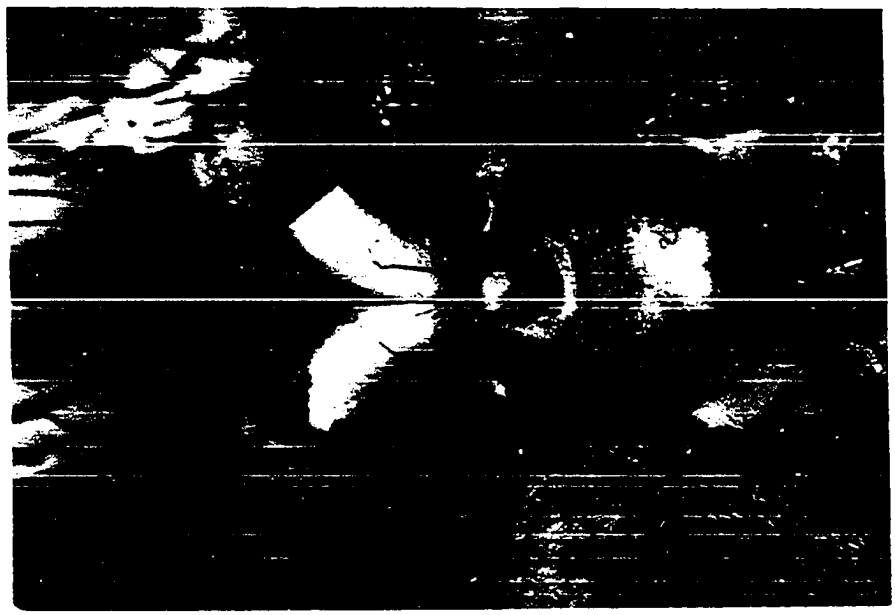

Figure 7.
Ventral view of the brain of the dog. 1. Arteria ethmoidalis interna. 2. Arteria ophthalmica interna. 3. Arteria carotis interna. 4. Arteria cerebri media. 5. Arteria cerebri rostralis. 6. Rami caudomediales (posteriomediales) of arteria communicans caudalis (pars proximalis). 7. Arteria corporis callosi (mediane) communis. 8. Rami caudolaterales (posteriolaterales) of arteria communicans caudalis (pars proximalis).

Figure 8.
Lateral view of the brain of the dog around the mesencephalon. 1. Arteria communicans caudalis (pars proximalis). 2. Rami caudolaterales branches of no. 1. 3. Arteria choroidea rostralis. 4. Arteria cerebri caudalis. 5. Common stem of the arteria choroidea caudalis and ramus ad tectum mesencephali rostralis. 6. Arteria cerebelli rostralis. 7. Ramus ad tectum mesencephali intermedius. 8. Ramus ad pontem rostralis. 9. Arteria cerebelli media.


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Figure 9.
A view similar to Figure 8. 1. Arteria cerebri caudalis. 2. Arteria choroidea caudalis. 3. Ramus ad tectum mesencephali rostralis. 4. Ramus ad tectum mesencephali intermedius. 5. Ramus ad tectum mesencephali caudalis. 6. Arteria cerebelli rostralis.

Figure 10.
A view similar to Figure 9 after removal of cerebellar hemisphere.
1. Arteria cerebri caudalis. 2. Arteria choroidea caudalis. 3. Ramus ad tectum mesencephali rostralis. 4. Ramus ad tectum mesencephali intermedius. 5. Ramus ad tectum mesencephali caudalis.


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Figure 11.
Dorsolateral view of the mesencephalon of the dog. 1. Arteria cerebri caudalis. 2. Arteria choroidea caudalis. 3. Ramus ad tectum mesencephali rostralis. 4. Ramus ad tectum mesencephali intermedius. 5. Ramus ad tectum mesencephali caudalis. 6. Arteria basilaris.

Figure 12.
Dorsal view of the nucleus caudatus, thalamus and colliculus rostralis to show the plexus choroideus ventriculi tertii and plexus choroideus ventriculi lateralis. 1. Arteria choridea rostralis. 2. Rami choroidei caudales. 3. Plexus choroideus ventriculi lateralis. 4. Plexus choroideus ventriculi tertii.


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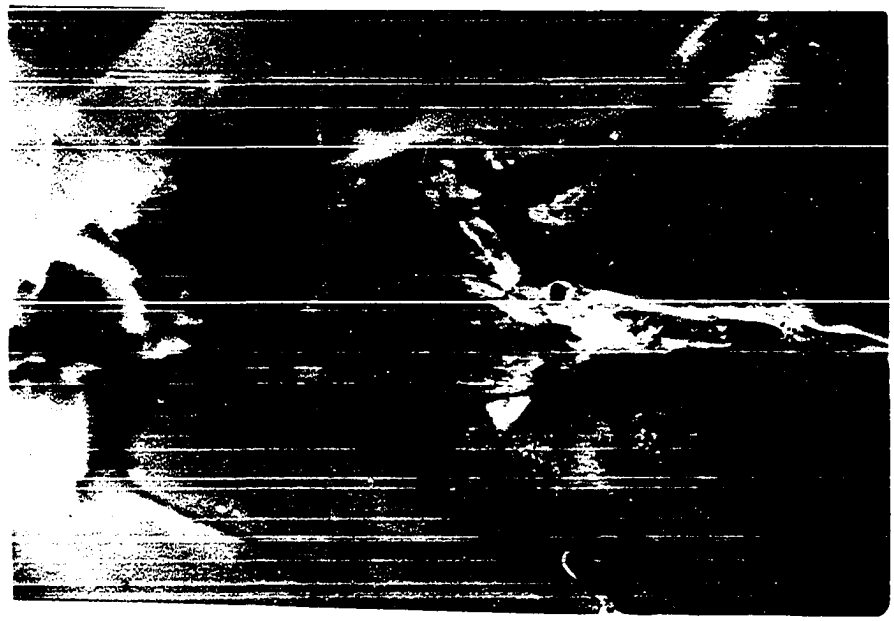
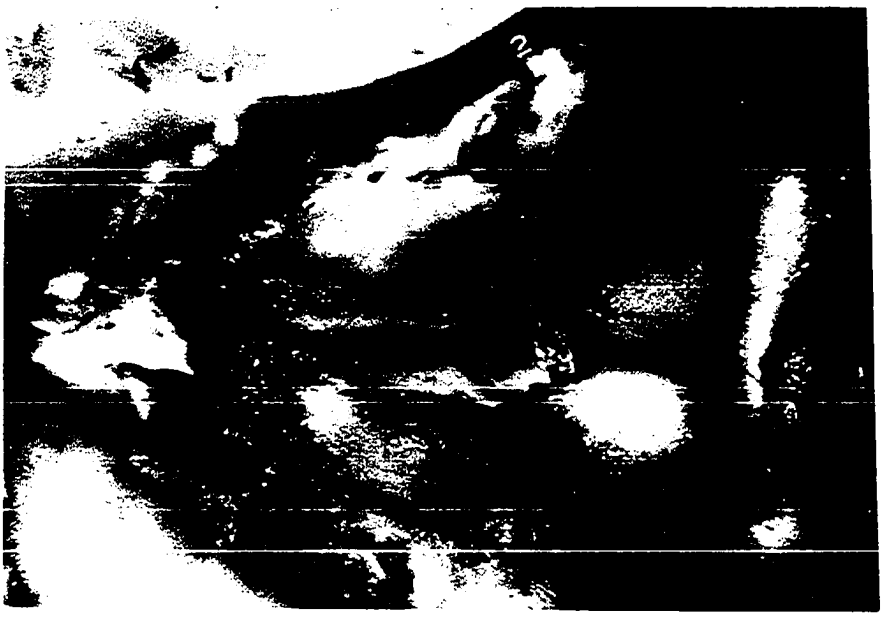


Figure 13.
A view similar to Figure 12, plexus choroideus ventriculi tertii reflected. 1. Arteria choroidea rostralis. 2. Rami choroidei caudales, few broken on the reflected plexus choroideus ventriculi tertii. 3. Plexus choroideus ventriculi lateralis. 4. Plexus choroideus ventriculi tertii.

Fiugre 14.
A view similar to Figure 13 with plexus choroideus ventriculi tertii removed. 1. Arteria choroidea rostralis. 2. Arteria choroidea caudalis. 3. Rami choroidei caudales. 4. Branches of the ramus ad tectum mesencephali rostralis. 5. Ramus ad tectum mesencephali intermedius. 6. Plexus choroideus ventriculi lateralis.

Figure 15.
A similar view as in Figure 14 showing the rami choroidei caudales.
1. Rami choroidei caudales. 2. Arteria choroidea rostralis. 3. Plexus choroideus ventriculi lateralis.

Figure 16.
Ventral view of the brain of the dog showing branches of the arteria basilaris. 1. Arteria basilaris. 2. Ramus medullaris. 3. Arteria cerebelli caudalis accessorius. 4. Arteria cerebelli caudalis. 5. Arteria cerebelli media. 6. Ramus ad pontem rostralis. 7. Ramus ad pontem intermedius.



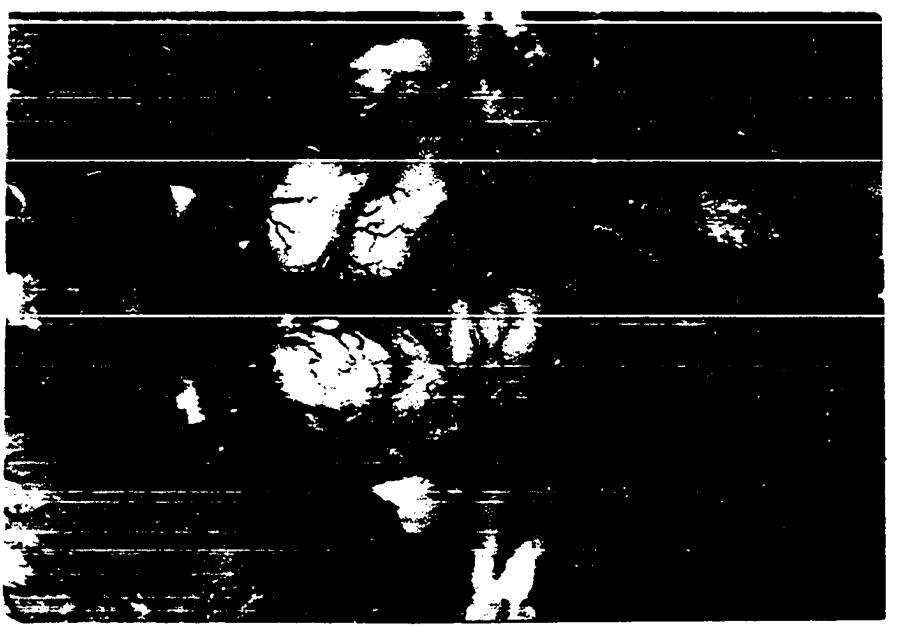
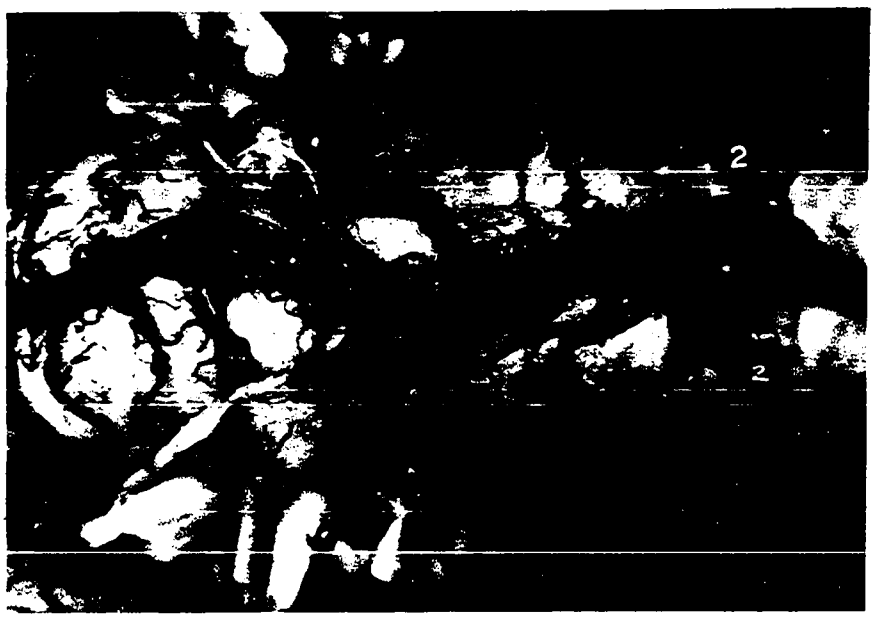


Figure 17.
Ventral view of the brain of the dog showing the branches of the arteria basilaris. 1. Arteria basilaris. 2. Arteria cerebrospinalis (vertebralis). 3. Ramus medullaris. 4. Arteria cerebelli caudalis accessorius. 5. Arteria cerebelli caudalis. 6. Arteria cerebelli media. 7. Ramus ad pontem rostralis. 8. Ramus ad pontem intermedius. 9. Ramus ad pontem caudalis.

Figure 18.
Lateral view of the medulla oblongata and adjoining area in the dog. 1. Arteria basilaris. 2. Ramus ad pontem rostralis. 3. Ramus ad pontem intermedius. 4. Ramus ad pontem caudalis. 5. Arteria cerebelli media. 6. Arteria cerebelli caudalis. 7. Arteria cerebelli caudalis accessorius. 8. Ramus medullaris.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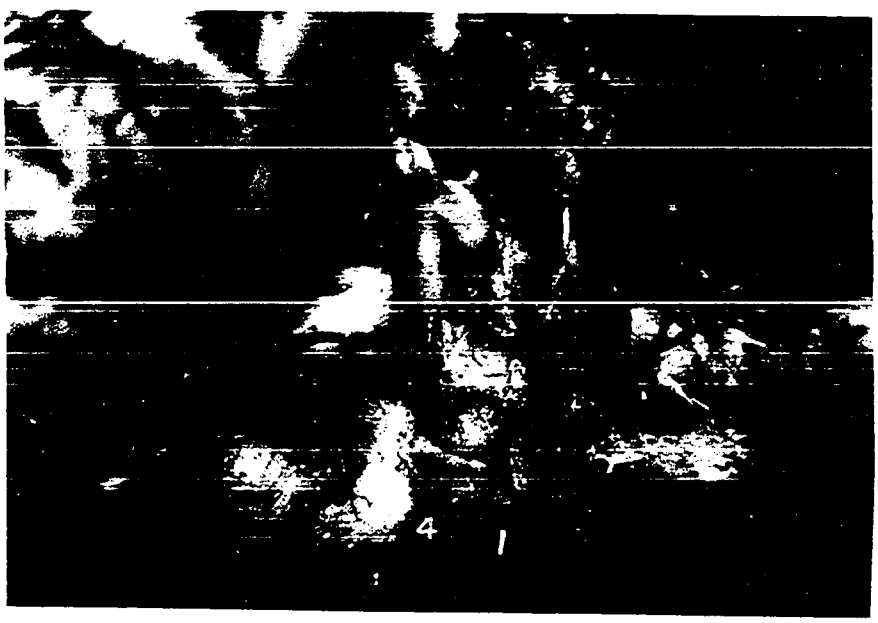
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Figure 19.
Dorsolateral view of the spinomedullary junction of the dog. 1. Arteria cerebelli caudalis accessorius. 2. Ramus medullaris. 3. Ramus caudalis of 2 and its distribution on the dorsal part of the spinomedullary junction. 4. Ramus caudalis of 2 and its continuation as arteria spinalis dorsalis.

Figure 20.
Lateral view of the spinomedullary junction of the dog. 1. Arteria cerebelli caudalis. 2. Arteria cerebelli caudalis accessorius. 3. Ramus medullaris. 4. Ramus caudalis of ramus medullaries to continue as arteria spinalis dorsalis.

Figure 21.
Dorsal view of the medulla oblongata and spinomedullary junction showing the distribution of the ramus medullaris and branches of arteria cerebelli caudalis. 1. Ramus rostralis of ramus medullaris. 2. Ramus caudalis of ramus medullaris. 3. Arteria spinalis dorsalis. 4. Branches of arteria cerebelli caudalis.

Figure 22.
Dorsal aspect of the caudal medulla oblongata and spinomedullary junction with cerebellum lifted up. 1. Arteria cerebelli caudalis. 2. Arteria cerebelli caudalis accessorius. 3. Rami choroidei arteria cerebelli caudalis. 4. Plexus choroideus ventriculi quarti.

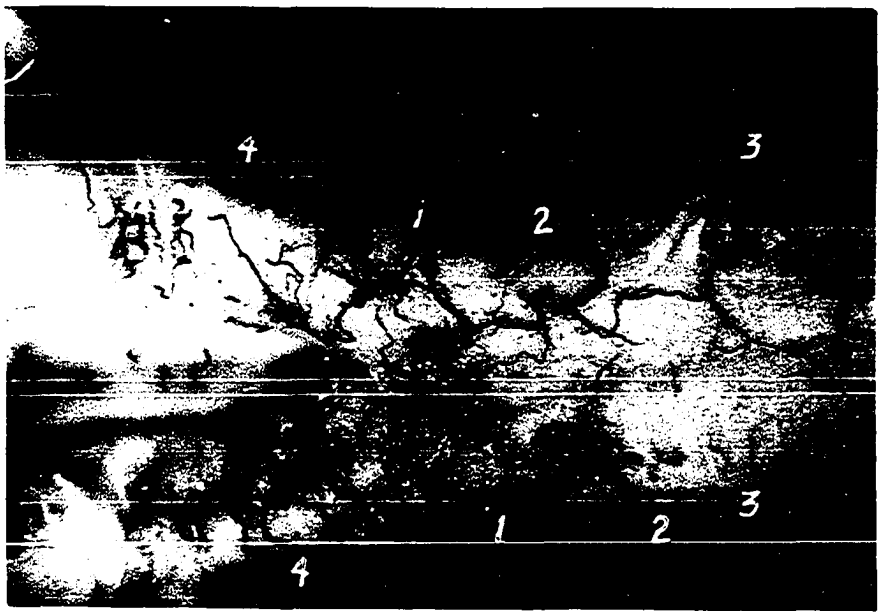
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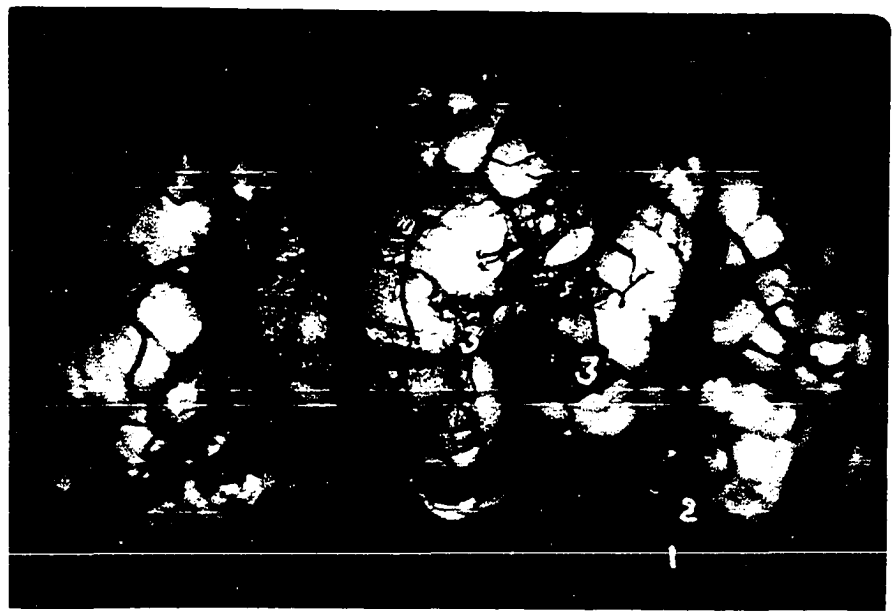
Figure 23.
Caudal view of the cerebellum of the dog. 1. Arteria cerebelli caudalis accessorius. 2. Arteria cerebelli caudalis. 3. Rami corticales arteriae cerebelli caudalis and caudalis accessorius.

Figure 24.
Rostral view of the cerebellum of the dog. 1. Arteria cerebelli rostralis. 2. Ramus medius. 3. Ramus intermedius. 4. Ramus lateralis.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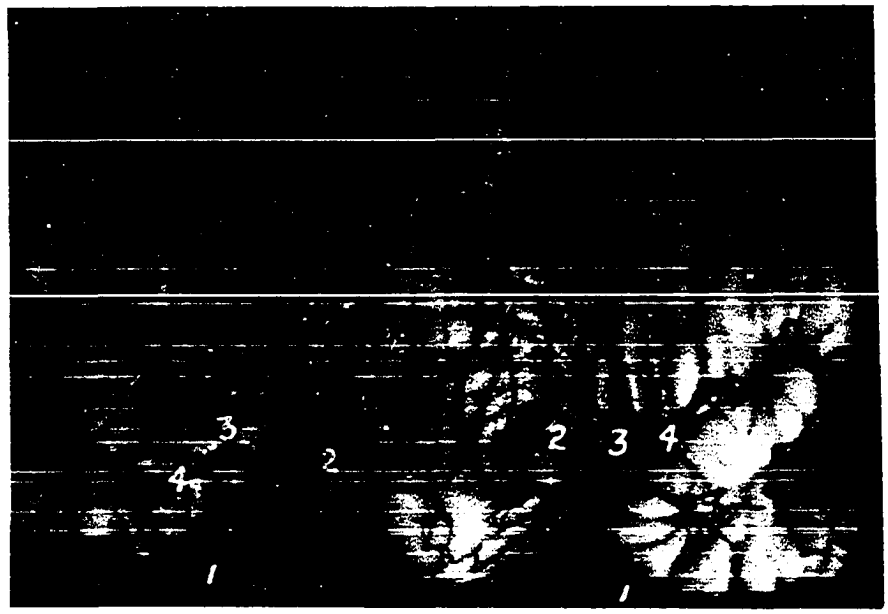
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Figure 25.
Lateral view of the medulla oblongata, pons and cerebellum of the dog.
1. Arteria cerebelli caudalis accessorius. 2. Arteria cerebelli caudalis.
3. Arteria cerebelli media. 4. Rami corticales arteria cerebelli media.

Figure 26.
Similar view as in Figure 26. 1. Arteria cerebelli media. 2. Arteria labyrinthi. 3. Rami corticales arteria cerebelli media.


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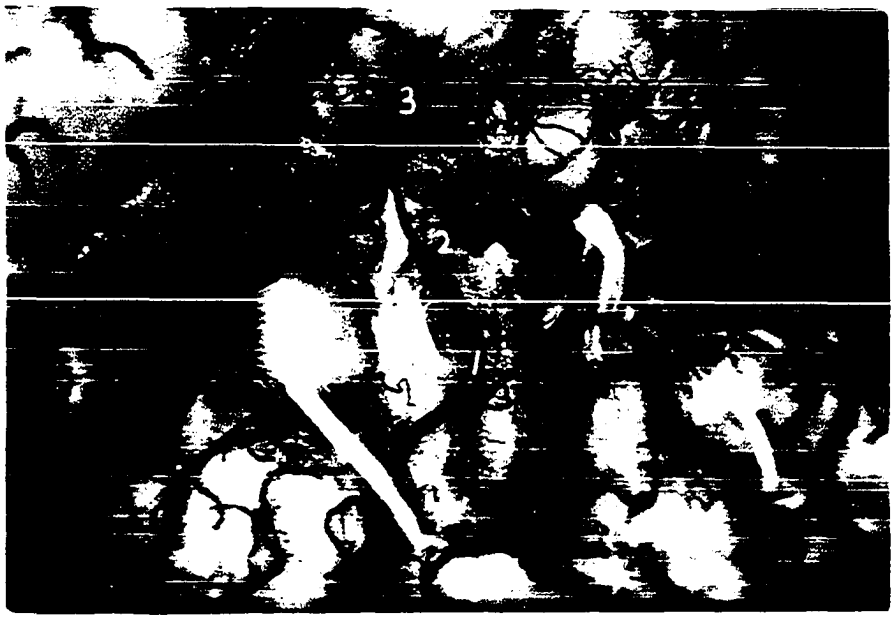
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Figure 27.
Midsagittal section of the brain stem of the dog showing rami paramedianes (medianes) of the arteria basilaris.

Figure 28.
Ventral view of the brain of the pig with rete mirabile epidurale rostrale in position. 1. Rete mirabile epidurale rostrale. 2. Arteria basilaris. 3. Arteria cerebrospinalis (vertebralis). 4. Arteria cerebelli caudalis. 5. Rami medullares.

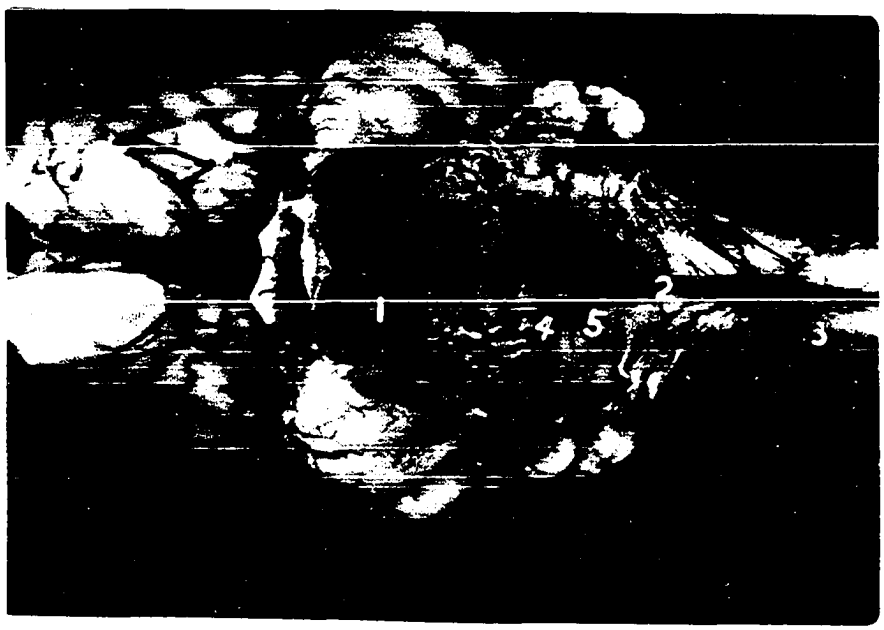
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Figure 29.
Ventral view of the brain of the pig after the rete mirabile epidurale rostrale removed. 1. Arteria carotis interna. 2. Arteria cerebri media. 3. Arteria cerebri rostralis. 4. Arteria ethmoidalis interna. 5. Arteria communicans caudalis. 6. Arteria cerebelli rostralis. 7. Arteria cerebelli caudalis. 8. Arteria basilaris. 9. Rami medullares.

Figure 30.
Lateral view of the brain of the pig. 1. Arteria cerebri media. 2. Rami corticales arteria cerebri media.

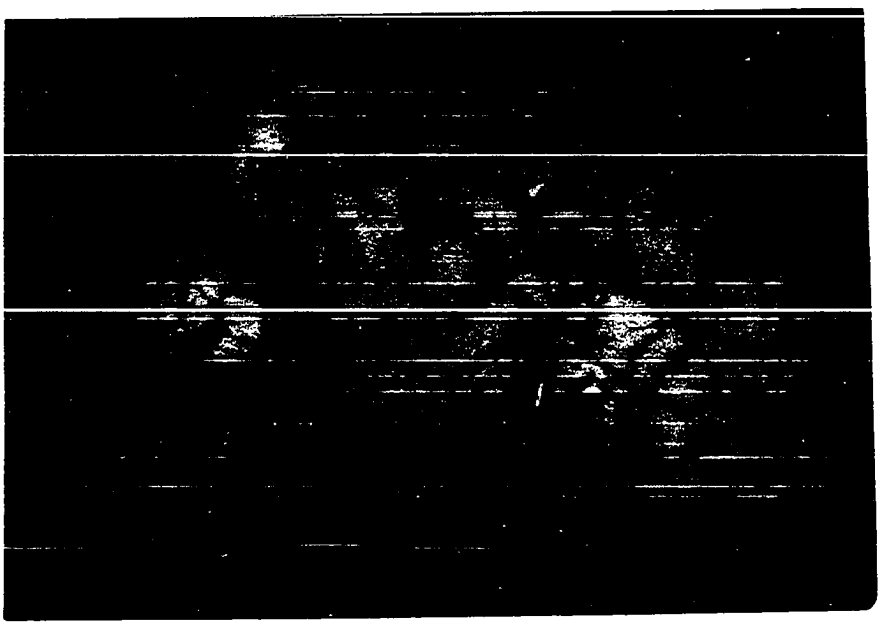


Figure 31.
Dorsal view of the brain of the pig. 1. Rami corticales arteria cerebri rostralis. 2. Rami corticales arteria cerebri media. 3. Rami corticales arteria cerebri caudalis.

Figure 32.
Midsagittal view of the brain of the pig. 1. Arteria corporis callosi (mediane) communis. 2. Rami corticales of arteria corporis callosi (mediane) communis. 3. Rami corticales arteria cerebri caudalis.

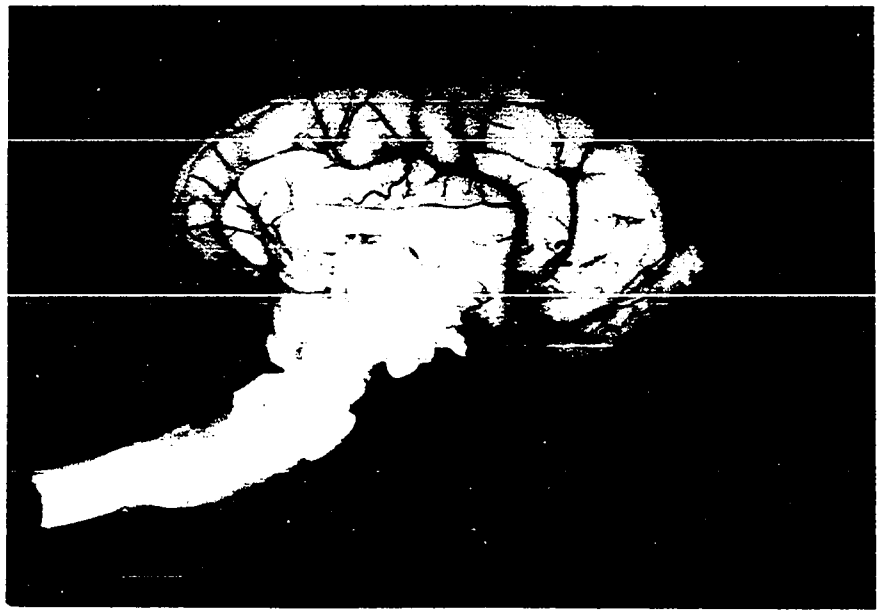
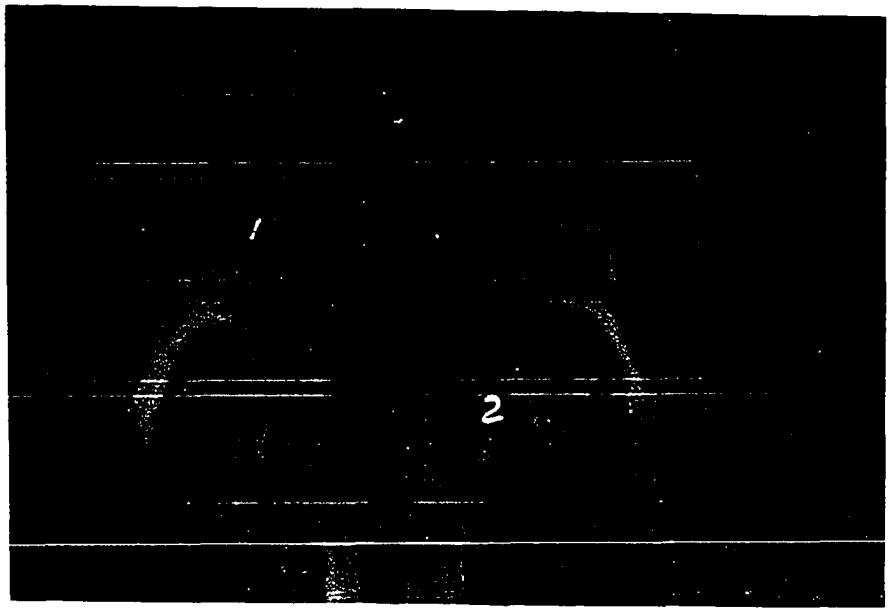


Figure 33.
Medial view of the two halves of the midsagittal section of the brain of the pig. 1. Arteria corporis callosi (mediane) communis. 2. Rami dorsomediales (caudomediales) of the arteria communicans caudalis (pars distalis).

Figure 34.
Ventral view of the brain of the pig around optic chiasma. 1. Arteria carotis interna. 2. Arteria intercarotica rostralis. 3. Arteria ophthalmica interna. 4. Arteria cerebri media. 5. Arteria cerebri rostralis. 6. Arteria communicans caudalis.. 7. Arteria choroidea rostralis.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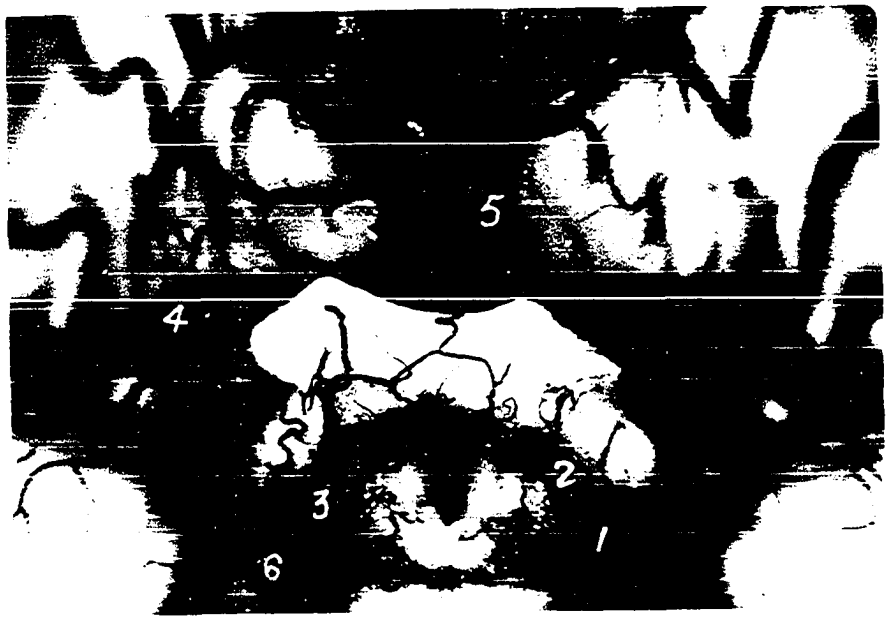
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Figure 35.
Ventral of the brain of the pig infront of the optic chiasma. 1. Arteria cerebri media. 2. Arteria cerebri rostralis. 3. Arteria ethmoidalis interna. 4. Arteria communicans rostralis.

Figure 36.
Ventral view of the brain of the pig around pons and mesencephalon.
1. Arteria communicans caudalis (pars proximalis). 2. Arteria communicans caudalis (pars distalis). 3. Arteria cerebri caudalis. 4. Arteria cerebelli rostralis. 5. Arteria basilaris. 6. Ramus ad tectum mesencephali rostralis. 7. Rami caudomediales or dorsomediales. 8. Ramus ad pontem rostralis.


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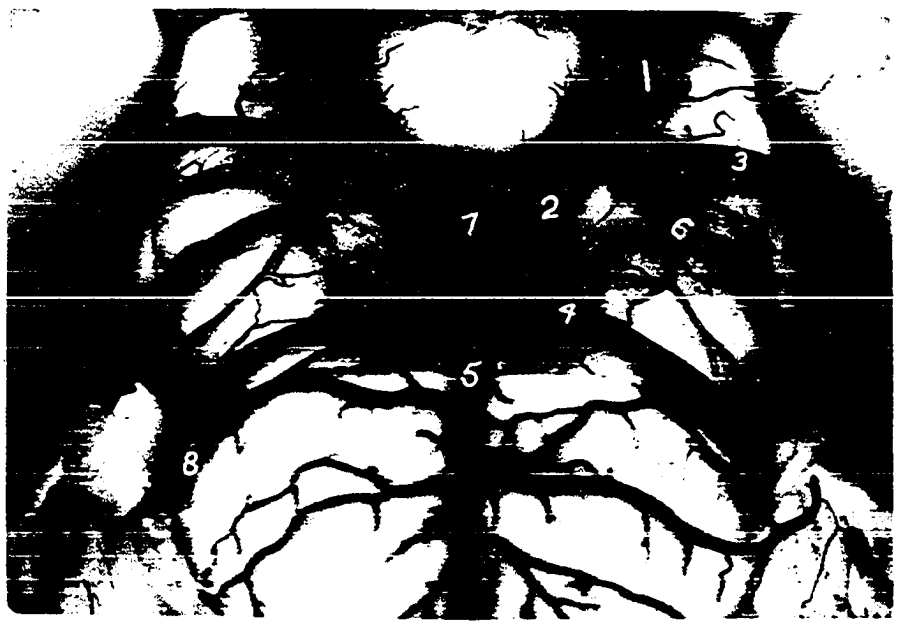
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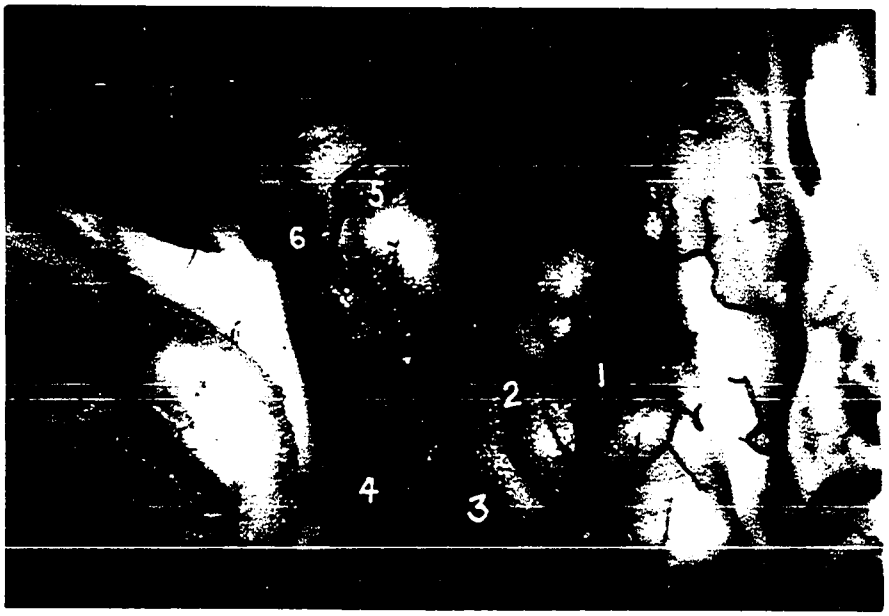
Figure 37.
Lateral view of the brain of the pig around the mesencephalon. 1. Arteria cerebri caudalis. 2. Arteria choroidea caudalis. 3. Ramus ad tectum mesencephali rostralis. 4. Arteria cerebelli rostralis. 5. Ramus ad tectum mesencephali intermedius. 6. Ramus ad tectum mesencephali caudalis.

Figure 38.
A view similar to Figure 37 showing the anastomosing branch from arteria cerebri caudalis for the arteria choroidea rostralis. 1. Ramus anastomoticus. 2. Plexus choroideus ventriculi lateralis. 3. Arteria choridea rostralis. 4. Rami perforantes of the arteria cerebri caudalis.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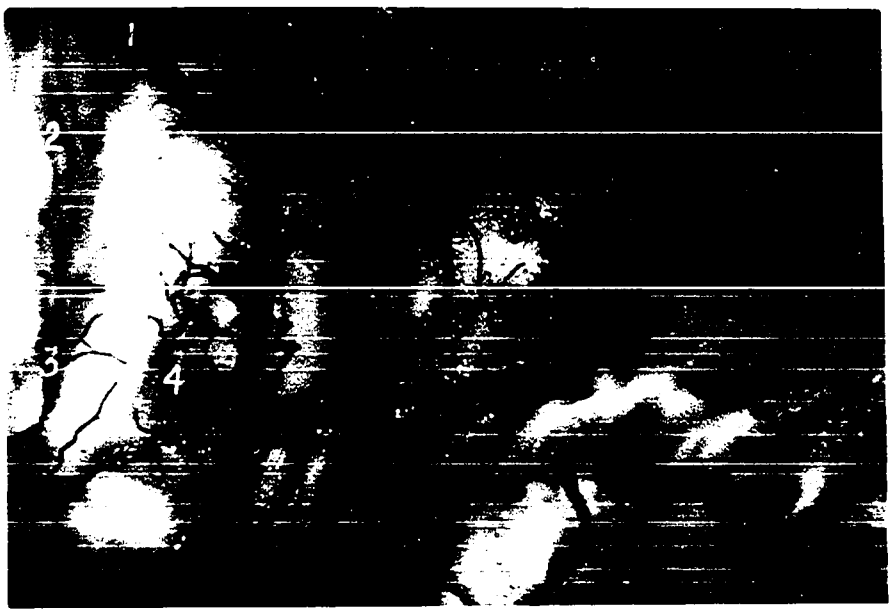
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Figure 39.
Dorsolateral view of the brain of the pig around the mesencephalon.
1. Arteria cerebri caudalis. 2. Ramus anastomoticus to arteria choroidea rostralis. 3. Arteria choroidea rostralis. 4. Plexus choroideus ventriculi lateralis.

Figure 40.
Dorsal view of the thalamic and mesencephalic areas. 1. Arteria cerebri caudalis. 2. Rami choroidei caudales. 3. Plexus choroideus ventriculi tertii.


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Figure 41.
Rostral aspect ofthe cerebellum of the pig. 1. Arteria cerebelli rostralis. 2. Ramus lateralis of the arteria cerebelli rostralis. 3. Ramus intermedius of the arteria cerebelli rostralis. 4. Ramus medius of the arteria cerebelli rostralis.

Figure 42.
Ventrolateral view of the medulla oblongata of the pig. 1. Ramus medullaris. 2. Arteria basilaris. 3. Plexus choroideus ventriculi quarti. 4. Arteria cerebelli caudalis.


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Figure 43.
Ventrolateral view of the medulla oblongata and spinomedullary junction of the pig. 1. Arteria basilaris. 2. Ramus medullaris. 3. Plexus choroideus ventriculi quarti. 4. Arteria cerebelli caudalis.

Figure 44.
Lateral view of the medulla oblongata, pons and cerebellum of the pig. 1. Arteria cerebelli caudalis. 2. Arteria cerebelli media. 3. Rami corticales of the arteria cerebelli media.


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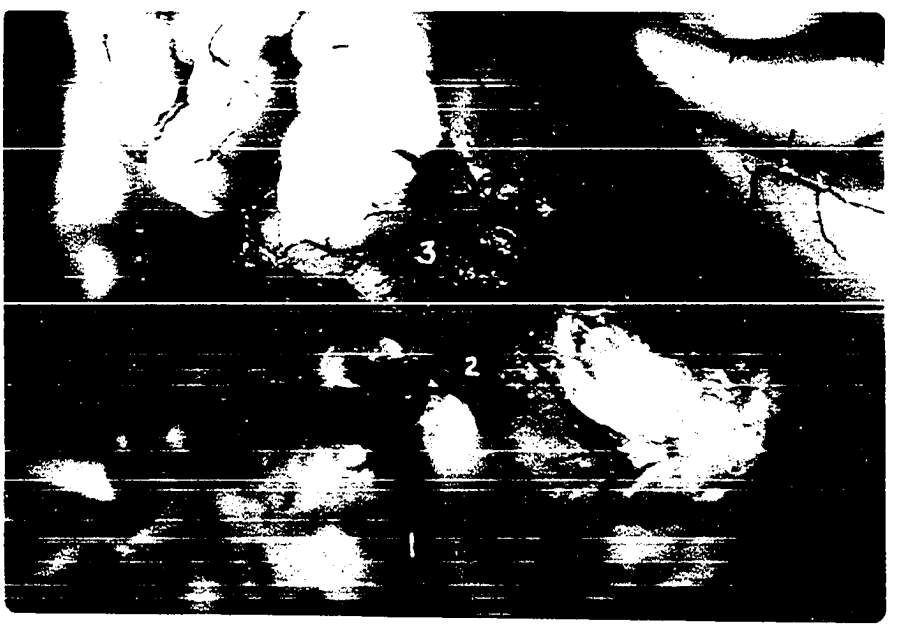
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Figure 45.
Caudal view of the cerebellum of the pig. 1. Arteria cerebelli caudalis. 2. Ramus lateralis of the arteria cerebelli caudalis. 3. Ramus intermedius of the arteria cerebelli caudalis. 4. Ramus medialis of the arteria cerebelli caudalis.

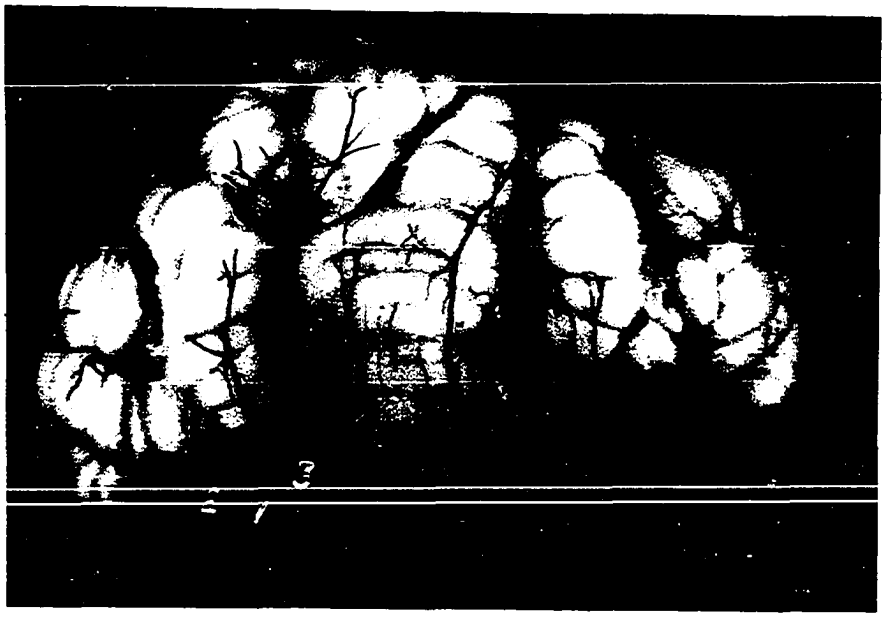
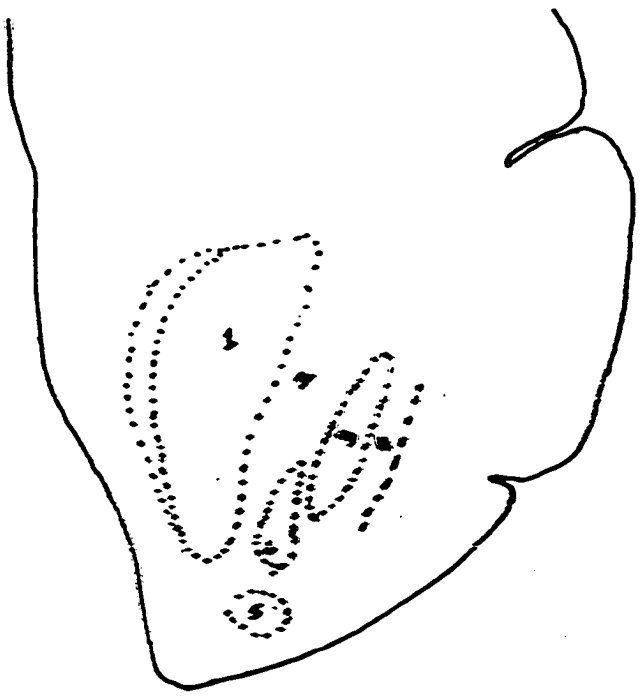


Figure 46a. (overlay).
Cross section of the brain of the dog at the level of the rostral part of the substantia perforata rostralis and maximum development of the nucleus caudatus. 1. Nucleus caudatus. 2. Capsula interna. 3. Claustrum. 4. Capsula externa. 5. Commissura rostralis. 6. Putamen.

Figure 46b.
Same as above. India ink injection.

Figure 47a. (overlay)
Cross section of the brain of the dog at the level of the septum pellucidum and just in front of the chiasma opticum. 1. Nucleus caudatus. 2. Ventriculus lateralis. 3. Capsula interna. 4. Area subcallosa. 5. Globus pallidus. 6. Putamen. 7. Claustrum. 8. Commissura rostralis. 9. Nucleus preopticus medialis. 10. Nucleus preopticus lateralis.

Figure 47b.
Same as above. India ink injection.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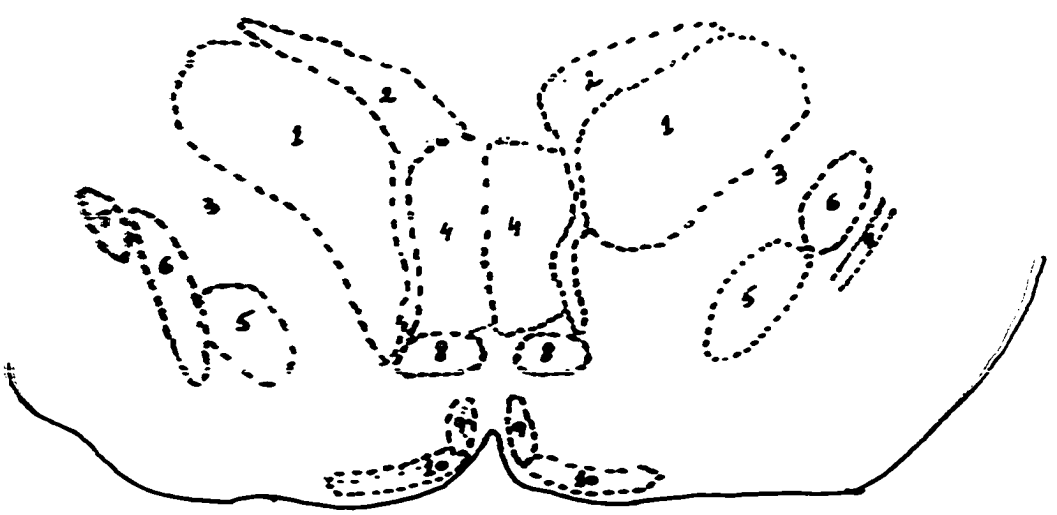
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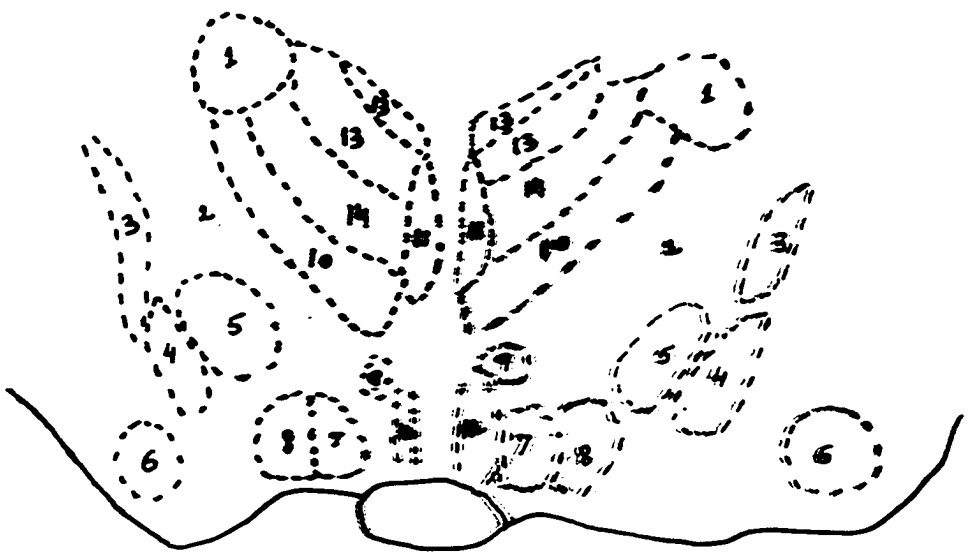
Figure 48a. (overlay)
Cross section of the brain of the dog at the level of the chiasma opticum, behind the commissura rostralis and at the level of the rostral thalamic areas. 1. Nucleus caudatus. 2. Capsula interna. 3. Putamen. 4. Globus pallidus. 5. Nucleus endopeduncularis. 6. Corpus amygdaloideum. 7. Nucleus preoptica medialis. 8. Nucleus preoptica lateralis. 9. Fornix. 10. Nucleus reticularis thalami. 11. Nucleus parataenialis. 12. Nucleus hypothalamicus paraventricularis. 13. Nuclei rostralis dorsalis and ventralis. 14. Nucleus rostralis medialis

Figure 48b.
Same as above. India ink injection.

Figure 49a. (overlay)
Cross section of the brain of the dog behind the chiasma opticum and at infundibulum. 1. Stria medullaris thalami. 2. Nuclei rostralis dorsalis and ventralis. 3. Nucleus ventralis rostralis. 4. Nucleus ventralis medialis. 5. Nucleus reticularis thalami. 6. Nucleus caudatus. 7. Nucleus parataenialis. 8. Nuclei intralaminares thalami. 9. Nucleus hypothalamicus paraventricularis. 10. Fornix. 11. Nucleus hypothalamicus rostralis. 12. Nucleus subthalamicus. 13. Nucleus endopeduncularis. 14. Tractus opticus. 15. Globus pallidus. 16. Putamen. 17. Corpus amygdaloideum.

Figure 49b.
Same as above. India ink injection.



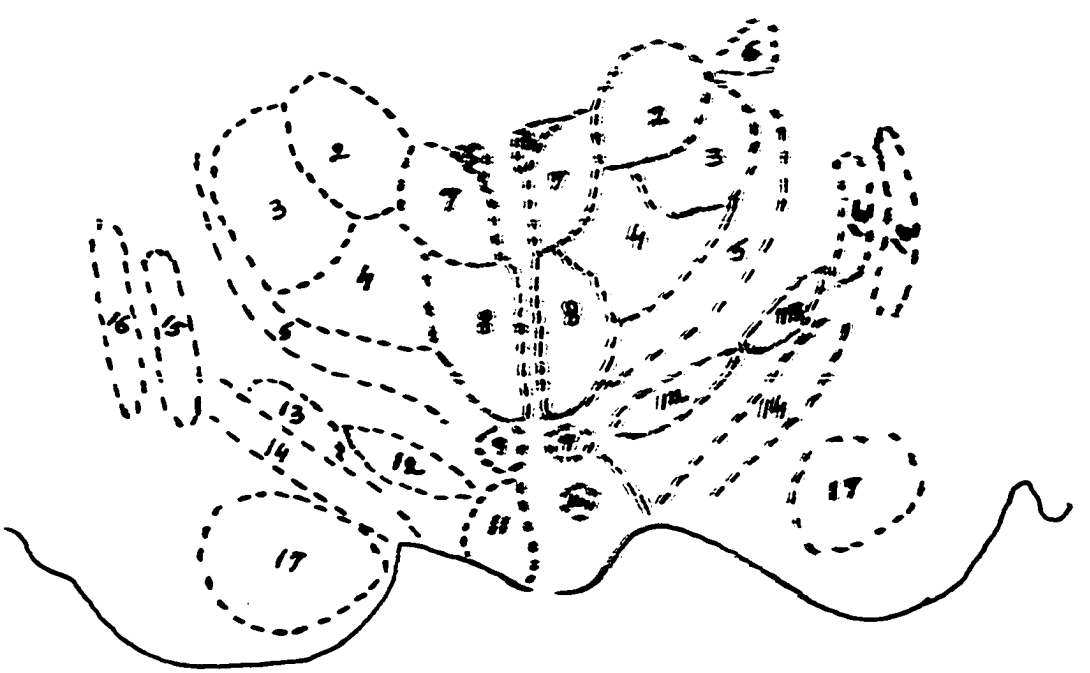
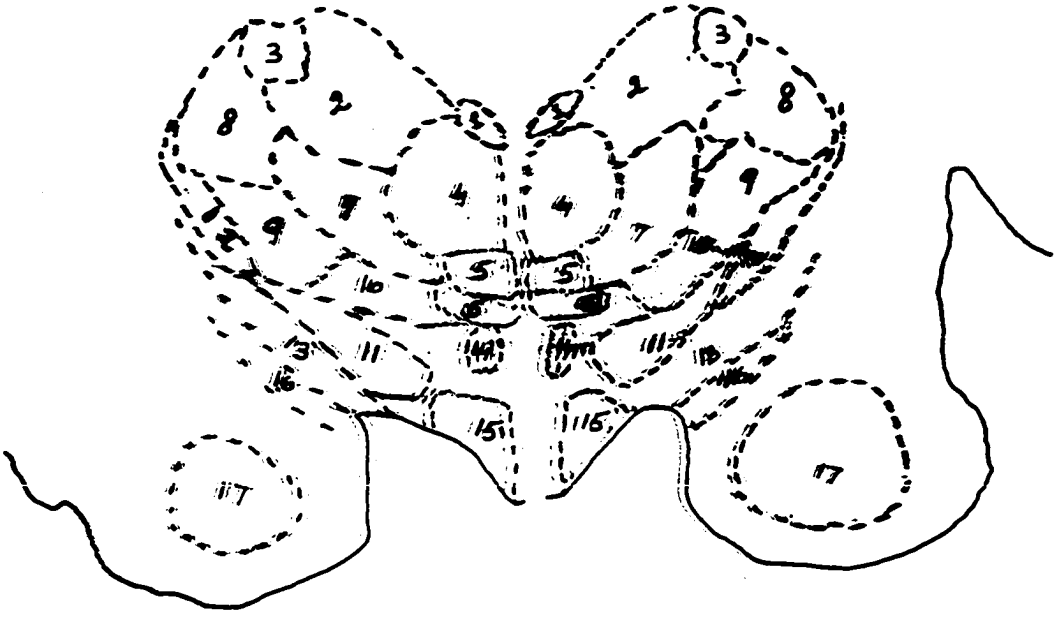


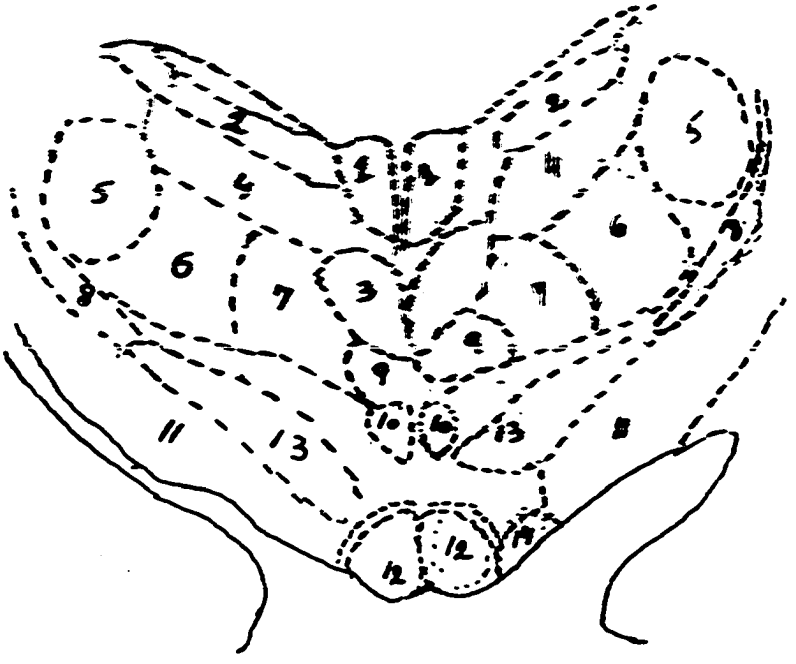
Figure 50a. (overlay)
Cross section of the brain of the dog at the level of the infundibulum and middle part of the lobus piriformis. 1. Stria medullaris thalami. 2. Nuclei rostralis dorsalis and ventralis. 3. Nucleus lateralis rostralis. 4. Nucleus dorsomedialis. 5. Nucleus centralis medialis. 6. Nucleus reuniens. 7. Nucleus centralis lateralis. 8. Nucleus ventralis rostralis. 9. Nucleus ventralis caudolateralis. 10. Nucleus ventralis caudomedialis. 11. Nucleus subthalamicus. 12. Nucleus reticularis thalami. 13. Crus cerebri. 14. Nucleus hypothalamicus dorsomedialis. 15. Nucleus hypothalamicus ventromedialis. 16. Tractus opticus. 17. Corpus amygdaloideum.

Figure 50b.
Same as above. India ink injection.

Figure 51a. (overlay)
Cross section of the brain of the dog at the level of the nucleus mamillaris and nucleus corporis geniculati lateralis. 1. Nuclei habenulares. 2. Pulvinar. 3. Nucleus dorsomedialis. 4. Nucleus lateralis caudalis. 5. Nucleus geniculati lateralis. 6. Nucleus ventralis caudolateralis. 7. Nucleus ventralis caudomedialis. 8. Nucleus reticularis thalami. 9. Nucleus parafascicularis. 10. Nucleus subparafascicularis. 11. Crus cerebri. 12. Corpus mamillaris. 13. Nucleus subthalamicus. 14. Nucleus mamillaris lateralis.

Figure 51b.
Same as above. India ink injection.





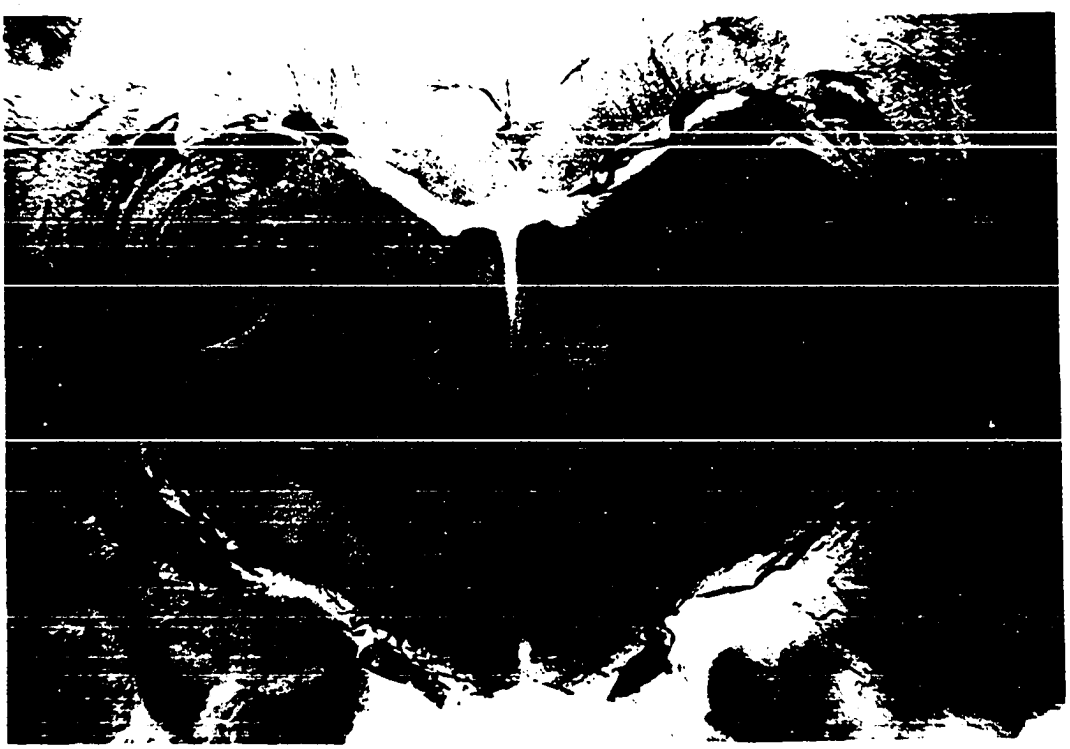
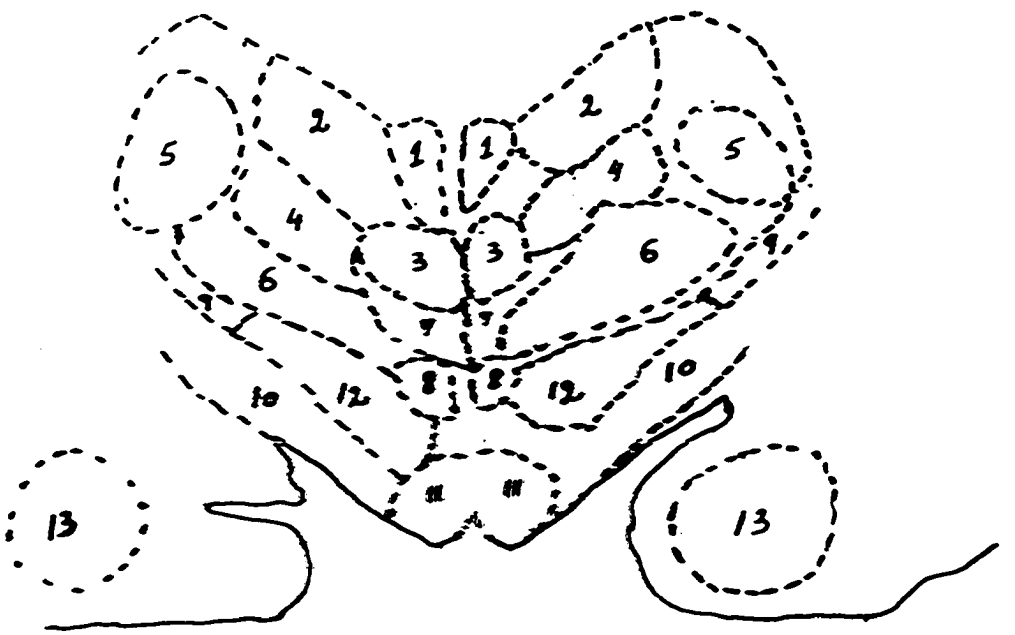


Figure 52a. (overlay)
Cross section of the brain of the dog slightly caudal to Figure 51a,b. Showing a similar disposition and distribution. 1. Nuclei habenulares. 2. Pulvinar. 3. Nucleus dorsomedialis. 4. Nucleus lateralis caudalis. 5. Nucleus geniculati lateralis. 6. Nuclei ventralis caudolateralis and caudomedialis. 7. Nucleus parafascicularis. 8. Nucleus subparafascicularis. 9. Nucleus reticularis thalami. 10. Crus cerebri. 11. Corpus mamillaris. 12. Nucleus subthalamicus. 13. Corpus amygdaloideum.

Figure 52b.
Same as above. India ink injection.

Figure 53a. (overlay)
Cross section of the brain of the dog at the level of the junction of the thalamus and colliculus rostralis. 1. Commissura caudalis. 2. Nucleus colliculus rostralis. 3. Pulvinar. 4. Nuclei habenulares. 5. Nucleus commissura caudalis. 6. Area pretectalis. 7. Nucleus geniculatum lateralis. 8. Substantia grisea centralis. 9. Nuclei Tegmenti. 10. Nucleus lateralis caudalis. 11. Nucleus geniculatum medialis. 12. Nucleus reticularis thalami. 13. Formatio reticularis. 14. Nucleus ruber or rubrum. 15. Substantia nigra. 16. Crus cerebri. 17. Fasciculus longitudinalis medialis. 18. Nucleus n. oculomotorii. 19. Decussatio tegmenti.

Figure 53b.
Same as above. India ink injection.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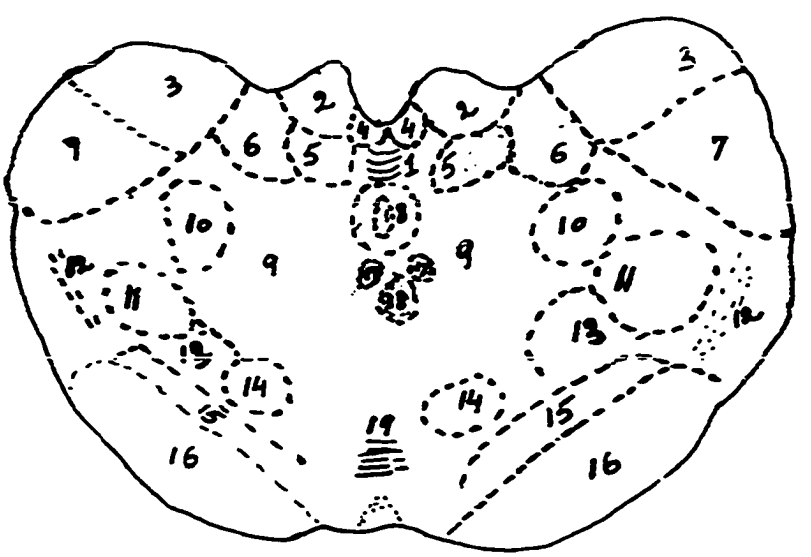
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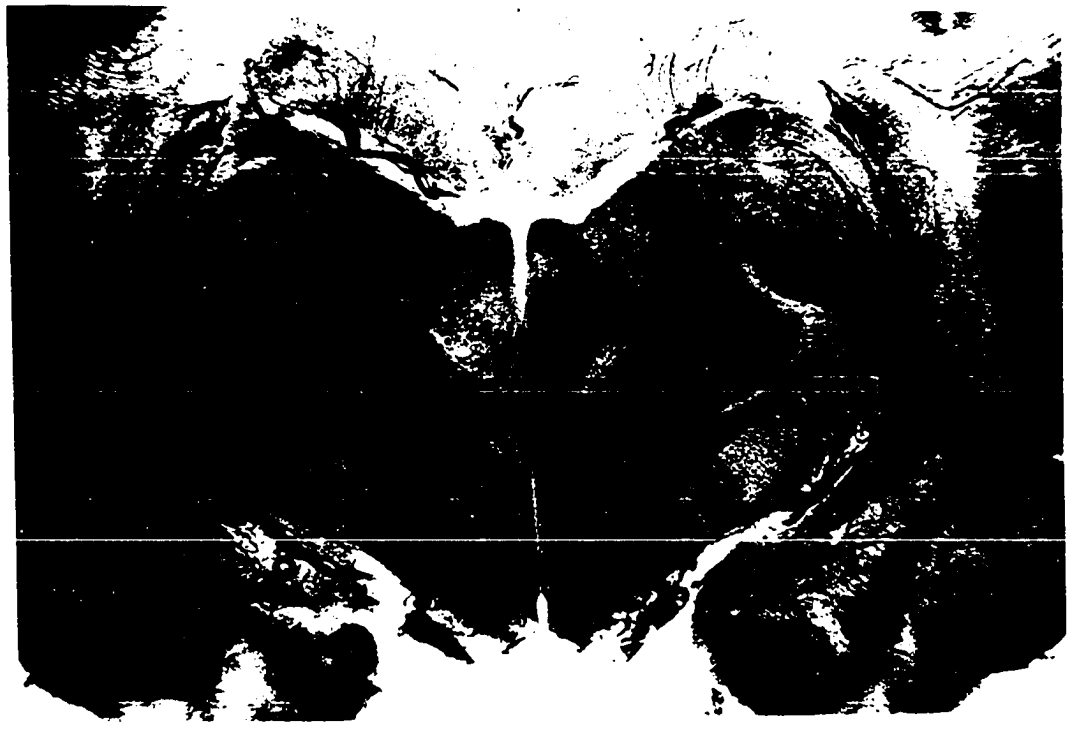
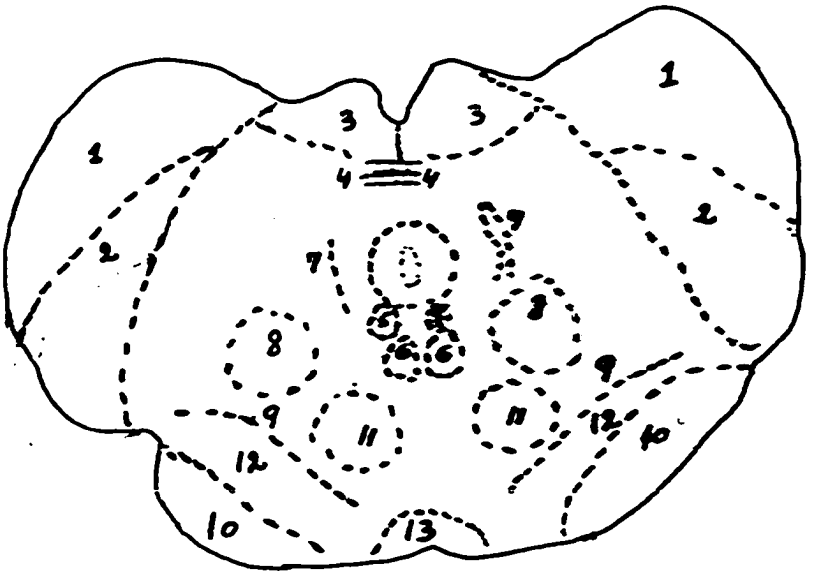


Figure 54a. (overlay)
Cross section of the brain of the dog slightly caudal to the Figures 53a,b. 1. Corpus geniculati lateralis. 2. Corpus geniculati medialis. 3. Nucleus colliculus rostralis. 4. Commissura caudalis. 5. Fasciculus longitudinalis medialis. 6. Nucleus n. oculomotorii. 7. Nucleus tr. mesencephali n. trigemini. 8. Nuclei tegmenti. 9. Lemniscus medialis. 10. Crus cerebri. 11. Nucleus rubrum or ruber. 12. Substantia nigra. 13. Nucleus interpeduncularis.

Figure 54b.
Same as above. India ink injection.

Figure 55a. (overlay)
Cross section of the brain of the dog at the level of the middle portion of the substantia perforata caudalis and middle part of the colliculus rostralis. 1. Nucleus colliculus rostralis. 2. Nucleus tr. mesencephali n. trigemini. 3. Nuclei tegmenti. 4. Brachium colliculi caudalis. 5. Corpus geniculati medialis. 6. Nucleus n. oculomotorii. 7. Lemniscus medialis. 8. Nucleus rubrum or ruber. 9. Nucleus interpeduncularis. 10. Substantia nigra. 11. Decussatio pedunculorum cerebellarium rostralium. 12. Crus cerebri. 13. Nuclei pontis.

Figure 55b.
Same as above. India ink injection.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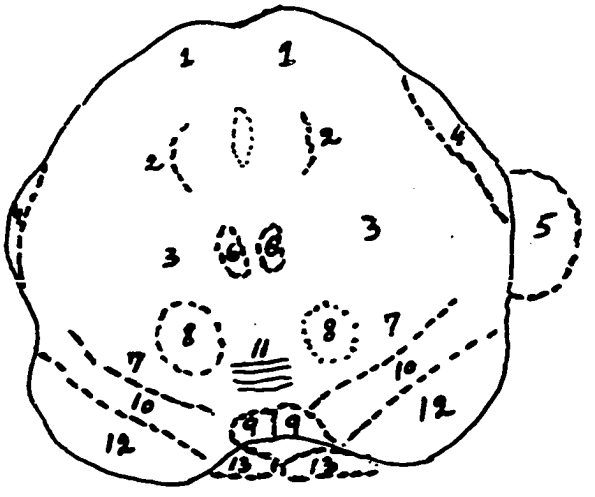
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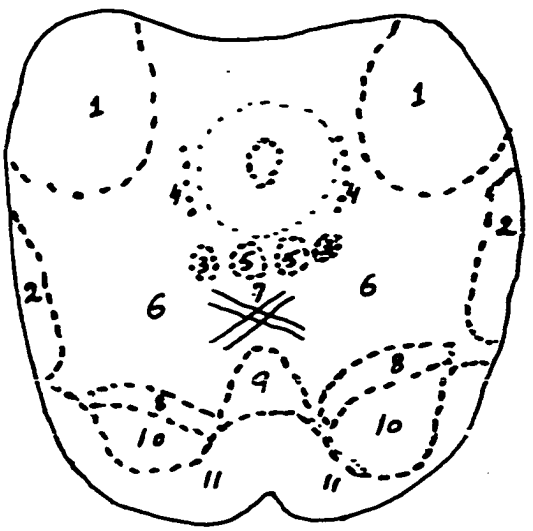
Figure 56a. (overlay)
Cross section of the brain of the dog at the level of the colliculus caudalis and caudal part of the substantia perforata. 1. Nucleus colliculus caudalis. 2. Nucleus bigeminalis. 3. Nucleus n. trochlearis. 4. Nucleus tr. mesencephali n. trigemini. 5. Fasciculus longitudinalis medialis. 6. Nucleus reticularis. 7. Decussatio pedunculorum cerebellarium superiorum. 8. Lemniscus medialis. 9. Nucleus interpeduncularis. 10. Crus cerebri. 11. Nuclei pontis.

Figure 56b.
Same as above. India ink injection.

Figure 57a. (overlay)
Cross section of the brain of the dog at the level of the anterior part of the pons. 1. Pedunculus cerebellaris rostralis. 2. Nucleus motorius n. trigemini. 3. Nucleus sensibilis pontinus n. trigemini. 4. Nucleus tr. mesencephali n. trigemini. 5. Pedunculus cerebellaris medius. 6. Nucleus lemnisci lateralis. 7. Lemniscus medialis. 8. Nucleus raphe or raphe. 9. Nucleus tegmenti guddinii. 10. Fasciculus longitudinalis medialis. 11. Nuclei pontis. 12. Fibrae pontis transversae. 13. Pyramis. 14. Nucleus reticularis.

Figure 57b.
Same as above. India ink injection.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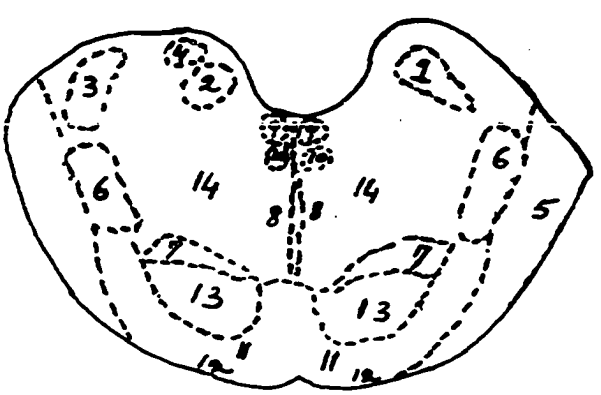
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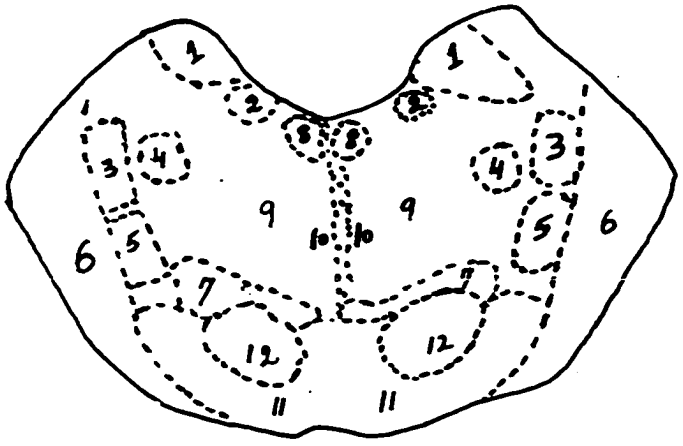
Figure 58a. (overlay).
Cross section of the brain of the dog at the level of the middle of pons. 1. Pedunculus cerebellaris rostralis. 2. Nucleus tr. mesencephali trigemini. 3. Nucleus sensibilis pontinus n. trigemini. 4. Nucleus motorius n. trigemini. 5. Nucleus lemniscus lateralis. 6. Pedunculus cerebellaris medius. 7. Lemniscus medialis. 8. Fasciculus longitudinalis medialis. 9. Nucleus reticularis. 10. Nucleus raphae or raphe. 11. Nuclei pontis. 12. Pyramis.

Figure 58b.
Same as above. India ink injection.

Figure 59a. (overlay)
Cross section of the brain of the dog at the level of the cerebellar nuclei, vestibular and cochlear nuclei. 1. Nucleus dentatus. 2. Nuclei interpositi cerebelli. 3. Nucleus fastigii. 4. Nuclei vestibulares medialis and lateralis. 5. Nucleus n. abducentis. 6. Fasciculus longitudinalis medialis. 7. Nucleus reticularis. 8. Pedunculus cerebellaris caudalis. 9. Tractus spinalis n. trigemini. 10. Nucleus tractus spinalis n. trigemini. 11. Nucleus olivaris superioris or nucleus dorsalis trapezoidei. 12. Pyramis. 13. Nuclei cochleares.

Figure 59b.
Same as above. India ink injection.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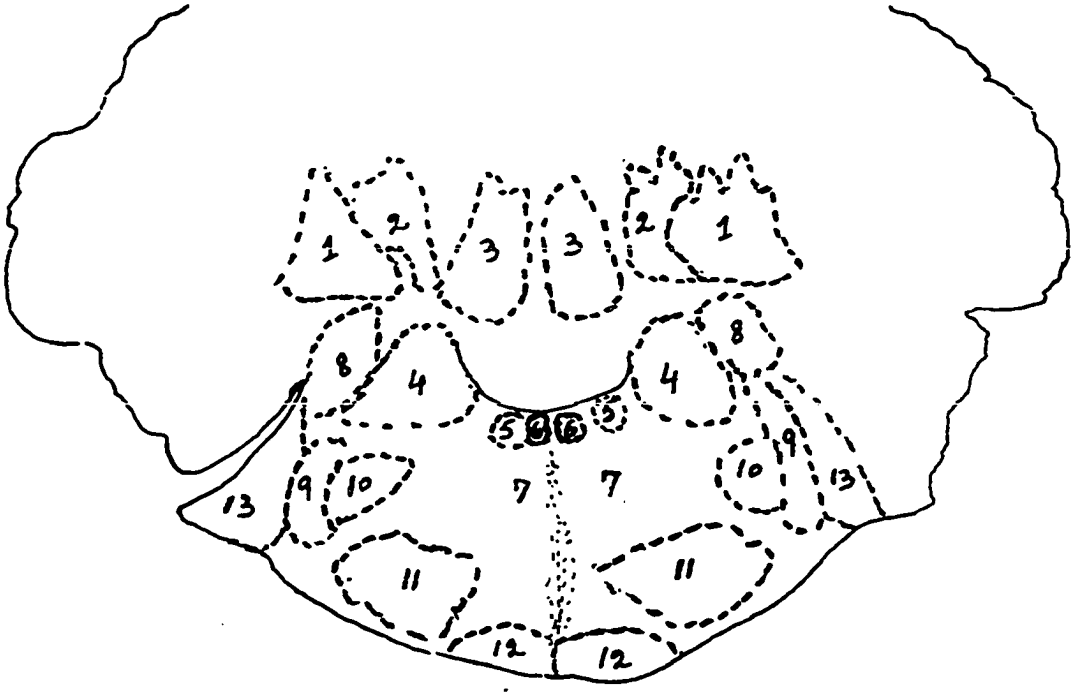
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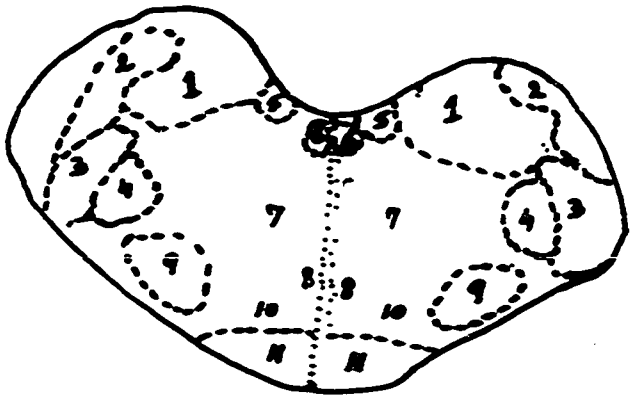
Figure 60a. (overlay)
Cross section of the brain of the dog at the level of the anterior part of the medulla oblongata. 1. Nuclei vestibulares lateralis and caudalis. 2. Pedunculus cerebellaris caudalis. 3. Tractus spinalis n. trigemini. 4. Nucleus tr. spinalis trigemini. 5. Nucleus prepositus. 6. Fasciculus longitudinalis medialis. 7. Nucleus reticularis. 8. Nucleus raphe or raphe. 9. Nucleus n. facialis. 10. Lemniscus medialis. 11. Pyramis.

Figure 60b.
Same as above. India ink injection.

Figure 61a. (overlay)
Cross section of the brain of the dog at the level of the maximal development of the nucleus olivaris inferioris. 1. Nucleus cuneatus medialis. 2. Nucleus cuneatus accessorius or lateralis. 3. Nucleus dorsalis n. vagi or nucleus parasympathicus n. vagii. 4. Nucleus intercalatus. 5. Nucleus n. hypoglossi or nucleus motorius n. hypoglossi. 6. Fasciculus longitudinalis medialis. 7. Nucleus tr. spinalis n. trigemini. 8. Nucleus ambiguus. 9. Nucleus reticularis lateralis. 10. Nucleus reticularis. 11. Nucleus raphae. 12. Lemniscus medialis. 13. Nucleus olivaris inferioris or nucleus olivaris. 14. pyramis.

Figure 61b.
Same as above. India ink injection.



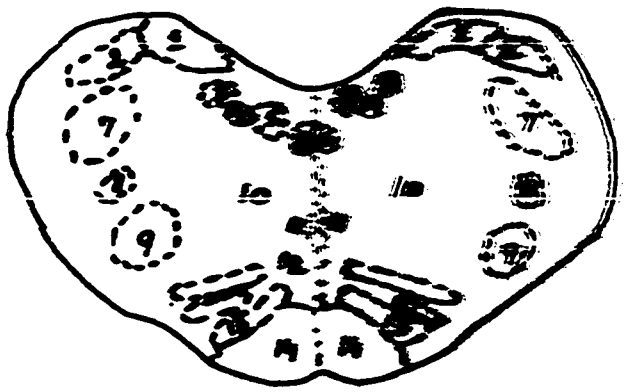
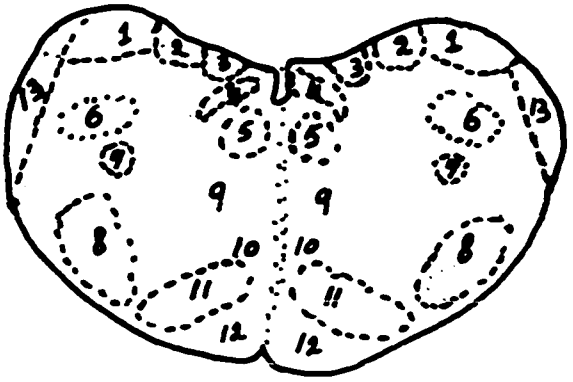


Figure 62a. (overlay)
Cross section of the brain of the dog at the level of the opening of the canalis centralis into the ventriculus quarti. 1. Nucleus cuneatus accessorius or lateralis. 2. Nucleus cuneatus medialis. 3. Nucleus gracilis. 4. Nucleus dorsalis n. vagi or nucleus parasympathicus n. vagi. 5. Nucleus n. hypoglossi or nucleus motorius n. hypoglossi. 6. Nucleus tr. spinalis n. trigemini. 7. Nucleus ambiguus. 8. Nucleus reticularis funiculi lateralis. 9. Nucleus reticularis. 10. Lemniscus medialis. 11. Nucleus olivaris inferioris or nucleus olivaris. 12. Pyramis. 13. Pedunculus cerebellaris caudalis.

Figure 62b.
Same as above. India ink injection.

Figure 63a. (overlay)
Cross section of the brain of the dog at the level of the spinomedullary junction. 1. Nucleus gracilis. 2. Nucleus cuneatus medialis. 3. Nucleus cuneatus accessorius or lateralis. 4. Pedunculus cerebellaris caudalis. 5. Tractus spinalis n. trigemini and nucleus tractus spinalis n. trigemini. 6. Nucleus ambiguus. 7. Nucleus reticularis funiculi lateralis. 8. Nucleus olivaris inferior or nucleus olivaris. 9. Nucleus reticularis. 10. Lemniscus medialis. 11. Nucleus dorsalis n. vagi or nucleus parasympathicus n. vagi. 12. Nucleus n. hypoglossi or nucleus motorius n. hypoglossi.

Figure 63b.
Same as above. India ink injection.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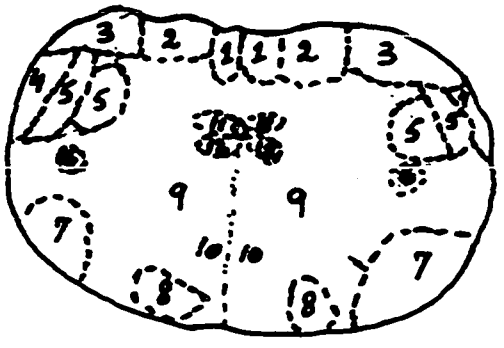
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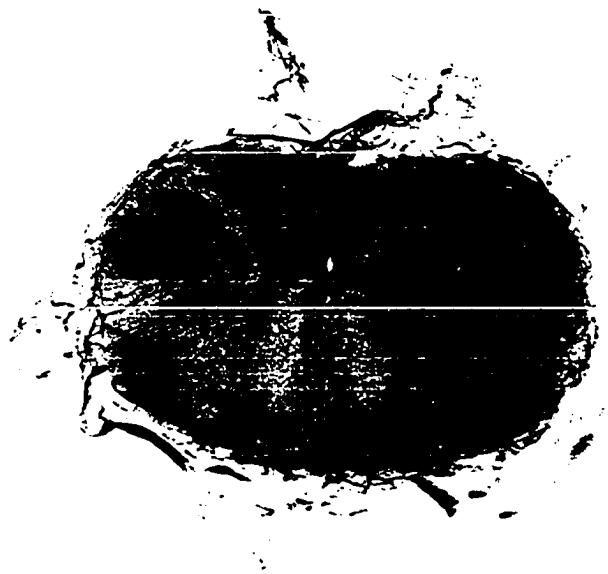
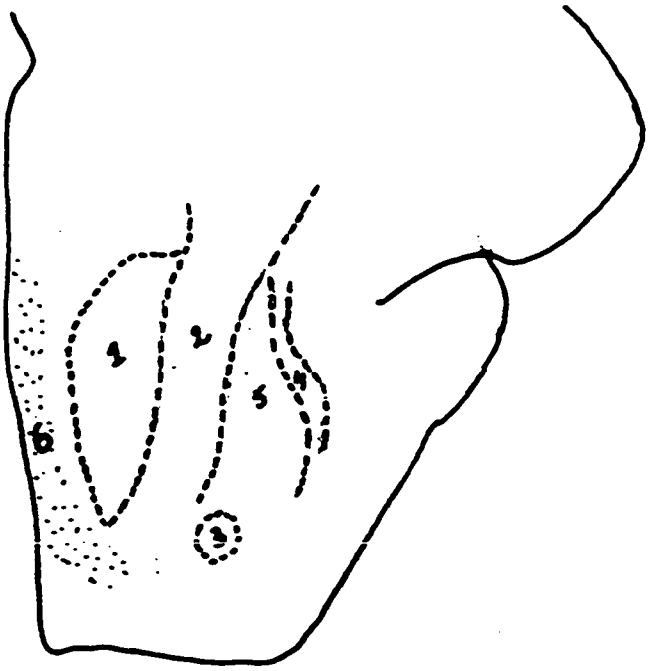


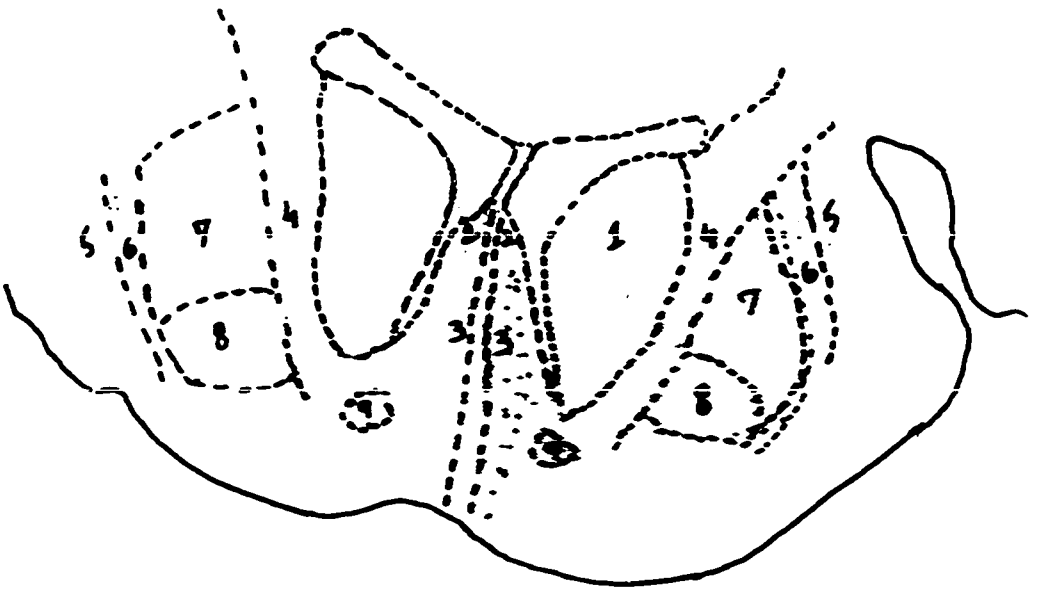
Figure 64a. (overlay)
Cross section of the brain of the pig at the level of the anterior part of the substantia perforata. 1. Nucleus Caudatus. 2. Capsula interna. 3. Commissura rostralis. 4. Claustrum. 5. Putamen. 6. Area subcallosa.

Figure 64b.
Same as above. Latex and India ink injection.

Figure 65a. (overlay)
Cross section at the level of the brain of the pig in front of the lobus piriformis. 1. Nucleus caudatus. 2. Septum pellucidum. 3. Area septalis. 4. Capsula interna. 5. Claustrum. 6. Capsula externa. 7. Putamen. 8. Globus pallidus. 9. Commissura rostralis.

Figure 65b.
Same as above. Latex and India ink injection.





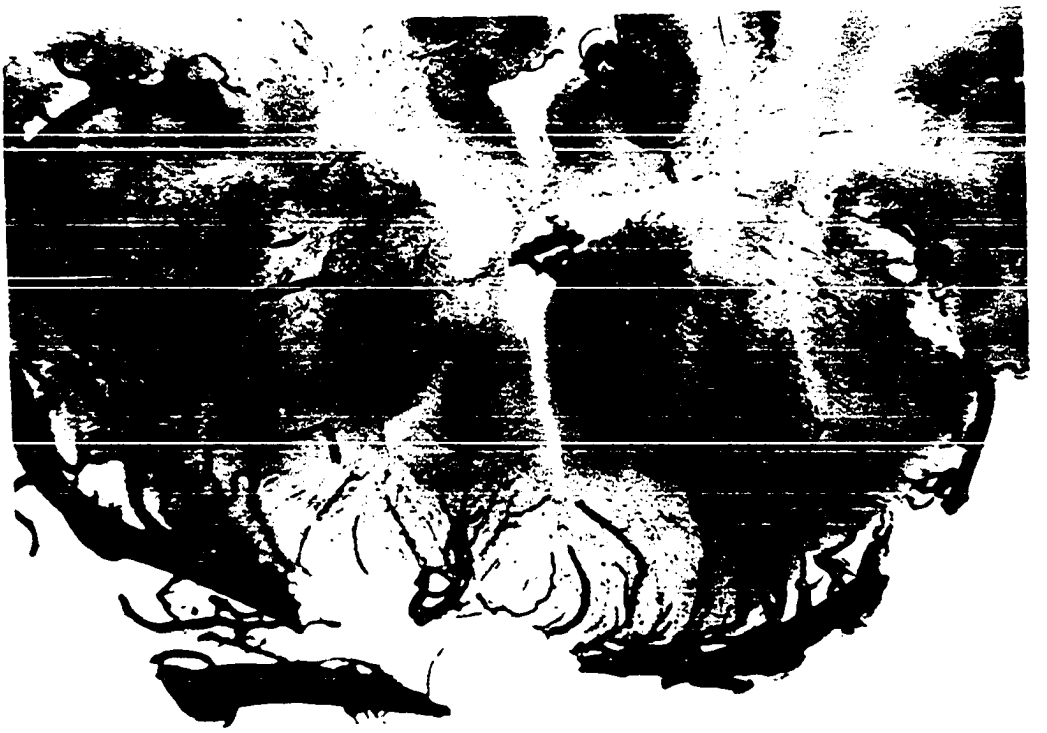
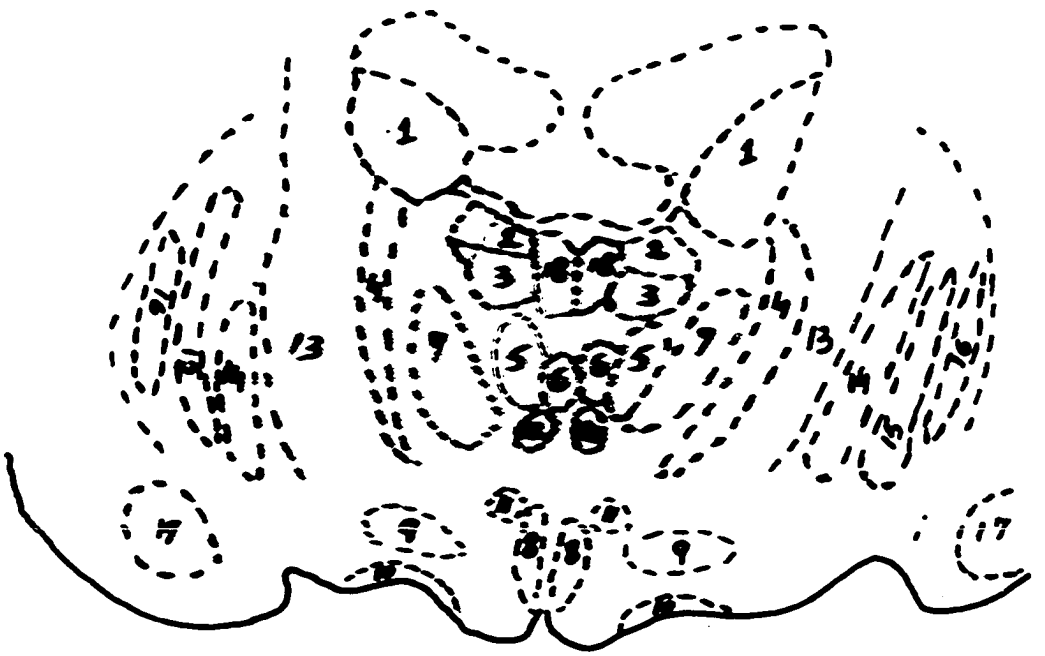


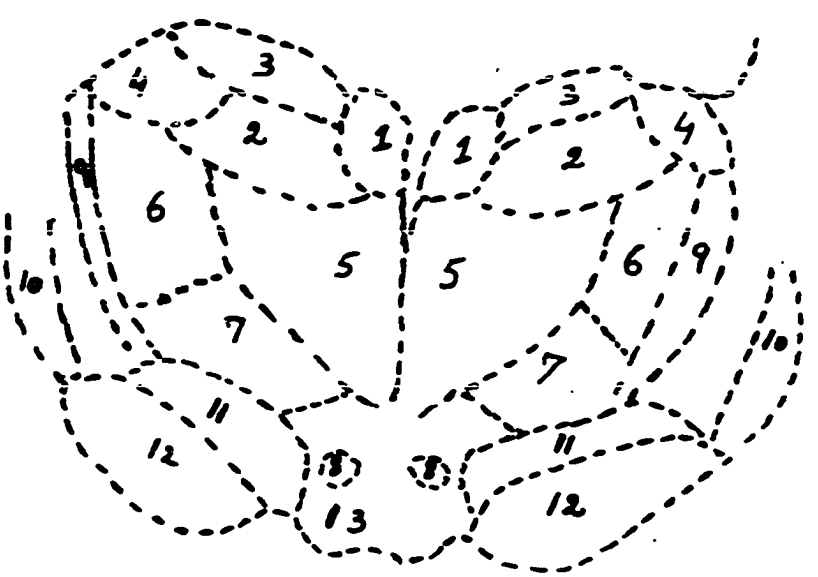
Figure 66a. (overlay)
Cross section of the brain of the pig at the level of the infundibulum.
1. Nucleus caudatus. 2. Nucleus rostralis dorsalis. 3. Nucleus rostralis ventralis. 4. Nucleus reticularis thalami. 5. Nucleus paracentralis. 6. Nucleus centralis medialis. 7. Nucleus ventralis rostralis. 8. Nucleus hypothalamicus paraventricularis. 9. Nucleus hypothalamicus lateralis. 10. Nucleus supraopticus. 1. Fornix. 12. Nucleus reuniens. 13. Capsula interna. 14. Nucleus endopedun cularis. 15. Globus pallidus. 16. Putamen. 17. Corpus amygdaloideum. 18. Nucleus parataenialis.

Figure 66b.
Same as above. Latex and India ink injection.

Figure 67a. (overlay)
Cross section of the brain of the pig at the level of the corpus mamillaris.
1. Nuclei habenulares. 2. Nucleus lateralis dorsalis. 3. Pulvinar. 4. Nucleus geniculati lateralis. 5. Nuclei intralaminares. 6. Nucleus ventralis caudolateralis. 7. Nucleus ventralis caudomedialis. 8. Fornix. 9. Nucleus reticularis thalami. 10. Tractus opticus. 11. Nucleus subthalamicus. 12. Crus cerebri. 13. Corpus mamillaris.

Figure 67b.
Same as above. Latex and India ink injection.





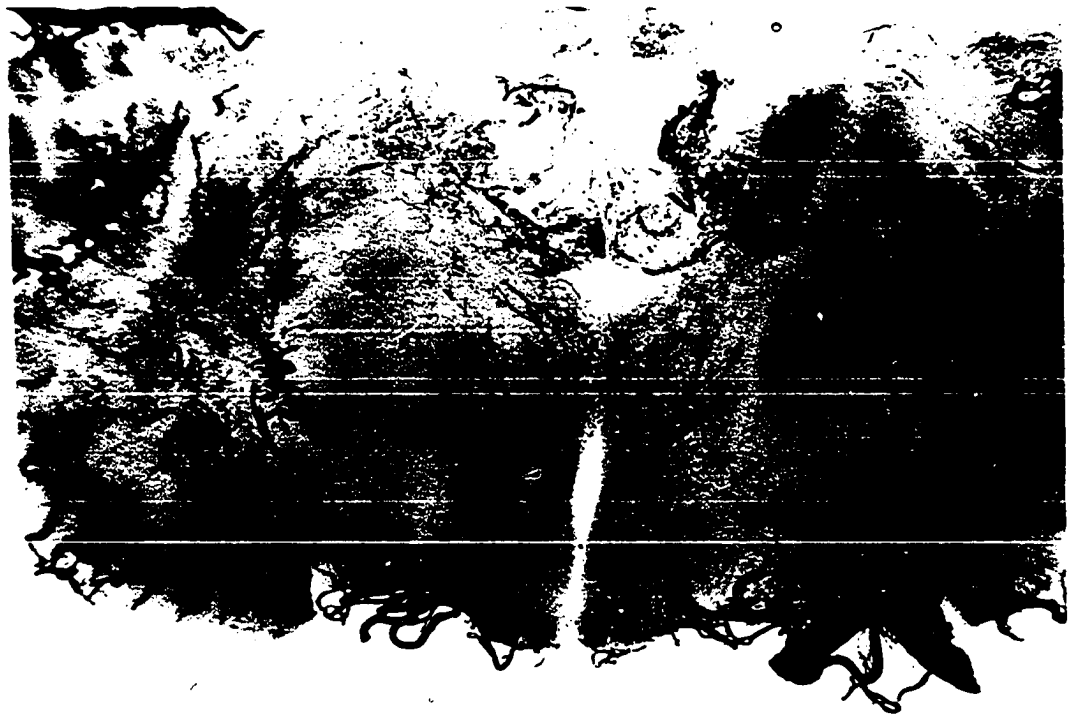
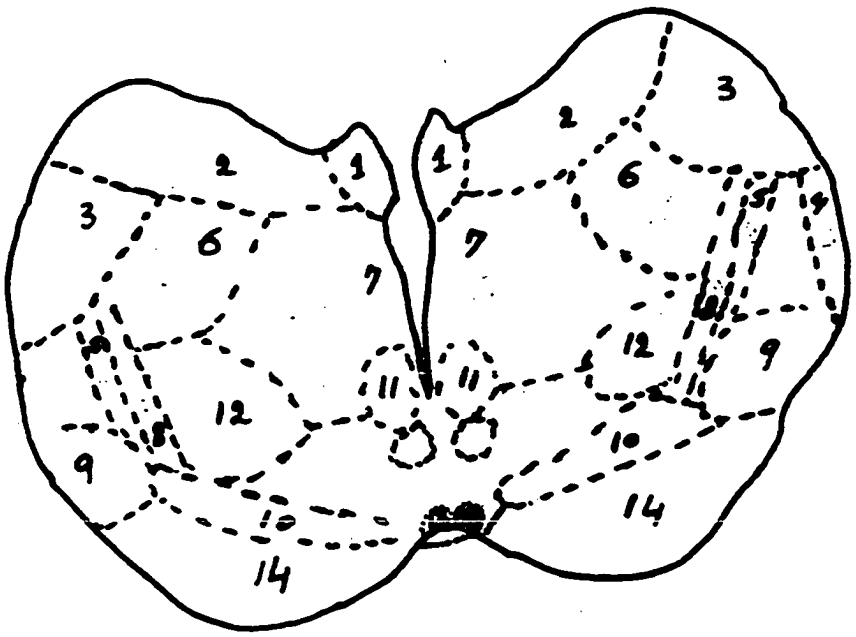


Figure 68a. (overlay)
Cross section of the brain of the pig level of the rostral part of the substantia perforata caudalis. 1. Nuclei habenulares. 2. Pulvinar. 3. Nucleus geniculati lateralis. 4. Tractus opticus. 5. Nucleus reticularis thalami. 6. Nucleus lateralis caudalis. 7. Nuclei intralaminares. 8. Lamina medullaris externa. 9. Nucleus geniculati medialis. 10. Nucleus subthalamicus. 11. Nucleus parafascicularis. 12. Nucleus ventralis medialis. 13. Nucleus mamillaris medialis. 14. Crus cerebri.

Figure 68b.
Same as above. Latex and India ink injection.

Figure 69a. (overlay)
Cross section of the brain ofthe pig at the level of the colliculus rostralis. 1. Nucleus colliculus rostralis. 2. Nucleus geniculati lateralis. 3. Nucleus geniculati medialis. 4. Commissura caudalis. 5. Nucleus tr. mesencephali n. trigemini. 6. Substantia grisea centralis. 7. Nucleus n. oculomotorii or Nucleus motorius n. oculomotori. 8. Nuclei tegmenti. 9. Crus cerebri. 10. Substantia nigra. 11. Lemniscus medialis. 12. Nucleus rubrum or ruber. 13. Decussatio tegmenti ventralis. 14. Nuclei interpeduncularis.

Figure 69b.
Same as above. India ink and latex injected.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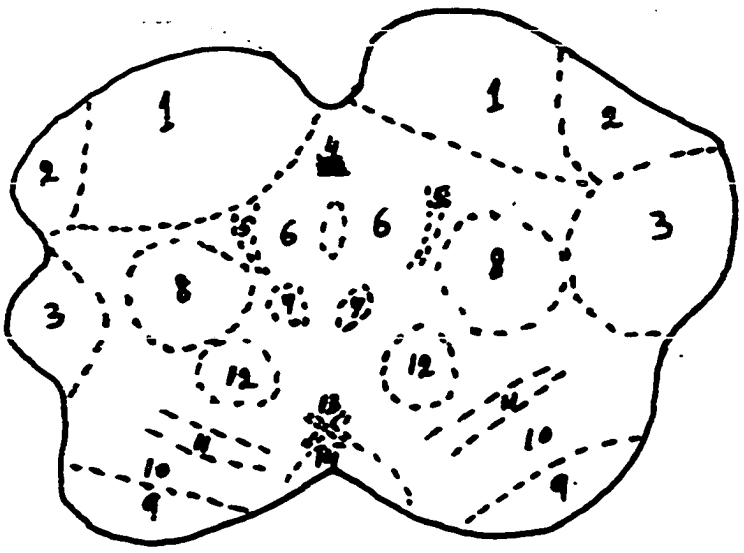
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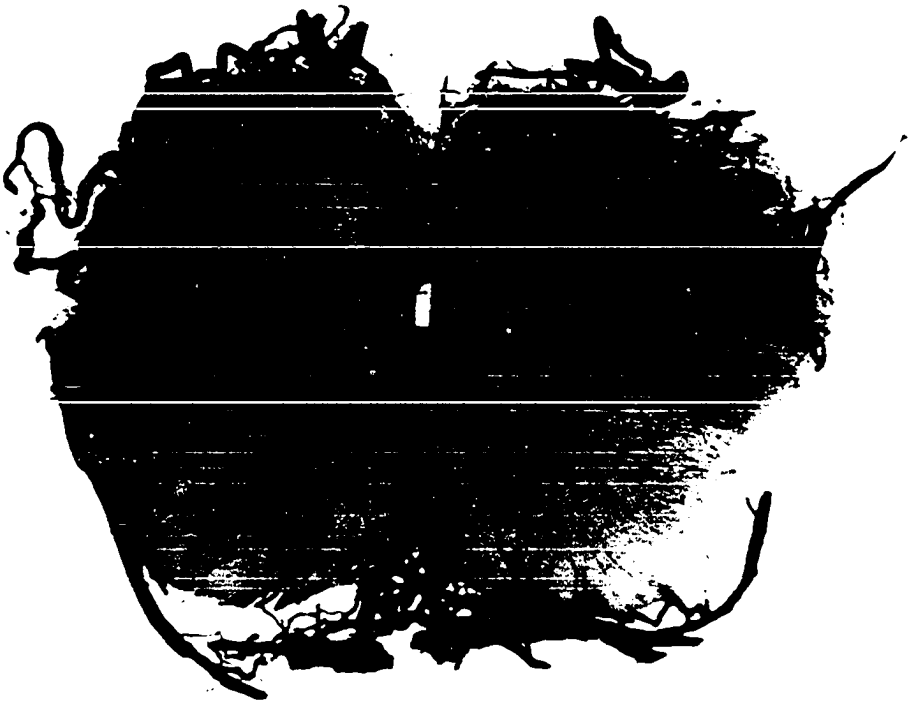
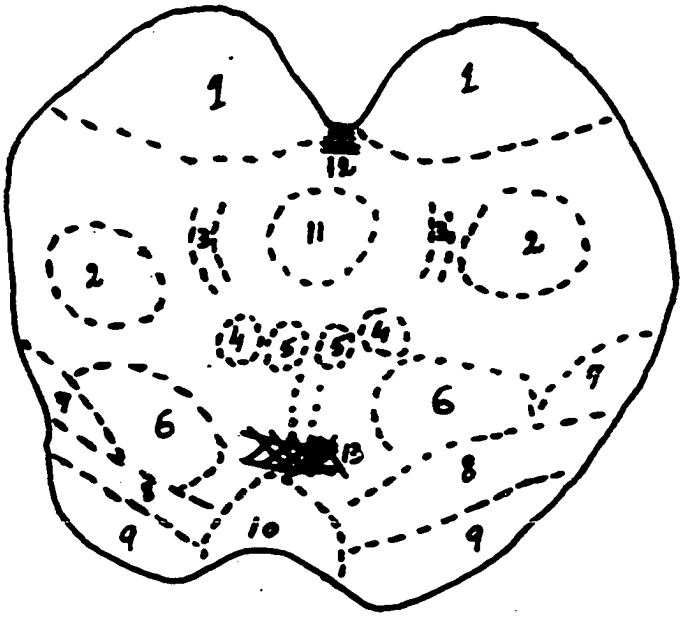


Figure 70a. (overlay)
Cross section of the brain of the pig at the level of the middle part of the mesencephalon. 1. Nucleus colliculus rostralis. 2. Nucleus colliculus. 3. Nucleus tr. mesencephali trigemini. 4. Nucleus n. trochlearis or nucleus motorius n. trochlearis. 5. Fasciculus longitudinalis lateralis. 6. Nucleus reticularis. 7. Lemniscus medialis. 8. Substantia nigra. 9. Crus cerebri. 10. Nucleus interpeduncularis. 11. Aqueductus mesencephali. 12. Commissura caudalis. 13. Decussatio pedunculorum cerebellarium rostralium.

Figure 70b.
Same as above. Latex and India ink injection.

Figure 71a. (overlay)
Cross section of the brain of the pig at the level of the middle of the pons. 1. Nucleus tractus mesencephali n. trigemini. 2. Nucleus motorius n. trigemini. 3. Nucleus sensibilis pontinus n. trigemini. 4. Nucleus tegmenti Guddenii. 5. Raphe or nucleus raphe. 6. Nucleus lemniscus lateralis and lemniscus lateralis. 7. Lemniscus medialis. 8. Nuclei pontis. 9. Nucleus reticularis. 10. Fibrae pontis transversae.

Figure 71b.
Same as above Latex injection.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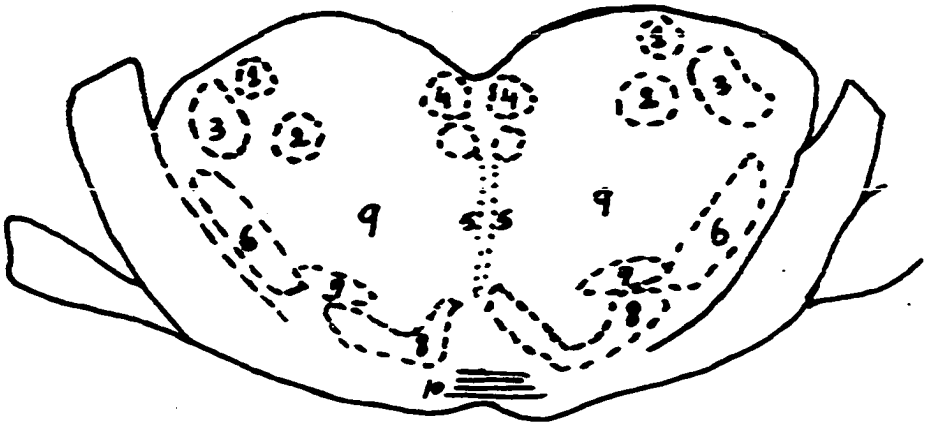
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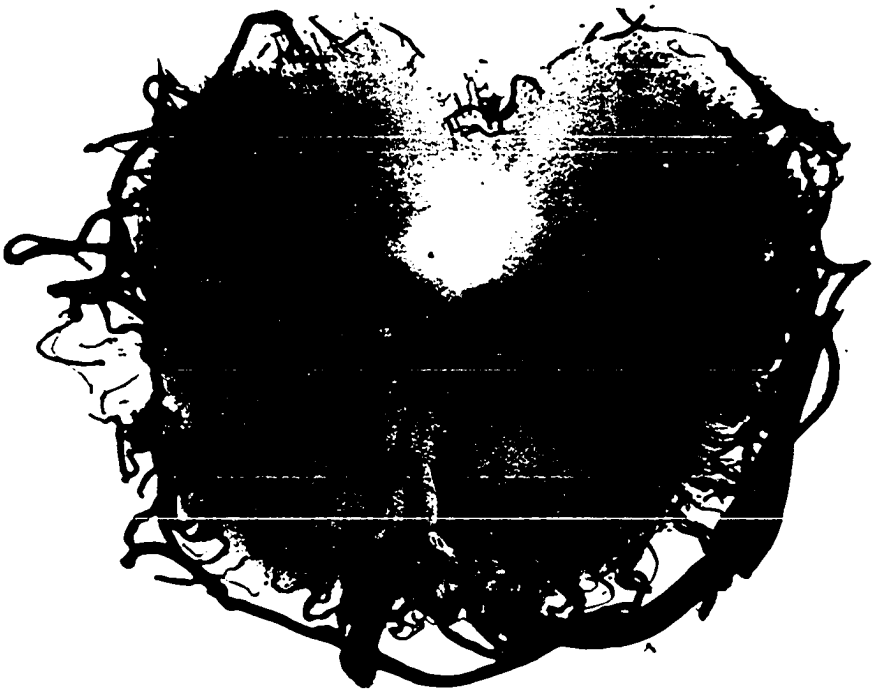


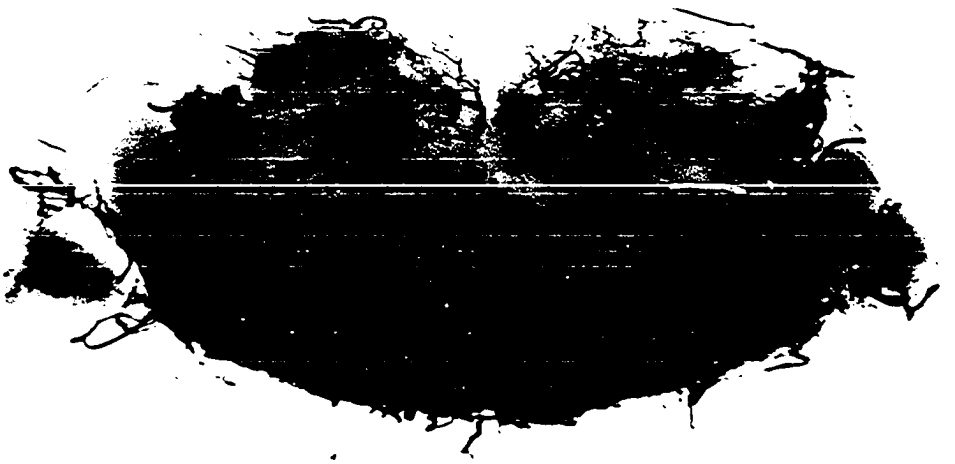
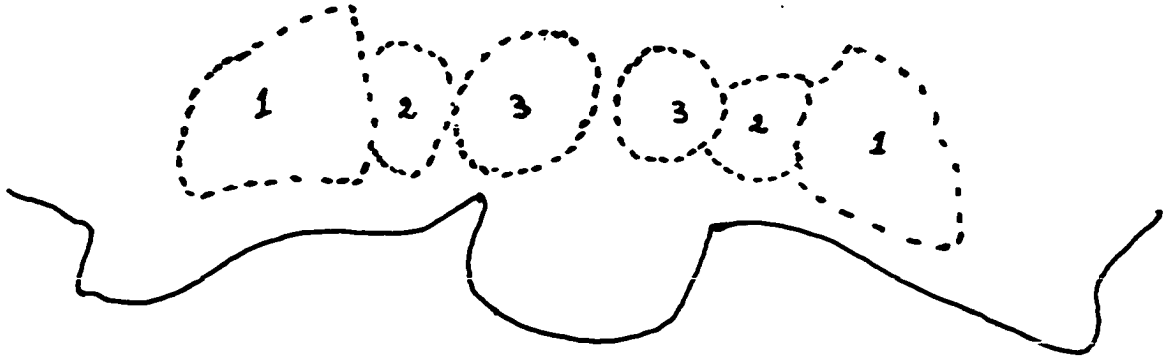


Figure 72a. (overlay)
Cross section of the cerebellum of the pig showing the cerebellar nuclei. 1. Nucleus dentatus. 2. Nucleus interpositi cerebelli. 3. Nucleus fastigii.

Figure 72b.
Same as above. Latex injection.

Figure 73a. (overlay)
Cross section of the brain of the pig at the level of the origin of the nervus vestibulocochlearis and nucleus n. facialis. 1. Fasciculus longitudinalis medialis. 2. Genu n. facialis. 3. Nucleus vestibularis medialis. 4. Nucleus vestibularis lateralis. 5. Pedunculus cerebelli caudalis. 6. Nucleus n. abducentis or nucleus motorius n. abducentis. 7. Nucleus reticularis. 8. Nucleus raphe or raphe. 9. Lemniscus medialis. 10. Pyramis. 11. Nucleus n. facialis or nucleus motorius n. facialis. 12. Nucleus tractus spinalis n. trigemini. 13. Tractus spinalis n. trigemini. 14. Nuclei cochleares.

Figure 73b.
Same as above. Latex injection.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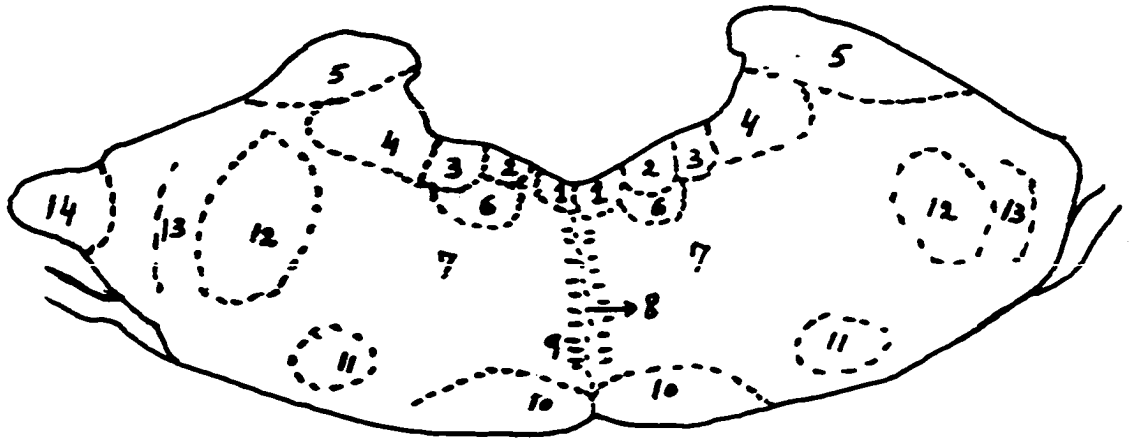
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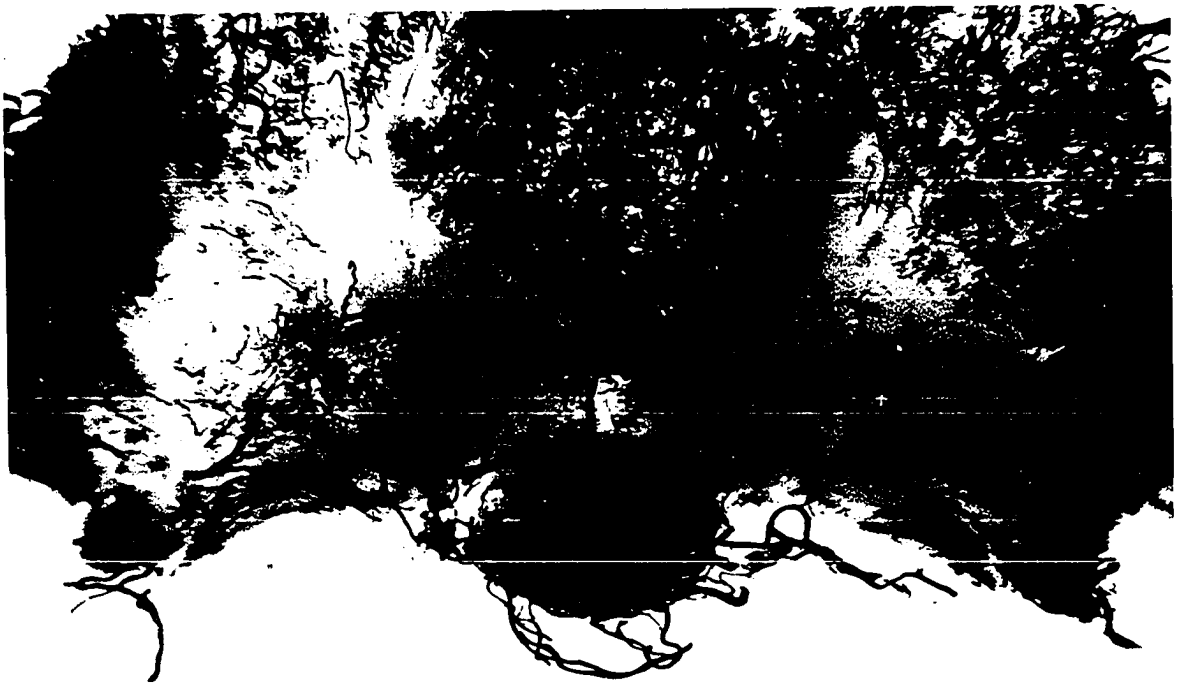


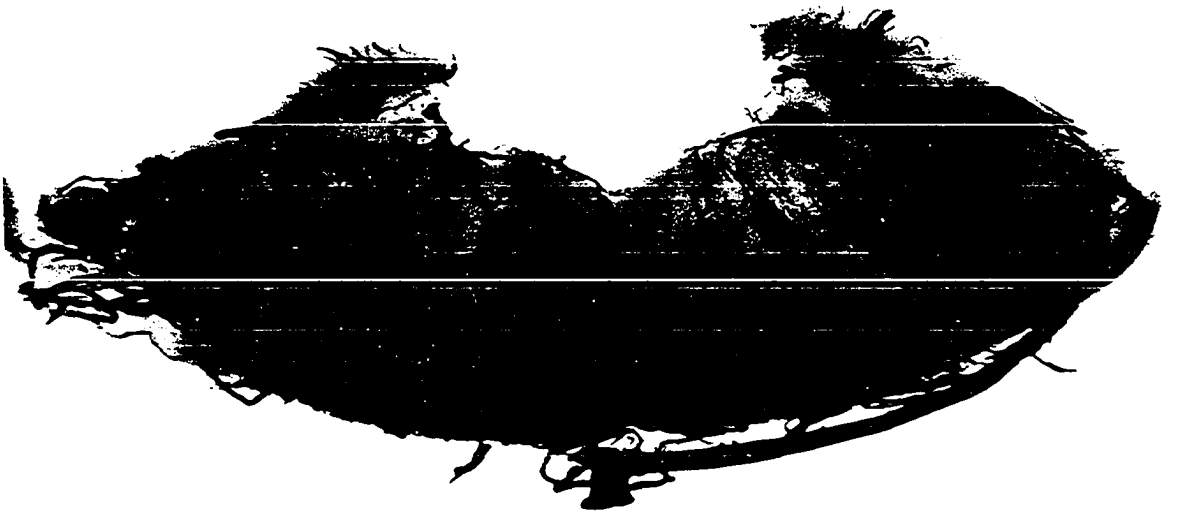
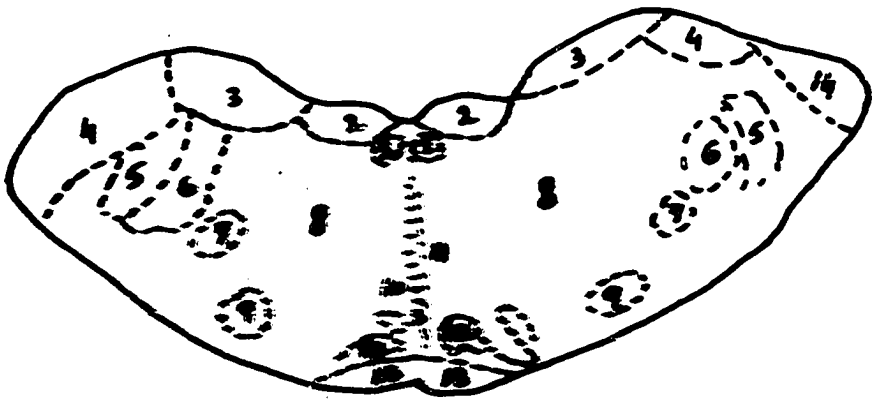


Figure 74a. (overlay)
Cross section of the rostral part of the medulla oblongata. 1. Fasciculus longitudinalis medialis. 2. Nucleus vestibularis medialis. 3. Nucleus vestibularis rostralis. 4. Pedunculus cerebelli caudalis 5. Tractus spinalis n. trigemini. 6. Nucleus tr. spinalis n. trigemini. 7. Nucleus ambiguus. 8. Nucleus reticularis. 9. Nucleus motorius n. facialis or nucleus n. facialis. 10. Lemniscus medialis. 11. Nucleus raphe or raphe. 12. Nucleus olivaris or nucleus olivaris inferioris. 13. Pyramis. 14. Nuclei cochleares.

Figure 74b.
Same as above. Latex injection.

Figure 75a. (overlay)
Cross section of the brain of the pig at the level of the middle of the middle part of the medulla oblongata. 1. Nucleus n. hypoglossi or nucleus motorius n. hypoglossi. 2. Nucleus dorsalis n. vagi or nucleus parasympathicus n. vagi. 3. Nucleus solitarius. 4. Nucleus Roller. 5. Fasciculus longitudinalis medialis. 6. Nucleus cuneatus medialis. 7. Nucleus cuneatus laterlis or accessorius. 8. Pedunculus cerebellaris caudalis. 9. Tractus spinalis n. trigemini. 10. Nucleus tr. spinalis n. trigemini. 11. Nucleus ambiguus. 12. Nucleus reticularis. 13. Nucleus reticularis lateralis. 14. Nucleus raphe or raphe. 15. Nucleus olivaris inferioris or nucleus olivaris. 16. Lemniscus medialis. 17. Pyramis.

Figure 75b.
Same as above. Latex injection.



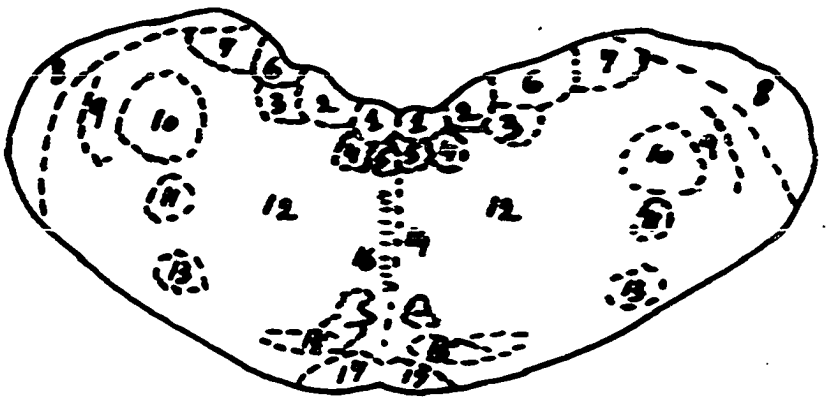
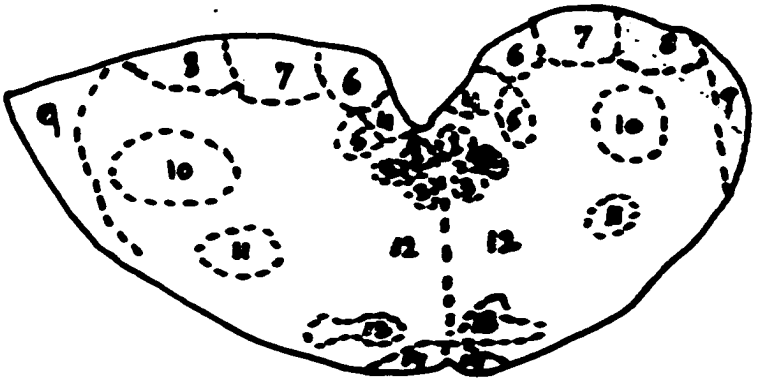


Figure 76a. (overlay)
Cross section of the brain of the pig at the level of the calamus scriptorius. 1. Nucleus n. hypoglossi or necleus motoius n. hypoglossic. 2. Nucleus Roller. 3. Fasciculus longitudinalis medialis. 4. Nucleus dorsalis n. vagi or nucleus parasympathicus n. vagi. 5. Nucleus intercalatus. 6. Nucleus gracilis. 7. Nucleus cuneatus medialis. 8. Nucleus cuneatus lateralis or accessorius. 9. Pedunculus cerebelli caudalis. 10. Nucleus tr. spinalis n. trigemini. 11. Nucleus ambibuus. 12. Nucleus reticularis. 13. Nucleus olivaris or nucleus olivaris infereioris. 14. Pyramis.

Figure 76b.
Same as above. Latex injection.

Figure 77a. (overlay)
Cross section of the brain of the pig at the spinomedullary junction. 1. Nucleus gracilis. 2. Nucleus cuneatus medialis. 3. Nucleus cuneatus lateralis or accessorius. 4. Pedunculus cerebellaris caudalis. 5. t. Nucleus tr. spinalis n. trigemini. 6. Nucleus fasciculi lateralis. 7. Nucleus olivaris or nucleus olivaris inferioris. 8. Nucleus dorsalis n. vagi or nucleus parasympthicus n. vagi. 9. Fasciculus longitudinalis medialis. 10. Nucleus n. hypoglossi.

Figure 77b.
Same as above. Latex infection.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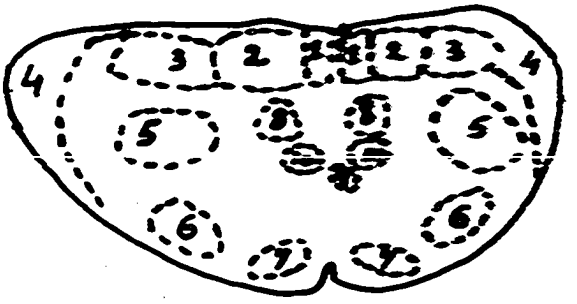
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Figure 78.
Dog No. E26. 2 months.
Showing a valve like structure in a pial branch of the anterior cerebral artery at the site of branching. Weigert's Resorcin Fuchsin elastic stain. X 1000.

Figure 79.
Dog No. 049. $5\frac{1}{4}$ months.
Showing a valve like formation in a pial branch of the posterior cerebral artery at the site of branching. Verhoeff's and Van Gieson's stain. X 1000.

Figure 80.
Dog No. 049. $5\frac{1}{4}$ months.
Showing a valve like structure at the site of branching in a pial branch of the posterior communicating artery. Hematoxylin and eosin stain. X 250.

Figure 81.
Dog No. 52. 7 years 6 months.
Showing a valve like structure at the site of branching in a pial branch of the anterior cerebral artery. Hematoxylin and eosin stain. X 250.

Figure 82.
Dog No. M37. 13 years and one month.
A valve like structure in an intracerebral branch of the anterior cerebral artery. Hematoxylin and eosin stain. X 250.

Figure 83.
Dog No. B99. 1 month and 19 days.
Pial branch of the anterior cerebral artery showing elastic fibers frayed from the internal elastic lamina. Weigert's Resorcin Fuchsin elastic stain. X 250.

Figure 84.
Dog No. B99. 1 month and 19 days.
Pial branch of the middle cerebral artery showing fragmented internal elastic lamina with few elastic fibers fraying. Weigert's Resorcin Fuchsin elastic stain. X 250.

Figure 85.
Dog No. E26. 2 months.
Showing the smooth muscle cells density in the tunica media of the basilar artery. Hematoxylin and eosin stain. X 400.

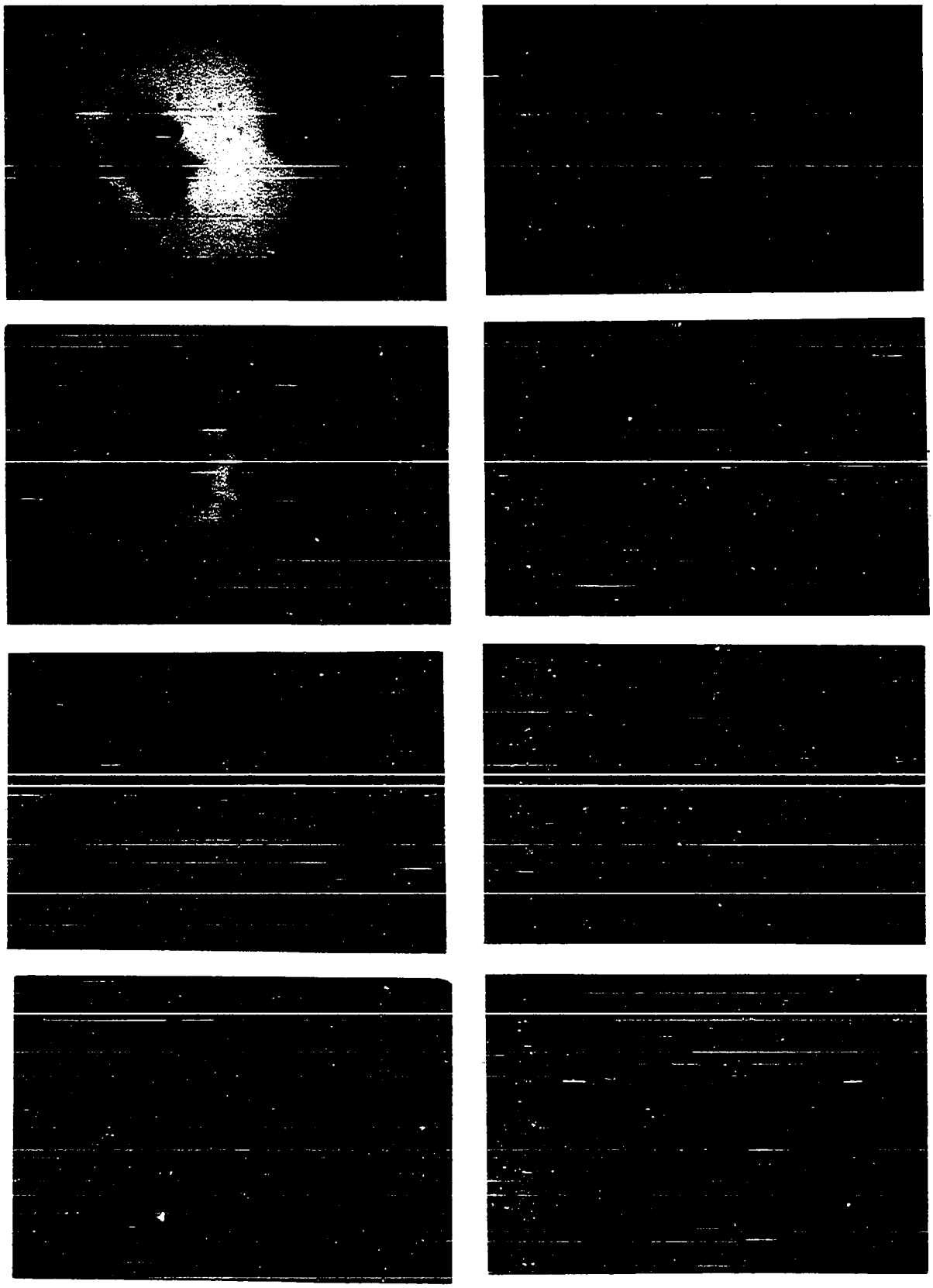


Figure 86.
Dog No. 049. 5½ months.
Showing the anterior cerebral artery almost devoid of elastic fibers in the tunica media. Weigert's Resorcin Fuchsin elastic stain. X 100.

Figure 87.
Dog No. 049. 5½ months.
Showing the same as in Figure 86, in the basilar artery. Weigert's Resorcin Fuchsin elastic stain. X 100.

Figure 88.
Dog No. 049. 5½ months.
Showing the elastic fibers in the tunica media of a branch of middle cerebral artery. Weigert's Resorcin Fuchsin elastic stain. X 100.

Figure 89.
Dog No. 049. 5½ months.
Showing the middle cerebral artery without any collagen infilteration in the tunica media. Mallory's Triple stain. X 100.

Figure 90.
Dog No. 049. 5½ months.
Showing a slight disruption of the internal elastic lamina with slight intimal thickening. Mallory's Triple stain. X 250.

Figure 91.
Dog No. 049. 5½ months.
Showing the subintimal changes, disruption of internal elastic lamina, disorganization of smooth muscle cells and slight collagen in the subintima. Mallory's Triple stain. X 1000.

Figure 92.
Dog No. 049. 5½ months.
Showing the medial defect in the middle cerebral artery. Mallory's Triple stain. X 100.

Figure 93.
Dog No. B48. 8 months.
Showing intimal thickening in the intracerebral branch of the anterior cerebral artery. Internal elastic lamina split and occlusion of the lumen. Weigert's Resorcin Fuchsin elastic stain. X 1000.

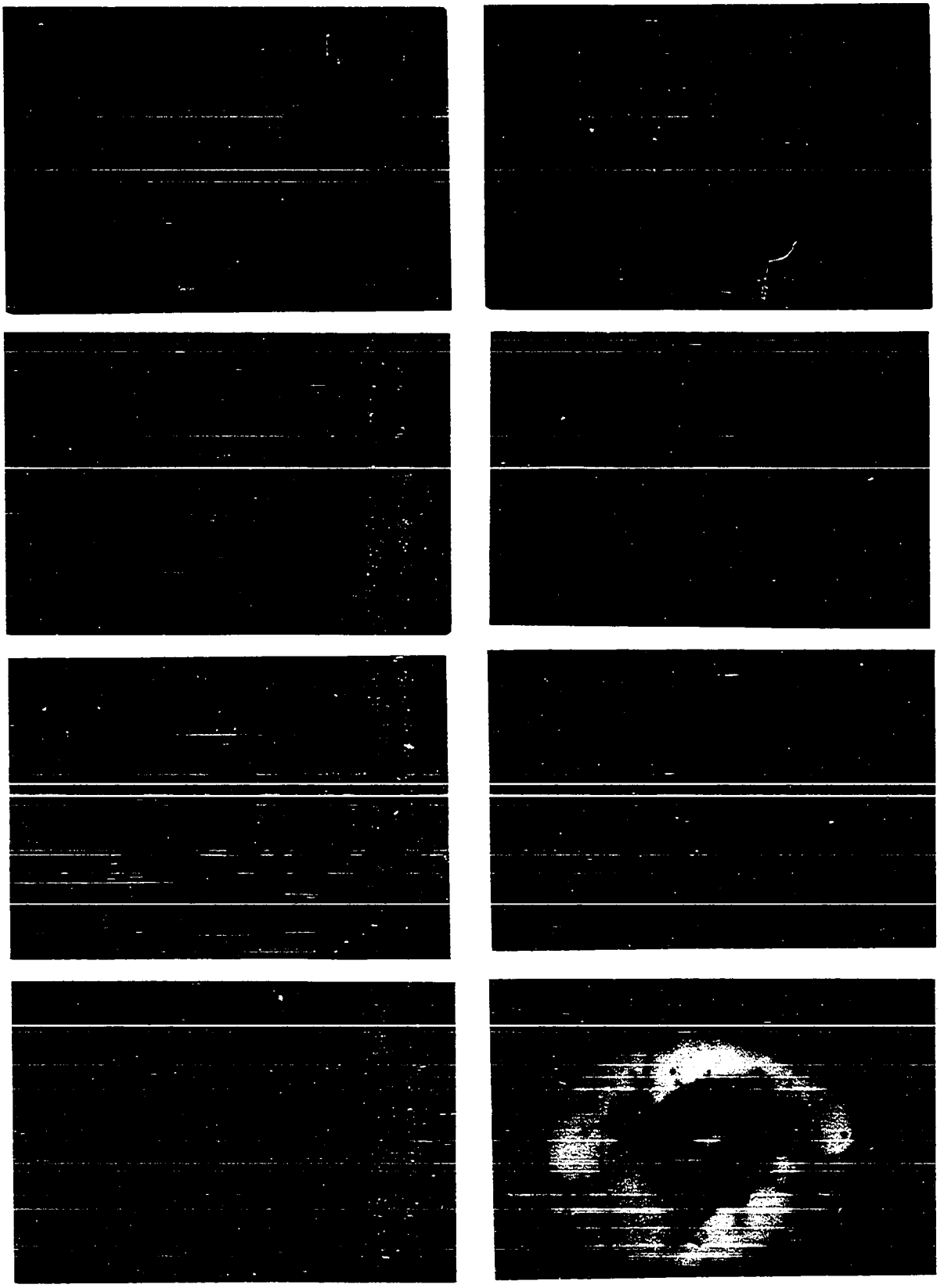


Figure 94.
Dog No. B48. 8 months.
Showing a branch of the middle cerebral artery with increased elastic fibers in the tunica media. Weigert's Resorcin Fuchsin elastic stain. X 250.

Figure 95.
Dog No. B48. 8 months.
Showing a branch of the middle cerebral artery with disrupted internal elastic lamina and increased collagen in the tunica media under it. Mallory's Triple stain. X 250.

Figure 96.
Dog No. 48. 8 months.
Showing a intracerebral branch of the posterior cerebral artery having fragmented elastic fibers from the internal elastic lamina occupying new locations in the tunica media. Slightly lameller. Weigert's Resorcin Fuchsin elastic stain. X 1000.

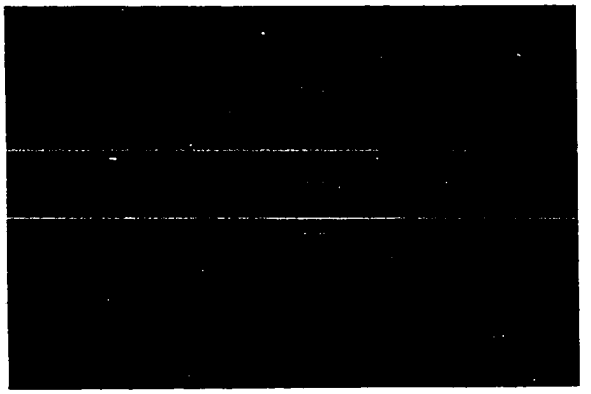
Figure 97.
Dog No. B56. One year.
Showing middle cerebral artery with slight intimal thickening and discontinuous internal elastic lamina. Mallory's Triple stain. X 100.

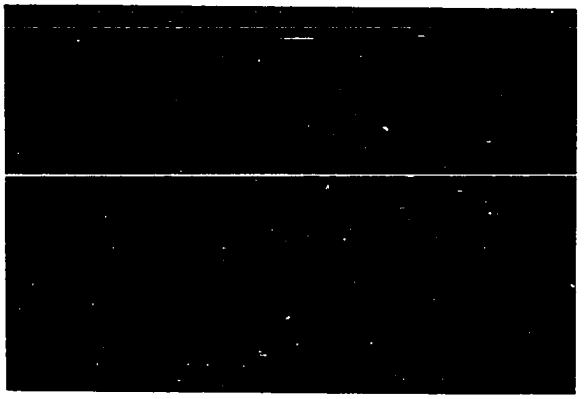
Figure 98.
Dog No. B56. One year.
Same as Figure 97 under X 250.

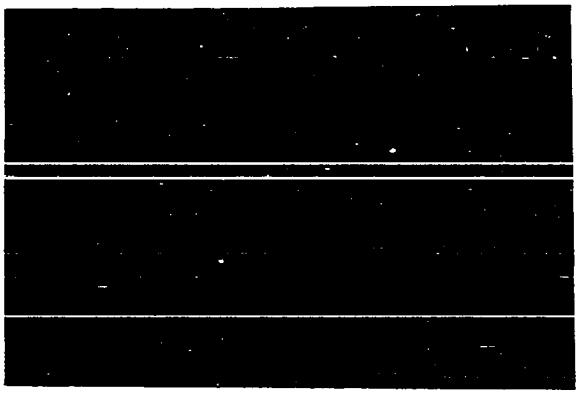
Figure 99.
Dog No. B56. One year.
Showing the split of the internal elastic lamina in intracortical branch of the posterior communicating artery. Weigert's Resorcin Fuchsin elastic stain. X 1000.

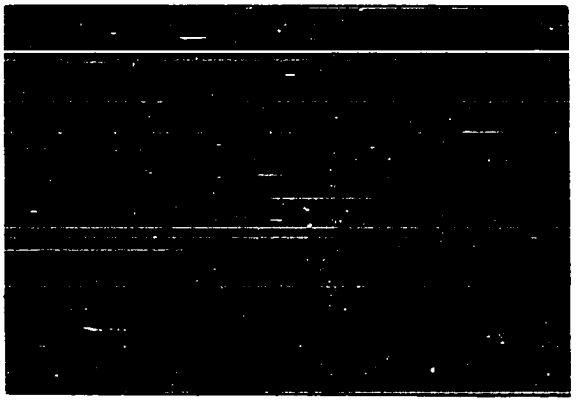
Figure 100.
Dog No. B56. One year
Showing the smooth muscle cells density in the tunica media of the basilar artery. Hematoxylin and eosin. X 250.

Figure 101.
Dog No. B37. 1 year, 2 months and 11 days.
Showing a branch of posterior communicating artery with internal elastic lamina split. Weigert's Resorcin Fuchsin elastic stain. X 1000.









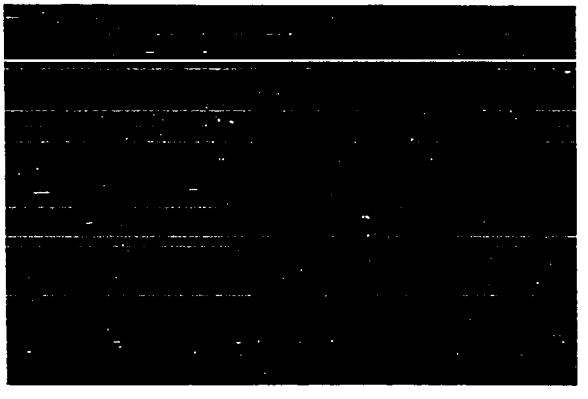


Figure 102.
Dog No. 21. 2 years and 17 days
Showing intracerebral branch of the anterior cerebral artery with focal duplication of the internal elastic lamina. Weigert's Resorcin Fuchsin elastic stain. X 1000.

Figure 103.
Dog No. 21. 2 years and 17 days.
Showing intracerebral branch of the posterior communicating artery with internal elastic lamina duplicated. Weigert's Resorcin Fuchsin elastic stain. X 1000.

Figure 104.
Dog No. 053. 2 years and 7 months.
Showing fraying of the internal elastic lamina in a branch of the posterior communicating artery. Weigert's Resorcin Fuchsin elastic stain. X 400.

Figure 105.
Dog No. B68. 2 years 8 months and 6 days.
Showing the fragmentation of internal elastic lamina, focal intimal thickening and collagen in the subintima of the basilar artery. Mallory's Triple stain. X 250.

Figure 106.
Dog No. 95. 4 years.
Showing disruption of the internal elastic lamina with large intimal thickening in a branch of the anterior cerebral artery. The thickening occluding the arteriole. Weigert's Resorcin Fuchsin elastic stain. X 1000.

Figure 107.
Dog No. 95. 4 years.
Showing the smooth muscle cell density in the tunica media of the middle cerebral artery. Hematoxylin and eosin. X 100.

Figure 108.
Dog No. 95. 4 years.
Showing the increase of the collagen in the tunica media and intima of the middle cerebral artery.
Mallory's Triple stain. X 250.

Figure 109.
Dog No. B118. 6 years and 7 months.
Showing a pial branch of the anterior cerebral artery with fragmentation of the internal elastic lamina and extensive intimal thickening occluding the vessel. Weigert's Resorcin Fuchsin elastic stain. X 1000.

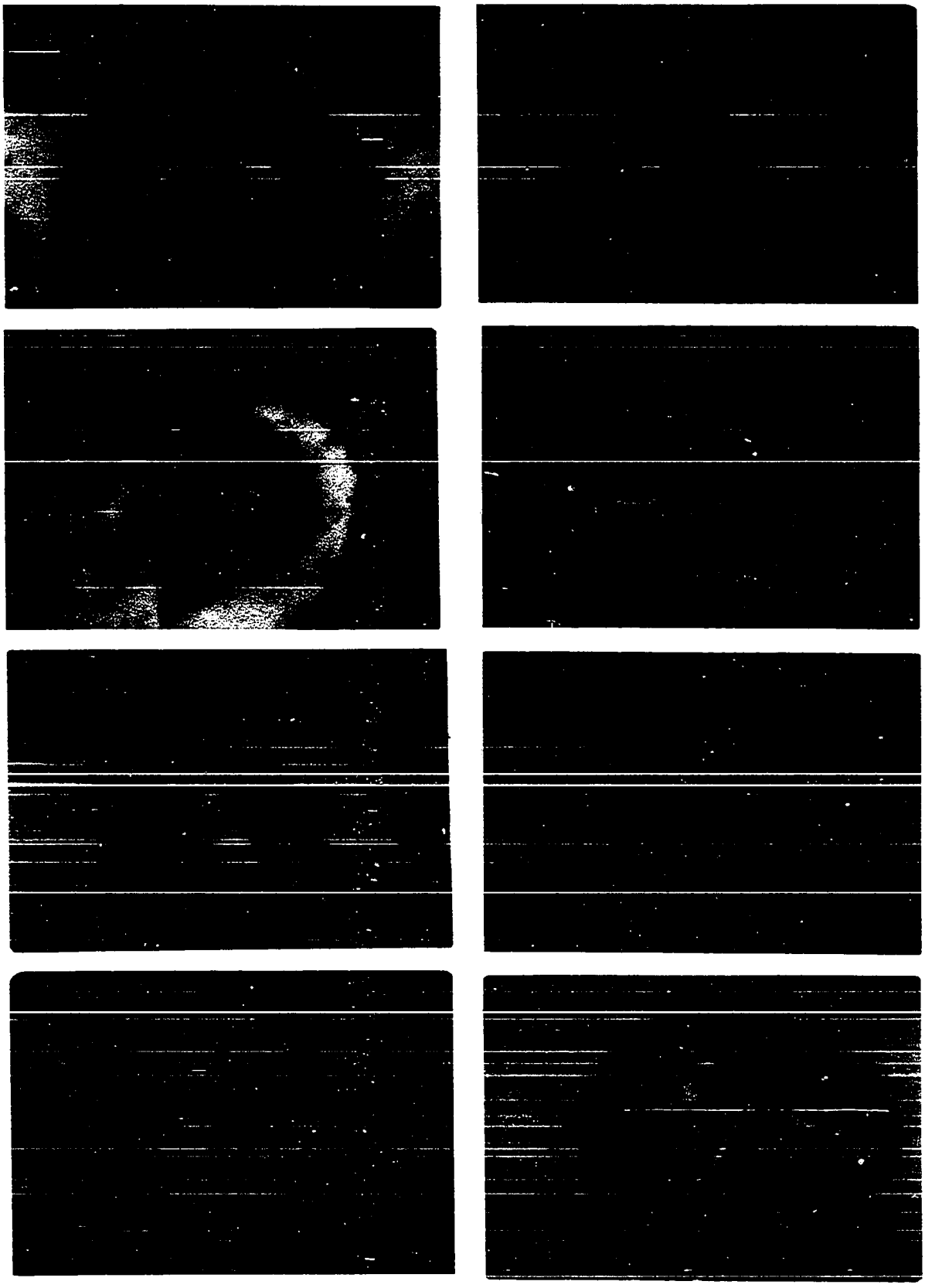


Figure 110.
Dog No. B119. 6 years and 10 months. Showing a pial branch of the anterior cerebral artery with increased elastic fibers in the tunica media. Weigert's Resorcin Fuchsin elastic stain. X 250.

Figure 111.
Dog No. B119. 6 years and 10 months. Showing middle cerebral artery with elastic fibers in the tunica media. Weigert's Resorcin Fuchsin elastic stain. X 250.

Figure 112.
Dog No. B119. 6 years and 10 months. Showing posterior cerebral artery with fibrous intimal thickening and fragmentation of the internal elastic lamina. Verhoeff's and Van Gieson's stain. X 250.

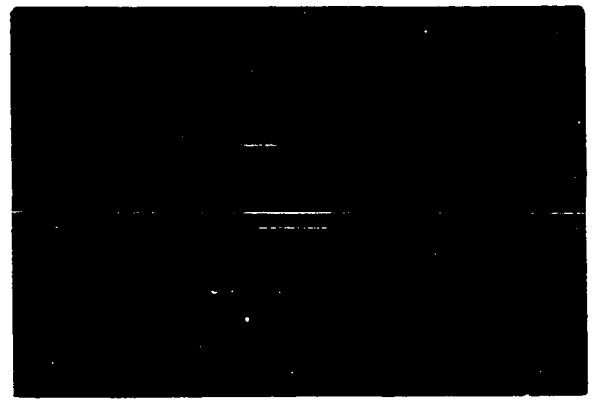
Figure 113.
Dog No. M52. 6 years and 6 months. Showing posterior cerebral artery with bilateral fibrous thickening. Mallory's Triple stain. X 100.

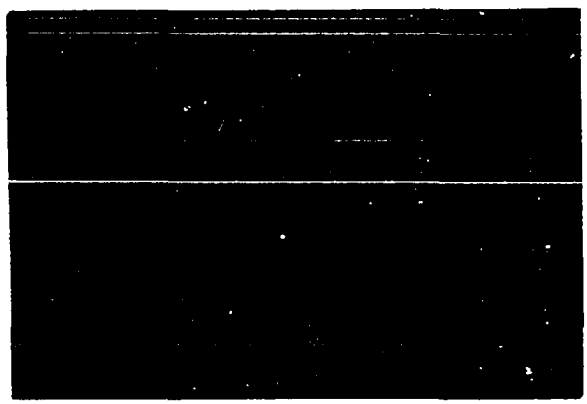
Figure 114.
Dog No. 9. 8 years and 8 months. Showing a branch of the middle cerebral artery with fibrous intimal cushion and medial defect. Mallory's Triple stain. X 250.

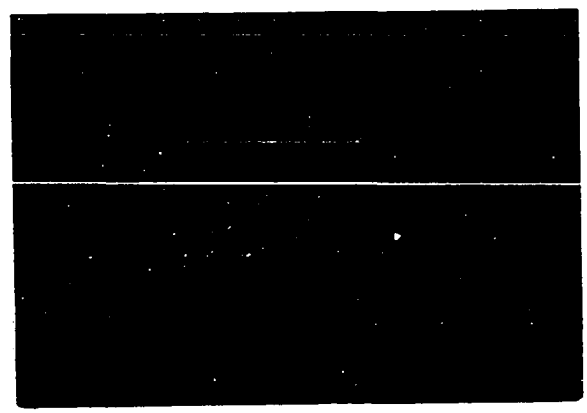
Figure 115.
Dog No. M53. 9 years. Focal fibrous subendothelial increase in a branch of the anterior cerebral artery. Mallory's Triple stain. X 100.

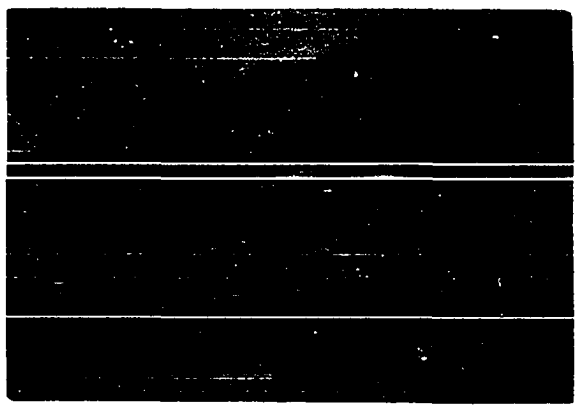
Figure 116.
Dog No. M53. 9 years. Intracortical branch of the anterior cerebral artery with intimal thickening occluding the lumen. Weigert's Resorcin Fuchsin elastic stain. X 1000.

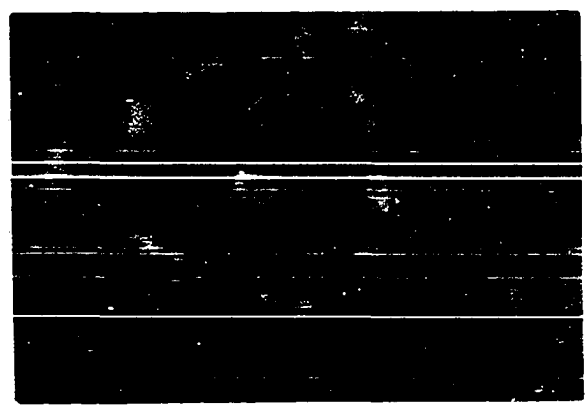
Figure 117.
Dog No. M53. 9 years. General subendothelial increase with its fibrosis in the middle cerebral artery. Mallory's Triple stain. X 100.

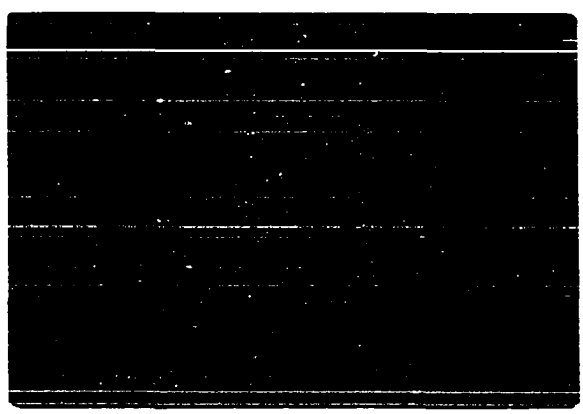












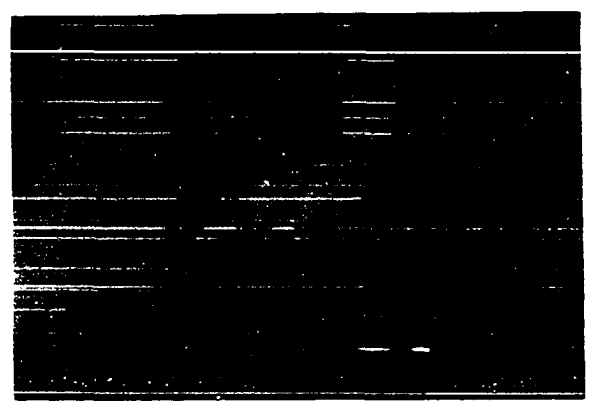


Figure 118.
Dog No. M53. 9 years.
Showing the smooth muscle cells density in the basilar artery.
Hematoxylin and eosin stain. X 250.

Figure 119.
Dog No. 6. 10 years.
Branch of the anterior cerebral artery showing intimal thickening with mesenchymal cells in it. Weigert's Resorcin Fuchsin elastic stain. X 400.

Figure 120.
Same as Figure 119 with Mallory's Triple stain. X 1000.

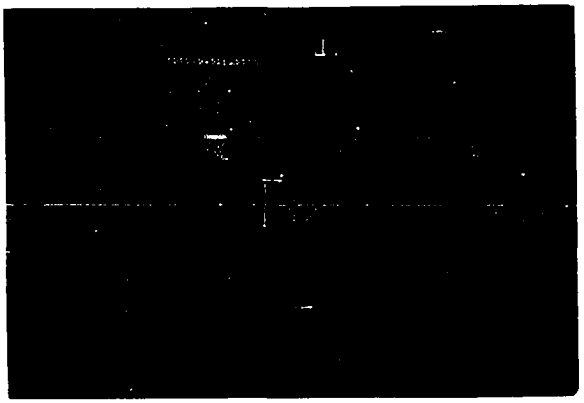
Figure 121.
Dog No. 6. 10 years.
Branch of the middle cerebral artery with intimal thickening and fibrosis of different layers. Mallory's Triple stain. X 250.

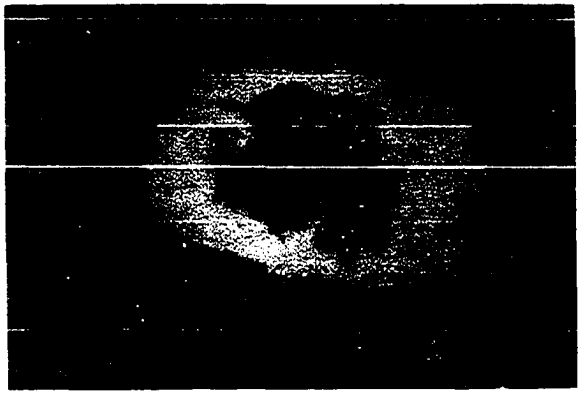
Figure 122.
Dog No. 6. 10 years.
Same as Figure 121 with Weigert's Resorcin Fuchsin elastic stain.
X1000.

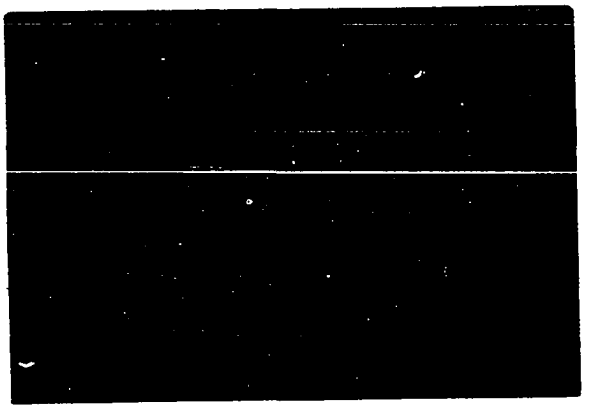
Figure 123.
Dog No. 6. 10 years.
Branch of the middle cerebral artery with fibrosed and fragmented elastic fibers in the tunica media. Weigert's Resorcin Fuchsin elastic stain. X 250.

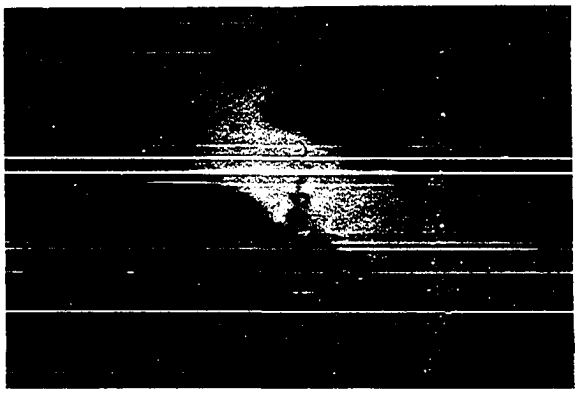
Figure 124.
Dog No. 6. 10 years.
Fibrosis of the different layers of the basilar artery. Mallory's Triple stain. X 250.

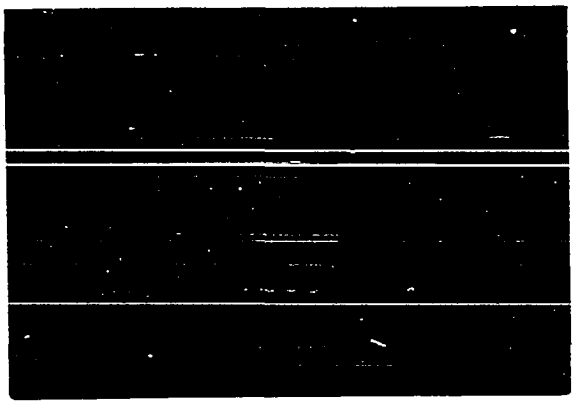
Figure 125.
Dog No. 6. 10 years.
Showing the presence of the acid mucopolysaccharides in the tunica media. Alican blue and PAS stain.
X 100.

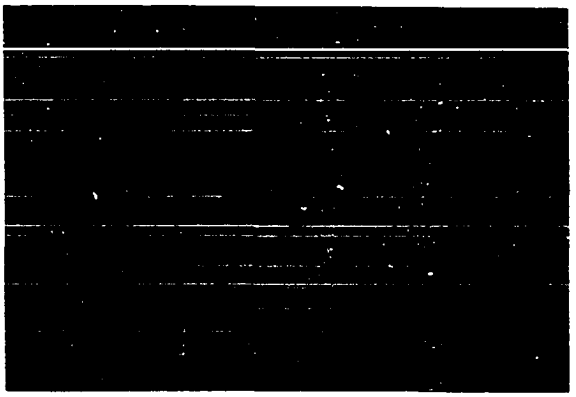












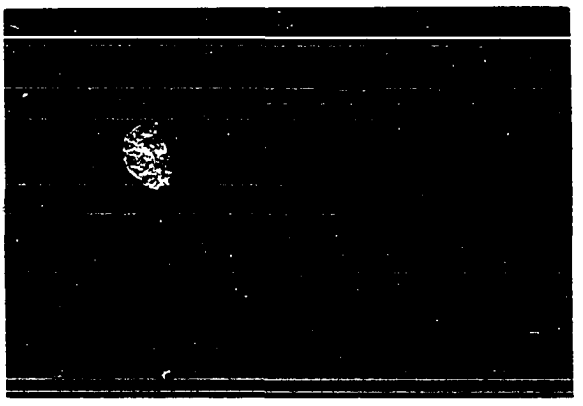


Figure 126.
Dog No. M49. 10 years and 3 months.
Branch of the anterior cerebral artery with smooth muscle like cells in the intimal thickening. Mallory's Triple stain. X 250.

Figure 127.
Dog No. M49. 10 years and 3 months.
Same as Figure 126 with Weigert's Resorcin Fuchsin elastic stain. X 250.

Figure 128.
Dog No. M39. 10 years and 3 months.
Same as Figure 127 at X 1000.

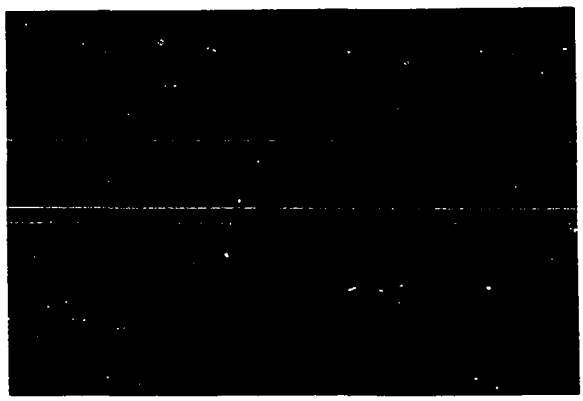
Figure 129.
Dog No. M49. 10 years and 3 months.
Branch of anterior cerebral artery with focal duplication of the internal elastic lamina, with intimal thickening having smooth muscle like cells.
Weigert's Resorcin Fuchsin elastic stain.
X 400.

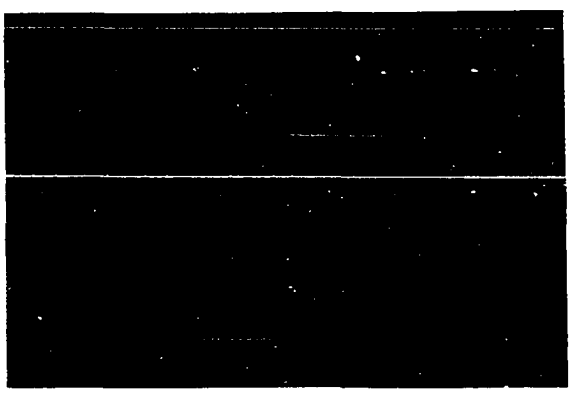
Figure 130.
Dog No. M49. 10 years and 3 months.
Intracortical branch of the middle cerebral artery with intimal thickening and internal elastic lamina fragmentation. Weigert's Resorcin Fuchsin elastic stain. X 1000.

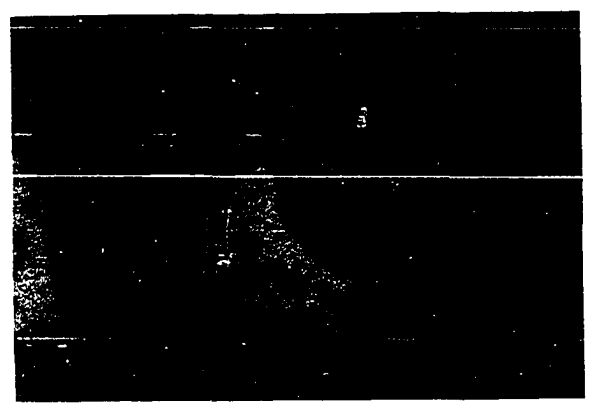
Figure 131.
Dog No. M49. 10 years and 3 months.
Fibrous intimal thickening and internal elastic lamina fragmentation in the basilar artery. Weigert's Resorcin Fuchsin elastic stain.
X 250.

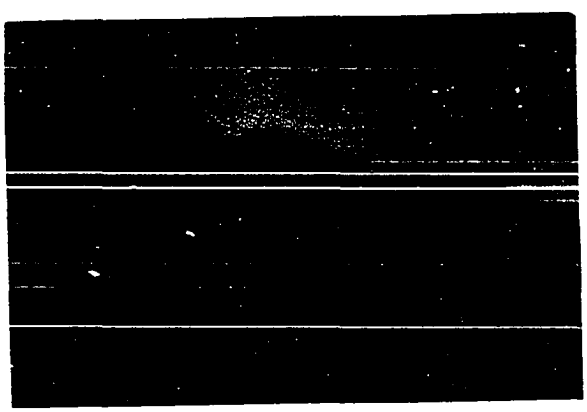
Figure 132.
Dog No. M49. 10 years and three months.
Showing acid mucopolysaccharides in the tunica media of the middle cerebral artery. Alican blue and PAS stain. X 100.

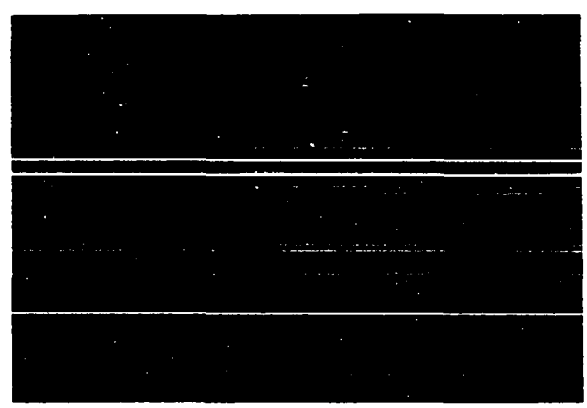
Figure 133.
Dog No. M42. 11 years and 2 months.
Perforating branch of the anterior cerebral artery with internal elastic lamina fragmentation and intimal thickening occluding the lumen.
Weigert's Resorcin Fuchsin elastic stain. X 1000.











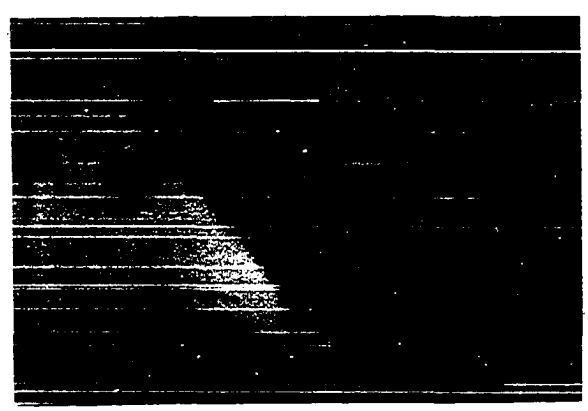


Figure 134.
Dog No. M44. 12 years
Pial branch of the anterior cerebral artery showing intimal thickening. Weigert's Resorcin Fuchsin elastic stain. X 100.

Figure 135.
Dog No. M44. 12 years.
Branch of the anterior cerebral artery with fragemented elastic fibers in the tunica media. Weigert's Resorcin Fuchsin elastic stain. X 250.

Figure 136.
Dog No. M44. 12 years.
Branch of the middle cerebral artery with fibrous intimal cushion and medial defect. Mallory's Triple stain. X 100.

Figure 137.
Dog No. M44. 12 years.
Same as Figure 136. X 250.

Figure 138.
Dog No. M44. 12 years.
Showing smooth muscle cells density in the tunica media of the basilar artery. Hematoxylin and eosin stain. X 250.

Figure 139.
Dog No. M37. 13 years and 1 month.
Showing the total fibrosis of the different layers of the middle cerebral artery. Mallory's Triple stain. X 40.

Figure 140.
Dog No. M37. 13 years and 1 month.
Same as Figure 139. X 250.

Figure 141.
Dog No. M37. 13 years and 1 month.
Showing the acid mucopolysaccharides in the tunica media of the middle cerebral artery. Alican blue and PAS stain. X 100.

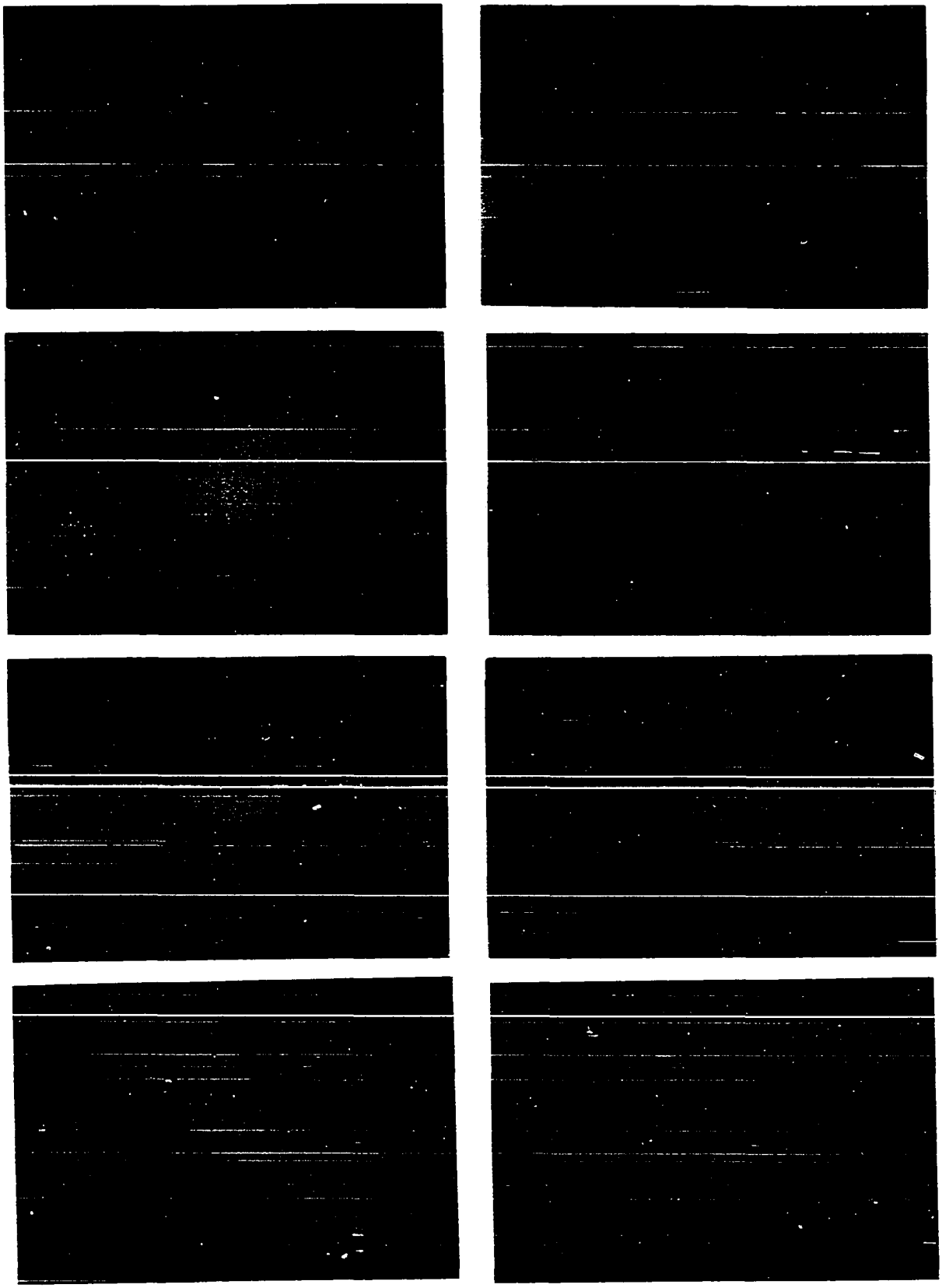


Figure 142.
Dog No. M36. 16 years.
Showing complete fibrosis of different layers of a branch of the anterior cerebral artery. Mallory's Triple stain. X 100.

Figure 143.
Dog No. M36. 16 years.
Showing the granulating and fragmenting elastic fibers in the tunica media of a branch of anterior cerebral artery. Weigert's Resorcin Fuchsin elastic stain. X 250.

Figure 144.
Dog No. M36. 16 years.
Showing the smooth muscle cell density in the tunica media of the middle cerebral artery. Hematoxylin and eosin. X 250.

Figure 145.
Dog No. M36. 16 years.
Showing fibrous intimal thickening of a branch of the posterior communicating artery. Verhoeff's and Van Gieson's stain. X 400.

Figure 146.
Dog No. M36. 16 years.
Pial branch of the middle cerebral artery with fibroblast like cells lining the luminal border of the thickened intima. Weigert's Resorcin Fuchsin elastic stain. X 400.

Figure 147.
Dog No. M36. 16 years.
Showing the degree of fibrosis of the different layers of the basilar artery and its branch. Mallory's Triple stain. X 400.

Figure 148.
Dog No. M36. 16 years.
Showing the smooth muscle cell density in the basilar artery. Hematoxylin and eosin. X 250.

Figure 149.
Dog No. M36. 16 years.
Showing the acid mucopolysaccharide in the tunica media of the basilar artery. Alican blue and PAS. X 400.

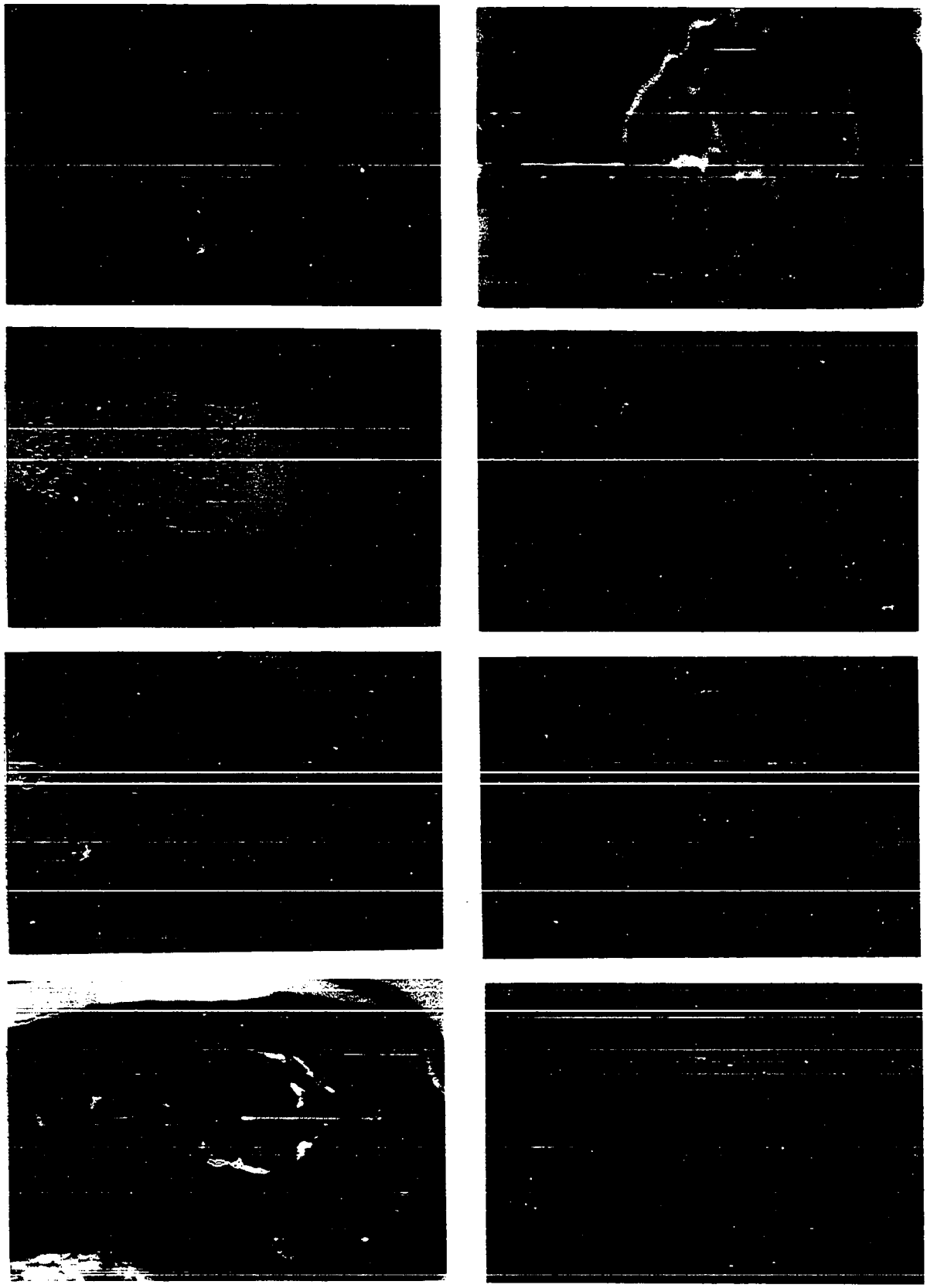


Figure 150.
Pig No. 1448B. 2 days
Pial branch of the anterior cerebral artery with duplication and fragmentation of internal elastic lamina. Weigert's Resorcin Fuchsin elastic stain. X 250.

Figure 151.
Pig No. 1448B. 2 days
Pial branch of the posterior communicating artery with a condition similar to that in Figure 150. Weigert's Resorcin Fuchsin elastic stain. X 250.

Figure 152.
Pig No. 1448B. 2 days.
A pial branch of the posterior communicating artery with early intimal cushion at the site of branching. Hematoxylin and eosin. X 250.

Figure 153.
Pig No. 5353. 2 months and 31 days.
Showing the intracortical branch of the posterior communicating artery with disruption of the internal elastic lamina. Weigert's Resorcin Fuchsin elastic stain. X 250.

Figure 154.
Pig No. 3923. 10 months and 15 days. Branch of the anterior cerebral artery with bilateral intimal cushions at the site of branching. Mallory's Triple stain. X 100.

Figure 155.
Pig No. 9442. 11 months.
Showing slight intimal thickening with disrupted internal elastic lamina in the basilar artery. Mallory's Triple stain. X 100.

Figure 156.
Pig No. 3430S. 1 year and 2 months.
Showing intimal cushions at the site of branching of the anterior cerebral artery. Mallory's Triple stain. X 100.

Figure 157.
Pig No. 3430S. 1 year and 2 months.
Same as in Figure 156. X 250.

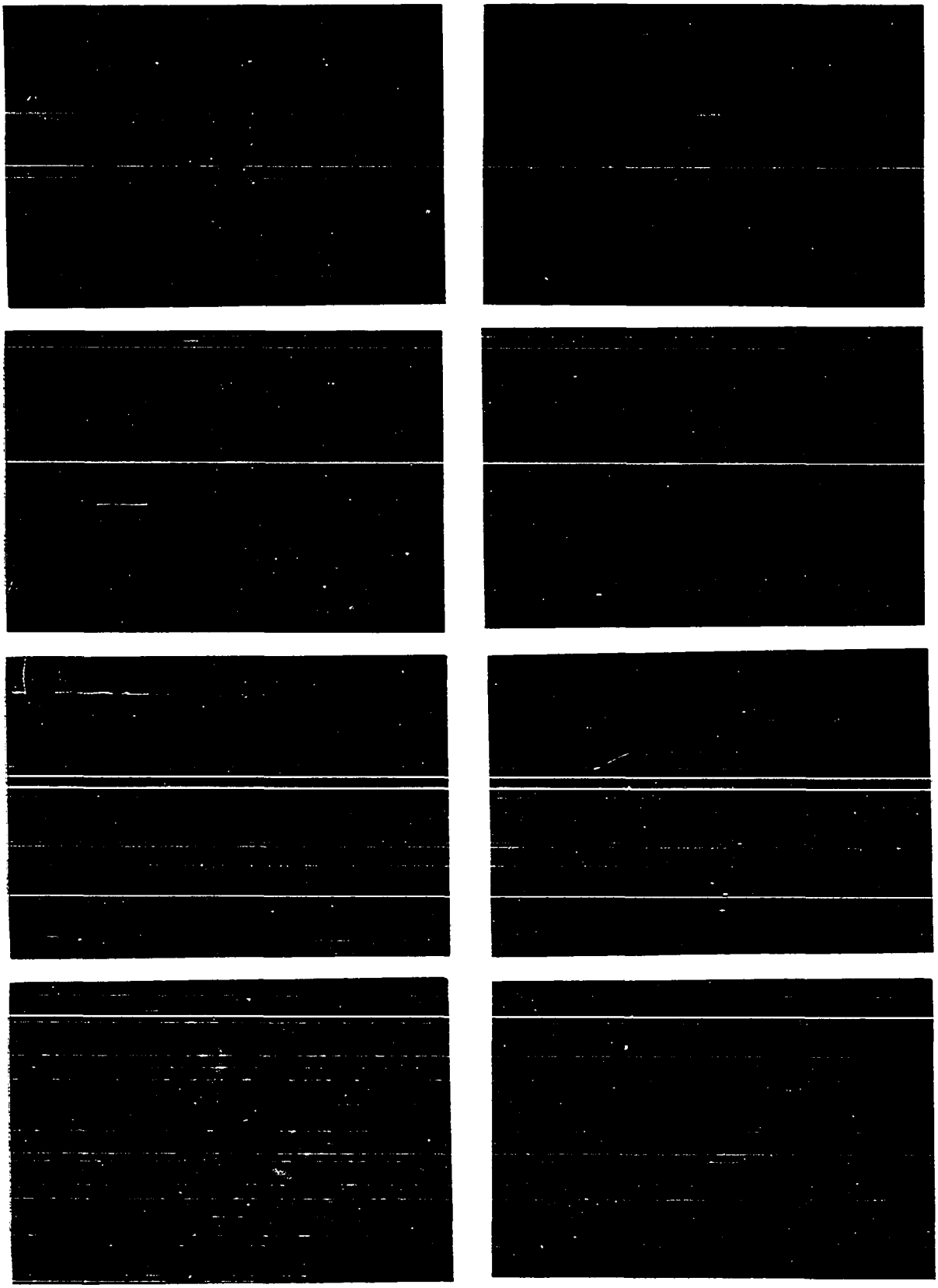


Figure 158.
Pig No. 3430S. 1 year and 2 months. Showing the disruption of the internal elastic lamina in the intracortical branch of the posterior cerebral artery. Weigert's Resorcin Fuchsin elastic stain. X 250.

Figure 159.
Pig No. 3430S. 1 year and 2 months. Fibrous intimal thickening of the basilar artery. Mallory's Triple stain. X 250.

Figure 160.
Pig No. 1362. 2 years and 11 months. Branch of the anterior cerebral artery with large intimal thickening occluding the arterial lumen. Verhoeff's and Van Gieson's stain. X 100.

Figure 161.
Pig No. 1362. 2 years and 11 months. Same as Figure 160. Mallory's Triple stain. X 100.

Figure 162.
Pig No. 1362. 2 years and 11 months.
Same as Figure 160 and 161. Mallory's Triple stain. X 250.

Figure 163.
Pig No. 1362. 2 years and 11 months.
Branch of middle cerebral artery with large intimal thickening and fragmented internal elastic lamina. Verhoeff's and Van Gieson's stain. X 100.

Figure 164.
Pig No. 1362. 2 years and 11 months.
Intracortical branch of the middle cerebral artery showing intimal thickening. Weigert's Resorcin Fuchsin elastic stain. X 250.

Figure 165.
Pig No. 1362. 2 years and 11 months.
Same as Figure 164. Alican blue and PAS stain. X 250.

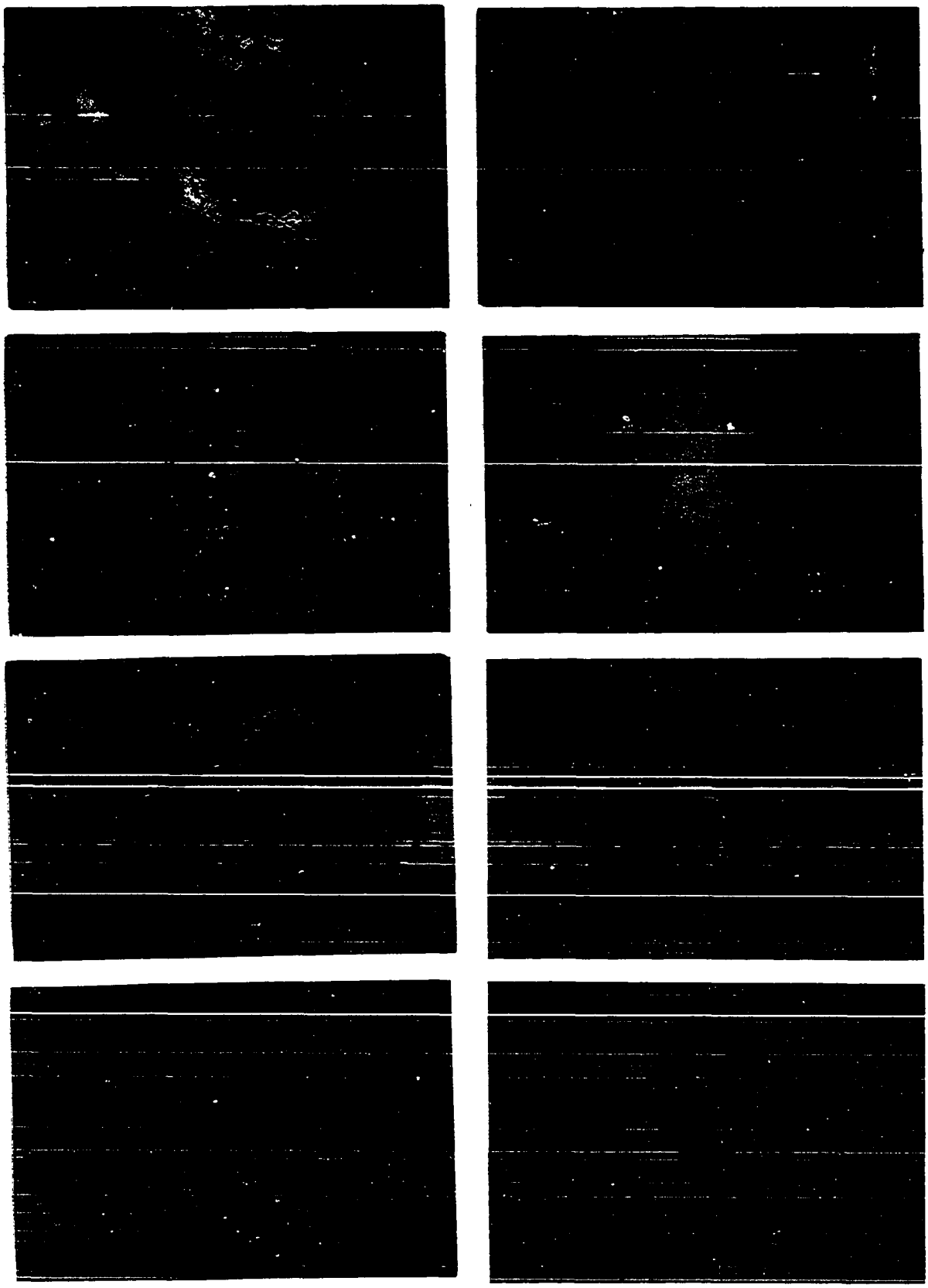


Figure 166.
Pig no. 1362. 2 years and 11 months.
Slight focal fibrous intimal thickening in a branch of the posterior communicating artery. Mallory's Triple stain. X 250.

Figure 167.
Pig No. 4631. 3 years and 10 months.
Increased acid mucopolysaccharides in the intimal thickenings of the branches of the middle cerebral arteries. Alican blue and PAS stain. X 100.

Figure 168.
Pig No. 4631. 3 years and 10 months.
Circumferential intimal thickening of a branch of the middle cerebral artery. Verhoeff's and Van Gieson's stain. X 250.

Figure 169.
Pig No. 4631. 3 years and 10 months.
Eccentric intimal thickening occluding partly a branch of the middle cerebral artery. Mallory's Triple stain. X 250.

Figure 170.
Pig No. 4631. 3 years and 10 months.
Same as Figure 169. Verhoeff's and Van Gieson's stain. X 250.

Figure 171.
Pig No. 4631. 3 years and 11 months.
Focal fibromuscular intimal thickening of a branch of the posterior communicating artery. Mallory's Triple stain. X 250.

Figure 172.
Pig No. 4631. 3 years and 11 months.
Eccentric fibromuscular thickening of a branch of the posterior communicating artery. Mallory's Triple stain. X 250.

Figure 173.
Pig No. 4631. 3 years and 11 months.
Same as in Figure 172. Alican blue and PAS stain. X 250.

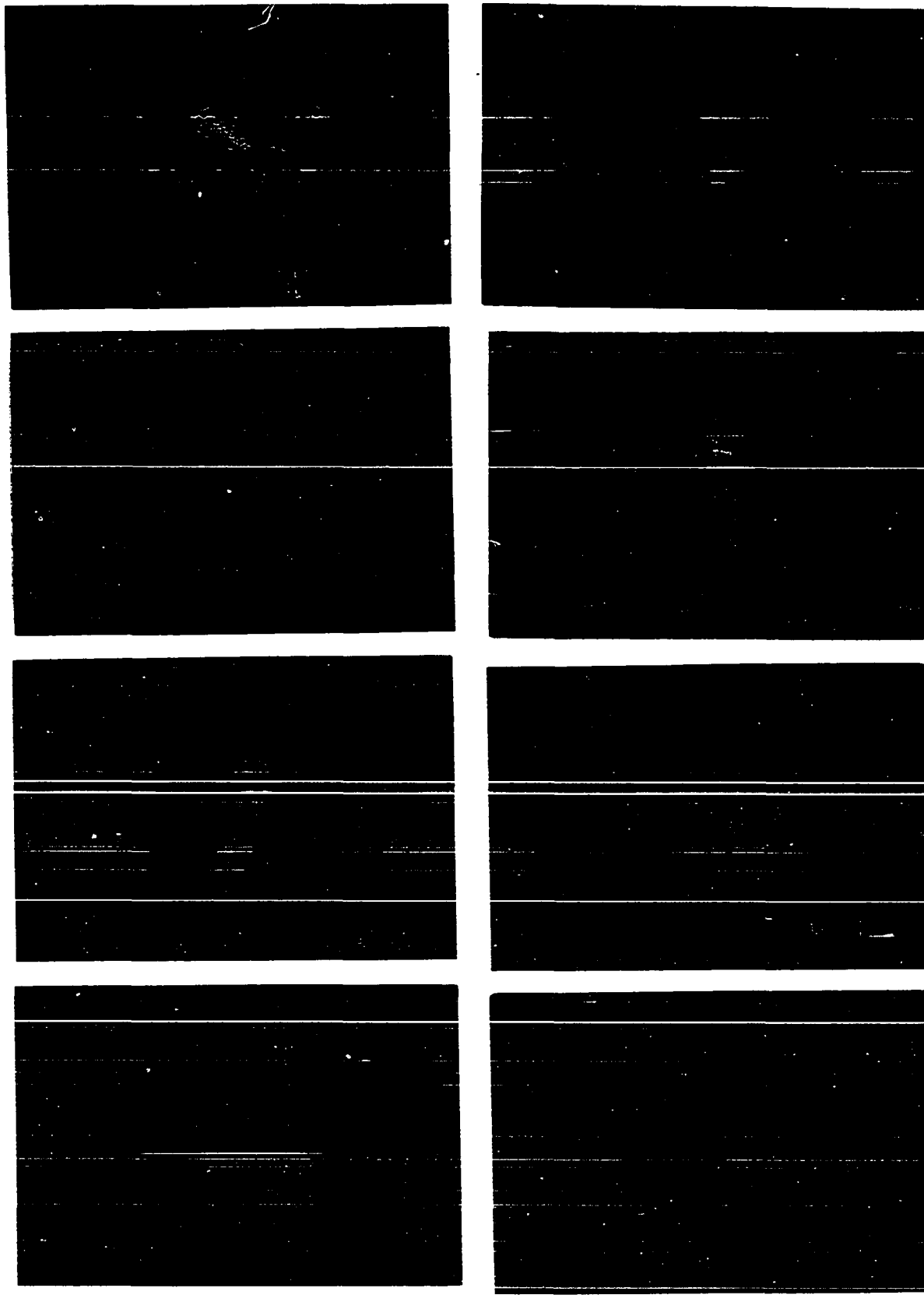


Figure 174.
Pig No. 4631. 3 years and 11 months. Showing the intimal cushions of the basilar artery at the site of branching having increased acid mucopolysaccharides in the fibrous cushions and arterial wall. Alican blue and PAS. X 100.

Figure 175.
Pig No. 4631. 3 years and 11 months. Same as in Figure 174. Mallory's Triple stain. X 250.

Figure 176.
Pig No. 4631. 3 years and 11 months. Smooth muscle cell density in the tunica media of the basilar artery. Hematoxylin and eosin. X 250.

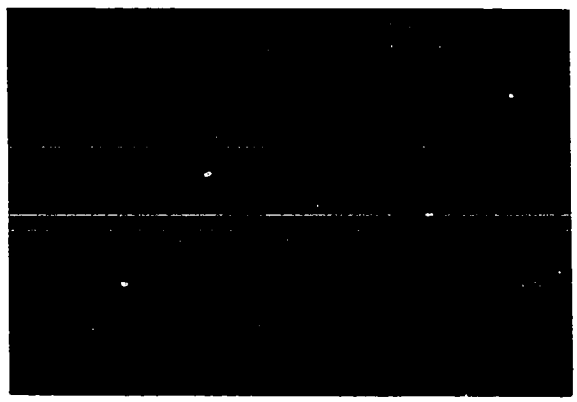
Figure 177.
Pig No. 3654. 5 years and 2 months. Acid mucopolysaccharides in the intimal thickening and tunica media of the middle cerebral artery. Alican blue and PAS. X 250.

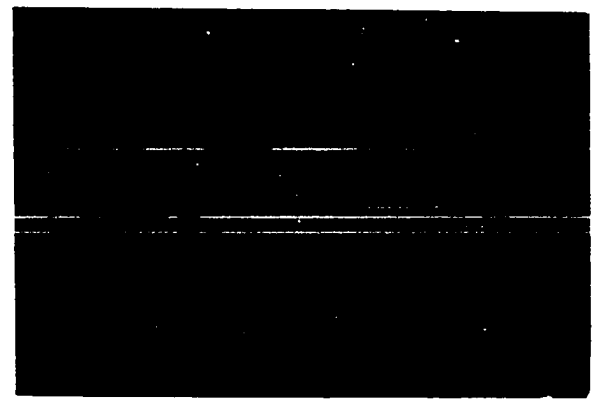
Figure 178.
Pig No. 3654. 5 years and 2 months. Basilar artery showing single intimal cushion at the site of branching Mallory's Triple stain. X 250.

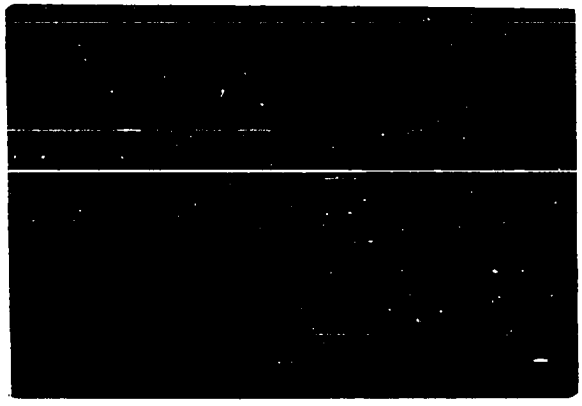
Figure 179.
Pig No. 3654. 5 years and 2 months. Branch of basilar artery showing three fibrous intimal cushions at the site of branching. Mallory's Triple stain. X 100.

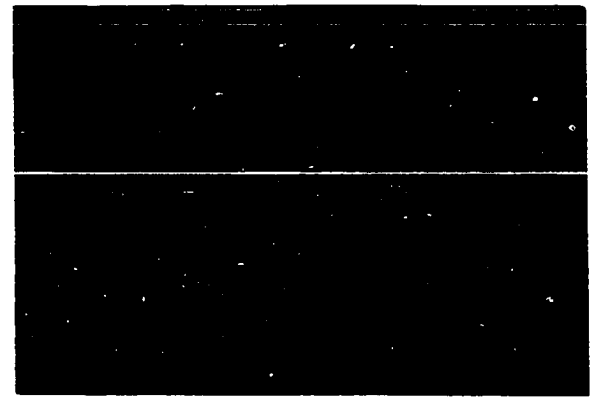
Figure 180.
Pig No. 3654. 5 years and 2 months. Eccentric fibrous intimal thickening occluding the arterial lumen of a branch of the basilar artery. Weigert's Resorcin Fuchsin elastic stain. X 100.

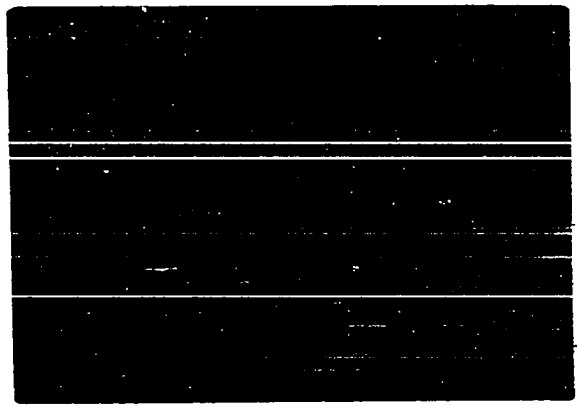
Figure 181.
Pig No. 1350. 6 years and 2 months. Intimal thickening with disrupted internal elastic lamina of a branch of the middle cerebral artery Mallory's Triple stain. X 100.

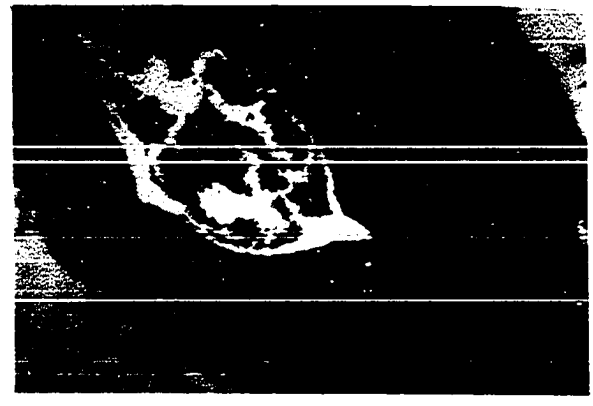


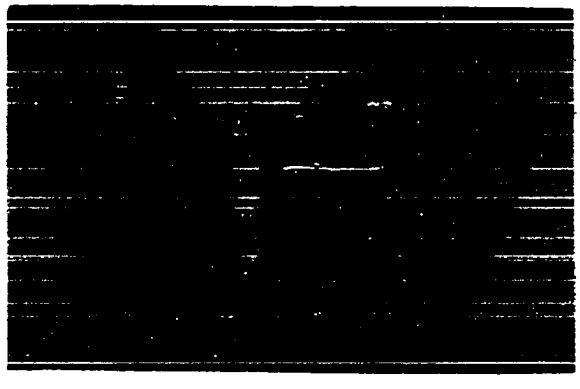












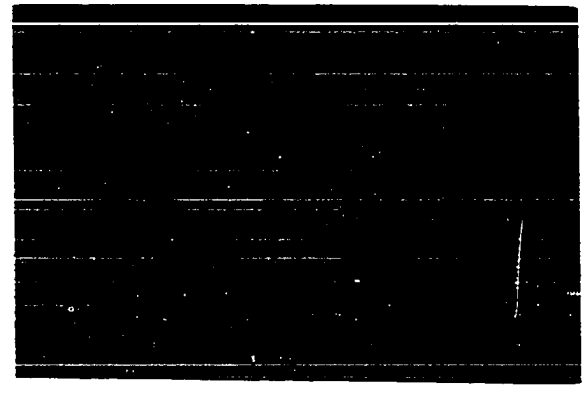


Figure 182.
Pig No. 1350. 6 years and 2 months.
A branch of the middle cerebral artery with disruption of internal elastic lamina. Weigert's Resorcin Fuchsin elastic stain. X 250.

Figure 183.
Pig No. 930-359. 6 years and 3 months.
Fibrous intimal cushion in a branch of the posterior communicating artery. Mallory's Triple stain. X 100.

Figure 184.
Pig No. 930-359. 6 years and 3 months.
Same as in Figure 183. Mallory's Triple stain. X 250.

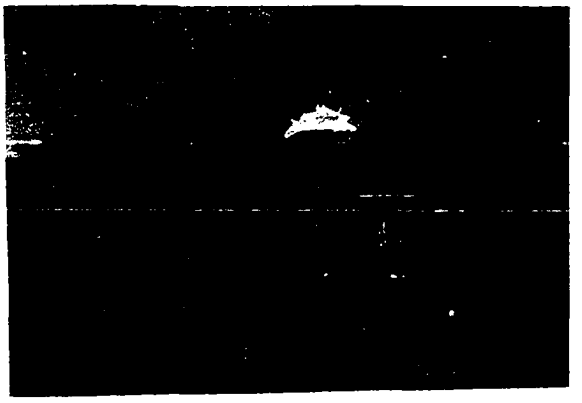
Figure 185.
Pig No. 930-359. 6 years and 3 months.
Showing the smooth muscle cell density in the tunica media of the middle cerebral artery.
Hematoxylin and eosin. X 250.

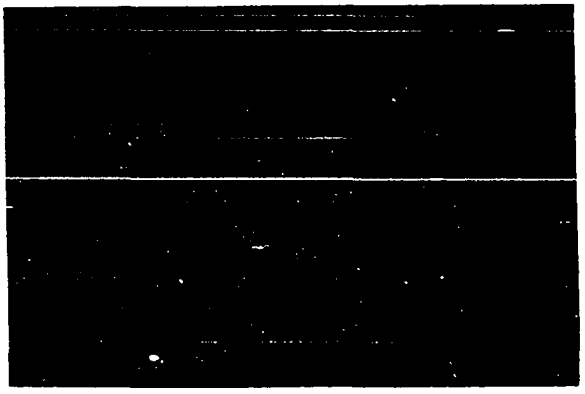
Figure 186.
Pig No. 930-359. 6 years and 3 months.
Showing the smooth muscle cell density in the tunica media of the basilar artery. Hematoxylin and eosin. X 250.

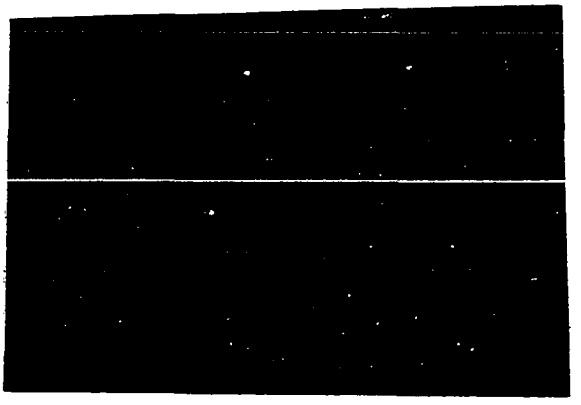
Figure 187.
Pig No. 312. 6 years and 10 months.
Focal fibrous intimal thickening in a branch of the posterior communicating artery. Mallory's Triple stain. X 100.

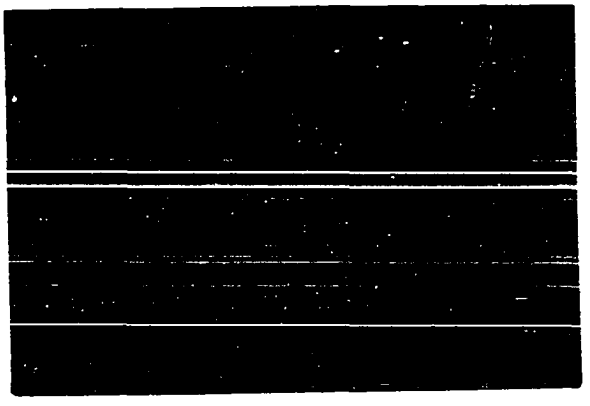
Figure 188.
Pig No. 312. 6 years and 10 months.
Same as Figure 187. Mallory's Triple stain. X 250.

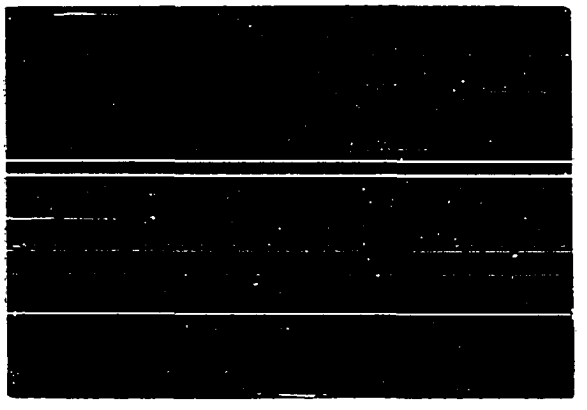
Figure 189.
Pig No. 119-259. 7 years.
Extensive fibrous intimal thickening of the middle cerebral artery with fragmented internal elastic lamina. Verhoeff's and Van Gieson's stain. X 100.











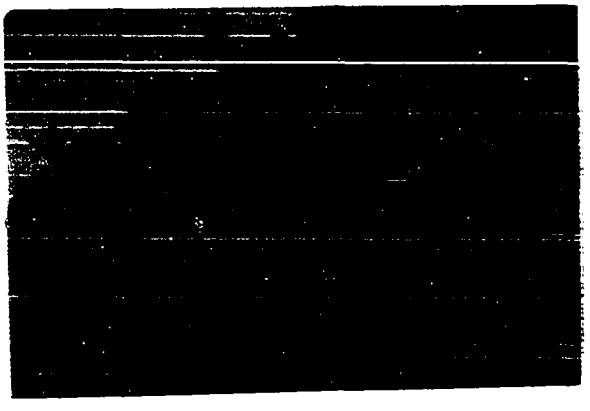


Figure 190.
Pig No. 119-259. 7 years.
Circumferential intimal thickening in the other middle cerebral artery. Verhoeff's and Van Gieson's stain. X 400.

Figure 191.
Pig No. 119-259. 7 years.
Same as Figure 190. Verhoeff's and Van Gieson's stain. X 100.

Figure 192.
Pig No. 119-259. 7 years.
Crescentic intimal thickening of a perforating branch of the middle cerebral artery. Verhoeff's and Van Gieson's stain. X 250.

Figure 193.
Pig No. 26-258. 7 years and 3 months.
A branch of the anterior cerebral artery showing a low eccentric intimal thickening. Weighert's Resorcin Fuchsin elastic stain. X 250.

Figure 194.
Pig No. 26-258. 7 years and 3 months.
Same as Figure 193 showing increased acid mucopolysaccharides. Alican blue and PAS. X 250.

Figure 195.
Pig No. 26-258. 7 years and 3 months.
Showing fibrous intimal thickening in a branch of the anterior cerebral artery. Weigert's Resorcin Fuchsin elastic stain. X 250.

Figure 196.
Pig No. 26-258. 7 years and 3 months.
Perforating branch of the middle cerebral artery with intimal thickening and increased acid mucopolysaccharides. Alican blue and PAS. X 100.

Figure 197.
Pig No. 26-258. 7 years and 3 months.
Same as Figure 196. Mallory's Triple stain. X 100.

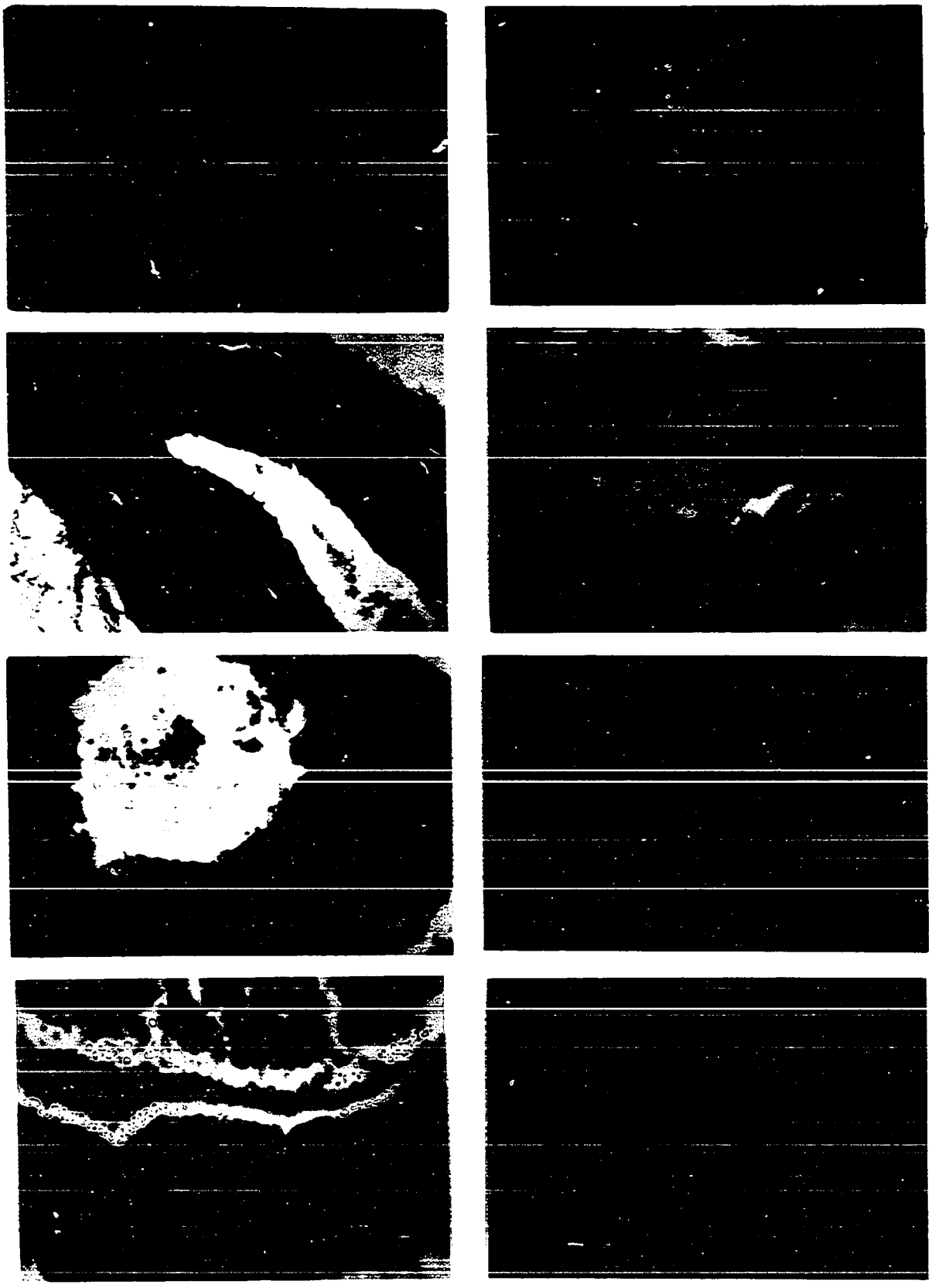


Figure 198.
Pig No. 26-258. 7 years and 3 months.
A branch of the middle cerebral artery with eccentric intimal thickening. Mallory's Triple stain. X 250.

Figure 199.
Pig No. 26-258. 7 years and 3 months.
A branch of the posterior communicating artery with intimal thickening and disrupted internal elastic lamina. Mallory's Triple stain. X 100.

Figure 200.
Pig No. 26-258. 7 years and 3 months.
A branch of the posterior communicating artery with eccentric intimal thickening. Mallory's Triple stain. X 100.

Figure 201.
Pig No. 26-258. 7 years and 3 months.
A branch of the basilar artery with eccentric intimal thickening occluding the arterial lumen. Mallory's Triple stain. X 100.

Figure 202.
Pig No. 26-258. 7 years and 3 months.
Same as Figure 201. Mallory's Triple stain. X 250.

Figure 203.
Pig No. 26-258. 7 years and 3 months.
Same as Figure 202. Weigert's Resorcin Fuchsin elastic stain. X 250.

Figure 204.
Pig No. 26-258. 7 years and 3 months.
Another branch of basilar artery with a condition similar to Figures 201 and 203. Weigert's Resorcin Fuchsin elastic stain. X 100.

Figure 205.
Pig No. 26-258. 7 years and 3 months.
Smooth muscle cell density in the basilar artery. Hemotoxylin and eosin stain. X 250.

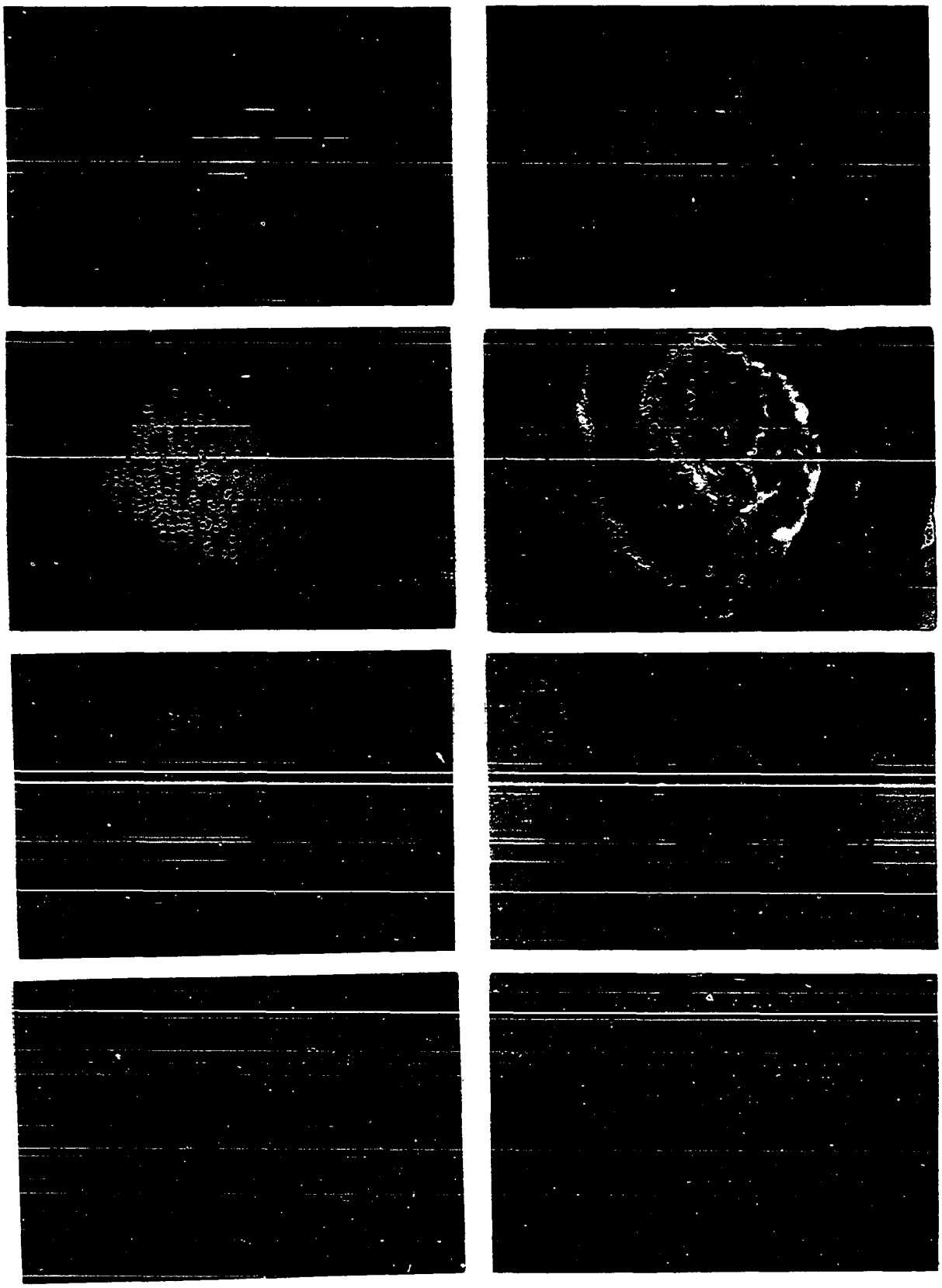


Figure 206.
Pig No. D1287-260. 8 years and 3 months.
Showing a branch of the anterior cerebral artery with focal intimal thickening. Verhoeff's and Van Gieson's stain. X 100.

Figure 207.
Pig No. D1287-260. 8 years and 3 months.
A branch of the middle cerebral artery with concentric intimal thickening. Verhoeff's and Van Gieson's stain. X 100.

Figure 208.
Pig No. D1287-260. 8 years and 3 months.
A branch of the middle cerebral artery with concentric intimal thickening. Verhoeff's and Van Gieson's stain. X 100.

Figure 209.
Pig No. D1287-260. 8 years and 3 months.
Same as Figure 207. Verhoeff's and Van Gieson's stain. X 400.

Figure 210.
Pig No. D1287-260. 8 years and 3 months.
Perforating branch of the middle cerebral artery with circumferential fibrous intimal thickening. Mallory's Triple stain. X 250.

Figure 211.
Pig No. D1287-260. 8 years and 3 months.
Low focal intimal thickening in a branch of middle cerebral artery. Verhoeff's and Van Gieson's stain. X 400.

Figure 212.
Pig No. D1287-260. 8 years and 3 months.
Branch of middle cerebral artery with focal intimal thickening. Verhoeff's and Van Gieson's stain. X 100.

Figure 213.
Pig No. 254. 9 years and 1 month.
Smooth muscle cells dividing the lumen of a branch of posterior communicating artery. Verhoeff's and Van Gieson's stain. X 100.

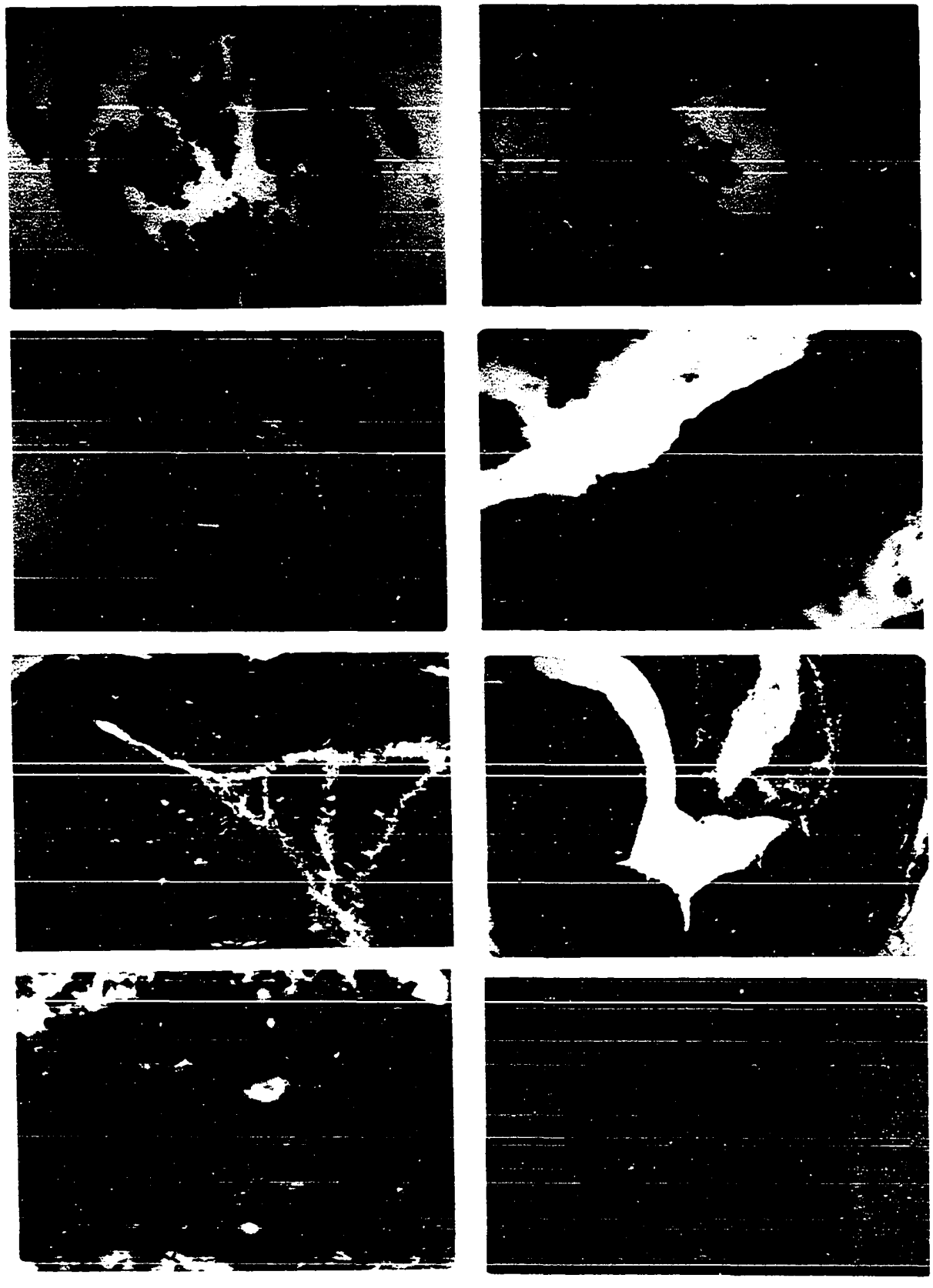


Figure 214.
Pig No. 254. 9 years and 1 month. Same as Figure 213. Verhoeff's and Van Gieson's stain. X 250.

Figure 215.
Pig No. 254. 9 years and 1 month. Focal intimal thickening in a branch of the posterior communicating artery. Verhoeff's and Van Gieson's stain. X 100.

Figure 216.
Pig No. 254. 9 years and 1 month. Intimal thickening of a branch of the basilar artery. Verhoeff's and Van Gieson's stain. X 100.

Figure 217.
Pig No. Merrick. 10 years. Branch of the anterior cerebral artery with intimal thickening and disrupted internal elastic lamina. Mallory's Triple stain. X 250.

Figure 218.
Pig No. Merrick. 10 years. Focal intimal thickening in a branch of the anterior cerebral artery, increased acid mucopolysaccharides. Alican blue and PAS stain. X 100.

Figure 219.
Pig No. Merrick. 10 years. Density of the smooth muscle cells in the tunica media of the middle cerebral artery. Hematoxylin and eosin. X 250.

Figure 220.
Dog No. C41. 11 months. Pigment in the neurons of the nucleus olivaris inferioris. Alican blue and PAS stain. X 250.

Figure 221.
Dog No. B95. 4 years. Pigment in the neurons of the nucleus olivaris inferioris. Alican blue and PAS stain. X 250.

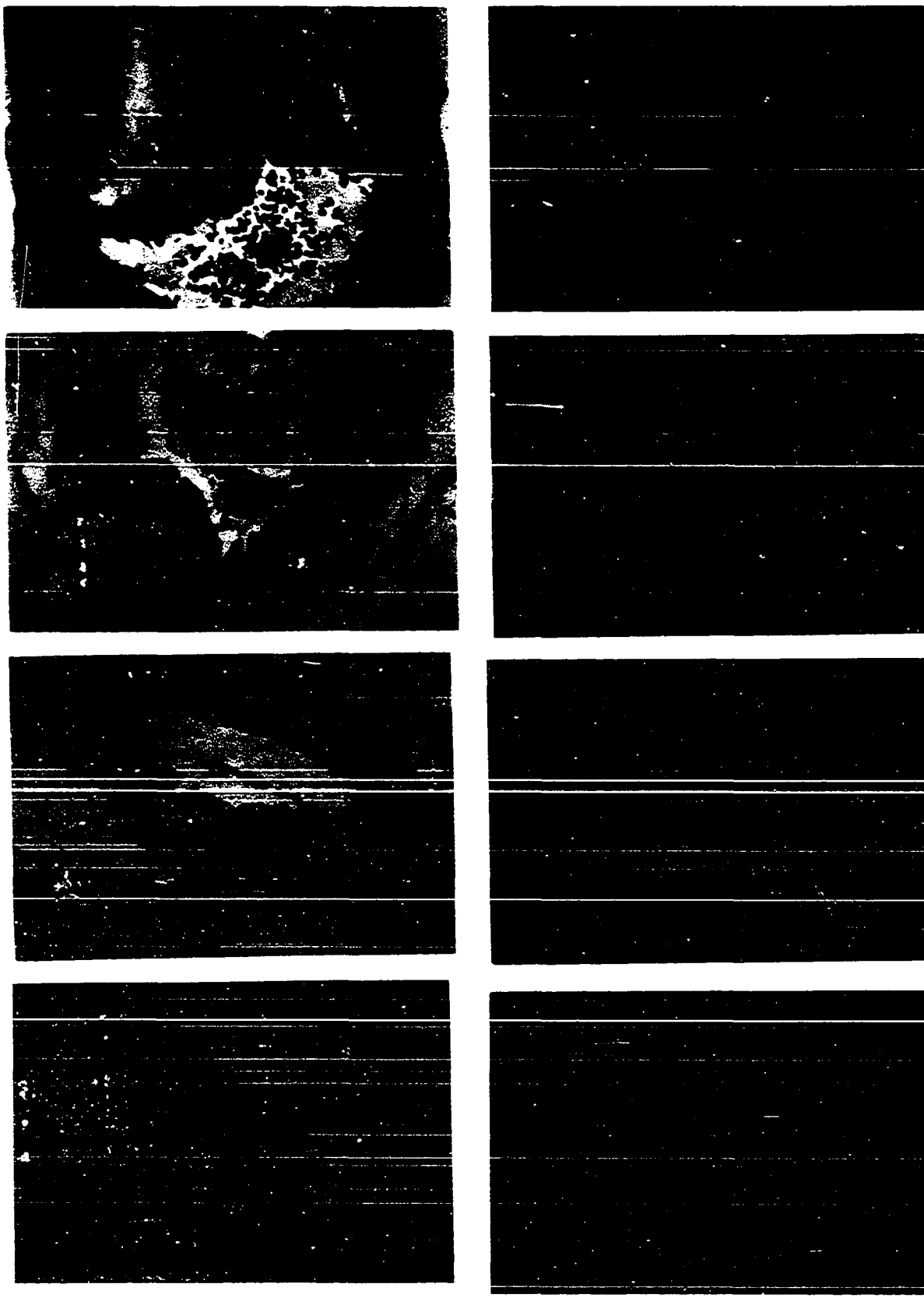


Figure 222.
Dog No. M44. 12 years.
Pigment in the neurons of the nucleus olivaris inferioris.
Alican blue and PAS stain. X 250.

Figure 223.
Dog No. 36. 16 years.
Pigment in the neurons of the nucleus olivaris inferioris. Alican blue and PAS stain. X 400.

Figure 224.
Dog No. C41. 11 months.
Pigment in the neurons of the nucleus hypoglossus. Alican blue and PAS stain. X 250.

Figure 225.
Dog No. B95. 4 years.
Pigment in the neurons of the nucleus hypoglossus. Alican blue and PAS stain. X 250.

Figure 226.
Dog No. M36. 16 years.
Pigment in the neurons of the nucleus hypoglossus. Alican blue and PAS stain. X 250.

Figure 227.
Dog No. M54. 9 years.
Pigment in the neurons of the dorsal motor nucleus of vagus.
Alican blue and PAS stain. X 250.

Figure 228.
Dog No. M44. 12 years.
Pigment in the neurons of the dorsal motor nucleus of the vagus.
Alican blue and PAS stain. X 250.

Figure 229.
Dog No. M36. 16 years.
Pigment in the neurons of the dorsal motor nucleus of the vagus.
Alican blue and PAS stain. X 250.

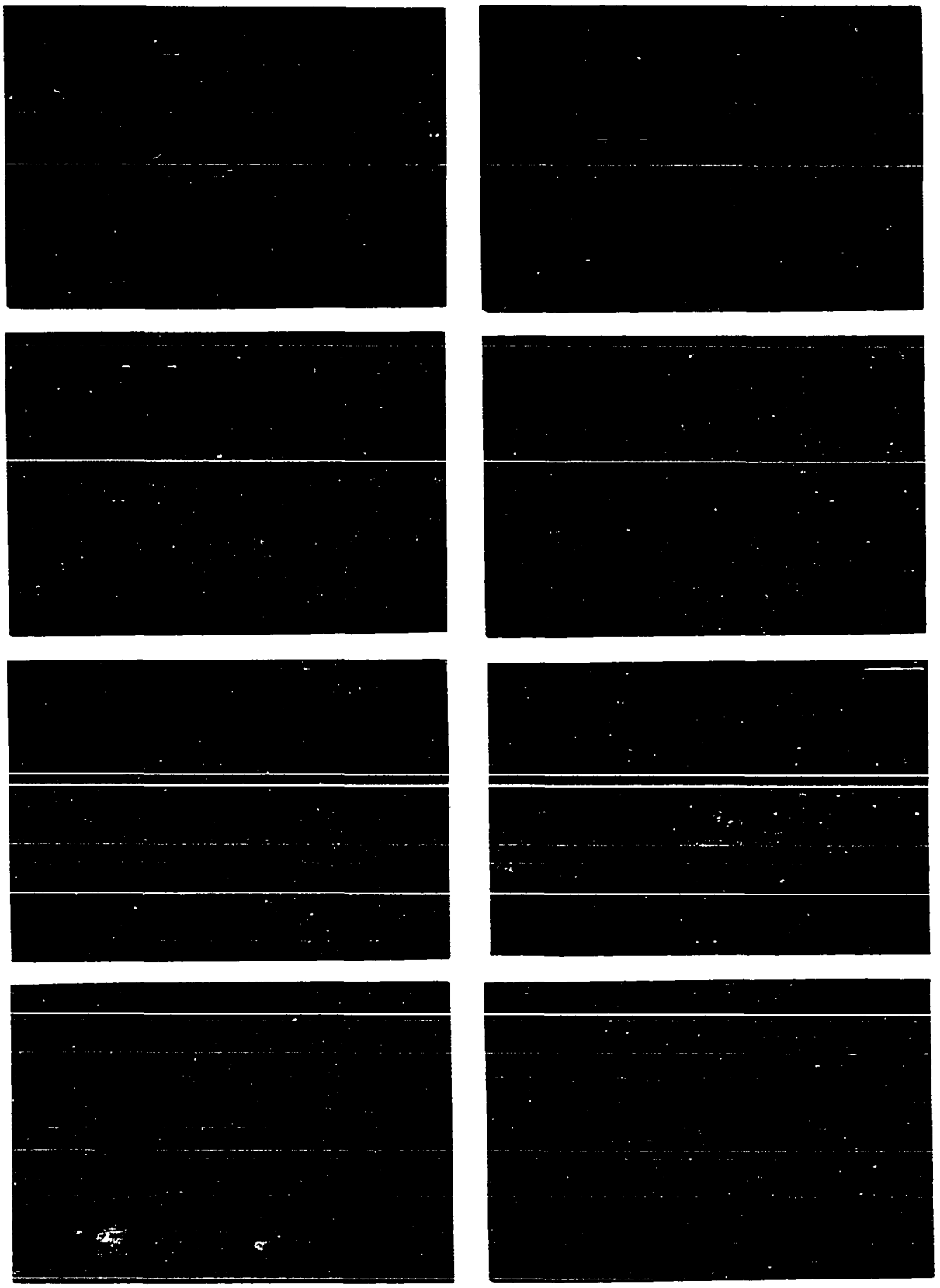


Figure 230.
Dog No. B80. 1 year and 7 months.
Pigment in the neurons of the nucleus cuneatus lateralis (accessorius). Alican blue and PAS stain. X 250.

Figure 231.
Dog No. B95. 4 years.
Pigment in the neurons of the nucleus cuneatus lateralis (accessorius). Alican blue and PAS stain. X 250.

Figure 232.
Dog No. M36. 16 years.
Pigment in the neurons of the nucleus cuneatus lateralis (accessorius). Alican blue and PAS stain. X 250.

Figure 233.
Dog No. C41. 11 months.
Pigment in the neurons of the nuclei vestibulares. Alican blue and PAS stain. X 100.

Figure 234.
Dog No. B118. 6 years and 7 months.
Pigment in the neurons of the nuclei vestibulares. Alican blue and PAS stain. X 100.

Figure 235.
Dog No. M37. 13 years and 1 month.
Pigment in the neurons of the nuclei vestibulares. Alican blue and PAS stain. X 250.

Figure 236.
Dog No. 21. 2 years and 17 days.
Pigment in the neurons of the nuclei cochleares. Alican blue and PAS stain. X 250.

Figure 237.
Dog No. M53. 9 years.
Pigment in the neurons of the nuclei cochleares. Alican blue and PAS stain. X 250.

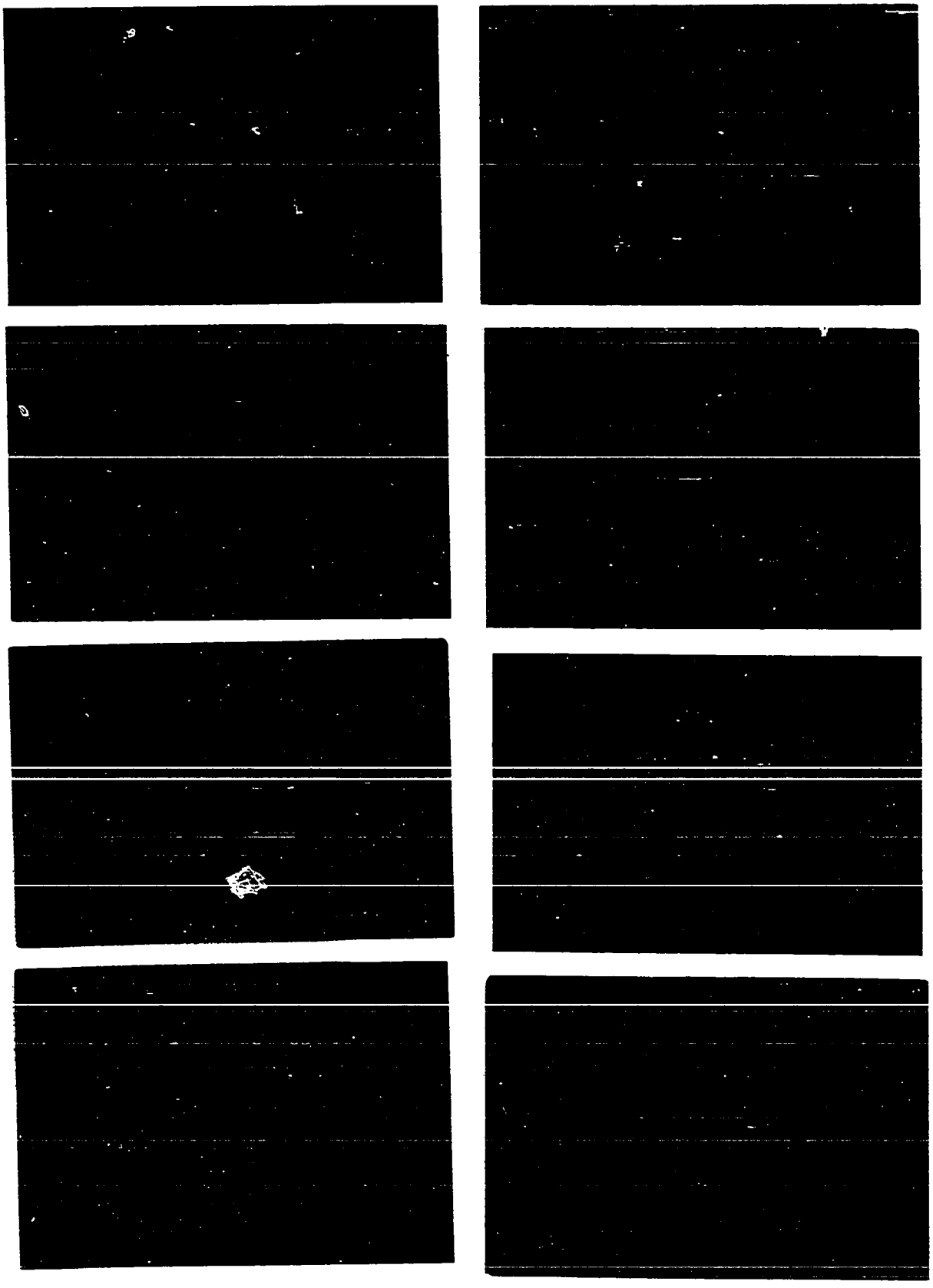


Figure 238.
Dog No. M37. 13 years and 1 month.
Pigment in the neurons of the nuclei cochleares. Alican blue and PAS stain. X 250.

Figure 239.
Dog No. B95. 4 years.
Pigment in the neurons of the nucleus of the nucleus dentatus. Alican blue and PAS stain. X 250.

Figure 240.
Dog. No. M37. 13 years and 1 month.
Pigment in the neurons of the nucleus dentatus. Alican blue and PAS stain. X 250.

Figure 241.
Dog No. B95. 4 years.
Pigment in the neurons of the nucleus fastigii. Alican blue and PAS stain. X 250.

Figure 242.
Dog No. M36. 16 years.
Pigment in the neurons of the nucleus fastigii. Alican blue and PAS stain. X 250.

Figure 243.
Dog No. C41. 11 months.
Pigment in the neurons of the nucleus ruber or rubrum. Alican blue and PAS stain. X 100.

Figure 244.
Dog No. M53. 9 years.
Pigment in the neurons of the nucleus ruber or rubrum. Alican blue and PAS stain. X 100.

Figure 245.
Dog No. M37. 13 years and 1 month.
Pigment in the neurons of the nucleus ruber or rubrum. Alican blue and PAS stain. X 100.

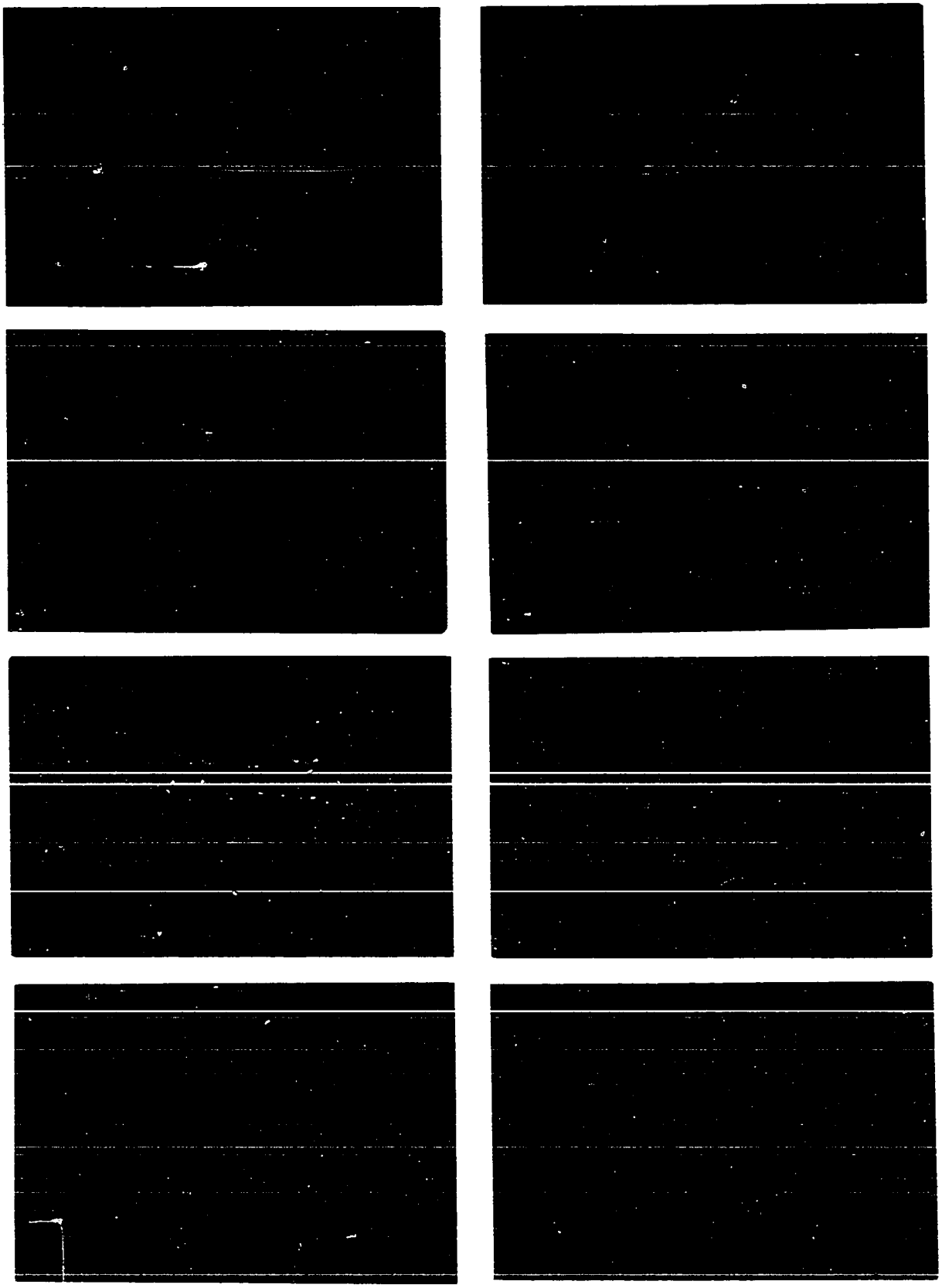


Figure 246.
Dog No. B68. 2 years, 9 months and 6 days.
Pigment in the neurons of the nucleus oculomotorius. Alican blue and PAS stain. X 250.

Figure 247.
Dog No. B95. 4 years.
Pigment in the neurons of the nucleus oculomotorius. Alican blue and PAS stain. X 250.

Figure 248.
Dog No. M37. 13 years and 1 month.
Pigment in the neurons of the nucleus oculomotorius. Alican blue and PAS stain. X 250.

Figure 249.
Dog No. B95. 4 years.
Pigment in the neurons of the thalamic area. Alican blue and PAS stain. X 250.

Figure 250.
Dog No. M36. 16 years.
Pigment in the neurons of the thalamic area. Alican blue and PAS stain. X 250.

Figure 251.
Pigment in the neurons of the gyrus hippocampalis. Alican blue and PAS stain. X 250.

Figure 252.
Dog. No. M36. 16 years.
Pigment in the neurons of the gyrus hippocampalis. Alican blue and PAS stain. X 250.

Figure 253.
Dog No. C41. 11 months.
Pigment in the large pyramidal cells of the frontal cerebral cortex. Alican blue and PAS stain. X 250.

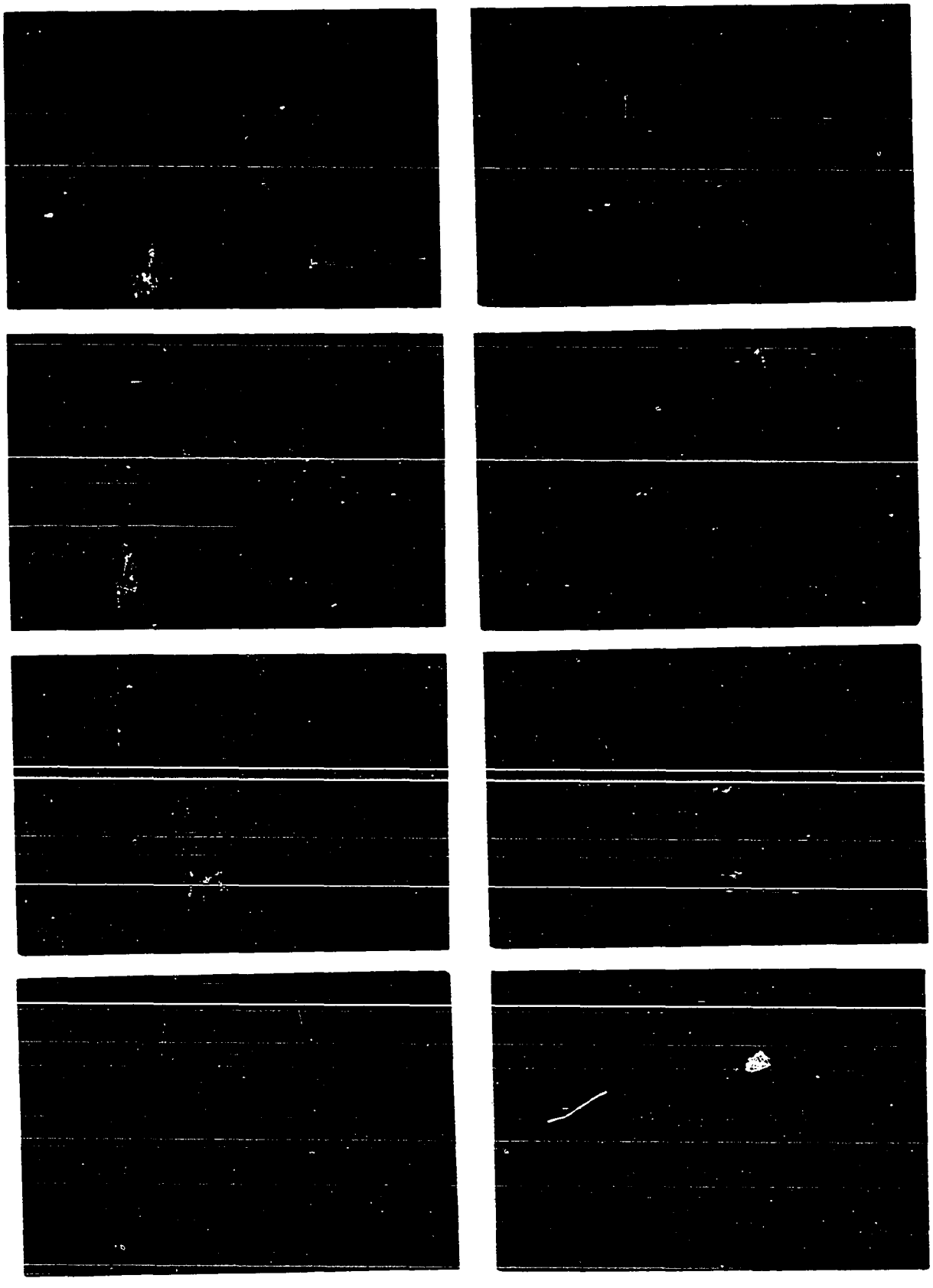


Figure 254.
Pig No. 3430S. 1 year and 2 months.
Autofluorescent pigment in the neurons of the nucleus olivaris inferioris. X 250.

Figure 255.
Pig No. Merrick. 10 years.
Autofluorescent pigment in the neurons of the nucleus olivaris inferioris. X 250.

Figure 256.
Pig No. 4491. 1 year and 11 months.
Autofluorescent pigment in the neurons of the nucleus hypoglossus.
X 400.

Figure 257.
Pig No. Merrick. 10 years.
Autofluorescent pigment in the neurons of the nucleus hypoglossus.
X 400.

Figure 258.
Pgi No. 4491. 1 year and 11 months.
Autofluorescent pigment in the neurons of the dorsal motor nucleus of the vagus. X 250.

Figure 259.
Pig No. Merrick. 10 years.
Autofluorescent pigment in the neurons of the dorsal motor nucleus of the vagus. X 250.

Figure 260.
Pig No. 4512. 2 years.
Autofluorescent pigment in the neurons of the nuclei vestibulares.
X 400.

Figure 261.
Pig No. Merrick. 10 years.
Autofluorescent pigment in the neurons of the nuclei cochleares.
X 250.

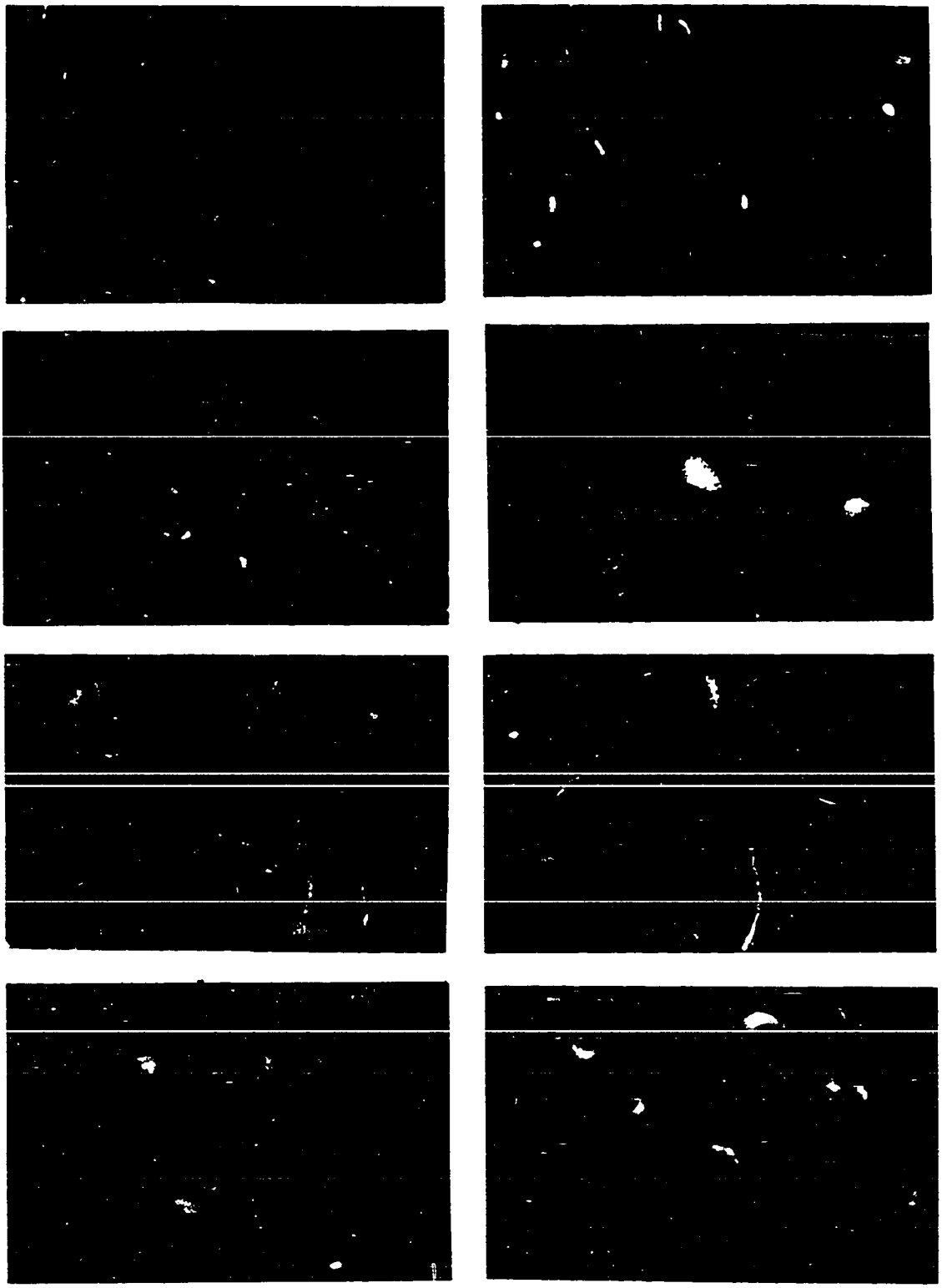


Figure 262.
Pig No. 4512. 2 years.
Autofluorescence pigment in the purkinje cells of the cerebellar cortex. X 400.

Figure 263.
Pig No. Merrick. 10 years.
Autofluorescence pigment in the neurons of the nucleus ruber or rubrum. X 250.

Figure 264.
Pig No. 1790. 3 years and 9 months.
Autofluorescence in the neurons of the gyrus hippocampalis.
X 400.

Figure 265.
Pig No. Merrick. 10 years.
Autofluorescence pigment in the purkinje cells of the cerebellar cortex. X 400.

Figure 266.
Pig No. Merrick. 10 years
Autofluorescence pigment in neurons of the thalamic area.
X 250.