1969

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69-15,617

HOLLOWAY, D.V.M., Clarke Lee, 1926-
CHANGES WITH AGE IN THE EYE OF THE DOG AND HOG FROM BIRTH TO SENILITY.

Iowa State University, Ph.D., 1969
Anatomy

University Microfilms, Inc., Ann Arbor, Michigan

CHANGES WITH AGE IN THE EYE OF THE DOG AND HOG FROM BIRTH TO SENILITY

by

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A Dissertation Submitted to the
Graduate Faculty in Partial Fulfillment of
The Requirements for the Degree of
DOCTOR OF PHILOSOPHY

Major Subject: Veterinary Anatomy

Approved:

Signature was redacted for privacy.
In Charge of Major Work

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Of Science and Technology
Ames, Iowa

1969

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INTRODUCTION

Much of the dilemma which has accompanied the evaluation of age changes in ocular tissues, as well as in other organs and tissues, has resulted from the difficulty in precisely defining aging and inadequately delineating the processes of normal growth, physiological aging, and pathological alteration.

In probing the intricate and oftentimes subtle changes created in biological tissues and organs by the mere existence of the tissue over a prolonged period of time, most investigators have developed a personal concept or definition of aging. Differences in the concepts or phrasing of a definition have generally reflected the individual's scientific approach, either dimensional, morphological, functional, or histochemical, to evaluating age-related changes. Although influenced by a specific scientific method of investigation or the investigator's personal interpretation of aging, each concept or definition as a rule has contributed to a better understanding of the overall process of senescence.

In addition, concepts and definitions of aging have indicated the investigator's opinion pertaining to the point of initiation of the process of aging. In a broad sense, Getty (1962) divided the life-cycle of warm-blooded vertebrates into three successive phases; namely,

growth, maturity, and senility. Furthermore, Getty (1966), as a result of extensive gerontological studies conducted in the Department of Veterinary Anatomy at Iowa State University, emphasized that unless one knew the normal histomorphological picture at the various age levels it was difficult at times to delineate physiological and pathological changes with age in the body tissue.

With specific reference to the eye, Duke-Elder (1938) considered senescent changes as continuous processes which started in the cradle or before and which were determined by heredity, constitution, and the inevitable effects of the continued stress and strain of life upon ocular tissue. On the other hand, Friedenwald (1952) designated only those changes which occurred commonly or universally in the aged eye as senescent changes.

A very simple and explicit interpretation of aging as related to the eye was presented by Francois (1958). Francois proposed that aging was an early biological phenomenon which consisted of a progressive alteration of the tissue to the extent that there was a marked difference in the anatomy of the eye in the young and in the aged.

In accord with the broad concepts of aging as proposed by Getty, Duke-Elder, and Francois, the goals and objectives of this study were formulated to determine the progressive changes which occurred in

the eye of the dog and hog from birth to senility. Initially, it was considered imperative to ascertain the specific tissue alterations which occurred during the period of life from birth to the attainment of physical maturity. To designate animals in this age period the term "maturation period" was utilized throughout this thesis; whereas, the term "postmaturation period" was used to designate the period of life from physical maturity to death.

The initial determination of tissue alterations which occurred during the maturation period established a basis for evaluating subsequent age-related changes in the postmaturation period. The diverse nature of changes found during the two age periods necessitated the utilization of a number of investigative techniques, each capable of revealing specific information with regard to either the dimensional, histological, or histochemical alterations attendant with aging.

Special emphasis was placed upon determining those changes with age which likely predisposed the constituent tissues of the eye to subsequent functional and pathological alteration. In this regard, an analysis of senescent changes in the vascular components of the eye was considered highly relevant.

Hopefully, the findings of this investigation pertaining to the dimensional, histological, and histochemical changes in the eye of the dog and hog with age, will constitute a collected source of

information of vital interest to a number of scientists with varied interests in ophthalmology and gerontology. Such information should assist the histologist in more precisely establishing the normal cytoarchitectural variants of the ocular tissues with age and aid the pathologist in the difficult and oftentimes impossible task of delimiting the processes of physiological aging and pathological alteration. A knowledge of the normal progressive tissue changes should benefit the physiologist in assessing the functional changes with age and should be of interest to the clinician in interpreting and explaining various ocular symptoms in the living animal. Information pertaining to senescent changes in the eye of the dog and hog should be of value to investigative efforts in human ophthalmology, since most of the senile changes reported in the human eye (Rones, 1938; Weale, 1963) were present in the ocular tissues of the dog and hog.

Admittedly, the broad scope of the present study prevented in-depth investigation of specific age-related changes in the eye of the dog and hog. It is hoped that this overview of ocular changes with age will stimulate and be of value to future in-depth investigations of specific changes with age in the eye of both animal and man.

LITERATURE REVIEW

General Considerations of Changes with Age in the Eye

Susceptibility of the eye to aging

According to Schofield (1961), no organ within the human body reflected the process of aging more readily than the eye. The eye, being constructed of many types of tissue each having a peculiar structure, developed senile changes of unusual variability and complexity. Schofield added, these changes were often so subtle and gradually progressive, one was not aware of their moment of onset.

Duke-Elder (1938) maintained that the avascularity of certain ocular tissues, an optical necessity, made these tissues prone to degenerative changes, and the lack of inflammatory response associated with avascularity made them peculiarly unresistant to infection. Bürger (1958) commented that the avascularity of the cornea and lens rendered these structures of particular interest in the measurement of the aging processes since they do not participate in the usual daily metabolic processes.

Tassman (1956) upheld the opinion that all structures of the eye were affected by senescent changes to some degree. Tassman considered most of these changes as more or less benign and, in essence, were part of the general aging process. Francois (1958)

agreed that senescent changes, in actuality, were part of some process of a more general nature but emphasized that senile modifications assumed special characteristics for each ocular tissue.

Characteristic changes of the aging eye

Rones, (1938) asserted that senile alterations in some ocular tissues were manifested by alterations in function, in others by visible degenerative disturbances, and at times senile variations were seen only by microscopic examination of the ocular tissues.

In general, Friedenwald (1952) summarized the senile changes of the eye as consisting of an increase in the density of the ocular tissues with age. Friedenwald characterized the increased density as being due to loss of water, increased interstitial fibrillar tissue, loss of fat and elasticity, and an accumulation of various inert materials within the densified tissue. Bürger (1958) noted that bradytrophic tissues, of which the cornea and lens were excellent examples, in general, have a common fate, a loss of water with increased age. According to Bürger, this process of progressive desiccation led to an increased density of the tissues, which was accompanied by an increase in protein content. As a consequence of reduced exchange of nutrients and faulty transport of waste products, various "slag substances" such as inorganic calcium and organic cholesterol accumulated in the tissues.

Functionally, Burn (1951) noted that as senescent changes progressed in the structures of the eye, visual acuity was diminished, light sense and dark adaptation became less sensitive, accommodative ability was reduced, and the visual field became smaller.

Relationship of senescent changes in the eye to ocular diseases

Burn (1951) included glaucoma, arteriosclerotic retinopathy, and senile ectropion as diseases of old age in which senescence played a part but was not necessarily the essential causative factor.

Friedenwald (1952) related senescent changes in the eye to sclerotic changes in the blood vessels, cataract, and glaucoma. Specifically referring to cataract, Friedenwald continued, if those instances of cataract which were clearly due to injury, metabolic disease, and congenital defects were set aside, and only the idiopathic forms of the disease were considered, this phenomenon was clearly related to advancing age. The diseases of which increased intraocular pressure was the chief symptom were noted as being multifarious, but if cases due to congenital malformation and cases secondary to injury or inflammation of the eye were excluded, the incidence of primary glaucoma was restricted almost exclusively to the age period beyond middle life.

Changes with Age in the Cornea

Weale (1963) in an excellent treatise pertaining to the aging eye, emphasized the importance of age-related studies of the geometry, the mechanical properties, and the structure of the cornea, especially, since these specific entities were of great significance in connection with inquiries related to ocular rigidity and intraocular pressure. Weale also pointed out that the cornea was the first and principal refracting surface of the eye and the eye's last line of defense against foreign bodies. According to Weale, the small amount of existing gerontological research pertaining to the cornea was directly or indirectly related to these two functional aspects.

Histologically and dimensionally, Whiteford (1956) found the cornea to be relatively immature in the newborn puppy. In the eight week old puppy, according to Whiteford, the cornea appeared histologically mature.

Prince et al. (1960) presented an outstanding description of the normal microscopic anatomy of the cornea and its constituent parts in the dog and hog. Prince included the normal size ranges of the corneal structures but gave no details as to the age at which these dimensions were attained. Prince further noted a general similarity in the cytoarchitecture of the cornea of the dog and hog and the conventional mammalian cornea. Inasmuch as all mammalian corneas

conformed to a basic histological pattern and since information pertaining to changes with age in the cornea as well as other ocular structures of the dog and hog was extremely sparse, the inclusion of references to age-related changes in the eye of man and species of animals other than the dog and hog was considered pertinent to the present investigation.

The horizontal and vertical corneal diameters of man, according to Wolff (1961), reached adult dimensions at approximately two years of age. Smith (1890), after measuring the horizontal corneal diameter of 250 men and women, concluded that the human cornea attained adult diameter size early in life and changed very little with age. A slight decrease in the horizontal corneal diameter was detected by Smith in patients over 40 years of age. Berliner (1949) noted that the central thickness in addition to the diameter sizes of the cornea were more or less independent of adult age.

Wolff (1961) stated that the neonatal human cornea was more or less spherical in shape, and that the corneal surface flattened with age. In addition to flattening, Hogan and Zimmerman (1962) found the cornea tended to become thinner with age. Weale (1963) noted that the tendency to flatten was greater in the younger years and postulated that this tendency might be due to the rapid growth of the eyeball during the period of maturation and growth.

Wolff (1961) also detected the cornea to be curved more in one meridian than another, and explained that astigmatism was the result of the unequal curvatures. In the young, the vertical curvature was generally observed as being greater than the horizontal curvature ("astigmatism with the rule"); whereas, in patients over 40 years of age the reverse was observed ("astigmatism against the rule"). These age-related alterations in the vertical and horizontal curvatures of the cornea were considered normal for the emmetropic eye. Marin-Amat (1956) hypothesized that the changes with age in the corneal curvature were possibly due to the activity of certain of the extraocular muscles. Marin-Amat elucidated by postulating that the orbicularis oculi and the medial rectus muscles exerted a moulding effect upon the cornea. Marin-Amat proposed that the moulding effect of the orbicularis was greater than the medial rectus in the young and therefore tended to increase the corneal curvature in the vertical meridian. Whereas, in the adult, the activity of the medial rectus was increased due to the performance of more systematic and close visual work. Consequently, the moulding effect of the medial rectus became predominant and tended to increase the curvature in the horizontal meridian.

Senile alterations in the corneal epithelium were observed by Fischer (1948) and were attributed to a change in hydration of the

epithelium. The change in hydration resulted in intracellular fluid being transported to the intercellular spaces with a subsequent decrease in the refractive index of the epithelium and a loss of its youthful luster.

The principal changes attributable to age in the substantia propria were a decrease in the number of corneal corpuscles (Wolff, 1961), and an increase in the density of the stroma (Fischer, 1948). Maurice (1962) suggested that the increase in stromal density was responsible for an increase in light scatter and a slowdown of protein transport through the cornea.

Symthe (1958) stated that Descemet's membrane in all animals increased in thickness with age. Smythe characterized Descemet's membrane in the young animal as being elastic and moderately thick. In the aged animal the membrane was more fibrous, less elastic, and markedly increased in thickness. Numerous authors (Duke-Elder, 1938; Rones, 1938; Kornzweig, 1951; and Feeney and Garron, 1961) reported an increase in thickness with age of Descemet's membrane in man. Each of the forenamed investigators also described the existence of focal, nodular thickenings which projected from the peripheral portion of Descemet's membrane into the anterior chamber. According to Feeney and Garron (1961), these excrescences were described by Hassal in 1851, and by Henle in 1866; subsequently, they

have been commonly referred to by the eponym, Hassal-Henle warts. According to Duke-Elder (1938), Hassal-Henle warts were hyaline-like nodules produced by overactivity of the endothelial cell and were similar in structure to nodules attached to the lens capsule, and Bruch's membrane. In man, Hassal-Henle warts were observed universally in patients over 20-30 years of age. Duke-Elder added that if the warts were present in sufficient numbers the enlargements interfered with the semipermeable characteristics of the endothelium and allowed excessive amounts of aqueous humor to penetrate the substantia propria. Feeney and Garron (1961) found that the warts stained similarly to Descemet's membrane and appeared to be thickenings of the membrane. These workers also noted that the nodular surface of the warts was covered by a thin attenuated process of the endothelial cell and that normal appearing endothelial cells occupied the depressions between warts.

Rones (1938) and Feeney and Garron (1961) described a bilateral corneal disease, cornea gutatta, which involved the central portion of the corneal endothelium and Descemet's membrane. Feeney and Garron commented that lesions of cornea gutatta were considered in the past to be similar to Hassal-Henle warts. However, these investigators found distinct differences in the two lesions. Feeney and Garron described the hyaline excrescences of cornea gutatta

as mushroom-like projections with flat tops. These excrescences contained no fissures and were not covered with endothelial projections as were the Hassal-Henle warts.

Magrane (1959) reported the occurrence of a dystrophic alteration of the corneal endothelium of the dog. This corneal alteration was not considered by Magrane to be caused by an inflammatory agent or an allergic reaction, but was a result of the wear and tear of aging. Donn (1966) noted a similar clinical entity in man, Fuch's epithelial endothelial dystrophy, which appeared usually in the fifth decade of life, was more common in female patients, and the incidence was only one in every 2000 eye patients. A malfunction of the corneal endothelium was considered to be the motivating cause for this dystrophy.

Rones (1938) observed that the corneal endothelial cell of the elderly was extremely variable in size and that the nuclei also varied greatly in size, form, and staining qualities. According to Stocker (1953) the endothelial cell tended to be flatter and more attenuated in adults than in children. Stocker suggested that the tendency to become more attenuated denoted a possible increase in tension upon the endothelial cell.

Schofield (1961) considered the phenomenon generally known as arcus senilis to be one of the most obvious and classical examples of

aging in the eye. Schofield characterized the lesions of arcus senilis as consisting of an opaque ring of lipid deposition at the periphery of the cornea. The opaque ring was observed to appear initially in either the upper or lower segments of the cornea and increased in extent until a complete lipid circle was formed in the vicinity of the limbus. Typically, a narrow lipid-free zone separated the opaque ring from the limbus.

In an evaluation of the incidence of arcus senilis in dogs, Krotova (1963) found with the aid of the slit lamp an ill-defined arcus senilis in a few four year old dogs; whereas, arcus senilis was visible in almost 50 per cent of the five year old dogs. Variable degrees of arcus senilis were found in all dogs over six years of age.

In a sizable number of human patients, Forsius (1954) observed clearly demonstrable lesions of arcus senilis in 40 per cent of the healthy males and 30 per cent of the healthy females. No patients over 50 years of age were without some degree of arcus senilis.

Histologically, arcus senilis was characterized by Friedenwald (1952) as consisting of an infiltration of Bowman's and Descemet's membranes and the substantia propria with cholesterol esters and neutral fats. Friedenwald pointed out that similar infiltrations occurred in the perivascular tissues of the iris, the sclera, the subepithelial tissues of the ciliary body, and Bruch's membrane.

Although there was unanimity among numerous investigators that lipid deposition does occur in ocular tissues, the exact nature of the lipid and the process by which it was deposited was debatable. Attias (1912) suggested that arcus senilis was the result of the deposition of globules containing stearins and palmitins into the substantia propria. Schofield (1961) pointed out the possible relationship of arcus senilis and a high serum cholesterol. In support of this possible relationship, Verse (1916, 1925) and Janes (1964) produced typical lesions of arcus senilis in rabbits by increasing the cholesterol content of the diet. Verse (1925) concluded that cholesterol served only as a vehicle for the fatty substances. Janes (1964) found by using the Schultz test for cholesterol that the majority of the sudanophilic material in the lesions was not cholesterol per se, but more likely a degradation product of cholesterol or that it was cholesterol closely bound to some other lipid which accepted a lipid stain.

In man, Forsius (1958) demonstrated that patients with either juvenile or senile forms of arcus senilis had higher levels of serum cholesterol and total lipids than patients without arcus senilis. Rodstein and Zeman (1961) compared indices of the degree of arcus senilis and electrocardiographic evidence of coronary artery disease and retinal arteriosclerosis. These authors concluded there was a

progressive increase in the frequency and degree of arcus senilis in the seventh, eighth, and ninth decades of life, and there was an apparent correlation between the degree of arcus senilis and the degree of coronary and retinal arteriosclerosis.

Cogan and Kuwabara (1955) offered an interesting hypothesis regarding the genesis of arcus senilis. Cogan and Kuwabara proposed that the appearance of visible fat in the cornea was not solely attributable to the unmasking of preformed fat, nor to infiltration by preformed serum lipids, but resulted from a process of local fat synthesis. The process of local fat synthesis required the presence of degenerating tissue, exogenous oleic acid, and an unknown serum factor. In essence, these authors believed that the neutral fat thus formed resulted from an intracellular enzymatic process common to all cells of the cornea.

Burn (1951) classified mild deposition of pigment granules in the cornea of elderly humans as simple senile change. Pigmentary infiltration of the cornea in the dog was noted by Nicolas (1925) to occur during the first two years of life, and that the frequency of infiltration increased with age. Magrane (1959) stated that pigmentary infiltration in the dog was usually secondary to some inflammatory condition. Roberts (1954) indicated that practically all invasive pigment in the cornea was melanin, and that pigmentation of the superficial

cornea originated from the germinal epithelium, and to a limited extent, from pigment adjacent to the limbus. Roberts observed that pigmentation in the deeper portions of the substantia propria adjacent to Descemet's membrane originated from the uveal tract.

Changes with Age in the Sclera

Whiteford (1956) noted that the sclera appeared histologically mature in dogs six to eight weeks of age, however, scleral thickness continued to increase until approximately seven months of age. The continued increase in thickness was characterized by an increase in fiber content and a decreased number of connective tissue cells. Whiteford observed scleral pigmentation in the dog to be scanty at birth but relatively abundant by eight weeks of age.

According to Prince et al. (1960), the sclera in both the dog and hog varied greatly in thickness in different regions of the sclera. In the dog, typical measurements of the scleral thickness at the corneo-scleral junction, the equator, and the posterior pole were 1.0 mm., 0.28 mm., and 0.80 mm., respectively. Similar measurements in the hog were 0.55 mm., 0.25 mm., and 0.90 mm., respectively.

Friedenwald (1952) observed that the sclera was thinner in older than younger individuals; whereas, Vannas and Teir (1960) observed the opposite. Individual scleral fibers, according to Schwarz (1953),

increased in thickness with age. In addition to the latter factor, Schwarz considered total scleral thickness to be dependent upon other factors such as the state of hydration, lipid content, and mineral deposition.

Schofield (1961) attributed the principal senile change in the human sclera to fatty infiltration of the scleral stroma. Other changes in the sclera which Schofield attributed to aging were sclerosed vessels, granular calcium deposits, and solid calcium and hyaline plaques.

Cogan and Kuwabara (1959b) also observed calcium deposits in the aged sclera which were present either in the form of fine granules or calcified plaques. These authors noted that calcified plaques were usually located near the tendinous insertions of the horizontal recti muscles, and that the sclera was relatively translucent at the site of these plaques. Although hyalinization of the stroma was not noticed, apatite crystals were frequently found in the translucent area. Duke-Elder (1938) detected both calcium and hyaline plaques close to the scleral insertion of the lateral rectus muscle and suggested a mechanical factor as being responsible for plaquation at this site.

Nicolas (1925) stated that osseous formations were occasionally found in the posterior aspects of the sclera in all animals. Nicolas said these formations were attributable to either senescent alteration or to inflammation of the sclera.

Changes with Age in the Iris

Whiteford (1956) observed in the iris of the one-day old puppy that iridal muscles were discernible, pigmentation was scant, and the anterior epithelium was relatively well developed. At this age the iris was characterized by the presence of many immature blood vessels. In dogs six to eight weeks of age, according to Whiteford, the iris appeared histologically mature.

Rones (1938) commented that the most noteworthy senile alteration in the iris of man was manifested by sclerotic changes in the blood vessels. Sclerosis of the iridal blood vessels was said to be characterized by thickening and hyalinization of the adventitia to the point that differentiation between the adventitia and the usually dense iridal stroma was difficult. Little alteration was noted in the tunica intima, consequently, the lumens of the iridal vessels were only slightly narrowed. Rones also stated that fat deposition did not occur in the iris as the result of age.

The fact that the diameter of the pupil decreased with age was documented by numerous authors (Birren, Casperson, and Botwinick, 1950; Kumnick, 1956; and Kadlecova, Peleska, and Vasko, 1958).

Kornzweig (1954) postulated that the senile decrease in pupillary response was due to atrophy of the dilator muscle. Rones (1938) observed atrophy of the dilator but not the sphincter muscle of the

iris; whereas, Larsson and Österlind (1943) attributed the failure in pupillary dilation to muscle degeneration and vascular changes, and the latter change was said to be the first histological sign of iridal senility.

Senile myosis and rigidity of the pupil were explained by Rones (1938) as being due to connective tissue proliferation and possible hyalinization of the marginal areas of the pupil. Most of the proliferative changes occurred between the sphincter muscle and the pigment epithelium. Intermuscular septa were involved in the proliferative process, but the muscle fibers remained free from alteration.

Depigmentation of the posterior epithelium of the iris was observed to occur with regularity in the aged (Schofield, 1961; Friedenwald, 1952). Both authors based the fading of the iris and the appearance of pale, patchy areas at the pupillary margin in the aged person as attributable to this process. Schofield (1961) also observed that much of the degenerated pigment spread into the iridal stroma, and that some of the liberated pigment migrated from the iris onto the corneal endothelium and into the uveo-scleral meshwork. Blockage of the aqueous flow by deposition of pigmentary debris at the latter site was considered by Schofield to be a possible factor in the production of chronic glaucoma.

In the human iris, Hogan and Zimmermann (1962) noted an age-related obliteration of the surface crypts and a tendency toward flattening of the iridal surface.

Changes with Age in the Ciliary Body

Whiteford (1956) investigated the microscopic changes in the ciliary body of the dog from birth to two years of age, and observed that the mature features of the ciliary body were absent at birth. At birth, the ciliary muscle contained numerous undifferentiated mesenchymal cells dispersed throughout the fiber components. The ciliary processes were adherent to the surface of the iris, and the epithelium of the processes was smoother than in the older dog. At six to eight weeks of age, the ciliary body was observed to appear histologically mature.

Smythe (1958) noted that in animals of all species the ciliary muscle became fibrosed with age, and considered the fibrotic changes to be a factor which interfered with the power of accommodation. Animals, according to Smythe, were normally incapable of accommodation to the same extent as man.

Senile changes in the ciliary body of man were described by numerous authors. (Kerschbaumer, 1888; Herbert, 1923; Van der Hoeve and Flieringa, 1924; Rones, 1938; Schofield, 1961; and Hogan and Zimmerman, 1962). These authors were generally in accord with

regard to the principal senile changes in the ciliary structures.

Kerschbaumer (1888) found that the ciliary processes increased in length and in overall size as age increased. Rones (1938) considered the progressive elongation and extensive branching of the ciliary processes as an important prelude to glaucoma. Rones explained, as the processes became more elongated, the iris was pushed forward, the anterior chamber angle decreased, and aqueous flow was impeded.

Rones (1938) pointed out that progressive hyperplasia of the outer nonpigmented epithelial cells was a most important part of the aging process of the ciliary body. Hyperplasia of these cells resulted in the formation of either large, flat excrescences, or knob-like swellings which were attached to the processes by either short or long stalks. Rones concluded that hyperplasia of the nonpigmented epithelial cells unquestionably interfered with their function as a dialyzing membrane for the formation of aqueous fluid. Hyperplasia of the pigmented epithelial cells of the ciliary processes usually accompanied hyperplasia of the nonpigmented cells, and the hyperplastic cells of both epithelia were frequently admixed.

Schofield (1961) noted that hyperplasia of the ciliary epithelial cells near the ora serrata (pars plana region) formed small knob-like elevations which projected into the vitreous. Often these

elevations fused and underwent cystic degeneration. The pars plana cysts thus formed were frequently greatly enlarged and pushed the iris forward.

Hogan and Zimmerman (1962) stated that in the aged individual the connective tissue core of the ciliary process frequently became hyalinized. Thickening of the subepithelial basement membrane and calcium depositions were characteristically present in the hyalinized ciliary processes. Progressive sclerosis and eventual obliteration of the blood vessels in the ciliary processes were also linked to the aging process. Hogan and Zimmerman also observed that the ciliary muscle tended to become atrophic and hyalinized in the aged eye.

Van der Hoeve and Flieringa (1924) found that the ciliary muscle decreased in thickness with age. Histologically, the nuclei of the ciliary muscle were decreased in number and the interstitial connective tissue fibers became fibrosed. In spite of these changes, there was no loss in muscle power. These authors attributed the declining power of accommodation in the aged person to lenticular changes.

Rones (1938) noted that lipid droplets were deposited within and between the muscle fibers. In Rones' view, lipid infiltration undoubtedly impaired the function of the ciliary muscle.

According to Kerschbaumer (1888), senile alterations were more frequent and were apparent at an earlier age in hypermetropic

than in emmetropic or myopic eyes.

Changes with Age in the Choroid

Whiteford (1956) observed that the choroid of the dog at birth ranged from 0.15 mm. to 0.20 mm. in thickness. At six weeks of age the choroid appeared histologically mature although at this age the choroid measured only 0.10 mm. in thickness. Whiteford explained the reduction in thickness of the more mature choroid as being due to a reduction in the size of the choroidocapillaris layer. Whiteford also noted that choroidal pigmentation was as extensive as in the mature choroid. Prince et al. (1960) observed that the choroidocapillaris layer and Bruch's membrane (Lamina basalis) were inconspicuous in the mature canine choroid.

Weale (1963) commented that the aging phenomena in the choroid were not uniform either along or across this complex tissue. Weale added that some parts, namely the suprachoroidea, were highly resistant to the passage of time, and other parts, such as Bruch's membrane, were frequent sites of senile change.

Schofield (1961) asserted that the vascular system was the first site of senile change in the choroid and that vascular changes most often occurred in the posterior portion of the choroid. Inasmuch as the nutrition of the outer layers of the retina was considered to be derived almost entirely from the choroidocapillaris, Rones (1938),

Tassman, (1951), Schofield (1961), and Prince (1965) attached great significance to senile sclerosis of the choroidocapillaris in the development of senile changes in the retina. Wood (1915) designated marked thickening and hyalinization of the media of the choroidal arteries as being prominent manifestations of the aging process in the eye of man. According to Wood, these vascular changes were initiated in middle life even in the absence of any evidence of generalized arteriosclerosis.

According to Sommers (1949), senile alterations in the choroidal vessels were manifested by fibrous proliferation of the tunica media, loss of medial nuclei, and perivascular accumulation of chromatophores. However, changes in the tunica intima were seldom observed. Although less extensive, Sommers found venous sclerosis to be frequently concomitant with arterial sclerosis.

Kerschbaumer (1892) acknowledged the embryological relationship of the retinal pigment epithelium and the sensory portion of the retina. However, Kerschbaumer maintained that senile changes of the pigment epithelium were more closely linked to changes in the choroid than to changes in the retina.

Friedenwald (1952) pointed out that Bruch's membrane increased uniformly in thickness with age. The appearance of "colloid bodies" (drusen) on Bruch's membrane was considered by numerous authors

to be a common manifestation of senility (Duke-Elder, 1938; Rones, 1938; Sommers, 1949; Friedenwald, 1952, Schofield, 1961; Hogan and Zimmerman, 1962).

Rones (1938) described in detail the formation of these "colloid bodies" on Bruch's membrane. Rones noted that of the two layers which comprise Bruch's membrane, only the cuticular or innermost layer thickened as age increased. Initially numerous basophilic granules were observed to accumulate within the cuticular membrane. The accumulation of granules subsequently gave rise to more compact structures which varied in form and height. At first the compact formations appeared granular but later were more hyaline in nature. The elevated "colloid bodies" were often covered with normal pigment epithelium.

Both Schofield (1961) and Hogan and Zimmerman (1962) asserted a common belief that "colloid bodies" resulted from aberrent secretory activity of the retinal pigment epithelium. Hogan and Zimmerman (1962) also observed that the senile eye often contained granular deposits on Bruch's membrane which resulted from lipoidal degeneration of the retinal pigment epithelium. Structurally, these deposits were less rounded and contained calcium granules more frequently than "colloid bodies".

Hogan and Zimmerman also described lipoidal infiltration of the choroidal stroma which these authors postulated was linked with senile lipoidal infiltration of the cornea in man. Massive infiltration of lipids was found in all layers and segments of the choroid in rabbits fed high cholesterol diets (Janes, 1964).

Kerschbaumer (1888) detected an increase in fibrous connective tissue in the choroid of the aged eye. Hogan and Zimmerman (1962) attributed atrophy and depigmentation of the peripheral choroid in the aged to fibrosis, hyalinization, and occlusion of the choroidal vessels.

Changes with Age in the Lens

Whiteford (1956) described the lens of the newborn puppy as a spherical structure which pushed the iris forward and created a shallow anterior chamber. The lens capsule was found to be considerably thinner at birth than at maturity. The anterior lens epithelium was visible at birth; the posterior epithelium was incorporated into the lens nucleus.

Nicolas (1925) examined the lenses of dogs at birth and found an active network of hyaloid vessels on the lenticular surfaces but noted that resorption of this fetal vascular network was completed shortly after birth.

Prince et al. (1960) commented that it was very doubtful that the lens of the dog was as complex in structure as the lens of man. Prince et al. expounded on this statement by noting that little variation occurred in the thickness of the anterior capsule of the dog, apart from a gradual transition from a thicker anterior to a thinner posterior capsule. Nor was an elongation of the cuboidal epithelium present in the equatorial portion of the lens of the dog. Prince et al. found the lens of the hog to be more comparable to the human lens.

According to Friedenwald (1952), the lens contained from birth to senility both embryonal and senile portions and that the difference in an old and a young lens was in the relative proportion of young and old tissues. Therefore, senescense in the lens was primarily characterized by a progressive accumulation of inert desiccated tissue in the center of the lens. Friedenwald further noted that the growth rate of the lens in man declined gradually as age advanced, but never ceased unless death of the tissue occurred as a result of cataract formation. In contrast to Friedenwald's observations, regarding lenticular growth in man, Krause (1934) and Brown and Evans (1935) found that the lenses of animals ceased growing at a relatively early age.

Rones (1938) explained the method by which the size of the lens was prevented from reaching undue proportions in man as consisting of a continuous process of peripheral apposition of new lens fibers and a subsequent compression of the older fibers into a compact centrally located nucleus. The laminar structure of the lens produced by this process was viewed with the aid of the slit lamp and described by numerous investigators (Berliner, 1949; Weale, 1963; and Goldmann, 1964). Goldmann utilizing a more sophisticated optical instrument than the slit lamp was able to estimate the age of an individual by ascertaining the number and position of the lenticular strata (lenticular disjunction stripes).

Biochemically, the progressive nuclear sclerosis attendant with aging, was characterized by increased amounts of insoluble protein, phospholipids, cholesterol, and calcium. There was a relative increase of sodium as compared to potassium. Water and glutathione were decreased as a result of the sclerotic process (Friedenwald, 1952). Most literature consulted was essentially in accord with the aforementioned biochemical alterations, although the increase in calcium with age was not observed by some investigators. Bürger (1963) studied the chemical composition of lenses from calves, cows, dogs, and horses and determined that calcium levels were low in the lenses of these animals and did not increase with age. Adams (1929)

and Grabar and Nordmann (1933) failed to find a significant increase in lenticular calcium in normal human lenses, representing an age range of eight decades. In contrast to these findings, Fischer (1933) found that the calcium content in the lenses of young calves was 0.5 mg. per cent wet weight and in older cattle it was 6.0 mg. per cent wet weight. Mackay, Stewart, and Robertson (1932) stated that in man there was a tendency for calcium to accumulate in the lens with age and that this trend was accentuated in cataractous lenses. Hogan and Zimmerman (1962) outlined the ionic shifts which accompanied cataract formation as consisting of a progressive loss of potassium and an increase in sodium and calcium cations. Weale (1963) concluded that calcium accumulation in the lens was not necessarily restricted to old age, furthermore, that its concentration at any given age depended upon the species being studied.

Schofield (1961) classified nuclear cataract as an extension or intensification of the normal process whereby the central fibers of the lens were compressed into laminated layers. According to Schofield, the continued compression of the centrally located lens fibers eventually resulted in the formation of a homogenous nuclear mass.

According to Catcott and Magrane (1959) a great majority of canine cataracts were associated with the advent of senility, and that

generally some degree of lenticular opacity was present in all dogs by seven or eight years of age. Smythe (1958) noted some degree of opacity in most old animals, but hesitated to compare these opacities to the true senile cataract of man.

Changes with Age in the Retina

Parry (1953a) proposed that the postconception age of the dog was a more reliable guide in evaluating the physiological maturation of the retina than the post-natal age. Utilizing this criteria, Parry precisely outlined the sequence of histological maturation changes in the canine retina. At the 60th day postconception a rod and cone layer was not visible, the inner and outer nuclear layers formed a single combined nuclear layer, optic nerve fibers were inconspicuous, and differentiation of the tapetum from the choroid was indistinct. About the 62nd day postconception, cleavage of the combined nuclear layers began in the region of the area centralis, and was completed by the 66th to 68th day. Also during this period, retinal blood vessels became conspicuous and slightly raised above the inner surface of the retina, rods and cones remained immature, the tapetum became more distinct, and the choroid contained more pigment. Near the 80th day postconception, the adult staining reactions of the retina were evident, and the outer and inner limbs of the rods and cones were distinct. Between the 85th and 95th days postconception, the rods and cones

reached their adult size. At this stage of development numerous newly formed capillaries were visible in the inner nuclear and outer plexiform layers. The choroidocapillaris was well developed by this age. By the 100th to 105th day postconception, the retina and tapetum appeared as in the mature animal. Parry further noted that once the retina of the dog attained maturity little change in structure occurred up to the age of six years.

Histologically, Whiteford (1956) found the retina to be the least developed structure of the eye in the newborn puppy. Whiteford observed that the retina appeared histologically mature in dogs six weeks of age.

The most striking senile changes in the retina were observed by Rones (1938) at the ora serrata, the macular region, and in the blood vessels. The macular region and ora serrata were noted by Kornzweig, Feldstein, and Schneider (1959) as receiving the poorest blood supply of the retina, and therefore rapidly affected when circulation and nutrition were impaired. Prince et al. (1960) described an area near the posterior pole of the retina in the dog and hog, the area centralis, which was relatively free of large blood vessels and was relatively comparable to the macula in man.

Cystic degeneration of the peripheral retina was observed in the aged dog, ox, and horse by Nicolas (1925) and Smythe (1958). Nicolas

(1925) described these cystic formations in animals as being about the size of a pea and similar in structure to senile cystic alterations of the human retina. As reported by Everett (1957) and substantiated by Okun, Rubin, and Collins (1961), cystic degeneration of the peripheral retina was a very common finding in the eye of the senile dog. Senile peripheral cystic degeneration was described as occurring frequently in the aged human retina (Rones, 1938; Friedenwald, 1952; Schofield, 1961; Hogan and Zimmerman, 1962, and Prince, 1965). Schofield (1961) stated that this alteration commenced in most human retinas about the age of 50 years and was characterized by the development of cystic spaces between the outer and inner nuclear layers. In time, these cystic spaces fused and formed interlacing channels which involved increasingly larger portions of the peripheral retina. Friedenwald (1952) questioned the general assumption that the process of cystic degeneration was due to local arteriosclerosis, since the area involved was remote from its parent arterial supply. Friedenwald further added that lesions of this type were not found in the dog, an animal notoriously free from arteriosclerosis. Sommers (1949) postulated that sclerosis of the retinal vessels was a sequela rather than the causative factor of peripheral cystic degeneration.

Peripheral retinal atrophy was described by Rones (1938) as occurring frequently in aged humans. According to Rones, the

lesions were characterized by a reduction in size of the nerve fiber, ganglion cell, and inner nuclear layers, along with a disappearance of the rod and cone elements, and hypertrophy of the retinal connective tissue.

The term peripheral chorioretinal degeneration or atrophy was applied to another form of peripheral retinal degeneration by various investigators (Teng and Katzin, 1953; Okun, 1960; and Hogan and Zimmerman, 1962). The lesions attendant with this degenerative alteration usually developed after 40 years of age in man, were bilateral, and the extent and incidence increased progressively with age. The lesions were manifested microscopically by an abrupt disappearance of the pigment epithelium, the rods and cones, and the outer nuclear layer. Lesser degrees of degeneration and disorganization were present in the other retinal layers. In cases of peripheral chorioretinal degeneration, retinal vessels were not significantly altered, however, choroidal vessels were extremely attenuated and often replaced by fibrous connective tissue. Okun (1960) considered the lesions associated with peripheral chorioretinal degeneration to be related to aging and atherosclerosis. In 12 out of 50 senile dogs examined, Okun, Rubin, and Collins (1961) found large patches of peripheral chorioretinal atrophy, within which were areas of marked retinal thinning to the point of hole formation in the retina.

Magrane (1965) asserted that degeneration in its varying forms was the most common affection of the canine retina. Generally, Magrane recognized two types of retinal atrophy: 1) the hereditary form; and, 2) degeneration as a sequela to systemic disease (distemper), chorioretinitis, and nutritional deficiences.

The occurrence of hereditary progressive retinal atrophy in a number of breeds of dogs was well documented by various investigators (Hodgman, Parry, Rasbridge, and Steel, 1949; Parry, 1953b; Magrane, 1965; and Barnett, 1965b, 1965c).

Parry (1954) reported the presence of central progressive retinal atrophy associated with pigment epithelial dystrophy in a group of 15 dogs of various breeds. According to Parry, this syndrone was quite distinct, both clinically and histopathologically, from hereditary retinal atrophy. Parry observed hypertrophy of the pigment epithelium, followed by atrophy of the rods and cones early in the life of these dogs. Three progressive phases of pigment epithelial dystrophy were distinguished: 1) generalized hypertrophy of the pigment epithelial cells, 2) the formation of isolated giant pigment epithelial cells, and 3) finally the formation of "multicellular nests" of hyperplastic pigment epithelial cells. Parry considered inadequate choroidal circulation as a possible causative factor in the initiation of lesions in the pigment epithelial cell of the retina.

Barnett (1965a) stated in the abstract of an excellent series of articles pertaining to canine retinopathies that in spite of the recognized importance of heredity in progressive retinal atrophy in the Irish Setter, and the familial incidence of this type of blindness in other breeds of dogs, the influence of genetics on retinal atrophy was not fully acknoledged.

Schofield (1961) reported that the most common senile change in the retina of man occurred in the retinal vessels, especially in the arterioles. Fibrous replacement of the vascular wall and patchy endothelial proliferation were described as being characteristic of the age changes in the retinal vessels of man. However, Schofield pointed out, atheromatous degeneration was less common in the retinal arteries than in other arteries of the body. Schofield cautioned that lesions in the retinal vessels might appear different to vascular lesions in other arteries of the body since the retinal vessels were unique in structure. The portion of the central retinal artery within the optic nerve corresponded structurally to the aorta and coronary arteries. (Prince et al. (1960) did not find a central retinal artery in the dog and hog; retinal arteries emanated from the long posterior ciliary arteries in these species.) After penetrating the lamina cribrosa, Schofield added, the wall of the retinal arteries progressively decreased in thickness, and past the

first or second bifurcation the muscle coat separated into isolated fibers, leaving in many places only an endothelial lining, a basement membrane, and an adventitia which originated from the parent vessels.

Rones (1938) discussed sclerotic changes in the retinal vessels thoroughly and concluded that arteriosclerosis of the retinal vessels was related to aging; whereas, arteriolosclerosis, commonly present in conjunction with hypertension, cardiac involvement, and renal impairment, had no relationship with the normal aging process. Rones described the age-related arteriosclerotic alterations as consisting of nodular, intimal proliferations of connective and elastic tissue, with occasional deposition of lipids in the thickened wall.

Friedenwald (1949) demonstrated a PAS-positive basement membrane beneath the endothelium of the entire retinal vascular tree. Friedenwald observed that the intensity of the PAS staining properties of the basement membrane increased with the age of the individual.

Loss of cellularity in the peripheral retinal capillaries was considered by Kuwabara, Carroll and Cogan (1961) as a prominent feature of the aging process in the retina. These authors attributed the loss of cellularity to cystic degeneration of the retina rather than to the degree of systemic arteriosclerosis.

Benedict and Wagener (1961) detected several types of changes in retinal vessels which increased in frequency and severity with the passing of time. These lesions were classified in the order of their increasing severity as arteriolar spasm, arteriolar hypertrophy, arteriolar fibrosis, and arteriolar necrosis.

Tower (1955) and Tassman (1956) expressed the opinion of some investigators that on the basis of present knowledge it was doubtful if true physiological aging of the retinal vessels actually occurred.

Krotova (1963) utilizing the slit lamp found that the retinal arteries became narrow and tortuous, and the veins slightly dilated and stretched in most dogs over six years of age.

MATERIALS AND METHODS

All ocular specimens utilized in this study were systematically collected from animals from which other tissues, organs, and organ systems were collected for evaluation as part of an overall departmental gerontology project. It was considered appropriate to briefly describe the history and scope of the overall project.

A comprehensive gerontological program was envisioned and instigated in the Department of Veterinary Anatomy, Iowa State University over ten years ago by Dr. Robert Getty. The implementation of this program was deemed vital due to a lack of factual information pertaining to the normal changes which occur with age in the tissues and organs of domestic animals. Such information would also be beneficial as a basis for comparative gerontological studies between man and the domestic animals; particularly, since there is no dividing line between human and animal gerontology (Getty 1962, 1966). Acknowledging the value of such a comprehensive gerontological study involving domestic animals, the program was supported by grants awarded by the National Institutes of Health and Gaines Division of General Foods Corporation. Consequently, a colony of purebred Beagle dogs has been maintained by the Department of Veterinary Anatomy since 1957, and tissues have been systematically collected

from these animals at predetermined ages. Hogs utilized in the departmental project were obtained from the Swine Nutrition Farm, Iowa State University.

Certain phases of the overall gerontology project have been presented and have included aging studies related to the uterus of the growing pig (Hadek and Getty, 1959), the cardiovascular system of the hog (Skold and Getty, 1961; Getty and Skold, 1962; Skold, Getty, and Ramsey, 1966; Getty, 1965; Getty, 1966), the gastric mucosa of the pig (Archer, 1963), the canine thyroid (Haensly, Jermier, and Getty, 1964), the canine adrenal (Haensly and Getty, 1965, 1968), the brain of the dog and pig (Whiteford and Getty, 1966), the spinal cord and dorsal root ganglia of the dog and hog (Few and Getty, 1967), and cardiac muscle of the dog (Munnell and Getty, 1968a, 1968b).

At the present, aging studies related to the adrenal gland, the cerebral vasculature, and the kidney are in progress by co-workers in the Department of Anatomy, Iowa State University. Additional evaluations of changes with age in the thyroid gland and the cardiovascular system are being pursued. Tissues from other organs have been collected and adequately preserved for future age-related studies. The eventual goal of the departmental project is to include all tissues in a comprehensive and comparative analysis of the changes which occur with age in the dog and hog.

Anamnesis of the Experimental Subjects

Dogs

Eyes from 86 dogs ranging in age from one day to 13.1 years of age were included in this study. Each dog originated from sources with known environmental conditions and was accompanied by a fully documented history.

Sixty-seven of the dogs were reared in the dog colony of the Department of Veterinary Anatomy, Iowa State University. The remainder of the dogs were obtained from the Post Division, Gaines Research Kennels, Saint Anne, Illinois. Data pertaining to the breed, sex, age, weight, diet, and origin of each animal was presented in tabular form (Table 1).

Dogs were maintained on a controlled dietary regimen throughout their entire life. Postweaning diet for all dogs consisted of a dry commercial dog food[1] which contained adequate supplements of vitamins and minerals.

The general health of the dog colony was maintained by the combined practices of good kennel sanitation, preventive medicine techniques, and isolation from uncontrollable external environmental

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[1]Supplied by Gaines Dog Food Division, General Foods Company, Kankakee, Illinois.

influences. Kennel sanitation was facilitated by the utilization of concrete runs, easily cleaned "hutch type shelters", and water connections capable of transmitting copious quantities of hot water to all areas of the animal quarters.

Preventive medicine techniques included routine inoculations for canine distemper and infectious canine hepatitis, and periodic fecal examinations followed by anthelmintic treatment if indicated.

Hogs

Eyes from 108 hogs ranging in age from 0.1 month (three days) to 8.0 years of age were utilized in this study. All porcine subjects were obtained from the Swine Nutrition Farm, Iowa State University or from other sources by special purchase. All hogs were free of visible clinical symptoms of disease at the time of euthanasia. Data pertaining to the precise age, breed, sex, and weight was available on all porcine subjects (Table 2).

Collection and Preservation of Tissues

Euthanasia and the collection and preservation of tissues were accomplished in a similar manner for the dog and hog. Electrocution was used as the method for euthanasia in all experimental subjects. A simple electrocution device was employed which consisted of two spring-clip electrodes wired to an electrical plug

capable of being inserted into a 110 volt alternating current outlet. One spring-clip electrode was attached to the animal's ear; the other electrode was attached to the anal mucosa. Successive electrical shocks, each of approximately 60 seconds duration, were administered to the animal. The shocks were repeated until respiration ceased to reoccur following the termination of the flow of electricity.

Partial exsanguination of each animal was accomplished by incising the skin and subcutaneous tissues of the axillary region and exposing and severing the large vessels in the region. Following the cessation of appreciable hemorrhage, the animal was decapitated at the atlanto-occipital articulation.

Eyes were enucleated in toto by reflecting the skin and ocular adnexa and carefully dissecting around the internal surface of the periorbita to the apex of the globe. Extirpation of the globe was completed by severing the optic nerve approximately one cm. caudal to the globe.

Upon removal of the globe, the orbital fascia (Fasciae orbitale) and the external muscles of the eye were removed, and the entire globe was immersed in 1000 ml. of ten per cent neutral buffered formalin.

This fixative was prepared by the following formula:

Formaldehyde, 40 per cent	100 ml.
Tap Water	900 ml.
Sodium Phosphate, dibasic	7 gm.
Sodium Phosphate, monobasic	4 gm.

Processing of the Tissues

All globes were allowed to remain in the fixative for at least 48 hours. Prior to subsequent processing, the external dimensions of the bulbus oculi and the keratometric measurements of the corneal curvatures were ascertained. All globes were then washed for 12-24 hours in running tap water in order to remove excess acids from the tissues. One eye from each dog and hog utilized in this investigation was prepared for paraffin embedment; the other eye from a number of these dogs and hogs (Tables 1, 2) was prepared for embedment in gelatin preparatory to making frozen sections.

Paraffin sections

After washing in tap water, the globe was placed in 70 per cent ethanol for 24 hours. The lateral calotte was then removed by cutting the globe with a sharp razor blade from the corneoscleral junction, being sure to include enough of the cornea to open the anterior chamber angle, to a point approximately five mm. lateral to the optic nerve. This procedure was repeated on the medial aspect of the

globe in removing the medial calotte. The medial and lateral calottes and the central portion of the globe which contained the lens and optic nerve were dehydrated, cleared, and infiltrated according to the following schedule:

Ethanol, 80 per cent	2 Hours
Ethanol, 95 per cent	2 Hours
Ethanol, 95 per cent	2 Hours
Ethanol, absolute	2 Hours
Ethanol, absolute	2 Hours
Ethanol, absolute-xylene (equal parts)	2 Hours
Chloroform	2 Hours
Chloroform	4 Hours
Xylene	1 Hour
Xylene	1 Hour
Bioloid paraffin[1] bath	2 Hours
Bioloid paraffin bath	2 Hours

Tissues were transferred from the last paraffin bath to a stainless steel embedding tray containing melted Bioloid paraffin, and the tray was placed for 20 - 30 minutes in a vacuum oven maintained at a temperature of 60^{0} C. and vacuum of 300-350 mm. of Hg. Embedment was accomplished by removing the embedding tray from the vacuum oven, positioning the tissues, and allowing the paraffin to solidify at room temperature.

Sections from the paraffin blocks were cut on a rotary microtome at a thickness of eight microns. Sectioning of the portion of

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[1] Bioloid-Will Scientific, Incorporated, Rochester, New York.

the globe which contained the lens was facilitated by placing for two to three minutes a warm, moist cloth over the surface of the block from which sections were to be taken. This procedure was immediately followed by the application of ice cubes to the face of the block and to the microtome blade until both were thoroughly chilled. Usually, four to five complete sections which contained unshattered lenses were attainable before repeating the applications of heat and cold to the block face.

Frozen sections

After washing the intact globe in running tap water for 12 - 24 hours, the medial and lateral calottes were removed in the same manner as outlined for the processing of tissues for paraffin embedment. In an eye destined for gelatin embedment, the lens was also removed and embedded separately. The central portion of the eye, the calottes, and the lens were embedded in gelatin according to the technique described by the Armed Forces Institute of Pathology (1960). As suggested by this source, the time required for gelatin infiltration was reduced by placing the specimens in a vacuum oven maintained at a temperature of 40° C. and exposing the tissues for two hours to a vacuum of 300 - 350 mm. Hg. Utilizing a Histo-Freeze[1]

[1] Histo-Freeze - Scientific Products, Division of American Hospital Supply Corporation, Evanston, Illinois.

freezing unit attached to a sliding microtome, frozen sections were cut at a thickness of 15 microns.

Staining Procedures

Paraffin sections

Sections from the calottes and the central portion of the eye were routinely stained with the following techniques: hematoxylin and eosin, Weigert's resorcin-fuchsin, Von Kossa's, alizarin red S, colloidal iron, and periodic acid Schiff (PAS).

Slides stained with hematoxylin and eosin were used for a general survey of the histological changes attendant with aging in the component tissues of the eye. Slides stained with this technique were also helpful in making microscopic measurements of the constituent cells and tissues of the eye. The procedure as outlined by the Armed Forces Institute of Pathology (1960) was employed in carrying out this staining technique.

Weigert's resorcin-fuchsin elastic stain combined with a counterstain of picric acid and acid fuchsin (Van Gieson's solution) was utilized to demonstrate alterations in the elastic and collagenous components of the eye. This combined procedure, initially described by Mallory (1938), was outlined in detail by the Armed Forces Institute of Pathology (1960). Slides stained by this procedure were

extremely beneficial in evaluating vascular changes with age as well as useful adjuncts to hematoxylin and eosin stained sections in assessing the overall changes with age in the tissues of the eye.

The colloidal iron technique of Rinehart and Abul-Haj (1951) was employed to visualize changes with age in the basic component of the ground substance, the acid mucopolysaccharides, of the ocular tissues. In addition, changes with age in the arteries, the membranous structures, and the connective tissues of the eye were well defined in slides stained with this technique.

Von Kossa's silver substitution for calcium technique (Armed Forces Institute of Pathology, 1960) and the dye-lake method for demonstrating calcium with alizarin red S (McGee-Russell, 1958) were applied in order to demonstrate mineral accumulation in the ocular tissues. According to McGee-Russell (1958), the alizarin red S technique was more definitive for calcium than the silver substitution method.

The periodic acid-Schiff staining technique as described by Friedenwald (1949) was adopted for use in this investigation for its capability to stain subtle alterations in the ocular vessels. Hyaline changes, colloid droplets, and changes in the basement membranes of the ocular tissues were usually well stained with this technique.

Frozen sections

All frozen sections were stained with oil red O fat stain in accord with the technique described by Bell (1959). The gelatin embedment apparently had no effect on the uptake of the stain by the lipid accumulations. However, the embedding media was lightly stained with the hematoxylin counterstain but did not seriously hinder the visualization of the lipid deposits.

Dimensional Studies and Statistical Analyses

The measurements and statistical analyses of dimensional changes with age in the ocular tissues were conducted in a similar manner for the dog and hog. Of the 86 dogs utilized in this investigation for the evaluation of histological and histochemical changes with age, only 78 dogs were included in the study of dimensional changes; whereas, all 108 hogs utilized in the histological and histochemical evaluations were included in the dimensional studies.

Since many of the eyes were collected and fixed in ten per cent neutral buffered formalin prior to the initiation of this study, all gross measurements of the bulbus oculi and corneal diameters, and all keratometric measurements of the corneal curvatures were performed after formalin fixation of the intact globe. In order to diminish the distortion and to some extent the shrinkage effects

created by formalin fixation, all eyes were injected with ten per cent neutral buffered formalin immediately prior to making gross measurements. A 26 gauge hypodermic needle with a formalin-filled syringe attached was inserted at a point near the corneoscleral junction into the anterior chamber. Sufficient formalin was injected into the anterior chamber to elevate and standardize the intraocular pressure of each eye to a common pressure of 120 mm. Hg. Intraocular pressure was ascertained with the Schioetz-Trylon tonometer. The induced intraocular pressure far exceeded the normal intraocular pressure of the dog in the vital state, but was mandatory in order to eliminate all undulations in the fixed corneal surface. Gross measurements of the external dimensional parameters of the bulbus oculi and cornea were measured with a precision caliper, and the curvatures of the anterior surface of the cornea were determined with a Bausch and Lomb keratometer.

Microscopic measurements of various component structures and cells of the eye were made from stained sagittal sections of the eye. A filar micrometer eyepiece inserted into the eyepiece tube of a microscope was employed to secure microscopic measurements.

Statistical analyses of the data were by the methods for linear and curvilinear regression as described by Snedecor (1967).

Analyses of the dimensional changes with age were conducted on the IBM 360/50 computer, Computation Center, Iowa State University, Ames, Iowa.

Designation of Age Groups

Histological and histochemical evaluations

In order to quantify the incidence of histological and histochemical changes at different age levels, the 86 dogs were divided into six age groups. The class intervals for the various age groups were selected to represent specific developmental, maturation, and senescent periods in the life span of the dog. The designated age groups and respective class intervals were as follows:

Age Group I	0.1 - 4.0 months of age
Age Group II	5.4 - 9.9 months of age
Age Group III	11.0 - 12.9 months of age
Age Group IV	1.5 - 4.4 years of age
Age Group V	6.0 - 9.9 years of age
Age Group VI	10.0 - 13.1 years of age

Age Group I included dogs in puppyhood and up to the age of the initiation of permanent dentition in the Beagle (Gaines Dog Research Center, 1965). Dogs in Age Group II represented the period of adolescence in man. Developmental changes in dogs in this age group were characterized by puberty and rapid somatic growth. The relatively short age interval of Age Group III was purposely set to include dogs which had recently attained mature growth (Gaines Dog

Research Center, 1965). Class intervals for Age Groups IV, V, and VI were designated to correspond respectively to the periods of adulthood, middle age, and senescence in man.

The 108 hogs were divided into five age groups. The age groups and the class intervals for the hog were as follows:

Age Group I	0.1 - 6.0 months of age
Age Group II	6.2 - 11.9 months of age
Age Group III	1.2 - 2.9 years of age
Age Group IV	3.1 - 5.9 years of age
Age Group V	6.0 - 8.0 years of age

The reduced number of class intervals in the hog as compared to the dog was necessitated by the shorter age range of hogs available for study. The developmental characteristics represented by hogs in Age Group I included infancy, usually puberty (Rice and Andrews, 1951), and a period of extensive somatic growth. In comparison to the age periods in the life of man, hogs in Age Groups II, III, IV, and V were considered to represent the periods of early adulthood, adulthood, middle age, and senescence, respectively.

Statistical evaluation of dimensional changes

For the purpose of statistical analyses of dimensional changes with age, dogs and hogs were divided into a Maturation Age Group and a Postmaturation Age Group. Dogs up to 13.0 months of age and hogs up to 12.0 months of age were included in the Maturation Age Group of the two species. Animals older than these designated ages were placed in the Postmaturation Age Group.

RESULTS

Bulbus Oculi

Statistical evaluation of dimensional change with age

Transverse, vertical, and anteroposterior diameters

Dog A curvilinear relationship (Graph 1) existed between the size of the transverse, vertical, and anteroposterior diameters of the bulbus oculi and age in the Maturation Age Group (0.1 - 13.0 months). In the one-day old puppy the transverse, vertical, and anteroposterior diameters were 11.42 mm., 10.50 mm., and 10.41 mm., respectively. The bulbus oculi reached its mature dimensions at ten months of age. At this age the transverse, vertical, and anteroposterior diameters were 22.19 mm., 21.50., and 20.77 mm., respectively.

There was no significant change in the transverse or vertical diameters of the bulbus oculi in the Postmaturation Age Group (1.5 - 13.1 years). However, the anteroposterior diameter increased linearly with age, and the regression coefficient was significant (Graph 2). This increase ranged from 20.71 mm. at 1.5 years to 22.21 mm. at 13.1 years of age. The correlation between the anteroposterior diameter and age was significant in the Postmaturation Age Group. In the order of their relative size at 13.1 years of age,

the transverse diameter was 22.32 mm., the anteroposterior diameter was 22.20 mm., and the vertical diameter was 21.50 mm.

Hog Statistical analyses of the transverse, vertical, and anteroposterior diameters of the bulbus oculi, measured in 22 hogs in the Maturation Age Group (0.1 - 12.0 months) revealed a curvilinear increase with age in each diameter (Graph 3). Maximum growth was reached in the transverse and vertical planes at 11.0 months of age, with maximum diameters of 26.65 mm. and 24.66 mm., respectively. The anteroposterior diameter reached a maximum size of 22.18 mm. at nine months of age.

In 86 hogs in the Postmaturation Age Group (1.2 - 8.0 years), the transverse, vertical, and anteroposterior diameters increased significantly with age (Graph 4). The increase in size of the transverse and vertical diameters was determined to be curvilinear with respect to age. The transverse and vertical diameters reached their maximum size at six years of age and were 28.76 mm. and 27.72 mm., respectively. A slight decline was noted in these two parameters between the sixth and eighth years of age.

The anteroposterior diameter increased linearly throughout the postmaturation period in yearly increments of 0.27 mm. The

regression coefficient was significant and the correlation between the anteroposterior diameter and age in the Postmaturation Age Group was also significant.

Cornea

Statistical evaluation of dimensional change with age

Transverse and vertical corneal diameters

Dog In the Maturation Age Group, the transverse and vertical diameters of the cornea increased curvilinearly with age (Graph 5). All regression coefficients were significant. The maximum diameter size was reached in both planes at ten months of age. The transverse diameter increased from 8.07 mm. in the one-day old puppy to 16.72 mm. at ten months of age. During the same period the vertical diameter increased from 7.51 mm. to 15.36 mm.

There was no significant change in either of the corneal diameters in the Postmaturation Age Group (Graph 6).

Hog A curvilinear relationship existed between the size of the transverse and vertical diameters of the cornea and age in the Maturation Age Group (Graph 7). In this age group a maximum transverse diameter of 16.94 mm. was reached at 11 months of age, and a maximum vertical diameter of 14.12 mm. was attained at 12.0 months of age. The slope of the regression line indicated the transverse and

vertical corneal diameters in the three-day old pig to be 10.87 mm. and 9.35 mm., respectively.

The transverse and vertical corneal diameters increased significantly with age in the Postmaturation Age Group (Graph 8). The transverse diameter increased linearly throughout the post-maturation age period at a rate of 0.36 mm. per year. The transverse diameter at eight years of age was 20.49 mm. The postmaturation increase in the vertical diameter was curvilinear in relation to age. The vertical corneal diameter was 14.90 mm. at 1.2 years, 16.69 mm. at 6.0 years, and 16.13 mm. at 8.0 years of age.

Curvature of the anterior surface of the cornea

Dog In the one-day old puppy, the anterior surface of the cornea (Facies anterior) was found to be spherical; e.g., the curvature in the transverse and vertical planes was equal. At this age the curvature in both planes was 56.00 diopters (Radius of Curvature = 6.05 mm.).

In the Maturation Age Group, the transverse and vertical corneal curvatures decreased markedly with age (Graph 9). The regression of both the transverse and vertical corneal curvatures was curvilinear with respect to age. The vertical curvature was found to decrease at a slightly more rapid rate than the transverse curvature. Curvilinear change in the corneal curvature stabilized

at the tenth month of age, and minimal regression was noted during the succeeding months of the maturation period. At ten months of age, the transverse and vertical curvatures were 42.06 diopters (Radius of Curvature = 8.02 mm.) and 40.93 diopters (Radius of Curvature = 8.22 mm.), respectively.

In the Postmaturation Age Group, the transverse and vertical corneal curvatures decreased linearly with age (Graph 10). Linear decrease in the transverse plane was not significant, whereas, the regression coefficient of the vertical curvature was significant. Correlation between the size of the vertical curvature and age was significant. In this age group, vertical corneal curvature decreased from 42.71 diopters (Radius of Curvature = 7.91 mm.) at 1.5 years to 38.46 diopters (Radius of Curvature = 8.76 mm.) at 13.1 years of age. The slope of the regression line indicated that the maximum and minimum measurements in the transverse plane were 39.53 diopters (Radius of Curvature = 8.54 mm.) at 1.5 years, and 38.10 diopters (Radius of Curvature = 8.86 mm.) at 13.1 years of age.

Hog Linear regression analysis revealed that in the three-day old pig the vertical corneal curvature was 51.31 diopters (Radius of Curvature = 6.58 mm.), and the transverse corneal curvature was 49.79 diopters (Radius of Curvature = 6.78 mm.).

Both the transverse and vertical corneal curvatures followed a significant linear decrease with age in the Maturation Age Group (Graph 11). The vertical curvature decreased at a rate of 1.24 diopters per month, and the transverse curvature decreased 0.91 diopters per month. The greater decrease in the vertical curvature resulted in the two curvatures being equal at approximately five months of age. At 12 months of age the transverse curvature was 38.84 diopters (Radius of Curvature = 8.68 mm.), and the vertical curvature measured 36.51 diopters (Radius of Curvature = 9.25 mm.). Correlation between age and the vertical curvature was significant as was the transverse curvature.

In the Postmaturation Age Group, the transverse corneal curvature decreased linearly with age (Graph 12). The linear decrease in the transverse curvature during this period was significant. At 1.2 years and 8.0 years of age, the transverse curvature measured 37.18 diopters (Radius of Curvature = 9.11 mm.) and 35.78 diopters (Radius of Curvature = 9.46 mm.), respectively. This reduction in the transverse curvature with age represented a decrease of 0.21 diopters per year.

The vertical corneal curvature was curvilinear with respect to age in the Postmaturation Age Group (Graph 12). Curvilinear analysis revealed a decrease in the vertical curvature from 1.2 years to

5.0 years, and an increase in this parameter from six to eight years of age. The curvilinearity of the vertical curvature resulted in the transverse and vertical curvatures being equal at approximately two years and again at approximately seven years of age.

Total corneal thickness

Dog Total corneal thickness, measured at the geometric axis of the bulbus oculi, followed a curvilinear increase with age in the Maturation Age Group (Graph 13). Corneal thickness in the one-day old puppy was 0.348 mm., and increased to 0.786 mm. at 13 months of age. Approximately 72 per cent of this increase in thickness occurred during the first six months after birth.

Total corneal thickness increased linearly with age in the dogs in the Postmaturation Age Group (Graph 14). This increase in corneal thickness was not statistically significant. The average corneal thickness for the 32 dogs in this age group was 0.915 mm.

Hog Total corneal thickness in the three-day old pig was 0.926 mm. (Graph 15). Total corneal thickness increased linearly with age during the maturation period, and the linear increase was significant. Increase in thickness was at the rate of 0.033 mm. per month. Correlation between corneal thickness and age was significant.

Corneal thickness, in the Postmaturation Age Group, was curvilinear in relation to age (Graph 16). A maximum thickness of 1.352 mm. was noted at four years of age, after which the thickness decreased markedly to 1.047 mm. at eight years of age.

Substantia propria

Dog In the Maturation Age Group the substantia propria (Substantia propria corneae) increased in thickness from 0.345 mm. in the neonatal puppy to a maximum thickness of 0.737 mm. at 12 months of age (Graph 13). The increase in thickness was curvilinear in relation to age. Approximately 73 per cent of the total increase in thickness during this period occurred during the first six months of life.

From 1.5 years to 13.1 years of age, the substantia propria increased slightly with age but was not statistically significant (Graph 14). A maximum thickness of 0.878 mm. was observed at 13.1 years of age.

Hog In the Maturation Age Group, the thickness of the substantia propria increased linearly with age and was statistically significant (Graph 15). A thickness of 0.849 mm. was noted at three days of age, and the thickness increased throughout the

maturation period at the rate of 0.032 mm. per month. Correlation between the thickness of the substantia propria and age was significant.

In the Postmaturation Age Group, the substantia propria followed a curvilinear increase and decrease in thickness (Graph 16). A maximum thickness of 1.245 mm. was attained at four years, and was followed by a sharp reduction in thickness to 0.927 mm. at eight years of age.

Corneal epithelium

Dog The thickness of the corneal epithelium (Epithelium anterius corneae) measured at the geometric axis of the bulbus oculi was curvilinear in relation to age in 46 dogs in the Maturation Age Group (Graph 13). The epithelial thickness increased from 16.52 microns in the neonatal puppy to a maximum thickness of 61.54 microns at nine months of age. Eighty-seven per cent of this increase in thickness occurred during the first six months after birth.

There was no significant change in the thickness of the corneal epithelium in the Postmaturation Age Group (Graph 14). A maximum thickness of 64.48 microns was noted in this age group at 13.1 years of age.

Hog The thickness of the corneal epithelium, measured at the geometric axis, increased linearly with age in the Maturation Age Group, but this increase in thickness was not significant

(Graph 15). The corneal epithelial thickness measured 61.23 microns at three days and 77.63 microns at 12 months of age. The average corneal epithelial thickness in the 22 hogs in this age group was 64.21 microns.

A slight linear decrease in the thickness of the corneal epithelium was noted in the Postmaturation Age Group (Graph 16). This slight decrease was not significant. Corneal thickness ranged from 77.60 microns at 1.2 years to 71.34 microns at eight years of age. The average corneal thickness for the 86 pigs in this age group was 75.62 microns.

Descemet's membrane

Dog In the one-day old puppy the thickness of Descemet's membrane (Lamina limitans posterior) was 7.92 microns at the geometric axis of the bulbus oculi, and increased in thickness to 9.07 microns at 13 months of age. This increase was linear with respect to age but was not statistically significant (Graph 13).

In the Postmaturation Age Group, the thickness of Descemet's membrane increased linearly with age, and this increase was statistically significant. The thickness increased from 8.86 microns at 1.5 years to 20.53 microns at 13.1 years of age (Graph 14). The increase in thickness was at the rate of 1.01 microns per year.

Correlation between the thickness of Descemet's membrane and age during the postmaturation period was significant.

Hog A significant linear increase with age occurred in the thickness of Descemet's membrane in the Maturation Age Group (Graph 15). Thickness ranged from 4.04 microns at three days to 12.98 microns at 12 months of age. Increase in thickness was in increments of 0.74 microns per month. Correlation between the thickness of Descemet's membrane and age was significant for the Maturation Age Group.

The thickness of Descemet's membrane increased in the Postmaturation Age Group at the rate of 3.98 microns per year. This increase in thickness was linear with age, and was statistically significant. In this age group, a maximum thickness of 40.58 microns was observed at eight years of age (Graph 16). Correlation between the thickness of Descemet's membrane and age was significant.

Corneal endothelium

Dog The corneal endothelial cell (Endothelium camerae anterioris) decreased in thickness with age in the Maturation Age Group (Graph 13). The slope of the regression line revealed that in the neonatal puppy, the endothelial cell was 6.30 microns in thickness and at 13 months of age it was 5.60 microns. This decrease in

thickness was not statistically significant. The average endothelial cell thickness for the Maturation Age Group was 5.90 microns.

In the Postmaturation Age Group, the thickness of the corneal endothelial cell increased linearly with age but was not significant (Graph 14). This increase in thickness ranged from 4.19 microns at 1.5 years to 4.57 microns at 13.1 years of age. The mean endothelial cell thickness for this age group was 4.42 microns.

Hog The thickness of the corneal endothelial cell increased linearly with age in the Maturation Age Group (Graph 15). This increase in thickness was significant. At three days of age the endothelial cell thickness was 3.60 microns, and the thickness increased in monthly increments of 0.20 microns to a maximum thickness of 6.02 microns at 12 months of age. Correlation between corneal endothelial cell thickness for the Maturation Age Group was 4.76 microns.

There was no significant change in thickness of the corneal endothelial cell in the Postmaturation Age Group (Graph 16). The average endothelial cell thickness for the 86 hogs in this group was 5.61 microns.

Histological and histochemical changes with age

Maturation changes

Dog Certain processes of prenatal development were found to be incomplete in the cornea of the newborn puppy.

The corneal epithelium in puppies less than seven days of age consisted of a basal layer of cuboidal cells and one or two layers of squamous epithelial cells. The substantia propria comprised approximately 95 per cent of the total thickness of the cornea and contained a large number of irregularly shaped, primitive appearing mesenchymal cells (Figure 3). The nuclei of the latter cells were distinctly vesiculated. Descemet's membrane was discernible, but its thickness was less than the thickness of the adjacent mesenchymal endothelial cell. Viewed in profile, the nuclei of the endothelial cells appeared close to each other with little intervening cytoplasm.

In all puppies younger than seven days of age, the iris was adherent, either totally or partially, to the posterior surface of the cornea (Figures 3-6). The lens was partially attached or in close proximity to the posterior surface of the cornea (Figures 4-6). Amorphous material, cellular debris, and remnants of fetal blood vessels, indicative of recent dehiscence of the cornea, iris, and lens, were observed in the anterior chamber.

By two weeks of age the iris and lens were completely separated from the posterior corneal surface (Facies posterior) although cellular debris and remnants of fetal vasculature were still evident in the anterior chamber. The corneal epithelium was five to six cells in thickness, and prolific mitotic activity was noted in the basal layer of cuboidal cells. The corneal stromal cells were slightly less numerous and generally less embryonal than in the younger puppy.

By four weeks of age, the basal cells of the corneal epithelium were increased in height to low columnar cells, and mitotic activity was very apparent. Five to six layers of squamous epithelial cells surmounted the single layer of basal cells. At this age stromal cells were still numerous and were approximately equally divided between primitive mesenchymal type cells and the more mature fibrocytic type stromal cell. Descemet's membrane was the approximate thickness of the endothelial cell at this age.

By eight weeks of age the basal cells of the corneal epithelium were tall columnar in form. One or two layers of oval to polyhedral cells ("wing cells") were interposed between the single layer of basal cells and the well-developed strata of nonkeratinized squamous epithelial cells. Except for the presence of a few immature stromal

cells the histological appearance of the cornea at eight weeks of age was quite typical of the appearance of the mature cornea.

After eight weeks of age the maturation process was devoted essentially to growth of the constituent parts of the cornea. The great increase in the total thickness of the cornea between the second and twelfth months of age was principally due to a progressive increase in the number of collagenous lamellae in the substantia propria.

Hog In comparison, the cornea of the neonatal pig was more mature in histological appearance than the cornea of the neonatal puppy. All structural components of the cornea were visible in the newborn pig. The only histological features which distinguished the cornea of the newborn from the mature cornea were: a diminished thickness of the squamous epithelial strata (only two to three cells in thickness), the presence of numerous primitive stromal cells in the substantia propria, and a greater degree of cellularity in the endothelial layer.

By eight weeks of age, except for the presence of an occasional immature stromal cell, the cornea of the hog was mature in histological appearance.

Lipid deposition

Dog Lipid deposition was not found in the cornea of any dog younger than 11 months of age. In Age Group III (11.0 - 12.9 months of age) the incidence of lipid deposition was markedly increased (Table 3). In dogs older than 1.5 years (Age Groups IV - V, 1.5 - 13.1 years of age) lipid deposition in some degree was found to be almost universal.

In frozen sections stained with oil red O, lipids stained light to dark red depending upon the lipid concentration (Figures 7-10). In areas of slight deposition, lipids appeared homogenously blended with the tissue and imparted a pale reddish hue to the infiltrated tissue. In areas of moderate deposition, lipids appeared within the tissue in a fine granular to small globular form, and in areas of heavy infiltration lipids were accumulated into large amorphous conglomerations.

If present, lipid depositions were always found near the corneal periphery (Figure 9) and were generally separated from the corneo-scleral junction by a narrow lipid-free zone which measured approximately 60 microns in width.

In general, the degree of lipid deposition was increased with age. Also as age increased specific areas near the peripheral portion of the cornea were observed to be predilected to lipid deposition

Lipid infiltration in Age Group III (11.0 - 12.9 months of age) was slight and principally found in the subepithelial region of the substantia propria (Figure 10). Lipid depositions at this site extended along the deep surface of the corneal epithelium for distances ranging from 0.2 mm. to 1.0 mm.

In Age Group IV (1.5 - 4.4 years of age), in addition to subepithelial deposition, slight to moderate deposition was observed in the region of the substantia propria immediately adjacent to Descemet's membrane. In older dogs of this age group slight infiltration was also noted in the central region of the substantia propria (Figure 7).

In Age Groups V and VI (6.0 - 13.1 years of age), the extent of lipid deposition was progressively increased with age in all regions of the substantia propria. A particularly dense accumulation of lipid deposits was often observed in the lamellae of the substantia propria adjacent to Descemet's membrane (Figure 8). The dense accumulation was thickest near the corneal periphery (up to 70 microns in the older dogs) and gradually tapered to a narrow, thin line of deposition at the axial extent of the deposition. The axial extent of deposition in this region ranged from 0.5 mm. to 2.0 mm. from the corneal periphery. Occasionally, in cases of marked deposition in this area, lipids were also observed in Descemet's membrane (Figure 8).

Hog The incidence of lipid deposition in the cornea of the hog was found to be minimal (Table 4). The earliest age at which lipid deposition was observed was 4.6 years (Hog No. 392, Age Group IV, 3.1 - 5.9 years of age).

In Age Group V (6.0 - 8.0 years of age) the incidence of lipid deposition was moderately increased, but the degree of deposition was extremely slight in all individual observations. The slight amount of lipid deposition observed in hogs in this age group was present only in the region of the substantia propria adjacent to Descemet's membrane.

Corneal pigmentation

Dog In most dogs (79.1 per cent) pigmentation was observed along the scleral side of the corneoscleral junction (Table 5), and near the corneoscleral junction in the germinal cells of the corneal and conjunctival epithelium. Migration of pigment from these areas into the superficial structures of the cornea (superficial corneal pigmentation) was either absent or present in very minute quantities in the dogs utilized in this investigation.

The incidence of deep corneal pigmentation (pigment invasion originating from the uveal tract and occupying the posterior structures of the cornea) was found to increase progressively with age in the dog (Table 3). The incidence of pigment invasion was

negligible in dogs younger than six months of age, although moderate pigmentation was observed in one dog (Dog No. B69, Age Group I) four months of age. With one exception (Dog No. M42, 11. 2 years of age), some degree of deep corneal pigmentation was noted in all dogs over 1. 5 years of age.

Deep corneal pigmentation was characterized by narrow, elongated pigment containing cells in the posterior portion of the cornea (Figure 11). The pigmented cells appeared to enter the cornea by migrating between Descemet's membrane and the adjacent lamellae of the substantia propria. A moderate number of fibrocytic, histocytic, and leucocytic cells usually preceded or accompanied the pigment invasion.

Although the degree of deep corneal pigmentation in individual dogs was variable, in general, the degree and extent of pigmentation was progressively increased with age. Within the cornea, the pigmented cells either retained their narrow, elongated morphology and advanced axially along the deep surface of Descemet's membrane (Figure 11) or accumulated into focal pigment aggregations near the corneal periphery (Figure 12). In older dogs it was not uncommon to find pigment extending axially into the cornea for distances up to two mm. from the corneal periphery and focal pigment aggregations measuring up to 60 microns in an anteroposterior direction.

Peripheral thickening of Descemet's membrane (Hassal-Henle body) was frequently concomitant with the presence of focal pigment aggregations. The thickened portion of Descemet's membrane formed smooth, mound-like protuberances which projected into the peripheral portion of the anterior chamber (Figures 13, 14). The extent of protrusion into the anterior chamber ranged from 10 to 20 microns in the younger animals, and up to 70 microns in the older animals. The protuberances retained the normal staining characteristics of Descemet's membrane, and the endothelial cells covering the protuberances were markedly attenuated (Figure 13). Occasionally, focal pigment deposition was observed in the protuberances which increased the size of the protuberance and the extent of protrusion into the anterior chamber (Figure 14).

Irregularly shaped, fibro-pigmented nodules were observed on the posterior surface of the cornea in 8.2 per cent of the dogs. These nodules were found in the young dogs as frequently as in the old dogs and were not considered to be age-related lesions. They were described at this point due to the fact that pigment invasion of the nodule was a consistent feature of the lesion. The fibro-pigmented nodules were characterized by complete disruption of Descemet's membrane, extensions of collagenous fiber bundles from the substantia propria into the nodule, and pigment invasion of the

nodules. Fibrocytes and histocytes usually accompanied the invasive elements into the nodule (Figure 15).

Hog Significant corneal pigmentation was not observed in hogs less than one year of age (Table 4, Age Groups I, II). In hogs older than one year of age, the incidence of corneal pigmentation was found to increase progressively until six years of age. In hogs between six and eight years of age (Table 4, Age Group V) a slight decrease was noted in the incidence of corneal pigmentation.

In the majority of cases of corneal pigmentation in the hog, the invasive pigment elements appeared to originate from melanin pigments in the portion of the sclera adjacent to the corneoscleral junction. In these cases infiltration into the cornea was usually restricted to the middle one-third of the substantia propria. The invasive pigment elements were characteristically gathered into elongated wedge-shaped accumulations, with the basal portion of the wedge situated at the corneoscleral junction and the pointed end of the wedge directed axially into the substantia propria. The axial extent of pigment infiltration was usually greater in older hogs. It was not uncommon to see more than one wedge-shaped accumulation extending into the middle one-third of the substantia propria (Figure 16). Inflammatory cells were not observed in the area of the pigment infiltration.

Deep corneal pigmentation, which was the typical form of corneal pigmentation in the dog, was observed in only four hogs. In these four hogs focal accumulation or axial penetration of the pigment was not extensive. Hassal-Henle bodies were occasionally observed in the hog but were not accompanied by pigment invasion.

Mineralization

Dog Corneal mineralization was manifested by intracellular accumulation of mineral salts, likely calcium carbonates or phosphates, and by extracellular deposition of these salts in the tissues of the cornea. These two manifestations of corneal mineralization were frequently concomitant.

Intracellular mineralization was present most frequently in the stromal and endothelial cells and less frequently in the cells of the corneal epithelium (Table 3). The intracellular accumulations were clearly stained with Von Kossa's staining technic for calcium salts as fine, brownish to black granules (Figures 17, 18, 20). A greater concentration of granules was usually visible in the nucleus than in the cytoplasm. With the alizarin red S staining technic, the cells which contained mineral salts were stained more homogeneously, were orange to red, and usually contained a central core which stained a deeper red (Figures 19, 21). The

percentage incidence of intracellular mineralization was almost identical for the stromal and endothelial cell in all age groups (Table 3).

The intensity of intracellular mineralization was relatively moderate in dogs less than one year of age. In dogs over one year old, the degree of intracellular mineralization generally increased up to approximately ten years of age. A slight decrease in the intensity of intracellular mineralization was observed in dogs over ten years of age. As intracellular mineralization increased in intensity in the stromal and endothelial cells, the incidence of the diffuse and mineralized excrescent forms of extracellular mineralization was increased.

The incidence of intracellular mineralization in the corneal epithelium was extremely variable throughout the six age groups (Table 3). The intensity of intracellular mineralization in this cell was generally progressive with age and proportional to the incidence of diffuse extracellular mineralization in the anterior one-third of the substantia propria.

Diffuse extracellular mineralization was prominent in the collagenous lamellae of the substantia propria, particularly in the regions adjacent to the corneal epithelium and Descemet's membrane. Diffuse extracellular mineralization in the substantia propria was

characterized by a diffuse permeation of the stromal lamellae with fine granular deposits of mineral salts (Figure 20).

Focal areas of dense mineralization in the substantia propria were present in 26.7 per cent of the dogs (Table 3). In the dog these areas were found predominantly in the posterior one-third of the substantia propria, were irregular in outline, and measured up to 100 microns at their greatest dimension (Figures 17, 18).

Mineralized excrescences which projected from the posterior surface of the cornea into the anterior chamber were found in 56.9 per cent of the dogs (Table 3). The youngest dog (Dog No. B47) in which mineralized excrescences were found was eight weeks of age. The incidence of excrescences was progressively increased in each successive age group up to Age Group VI (10.0 - 13.1 years of age). A slight decline in the incidence of mineralized excrescences was observed in the latter age group.

The mineralized excrescences were irregularly spaced along the posterior surface of the cornea and were firmly attached to this surface by mineralized areas extending from Descemet's membrane into the excrescence (Figures 17, 21). Frequently, the mineralized area of attachment in Descemet's membrane also extended into the substantia propria.

The excrescences were positively stained for mineral salts with the alizarin red S (Figure 21) and Von Kossa (Figure 17) staining techniques and for acid mucopolysaccharides with the colloidal iron technique of Rinehart and Abul-Haj (Figure 22). In hematoxylin and eosin stained sections the excrescences stained basophilic (Figure 23).

The mineralized excrescences were variable in size, and the extent of protrusion into the anterior chamber was difficult to measure accurately due to shattering of the summit of the excrescence by the sectioning process. However, it was possible to approximate the extent of protrusion by the width of the attachment area on Descemet's membrane and by the amount of shattered mineralized material in the anterior chamber. Attachment areas in Descemet's membrane ranged in width from 10 to 80 microns. In the typical excrescence, the extent of protrusion into the anterior chamber was estimated to be nearly equal to the width of the excrescence at the attachment area. A few excrescences were attached to Descemet's membrane by narrow, pedunculated basal stalks which were surmounted by larger mineralized summits. Generally, the size and the number of excrescences were increased

with age. In the older dogs it was not uncommon to find mineralized excrescences scattered along the entire posterior surface of the cornea.

Hog The manifestations and the staining characteristics of corneal mineralization were similar in the dog and hog (Figures 17-28). The total incidence of corneal mineralization in the two species was relatively comparable except in the focal and excrescent forms of extracellular mineralization (Tables 3, 4).

The incidence (Table 4) of intracellular mineralization of the stromal, endothelial, and epithelial cells and diffuse extracellular mineralization of the substantia propria was extremely high in hogs up to one year of age (Age Groups I and II, 0.1 - 11.9 months of age). The incidence of each of these types of corneal mineralization was reduced in Age Group III (1.2 - 2.9 years of age) and remained relatively constant in Age Groups IV and V (3.1 - 8.0 years of age). The intensity of intracellular mineralization was usually proportional to the incidence of the more advanced forms of extracellular mineralization; e. g., focal mineralization and mineralized excrescences.

The total incidence of focal mineralization was greater in the hog than in the dog (Tables 3, 4). Focal mineralization in the hog was characterized by the presence of irregular foci of dense

mineral deposition in the anterior one-third of the substantia propria (Figure 26). Usually, these foci were adjacent to areas of intense intracellular mineralization or focal mineralized lesions in the corneal epithelium (Figure 27).

Mineralized excrescences on the posterior surface of the cornea were observed in only one hog (Hog No. 9310, 5.9 months of age) in Age Group I (0.1 - 6.0 months of age). The incidence of mineralized excrescences was markedly increased in Age Group II and remained at a nearly constant percentage level in the subsequent older age groups (Table 4). The incidence of mineralized excrescences was not as great in the hog as in the dog (Tables 3, 4). Generally, the size and extent of distribution of excrescences on the posterior surface of the cornea were not as extensive in the hog as in the dog.

Acid mucopolysaccharides

Dog Acid mucopolysaccharides were found to be a constant structural component of the cornea in dogs of all ages. An age-related increase or decrease in this basic component of the intercellular ground substance was not evident.

In sections stained with the colloidal iron technique of Rinehart and Abul-Haj, acid mucopolysaccharides were stained light to dark blue (Figures 4, 22, 28, 29). In the cornea acid mucopolysaccharides were found almost exclusively in the substantia propria. In

areas of the substantia propria where the lamellae were contiguous, mucopolysaccharides were almost imperceptible. However, close observation revealed that the stromal lamellae and the stromal cells were delicately embedded in a matrix of acid mucopolysaccharides.

Acid mucopolysaccharides were as a rule more distinctly visible in certain areas of the substantia propria than in others. These areas included: the posterior one-half of the limbal region, the area adjacent to the corneal epithelium, and the area immediately anterior to Descemet's membrane. In these areas the stromal lamellae were often noticably separated, and the mucopolysaccharides appeared distended and formed a lattice-like network within the enlarged interstitial space (Figure 29). Acid mucopolysaccharides were also distinctly visible and appeared to be concentrated in the sites of corneal mineralization (Figure 28).

Hog Acid mucopolysaccharides were found to be a constant structural component of the cornea in hogs of all ages. The location of specific areas in the substantia propria, in which mucopolysaccharides were more distinctly visible than in others, was similar to the pattern of distribution in the dog. However, in the hog acid mucopolysaccharides were generally more diffusely

spread throughout the substantia propria and stained more intensely with the colloidal iron technique (Figure 30).

In the substantia propria, acid mucopolysaccharides were particularly prominent in and adjacent to areas of focal mineralization, and adjoining mineralized excrescences on the posterior surface of the cornea.

Sclera

Statistical evaluation of dimensional change with age

Thickness of the sclera at the corneoscleral junction

Dog The thickness of the sclera measured at the corneoscleral junction in 46 dogs in the Maturation Age Group (0.1 - 13.0 months) increased with age. The increase in thickness was curvilinear in relation to age and the regression coefficients were significant (Graph 17). Thickness increased during the maturation age period from 0.316 mm. in the one-day old puppy to a maximum of 0.948 mm. at 10 months of age.

In 32 dogs in the Postmaturation Age Group (1.5 - 13.1 years) thickness increased slightly with age but was not statistically significant (Graph 18). The increase in thickness ranged from 0.883 mm. at 1.5 years to 0.957 mm. at 13.1 years of age.

Hog The thickness of the sclera at the corneoscleral junction measured in 22 hogs in the Maturation Age Group (0.1 - 12.0 months) increased linearly with age (Graph 19). The regression coefficient was significant. The slope of the regression line indicated the thickness to be 0.911 mm. in the three-day old hog and 1.419 mm. in the 12-month old hog. The increase in thickness was at the rate of 0.042 mm. per month. The correlation between scleral thickness at this site and age was significant.

In 86 hogs in the Postmaturation Age Group (1.2 - 8.0 years), the thickness of the sclera at the corneoscleral junction was curvilinear in relation to age (Graph 20). The thickness, as indicated by the regression line, was 1.179 mm. at 1.2 years, 1.458 mm. at 5.0 years, and 1.273 mm. at 8.0 years of age. The mean scleral thickness for this age group was 1.341 mm.

Scleral thickness at the geometric axis of the bulbus oculi

Dog Scleral thickness in the Maturation Age Group at this site increased curvilinearly with age and the regression coefficients were significant (Graph 17). Scleral thickness at the geometric axis of the bulbus oculi was 0.163 mm. at 0.1 month, 0.433 mm. at 9.0 months, and 0.399 mm. at 13.0 months of age.

There was no significant change in the thickness of the sclera at the geometric axis of the bulbus oculi in the Postmaturation Age Group (Graph 18).

Hog A significant curvilinear relationship existed between scleral thickness dependent upon age in the Maturation Age Group (Graph 19). The thickness of the sclera, as represented by the regression curve, was 0.581 mm. in the three-day old pig and increased to a maximum thickness of 1.375 mm. at eight months of age. Between eight and twelve months of age scleral thickness decreased to 1.191 mm.

During the postmaturation period, scleral thickness increased from 1.293 mm. at 1.2 years to 1.472 mm. at 5.0 years and then decreased to 0.966 mm. at 8.0 years of age. The regression coefficients for the curvilinear relationship between scleral thickness and age were significant (Graph 20).

Scleral thickness at the equator of the bulbus oculi

Dog The equatorial thickness of the sclera increased linearly with age from 0.126 mm. in the one-day old puppy to 0.208 mm. at 13 months of age (Graph 17). The linear increase in thickness was at the rate of 0.006 mm. per month, and the regression

coefficient was significant. The average thickness of the equatorial segment of the sclera in the 46 dogs in the Maturation Age Group was 0.173 mm.

There was no significant change in the thickness of the equatorial sclera in the Postmaturation Age Group (Graph 18). The mean thickness of the sclera at this site in the 32 dogs in this age group was 0.166 mm.

Hog In the Maturation Age Group, the equatorial thickness of the sclera was curvilinear with respect to age (Graph 19). The equatorial thickness of the sclera increased from 0.041 mm. at 0.1 month, to 0.390 mm. at nine months of age, then regressed to 0.340 mm. at 12.0 months of age.

A significant curvilinear relationship existed between equatorial thickness and age in the Postmaturation Age Group (Graph 20). During the period from 1.2 years to 4.0 years of age, the equatorial thickness increased from 0.377 mm. to 0.573 mm. and then decreased to a thickness of 0.349 mm. at eight years of age.

Histological and histochemical evaluation of age changes

Maturation changes

Dog The histological appearance of the sclera in the one-day old puppy was characterized by the presence of numerous, pleomorphic fibroblasts which were dispersed diffusely throughout

the scleral stroma. Scleral fibers were thin (approximately two microns in thickness) and fibrils were not visible with the resolution afforded by the light microscope. A moderate number of pigmented cells were observed throughout the scleral stroma and were most notably present in the vicinity of the choroid.

By two weeks of age the pleomorphic fibroblasts were greatly reduced in number, and the morphology of the cellular elements of the sclera was generally typical of the mature fibrocyte. Scleral fibers were moderately increased in number but only slightly increased in thickness.

By 2.5 months of age the sclera was essentially mature in histological appearance. At this age scleral fibers were noticeably increased in number and thickness, fibrils were visible in the individual stromal fibers, and elastic fibers were observed adjacent to and paralleling the course of the fibers.

The thickness of scleral fibers was found to increase progressively with age (Table 5). Also with increased age the fibrillar nature of the scleral fibers was more distinct, and elastic fibers were more abundant.

Scleral pigmentation was increased with age but appeared to be related to the degree of pigmentation in the uveal tract. Prominent pigment accumulations were observed only in the region of the

corneoscleral junction, and these accumulations were not prominent until approximately six months of age. Prominent accumulation of pigment was noted at the corneoscleral junction in 79.1 per cent of the dogs (Table 5).

Hog Numerous fibroblastic cells were observed in the sclera of the neonatal pig. However, in comparison with the dog fibrocytic cells were more mature in the hog at this age level. In the three-day old pig the mean thickness of ten randomly selected scleral fibers was 2.8 microns.

By 2.17 months of age the cellularity of the sclera was markedly reduced, and all fibrocytic cells were essentially mature in appearance. Scleral fibers were increased in number and in thickness, the fibrillar nature of the individual fibers was ascertainable, and thin elastic fibers were present throughout the scleral stroma. In essence, at approximately two months of age, or possibly earlier since specimens were not available for histological examination between three days and 2.1 months of age, the sclera was mature in histological appearance.

In pigs younger than six months of age, pigmentation was not pronounced in the sclera, except in the region of the corneoscleral junction. In the latter region slight pigmentation was found in 50 per cent of the pigs between the age of 0.1 month and 6.0 months

(Table 6). In hogs over six months of age, pigmentation of the total sclera was increased, but generally was not as extensive as in the dog, except in the region of the corneoscleral junction.

The thickness of individual scleral fibers was found to increase with age in the hog (Table 6).

Vascular changes

Dog The endothelial cells of the scleral venous plexus (Plexus venosus sclerae) were found to be a frequent site of intracellular deposition of mineral salts in all age groups (Table 5). In the early stages of intracellular mineral accumulation the cell outline and nucleus were distinguishable (Figure 31). With increased mineralization within the cell, cellular hypertrophy occurred and resulted in the formation of mineralized plaques which protruded into the lumen of the vessel (Figure 32). Frequently, a large portion of the vessel wall was mineralized, and the mineralized area extended into the adjacent scleral stroma.

Although mild intracellular mineralization was occasionally noted in the arterial endothelium, mineralized plaques of the arterial wall were rarely observed.

Intrascleral segments of the long posterior ciliary artery (Aa. ciliares posteriores longae) and its branches, the retinal (Aa. retinae) and short posterior ciliary arteries (Aa. ciliares

posteriores brevis), and the anterior ciliary artery (Aa. ciliares anteriores) were examined for possible histological alterations attendant with aging. In these arteries, spontaneous intimal and medial sclerosis were observed, and the incidence of each type of sclerosis was found to increase with age (Table 5).

In general, intimal sclerosis was the predominant type of spontaneous arteriosclerosis in dogs up to six years of age and was observed in one dog (Dog No. 072, Age Group I) 2.6 months of age. In dogs older than six years of age intimal and medial sclerosis were coexistant, and the percentage incidence of the two types was equal (Table 5).

In dogs in Age Groups I, II, and III (0.1 - 12.9 months of age) spontaneous intimal sclerosis was characterized by the presence of from one to three nodular plaques located around the circumference of the internal vascular wall (Figures 33, 34). The internal elastic membrane beneath the plaques was consistently fragmented or disrupted. Between plaques the internal elastic membrane was usually thickened but not disrupted. Typical components of the plaques consisted of elongated, spindle-shaped cells which appeared similar to smooth muscle cells or fibroblasts. There was little evidence of fibrotic changes in the early plaques. However, in sections stained with the colloidal iron technique of Rinehart and

Abul-Haj, acid mucopolysaccharides were clearly visible (Figure 34). The areas of blue staining matrix, indicative of acid mucopolysaccharides, were particularly evident around the cellular elements of the plaque. Fine granular deposits of mineral salts were occasionally noted in the intimal plaques of dogs in Age Group III (11.0 - 12.9 months of age). Lipid deposition was not observed in the intimal plaques of dogs in the three younger age groups. The tunica media of dogs in these age groups was essentially normal.

In dogs in Age Groups IV and V (1.5 - 9.9 years of age), nodular intimal plaques were more numerous than in the younger age groups (Figures 35-38). Reduplication and fragmentation of the internal elastic membrane was more pronounced than in dogs in the younger age groups, and the invasive cellular elements observed in the nodular plaques of younger dogs tended to be gradually replaced by fibrous connective tissue and/or by fragments of fine elastic fibers. With the appearance of collagenous fibers in the plaques, acid mucopolysaccharides tended to be diminished.

In dogs over ten years of age (Age Group VI, 10.0 - 13.1 years of age), the individual plaques appeared to coalesce and to form more uniform intimal thickenings which involved extensive portions of the internal vascular wall (Figures 39-42). Mineralization of the plaques was more frequently observed in dogs in this age group

and appeared usually in a coarse granular form scattered throughout the enlarged plaque (Figure 41). In frozen sections stained with oil red O, intimal plaques in the dogs over ten years of age were found to occasionally contain lipids in the form of densely stained globules or as lightly stained diffuse permeations of the entire plaque (Figure 43).

Although the incidence (Table 5) was not pronounced in dogs younger than six years of age (Age Groups I - IV), spontaneous medial sclerosis was observed in three dogs younger than six years of age, and was particularly evident in one dog (Dog No. B65, Age Group III) 3.6 years of age. The incidence (Table 5) of spontaneous medial sclerosis was increased in Age Groups V and VI (6.0 - 13.1 years), and was comparable to the incidence of intimal sclerosis in these age groups.

Spontaneous medial sclerosis of the intrascleral arteries was characterized by thickening of the tunica media. The medial thickening was produced largely by the progressive accumulation of an abundance of collagenous fibers and proliferations of smooth muscle cells (Figures 39, 40). Other contributing factors to the increased thickness were depositions of mineral salts and occasionally lipids.

Generally, in cross sections of the artery, the collagenous fibers were circularly arranged around the media. However, dense bundles of collagenous fibers were observed which surrounded individual smooth muscle cells or groups of smooth muscle cells. Smooth muscle cells within these "collagenous nests" appeared to be in varying stages of degeneration (Figure 40). "Collagenous nests" were most conspicuous near the periphery of the media, but were also evident, to a lesser degree, in the central portions of the media.

Mineral deposits were found in the form of coarse granules dispersed irregularly throughout the media or as small focal areas of more dense mineralization (Figure 41). Ossification was not found in any vessel. Acid mucopolysaccharides were present in varying degrees throughout the media and were most notable in the areas containing mineralized deposits (Figures 41, 42).

Hog In the portion of the sclera adjacent to the ciliary body, a prominent scleral venous plexus was not observed in the hog as in the dog. In the hog small veins were found in the sclera near the anterior chamber angle (Spatia anguli iridocornealis) and adjacent to the bulbar conjunctiva. The process of intracellular mineralization of the endothelial cell and subsequent plaquation of the walls of these vessels was similar to the process described in the scleral venous plexus in the dog. However, mineralized nodules

extending into the venous lumen or involving the adjacent scleral stroma were not as extensive in the hog as in the dog. However, within age group comparisons of the incidence of endothelial mineralization and mural plaquation were comparable in both species (Tables 5, 6).

Intrascleral segments of the long posterior ciliary and the anterior ciliary artery, and their branches were observed for histological and histochemical alteration attendant with aging. Spontaneous intimal and medial sclerosis were observed in these arteries, and the incidence of each type of vascular alteration in the various age groups was presented in tabular form (Table 6).

Alteration in the vascular structure was not apparent in hogs in the two youngest age groups (Age Groups I, II, 0.1 - 11.9 months of age). However, in Age Groups III, IV, and V (1.2 - 8.0 years of age) the incidence of spontaneous intimal and medial sclerosis was increased with age (Table 6).

As in the dog, reduplication, splitting, and fragmentation of the internal elastic membrane were characteristic features of spontaneous intimal sclerosis in the hog (Figures 44-47). In newly formed plaques spindle-shaped cells appeared to pass from the tunica media through the interrupted internal elastic membrane (Figure 44). Upon entering the subendothelial layer the cellular

elements tended to advance circumferentially beneath the endothelium and to form elongated, crescentric-shaped intimal plaques (Figures 45, 46). The invasive cellular elements were subsequently gradually replaced to a large extent by collagenous fibers. Mucopolysaccharides were obvious in the newly formed plaques but were diminished with the appearance of collagenous fibers. Moderate amounts of diffuse mineral deposits were observed in the plaques, but lipid infiltration was rarely observed in the early plaques.

Intimal plaques observed in hogs in the older age groups (Age Groups IV and V, 3.1 - 8.0 years of age) were frequently extensive, were typically crescentric in shape, and produced considerable narrowing of the lumen (Figure 46). Histologically, intimal plaques in these age groups were characterized by a predominance of collagenous fibers and a reduced number of cellular components (Figure 46). Acid mucopolysaccharides were demonstrable in intimal plaques in sections stained with the colloidal iron technique of Rinehart and Abul-Haj (Figure 47).

Spontaneous medial sclerosis was noted in varying degrees in the three older age groups (Age Groups III, V, 1.2 - 8.0 years of age). Thickening of the tunica media as a result of fibrosis and proliferation of smooth muscle cells was not as marked in the hog as in the dog. "Collagenous nests" as described in the dog, were

not observed in the hog. Coarse granules of mineral deposits and small focal areas of mineralization as well as diffuse lipid infiltration were occasionally observed in the tunica media of the hog. Ossification was not found in the tunica intima or media of any hog.

Lipid deposition

Dog The percentage incidence of lipid deposition was determined for each age group in three segments of the sclera, and the results were presented in tabular form (Table 5). The segments of the sclera included in this comparison were the segment adjacent to the ciliary body, the equatorial segment, and the posterior segment.

The incidence and intensity of lipid deposition were progressively increased with age. The increase in intensity was particularly marked in the posterior and equatorial segments. In these segments, fatty infiltration appeared initially in the scleral fibers adjoining the choroid. With subsequent increase in infiltration, lipid deposition progressively spread toward the peripheral fibers of the sclera. In older animals, lipid deposition was frequently observed throughout the entire thickness of the sclera. In such cases, the intensity of deposition was consistently greater in scleral fibers near the choroid.

In the segment of the sclera adjacent to the ciliary body, lipid infiltration was usually less intense than in the equatorial and posterior segments. In the ciliary segment of the sclera, a proclivity was observed for deposition in the scleral fibers near the scleral venous plexus.

In sections stained with oil red O, lipid infiltrates appeared light red in slight to moderate infiltrations and deep red in the heavier infiltrations (Figures 48-50). In heavy infiltrations the scleral fibers appeared to be homogeneously saturated with the stained lipids. Atheromatous thickening of the intimal lining of the large scleral veins was occasionally observed in cases of heavy lipid deposits in the scleral fibers (Figure 49).

Hog The incidence of lipid deposition in the sclera of the hog was slight in all age groups (Table 6). The youngest hog in which scleral lipid deposition was found was 2.8 years of age (Hog No. 3196, Age Group III). Lipid infiltration of the sclera in this hog was noted only in the ciliary segment and consisted of a very mild, diffuse permeation of the scleral fibers adjacent to the ciliary body.

Mild lipid infiltration was present in all three segments of the sclera in two hogs (Hog Nos. 190-10 and 392) in Age Group IV (3.1 - 5.9 years of age). Lipid infiltration of the sclera was observed

in only two hogs in Age Group V (6.0 - 8.0 years of age). In one of these hogs (Hog No. 221, 6.4 years of age) there was mild lipid permeation of the scleral fibers in only the posterior segment of the sclera. In the other hog (Hog No. 13-258, 8.0 years of age), mild lipid permeation of the scleral fibers was seen throughout the ciliary segment and to a lesser degree in the posterior segment of the sclera.

Extensive accumulations of globular fat were seen in the majority of hogs in the interstitial spaces of the sclera in the proximity of the optic nerve. In all cases, these extensive accumulations in the interstitial spaces of the sclera were adjacent to massive collections of extraocular fat cells. These extensive interstitial lipid accumulations appeared to originate from extraocular lipid cells and were not included in the calculation of the percentage incidence of lipids in the posterior segment of the sclera.

Mineralization

Dog Mineralization of the sclera was characterized by varying degrees of intracellular, diffuse extracellular, and dense focal deposition of mineral salts in the scleral tissues. In each age group, the percentage incidence of these various forms of mineralization was determined for the same segments of the sclera

which were evaluated for lipid deposition, and the results were presented in tabular form (Table 5).

Intracellular deposition (Figures 31, 32) was noted in the fibrocytic cells of all segments of the sclera, and in the endothelial cells of the scleral venous plexus and vortices veins. The total incidence (Table 5) of intracellular mineralization was greatest in the ciliary segment of the sclera. This trend was particularly noticeable in Age Group I (0.1 - 4.0 months of age). The intensity of intracellular deposition was slight to moderate in Age Groups I and II (0.1 - 9.9 months of age) and was increased markedly in subsequent age groups.

Diffuse extracellular mineralization was manifested by a diffuse permeation of the scleral fibers with granular deposits of mineral salts (Figure 51). The incidence of this form of mineralization was generally found to increase with age, although a slight decrease in incidence was noted in Age Group VI (10.0 - 13.1 years of age) in the ciliary and posterior scleral segments (Table 5). In the segment adjacent to the ciliary body mineral granules were diffusely spread throughout the sclera. In the equatorial and posterior segments, depositions tended to be concentrated near the choroid in the case of slight to moderate extracellular

mineralization (Figure 52). In the case of extensive mineralization in these two segments, extracellular depositions were more uniformly dispersed throughout the scleral stroma.

The incidence of focal mineralization in the sclera was variable in the six age groups. Despite the great variability, certain salient features characterized the incidence of focal mineralization in the sclera. These features included: a high incidence in Age Groups I, II, and III (0.1 - 12.9 months of age), maximum incidence in Age Groups IV and V (1.5 - 9.9 years of age), and a marked decrease in incidence in Age Group VI (10.0 - 13.1 years of age).

Dense foci of scleral mineralization were observed in one dog (Dog No. B50, Age Group I) 0.5 months of age. These foci were found in areas of the sclera adjacent to the cornea, the ciliary body, and the optic nerve. In the latter area, mineralization extended into the peripheral portion of the optic nerve. Extensive foci of mineralization were occasionally observed near the scleral insertion of the lateral and medial recti muscles.

In comparison, foci of mineralization were generally larger in the sclera than in the cornea. The staining properties of all forms of mineralization were similar in the sclera and in the cornea. Ossification was not observed in either the sclera or the cornea.

Hog The process of mineralization in the hog included the three forms of deposition observed in the dog; e. g., intracellular, diffuse extracellular, and focal mineralization. No difference was noted in the staining characteristics of mineral deposits in either species.

In general, the incidence of all forms of mineralization was greater in all scleral segments of the hog than in the dog (Tables 5, 6). The intensity of mineralization was also usually greater in the hog.

The greater incidence (Table 6) in the hog was especially evident in the equatorial segment of the youngest age group of hogs (Age Group I, 0.1 - 6.0 months of age). Areas of prolific focal and dense extracellular mineralization were observed in the equatorial segment at the point of insertion of the lateral and medial recti muscles in approximately 23 per cent of the hogs.

Iris

Statistical evaluation of dimensional change with age

Basal thickness

Dog The basal thickness of the iris was curvilinear in relation to age in the Maturation Age Group. The curvilinear increase

in thickness ranged from 0.082 mm. in the one-day old puppy to a maximum thickness of 0.237 mm. at nine months of age (Graph 21).

In the Postmaturation Age Group the basal thickness increased linearly with age (Graph 22). The linear increase in thickness was in yearly increments of 0.011 mm. and the regression coefficient was significant. At 13.1 years, the slope of the regression line indicated the basal thickness to be 0.304 mm.

Hog In the Maturation Age Group, the thickness of the basal portion of the iris was curvilinear with regard to age (Graph 23). Basal thickness of the iris increased from 0.192 mm. at 0.1 month of age to a maximum thickness of 0.456 mm. at 7.0 months of age.

From 1.2 years to 8.0 years of age there was a nonsignificant linear decrease in the basal thickness of the iris from 0.451 mm. to 0.384 mm. (Graph 24). The average basal thickness in the 86 hogs in the Postmaturation Age Group was 0.418 mm.

Central thickness

Dog In the Maturation Age Group, the central thickness of the iris was curvilinear with respect to age (Graph 21). Curvilinear increase with age ranged from 0.147 mm. at 0.1 month of age to a maximum thickness of 0.476 mm. at nine months of age.

Seventy-eight per cent of the increase in thickness occurred during the first five months of life.

In the Postmaturation Age Group, the central iridal thickness increased linearly with age, in yearly increments of 0.020 mm. The increase ranged from 0.386 mm. at 1.5 years to 0.616 mm. at 13.1 years of age. The regression coefficient and the correlation between age and the central iridal thickness were significant (Graph 22).

Hog A slight linear decline was noted in the central thickness of the iris during the first 12 months of life, but the regression coefficient was not statistically significant (Graph 23). The slope of the regression line revealed that the central thickness of the iris was dimensionally mature in the three-day old pig. The average central thickness for the 22 hogs in the Maturation Age Group was 0.610 mm.

The central iridal thickness increased linearly with age in the Postmaturation Age Group, and the regression coefficient was significant (Graph 24). The increase ranged from 0.569 mm. at 1.2 years to 0.833 mm. at 8.0 years of age. Increase in this dimension was at the rate of 0.038 mm. per year, and the correlation between central thickness and age was significant.

Histological and histochemical changes with age

Maturation changes

Dog In the one-day old dog, the iris was not completely separated from the posterior surface of the cornea (Figures 3, 4). Its appearance at this age was characterized by the presence of a large number of primitive mesenchymal cells dispersed throughout a faintly visible fibrous stroma. Thin-walled arteries and veins in the stroma were quite prominent, with the latter being particularly large and conspicuous. Both the dilator (M. dilator pupillae) and sphincter muscles (M. sphincter pupillae) were discernible. Pigmentation was extensive along the posterior border of the iris and obscured the superficial epithelium at this site. Melanocytes were scattered throughout the fibrous stroma, but their pigment content was not extensive.

By two weeks of age the iris was completely detached from the cornea. Primitive mesenchymal cells were reduced in number, and the fibrous nature, characteristic of the mature iris, was apparent. Melanocytes were larger, contained more melanin granules, and were more diffusely distributed in the stroma. Due to the increase in fibrous and pigmentary elements, the iridal vasculature was less conspicuous.

By one month of age, the surface of the extensive, continuous layer of pigment cells on the posterior surface of the iris assumed an undulating or fluted appearance. At this age the iris contained all the cytological elements and the structural features normally associated with the mature iris.

Hog In the three-day old pig the iris and cornea were completely separated and formed an "open" anterior chamber angle (Spatia anguli iridocornealis). Collagenous fibers were dispersed moderately throughout the stroma in a dense ground substance which stained positively for acid mucopolysaccharides. Stromal cells were slightly larger than in the more mature iris. Extensive vascularization was clearly visible, and the fibrous elements and mucopolysaccharides tended to accumulate around the arteries and to a lesser extent the veins. The sphincter muscle was prominent, but a well defined dilator muscle was not discernible. Pigmentation was extensive along the posterior border and a moderate number of tenuous melanocytes were observed in the iridal stroma.

At nine weeks of age the iris contained all the cellular and structural features of the mature iris. Fibrous connective tissue was increased in the stroma and around the vessels. A thick fibrous tunica adventitia was found to be characteristic for the hog. Pigmentation was increased in the posterior pigment epithelial

cells and in the stromal melanocytes. At this age the dilator muscle was discernible.

Lipid deposition

Dog The incidence of lipid deposition in the iris of the dog was negligible (Table 7). Lipid deposition was not found in the iris of dogs in any age group prior to Age Group V. In Age Group V, lipoidal infiltration was observed in one dog (Dog No. M51, 9.3 years of age), and in two dogs (Dog No. M49, 10.3 years of age; Dog No. M38, 10.4 years of age) in Age Group VI.

In all cases lipoidal infiltration was limited to the dense fibropigmentous connective tissue posterior to the central annulus of blood vessels (Circulus arteriosus iridis minor) (Figure 55). Small lipid droplets were observed in the intima and media of one artery near the central annulus of vessels in Dog Number M49.

Hog Lipid deposition was not found in the iris of any hog utilized in this investigation.

Mineralization

Dog Mineralization of the iris was observed in three distinct forms: 1) intracellular accumulation in the anterior (Endothelium camerae anterioris) and posterior (Pars iridica retinae) epithelial layers; 2) hypertrophy and hyperplasia of the mineralized

epithelia with subsequent formation of small nodular excrescences on the surface of the iris; and 3) multiple focal depositions of minerals in the iridal stroma.

Due to excessive fragmentation in a large number of mineralized irides, accurate evaluation of the percentage incidence of each form of mineralization was considered unfeasible. Therefore, the presence of any of the aforementioned forms in an individual specimen was considered indicative of iridal mineralization. Utilizing this criteria for calculating the percentage incidence, a high incidence of mineralization of the iris was found in all age groups (Table 7).

Intracellular accumulation of mineral salts in the epithelia was most prominent in Age Groups I and II (0.1 - 9.9 months of age). In the neonatal puppy extensive diffuse accumulation was noted along the line of fusion of the unseparated iris and cornea. Slight to moderate hypertrophy and hyperplasia of the mineralized epithelia followed by the formation of small surface excrescences were observed in dogs in Age Group II (5.4 - 9.9 months of age). These changes were accentuated and more extensive in dogs in Age Groups III and IV (11.0 months - 4.4 years of age). The mineralized surface excrescences did not attain the size nor were they as

numerous as similar appearing excrescences found on the posterior surface of the cornea.

Multiple focal deposits were the typical manifestation of iridal mineralization (Figure 61) in the two older age groups (Age Groups V, VI, 6.0 - 13.1 years of age). These deposits were usually sparsely distributed in the stroma and a predilection for a specific site of deposition was not observed.

Variations were observed in the typical manifestations of iridal mineralization as described for each age group as age groups.

Hog The three forms of mineralization observed in the iris of the dog were also found in the hog, and the total incidence of mineralization was approximately equal in both species (Tables 7, 8).

Intracellular mineralization of the epithelia followed by the formation of surface excrescences was not observed as frequently in the younger hogs as in the younger dogs. In the hog mineralization was typified by multiple focal mineral deposits in the stroma. The focal deposits usually ranged from 15 - 30 microns in size, but occasionally focal aggregates were found which measured up to 100 microns at their greatest dimension.

Fibrous and pigmentary changes

Dog Fibrous and pigmentary tissue elements initially observed in the iris of the one-day old dog were found to increase progressively with age. The progressive increase in these two tissue elements led to an increased density or sclerosis of the iridal stroma as age advanced.

In the posterior one-half of the iris, between the central annulus of blood vessels and the dilator muscle, an increase in both the fibrous and pigmentary tissue was noted (Figure 53). In this area, elongated, branching melanocytes were copiously interspersed in the stromal connective tissue and appeared to partially separate the latter tissue into fibrous bundles. In the anterior one-half of the iris, pigment proliferation was quite extensive and markedly increased the total thickness of the iris (Figure 54). Extensive fibrous proliferation in the anterior one-half of the iris was frequently evident in dogs in Age Groups V and VI (Table 7). These extensive proliferations tended to flatten the surface of the iris and to obliterate the iridal crypts. Consequently, the iris appeared more oval and less elongated in the aged dog (Figure 54).

Also with increased age fibrous and pigment tissue were observed to concentrate around the iridal vasculature. Other areas of extensive fibrous concentration were observed at the apex and

base of the iris. At the apex fibrous proliferations were noted between the sphincter muscle and the posterior border. Occasionally, in the basal area fibrous proliferations extended into the ciliary body and the ciliary processes.

In the two older age groups (Age Groups V, VI) hyperplasia of the pigment epithelium was frequently observed. The hyperplastic cells characteristically formed knob-like projections which protruded into the posterior chamber of the eye (Camera posterior bulbi) (Figure 54). Cystic spaces were also observed on the posterior surface of the iris as a result of hyperplasia of the pigment epithelium.

Hog The increase in size and density of the iris of the hog was primarily due to a progressive increase with age in the fibrous elements of the stroma. The addition of collagenous fibers was observed throughout the entire stroma but was particularly evident around the vasculature and in the area between the sphincter muscle and the posterior border of the iris. As fibrosis increased, a corresponding decrease was observed in the acid mucopoly-saccharides of the iridal ground substance.

Melanocytes, initially observed in the iridal stroma in the neonatal pig, were increased slightly during the first six months of life (Age Group I, 0.1 - 6.0 months of age). This increase occurred

primarily in the anterior portion of the iris, where the light-brown pigment bearing cells were small and pleomorphic. In the central region of the iridal stroma the melanocytes were not substantially increased in number. Those melanocytes present in this region were predominantly narrow and elongated. Generally, only a modest increase was noted in stromal pigmentation in subsequent age groups.

An increase with age was observed in pigmentation on the posterior border of the iris. This increase was characterized in Age Group II (6.2 - 11.9 months of age) by hypertrophy of the pigment epithelial cell followed by the formation of pigmented nodules which projected into the posterior chamber. In Age Groups III - V (3.1 - 8.0 years of age) hyperplasia of the pigment epithelial cell produced elongated pigment projections; portions of which were often extruded into the posterior chamber. In these age groups pigmentary debris was frequently found on the anterior surface of the lens, the posterior surface of the cornea, and in the anterior chamber of the eye.

Muscular changes

Dog The incidence of muscular atrophy of both the dilator and sphincter muscles of the iris was found to increase with age (Table 7). The incidence of senile atrophy of the sphincter

muscle was noticeably greater. The intensity of atrophic changes in the two muscles was generally increased with age.

Fibrous connective tissue, between the posterior apical border of the iris and the sphincter muscle, was typically increased in cases of sphincter muscle atrophy. Fibrous strands extending from the area of fibrous proliferation as well as pigmentary deposits tended to separate the muscle tissue into atrophic muscular bundles.

Atrophy of the dilator muscle was more difficult to detect due to the extensive pigmentation on the posterior border of the iris. Disruption of this muscle by these pigmentary elements was observed, as well as an increased amount of collagenous fibers within the muscular tissue.

In sharp contrast to atrophy of the dilator muscle, hypertrophy of this muscle was observed in a moderate number of dogs in Age Groups V and VI (Table 7). As compared to a thickness of approximately ten microns in the normal muscle, the increase in thickness attendant with hypertrophy of the dilator muscle ranged from 40 - 60 microns. Hypertrophy of the dilator muscle was characterized by a reduction in muscle nuclei, slight to moderate invasion by pigment granules and collagenous fibers, and a hyalinized appearance (Figure 54).

Hog Atrophy of the dilator muscle was initially observed in hogs in Age Group II (6.2 - 11.9 months of age). Atrophy in hogs in this age group was slight and restricted to areas adjacent to hypertrophic pigment epithelial cells. The incidence (Table 8) was markedly increased in Age Groups III - V (3.1 - 8.0 years of age), and the degree of atrophy was variable in each of these age groups. Atrophy varied from segmental atrophy, principally, beneath hypertrophic and hyperplastic pigment epithelial cells, to almost a total absence of the muscle in a few specimens. Invasion of the muscular tissue by small pigment granules was a characteristic feature of dilator muscle atrophy.

Hypertrophy of the dilator muscle was found in a small percentage (Table 8) of the hogs in Age Group II (6.2 - 11.9 months of age). The percentage incidence remained uniform in Age Groups II - IV (6.2 months to 5.9 years of age) but increased slightly in Age Group V (6.0 - 8.0 years of age). The severity of sphincter muscle atrophy increased with age in proportion to the extent of fibrosis. Invasion of the muscular bundles by pigmentary elements was not excessive in any age group.

Vascular changes

Dog The walls of the iridal arteries were found to be generally thicker, and were encircled by a denser tunica adventitia than arteries in other portions of the eye.

Medial thickening of the arteries of the iris was noticed initially in dogs approximately one year of age (Age Group III, 11.0 - 12.9 months of age). A slight increase in the cellularity of the media was observed, and fine collagenous fibers were faintly perceptible throughout the media. Invariably, the arteries were surrounded by varying degrees of pigment accumulation and dense fibrous connective tissue. Alteration in the intima of the vessels was not observed, nor was the caliber of the vascular lumen noticeably decreased.

The incidence of medial thickening was increased in the subsequent age groups (Table 7). In Age Group VI (10.0 - 13.1 years of age) medial thickening in some degree was observed in all dogs (Table 7). Medial thickening in this age group was characterized predominantly by an increase in collagenous fibers and to a lesser extent by hypertrophy of the smooth muscle cell. Fibro-cellular intimal plaques accompanied by interruption of the internal elastic membrane were observed occasionally in the larger iridal arteries. The size of these plaques was not extensive and did not appreciably alter the

caliber of the lumen. In a few smaller arterioles fibrous medial thickening was observed to occlude the lumen.

Hog An extensive fibrous tunica adventitia surrounded all iridal vessels in the hog. In the arterioles the thickness of the adventitia was typically two to three times the diameter of the other portions of the vessel. In the larger arteries and veins the relative thickness was not as great. The thickness of the tunica adventitia was observed to increase with age and was proportional to the general increase in iridal fibrosis.

Well defined intimal sclerosis was found in the iris of only one hog (Hog No. 190-10, 4.5 years of age). Fragmentation of the internal elastic membrane and subendothelial accumulation of cellular and fibrous elements were observed in this specimen.

Medial sclerosis was not observed in Age Groups I and II (0.1 - 11.9 months of age), but the incidence (Table 8) progressively increased in Age Groups III - V (1.2 - 8.0 years of age). Medial thickening was not marked in any age group and was characterized by a moderate proliferation of smooth muscle cells and an increase in collagenous fibers.

Ciliary Body

Statistical evaluation of dimensional change with age

Thickness of the basal lamina of the corona ciliaris

Dog The basal lamina (Lamina basalis) of the ciliary crown (Corona ciliaris) measured in the proximity of the anterior chamber angle of the eye (Spatia anguli iridocornealis) increased in thickness from 0.155 mm. in the one-day old puppy to 0.430 mm. at 13 months of age (Graph 25). The increase was curvilinear in relation to age during this period. Approximately 77 per cent of the increase in thickness occurred during the first seven months of life.

In the Postmaturation Age Group, the thickness of the basal lamina increased linearly with age (Graph 26), and the regression coefficient was significant. The thickness at 1.5 years was 0.349 mm., and increased at a yearly rate of 0.014 mm., to 0.508. at 13.1 years of age.

Hog The thickness of the basal lamina in the hog increased linearly with age in the Maturation Age Group, and the regression coefficient was significant (Graph 27). The thickness increased in monthly increments of 0.402 mm., from 0.542 mm. at 0.1 month to 1.042 mm. at 12.0 months of age. Correlation

between the thickness of the basal lamina of the corona ciliaris and age was significant.

There was a slight linear increase in the thickness of the basal lamina in the Postmaturation Age Group. The regression coefficient was not significant. The thickness ranged from 1.030 mm. at 1.2 years to 1.149 mm. at eight years of age (Graph 28).

Histological and histochemical changes with age

Maturation changes

Dog In puppies less than one week of age the ciliary body (Corpus ciliare) was composed largely of smooth muscle with very little connective tissue. Smooth muscle cells were numerous, closely packed together, and appeared larger than smooth muscle cells in the mature dog. Loosely arranged, primitive appearing connective tissue elements were observed in the region near the future anterior chamber angle. Small quantities of pigment were visible in both the muscular and lens connective tissue of the ciliary body. At this age the ciliary processes (Processus ciliares) were folded into compact rounded projections on the posterior aspect of the corona ciliaris. Extensions of highly vascularized connective tissue extended into the folds from the basal lamina. Pigmentation was extensive in the ciliary folds, but individual pigment epithelial cells were not discernible. The superficial epithelial cells covering

the ciliary processes were present in multiple layers composed of numerous small elongated cells. The multiplicity of superficial epithelial cells was also noted in the orbiculus ciliaris (Orbiculus ciliares). Pigment epithelial cells were prominent in the orbiculus region, but pigmentation was not as extensive as in the folded ciliary processes. In the one-day old puppy the retina was in close proximity to the folded ciliary processes, consequently, the orbiculus ciliaris was relatively short.

By one week of age, the ciliary processes were unfolded and were more elongated. Extensive branching of the processes was not observed at this age. Connective tissue was increased, and blood vessels were relatively reduced in the subepithelial core of the processes. A reduction was noted in the cellularity of the superficial epithelial layer in both the processes and the orbiculus ciliaris. Evidence of substantial maturation in the ciliary musculature was not observed at this age.

Formation of definite ciliary muscle bundles was found in puppies two weeks of age. Loose connective tissue and pigment occupied the spaces between the bundles. Superficial epithelial cells of the processes and in the orbiculus ciliaris were usually in a single layer composed of tall columnar cells.

By four weeks of age, the ciliary processes were noticeably longer, usually thinner, and more branched. The superifical epithelia were cuboidal to low columnar in form. Progressive growth of the eye resulted in an increase in the distance between the ciliary processes and the retina and an increase in the length of the orbiculus ciliaris. At four weeks of age the ciliary body resembled the mature structure in histological appearance.

Hog The histological development of the ciliary body in the three-day old pig was observed to be more advanced than in the neonatal puppy. In the three-day old pig, the ciliary processes extended into the posterior chamber (Camera posterior bulbi) as narrow, moderately branched prolongations which were covered by a single layer of cuboidal to low columnar epithelial cells. Pigmentation was prominent in the pigment epithelial cells, but connective tissue and vascularization was not extensive in the subepithelial core of the process. Superficial epithelial cells in the orbiculus ciliaris region were present in a single layer of tall columnar cells. Smooth muscle cells of the ciliary muscle (M. ciliaris) and connective tissue cells in the corona ciliaris were approximately equally divided between embryonal and mature appearing cells.

At two months of age the ciliary body and its constituent parts were mature in their histological appearance.

Lipid deposition

Dog Lipid deposition was not observed in any portion of the ciliary body in dogs in Age Groups I, II, and III (0.1 - 12.9 months of age). In Age Group IV (1.5 - 4.4 years of age) lipid deposition was found in the basal lamina (Lamina basalis) of the corona ciliaris and in the connective tissue core of the ciliary processes in a majority of the dogs (Table 9).

In Age Groups V and VI (6.0 - 13.1 years of age) the incidence of deposition was increased in the basal lamina (Table 9). Deposition in the basal lamina was universal in these age groups.

In the portion of the basal lamina immediately adjacent to the ciliary processes, dense, homogeneous, focal depositions were noted at the point of union of the basal lamina and the ciliary process. These focal depositions typically occupied the entire width of the individual process and frequently extended into its connective tissue core for a short distance (Figure 58). Small arterioles in the basal region of the process were often surrounded by dense accumulations of lipoidal infiltrates (Figure 59).

In the ciliary process proper, lipid depositions were randomly dispersed throughout the subepithelial connective tissue core (Figure 58). In this area lipid depositions were generally less

dense than in the basal portion of the process or in the basal lamina of the ciliary crown.

In one dog (Dog No. 7BA, 6.4 years of age) lipid deposition was noted in the ciliary muscle. Lipid infiltrates appeared to diffusely permeate the muscle fibers in this specimen.

Hog The percentage incidence of lipid deposition in the ciliary body of the hog was much less than in the dog (Tables 9, 10). The intensity of deposition also was not as great in the hog.

Lipid deposition was not observed in any portion of the ciliary body in hogs in age groups prior to Age Group III (1.2 - 2.9 years of age). In Age Groups IV and V, (3.1 - 8.0 years of age) an increase occurred in the incidence of deposition (Table 10).

The total incidence (Table 10) was greatest in the basal lamina of the corona ciliaris. At this site, diffuse, homogeneous depositions were observed in the connective tissue, and the depositions extended without interruption into the basal portion of the ciliary processes. Lipid depositions were also noted in the subepithelial core of the more peripheral portions of the ciliary processes (Figure 57).

A slight diffuse permeation of the ciliary muscle with lipid infiltrates was found in one hog (Hog No. 3093-259, 7.0 years of age).

Mineralization

Dog In the ciliary body, mineralization was found in the basal lamina and ciliary processes of the ciliary crown, the ciliary muscle, and the orbiculus ciliaris (pars plans). Mineral deposition was also noted in the portion of the corona ciliaris adjacent to the anterior chamber angle of the eye and in the trabecula meshwork. The percentage incidence of mineralization in each of these sites was determined for each age group and recorded in tabular form (Table 9).

In the one-day old dog, mineral salts were faintly visible in a diffuse form in the superficial epithelial cells (Pars ciliaris retinae) of the ciliary processes and the orbiculus ciliaris. Distinct intracellular accumulations were not apparent until approximately two months of age (Age Group I, 0.1 - 4.0 months of age). In dogs in Age Group II (5.4 - 9.9 months of age) increased intracellular mineralization occasionally resulted in hypertrophy and hyperplasia of the epithelial cells and the formation of small nodular excrescences on the surface of the ciliary processes and orbiculus ciliaris. Excrescences were usually larger in the portion of the pars ciliaris retinae covering the ciliary processes than in the orbiculus ciliaris region. Mineralization in the ciliary processes and the orbiculus was also characterized by the presence of small focal deposits in

the connective tissue stroma of these two ciliary structures. The incidence of mineralization in the orbiculus ciliaris region increased progressively with age except in Age Group V (6.0 - 9.9 years of age), in which a very slight decrease was noted (Table 9). A marked decrease in the incidence (Table 9) of mineralization in the ciliary processes occurred in Age Groups V and VI (6.0 - 13.1 years of age).

Mineralization in the basal lamina of the ciliary crown was characterized by granular mineral deposits notably in the connective tissue adjacent to the base of the ciliary processes (Figure 61). The incidence (Table 9) was variable in dogs younger than 12.9 months of age, but increased progressively with age in dogs in Age Groups IV, V, and VI (1.5 - 13.1 years of age). The degree of deposition at this site was also observed to increase with age.

Focal mineral deposits were observed in dogs in all age groups near the anterior chamber angle of the eye (Figure 60). These deposits were located in the anterior portion of the basal lamina and in the trabecula meshwork. Deposits in both areas were included in the calculation of the percentage incidence of mineralization at the chamber angle (Table 9). Small focal deposits with irregular outlines were distributed throughout this area. The size of the deposits typically measured 10 - 25 microns at their greatest

dimension. Larger focal deposits were occasionally observed which measured up to 75 microns at their greatest dimension. A marked diminution in the incidence (Table 9) of focal deposition at the chamber angle was noted in Age Group VI (10. 0 - 13. 1 years of age).

Mineralization was observed inn the ciliary muscle of dogs in all age groups (Table 9). In Age Group I (0. 1 - 4. 0 months of age) mineralization was manifested by a slight diffuse infiltration of the posterior muscle fibers. In subsequent age groups, small focal deposits were dispersed throughout all ramifications of the muscle. In dogs in Age Group VI (10. 0 - 13. 1 years of age) there was a reduction both in incidence (Table 9) and intensity of mineralization in the ciliary muscle.

Hog In the ciliary body of the hog mineralization was observed in the same sites as in the dog; e. g., the basal lamina and ciliary processes of the corona ciliaris, the orbiculus ciliaris, the ciliary muscle, and the anterior chamber angle of the eye. The incidence of mineralization was greater in all portions of the ciliary body in the hog than in the dog, except, in the orbiculus ciliaris. In the latter site the percentage incidence was approximately equal in both species (Tables 9, 10).

The manifestations of mineralization within the component structures of the ciliary body were similar in the hog and dog. Focal and multiple focal deposits tended to be more extensive in the hog. However, excrescence formation following hypertrophy and hyperplasia of the superficial epithelial cells in the orbiculus ciliaris was observed less frequently in the hog.

Fibrosis

Dog As age increased, an increase in fibrous connective tissue was noted in the ciliary body. The increase was particularly noticeable in the basal lamina of the corona ciliaris and in the ciliary muscle.

In the basal lamina, fibrous connective tissue was observed to accumulate in dense bundles at the base of the ciliary processes (Figures 62-64). The fibrous accumulations were not especially dense nor extensive in Age Groups I and II (0.1 - 9.9 months of age), although the incidence (Table 9) was increased in Age Group II (5.4 - 9.9 months of age). In subsequent age groups fibrous concentration at this site increased in incidence (Table 9) and in intensity with age.

In Age Groups V and VI (6.0 - 13.1 years of age) the incidence of fibrosis was elevated in the connective tissue core of the ciliary processes (Table 9). Collagenous fibers were principally increased around the small vessels of the subepithelial connective tissue core,

but often completely occupied the entire thickness of the core. Hyalinization of the connective tissue core of the process was frequently observed (Figure 62), and the incidence of hyalinization increased with age (Table 9).

The incidence of fibrosis was increased progressively with age in the ciliary muscle (Table 9). As age advanced, increasing amounts of collagenous fibers were found in the muscle, and the muscle fibers became noticeably separated and often atrophic. The incidence of ciliary muscle atrophy was increased as muscular fibrosis increased (Table 9).

An increase in pigment accumulation in the ciliary muscle was concomitant with the increase in fibrous connective tissue. In the small number of cases of muscular atrophy observed in dogs in Age Groups I and II (0.1 - 9.9 months of age) atrophy was primarily due to pigment accumulation in the ciliary muscle. However, in subsequent age groups both fibrous and pigment accumulations were present in the muscle fibers and in the enlarged spaces between muscle fibers. In Age Groups V and VI (6.0 - 13.1 years of age) fibrous elements were predominant over the pigmentary elements in the interstices. Atrophy of the ciliary muscle (Figure 64) was particularly extensive in dogs in Age Group VI (10.0 - 13.1 years of age).

Hog Fibrosis increased with age in the basal lamina, ciliary processes, and in the ciliary muscle of the hog.

In hogs in Age Group I (0.1 - 6.0 months of age) less than three months of age, prominent fibrous accumulation was not observed in the basal lamina. However, prominent accumulations were observed at this site in all hogs (Table 10) in Age Groups II - V (6.2 months - 8.0 years of age). The density and extent of fibrosis also increased with age. Fibrous elements from the basal lamina commonly extended deep into the connective tissue core of the ciliary processes.

The incidence (Table 10) and the degree of fibrosis of the ciliary processes were markedly greater in the hog than in the dog. Abundant accumulations of collagenous fibers were constantly found in the ciliary process adjacent to the iris and greatly increased the thickness of the process (Figure 56). The incidence of hyalinization of the ciliary processes was not as great in the hog as in the dog (Tables 9, 10).

The incidence of fibrosis and atrophy of the ciliary muscle was found to be greater in the hog than in the dog (Tables 9, 10). Extensive pigmentary invasion of the atrophic muscle bundles, as seen in the dog, was not observed in the hog.

Epithelial hyperplasia

Dog Hyperplasia of the superficial epithelial cells of the ciliary processes and the orbiculus ciliaris was found to be a common manifestation of aging in the dog. The incidence of epithelial hyperplasia increased progressively with age (Table 9) and, in general, the degree of hyperplasia also increased with age.

Senile epithelial hyperplasia was present in all dogs in Age Groups V and VI (6.0 - 13.1 years of age). Accumulations of hyperplastic cells were most frequently observed at the tips of the ciliary processes (Figure 65). Proliferative pigment epithelial cells were occasionally observed to invade the zone of hyperplastic superficial epithelial cells.

Hyperplasia of the superficial epithelial cells of the orbiculus ciliaris (pars plana region) was not as marked as in the ciliary processes. In the former area hyperplasia was accompanied by distension of the basement membrane of the epithelium and the formation of cystic spaces (pars plana cysts) which protruded into the vitreous body (Corpus vitreum). The usually circular cysts ranged in size from 25 microns up to 150 microns in diameter. The cystic spaces contained a mucoid-like material which stained positively for acid mucopolysaccharides with the colloidal iron technique of

Rinehart and Abul-Haj (Figure 66). The incidence of pars plana cysts, although slightly variable within age groups, was found to increase with age (Table 9).

Hog In the hog epithelial hyperplasia was observed in the superficial epithelial cells of the ciliary processes and in the orbiculus ciliaris. The incidence (Table 10) and extent of hyperplasia increased with age. As in the dog, hyperplasia was most evident at the tips of the ciliary processes. In the hog, the hyperplastic tips of the ciliary processes tended to be flattened in an oblique plane which conformed to the curvature of the anterior surface of the lens.

Hyperplasia of the superficial epithelial cells of the orbiculus ciliaris was not as extensive as in the ciliary processes. The incidence of pars plana cysts was not as great in the hog as in the dog (Tables 9, 10), and the size of the cystic spaces in the hog were typically much smaller.

Choroid

Statistical evaluation of dimensional change with age

Thickness at the geometric axis of the bulbus oculi

Dog In the Maturation Age Group a curvilinear relationship existed between the thickness of the choroid measured at the geometric axis of the bulbus oculi and age (Graph 29). Choroidal

thickness decreased from 0.084 mm. at 0.1 months to 0.076 mm. at four months of age. Between 4.0 and 12.9 months of age, choroidal thickness increased from 0.076 mm. to 0.138 mm.

In the Postmaturation Age Group, the choroid decreased linearly from 0.118 mm. at 1.5 years to 0.111 mm. at 13.1 years of age, and the regression coefficient was significant (Graph 30).

Hog The thickness of the choroid increased linearly with age from 0.093 mm. in the neonatal pig to 0.105 mm. at 12.0 months of age (Graph 31). This increase in thickness of the choroid in the Maturation Age Group was not statistically significant.

Choroidal thickness also increased linearly with age in the Postmaturation Age Group, and the regression coefficient was significant (Graph 32). The increase in thickness ranged from 0.094 mm. at 1.2 years to 0.150 mm. at 8.0 years of age. The increase during this period represented a yearly increase of 0.008 mm.

Thickness at the ora serrata

Dog The thickness of the choroid, measured at the ora serrata increased linearly with age in the Maturation Age Group (Graph 29). Thickness increased from 0.033 mm. at 0.1 month to 0.058 mm. at 12.9 months of age. Both the regression coefficient and the correlation between choroidal thickness and age were significant.

In the Postmaturation Age Group there was no significant change in the thickness of the choroid at the ora serrata (Graph 30). The mean choroidal thickness of the 32 dogs in this age group was 0.058 mm.

Hog The thickness of the choroid at the ora serrata increased from 0.038 mm. at 0.1 month of age to 0.053 mm. at 12.0 months (Graph 31). The increase in thickness was linear in relation to age, but the regression coefficient was not significant. The mean choroidal thickness for the 22 hogs in the Maturation Age Group was 0.046 mm.

There was no significant change in the choroidal thickness at this site in the Postmaturation Age Group (Graph 32). The mean choroidal thickness for the 86 hogs in this age group was 0.044 mm.

Maturation changes

Dog In the one-day old dog the choroid (Choroidea) was characterized by its extensive cellularity and vascularity, prominent pigmentation, and its relatively large size in comparison to the sclera. At the geometric axis of the bulbus oculi the choroid was approximately one-third the size of the adjacent portion of the sclera. Large thin-walled vessels were present in the outer one-half of the choroid, and numerous smaller vessels were discernible in the inner one-half. Extensive pigmentation hindered a detailed examination of the latter vessels. A highly cellular tapetum (Tapetum lucidum) was present

at this age, and the nuclei of the tapetal cells were oval to plump-spindle in shape. Bruch's membrane (Lamina basalis) was not visible at this age.

In the one-week old puppy, the choroidal vessels were organized into a more definite pattern of layered vascularization and were surrounded by extremely thin collagenous fibers. The cellularity of the tapetum was reduced, however, the majority of the remaining tapetal cells retained a primitive appearance.

Between one week and two months of age the gradual process of histological maturation was manifested by: 1) the formation of a definite layered vasculature; 2) a gradual increase in the collagenous fiber framework, especially around the blood vessels; 3) a reduction in the cellularity of the choroid proper and the tapetum; 4) a transformation in the morphology of the individual stromal cells from plump, primitive appearing cells to more mature spindle shaped cells, and 5) a reduction in the relative thickness of the choroid as compared to the sclera. At two months of age the choroid was essentially mature in histological appearance.

Hog In the three-day old pig the choroid was more mature in histological appearance than in the neonatal puppy. Although the walls of the vessels were very thin, a definite pattern of layered vascularization was apparent. Thin collagenous fibers were

distributed moderately throughout the stroma, and the majority of the fibrocytic cells were spindle-shaped and mature in appearance. A thin layer of capillaries (Lamina choroidocapillaris) was perceptible adjacent to the single layer of flattened pigment epithelial cells of the retina. As in the dog, Bruch's membrane was not visible at this age.

At two months of age the choroid appeared histologically mature. An outer layer of large vessels and an inner layer of smaller vessels were clearly distinguishable in the choroidal vascular layer (Lamina vasculosa). The choroidocapillaris was quite apparent at this age except in areas of dense pigmentation. Collagenous fibers and fibrocytes were increased in the choroidal stroma, and in most specimens melanocytes were numerous.

Lipid deposition

Dog The incidence of lipid deposition was determined for each age group in three arbitrarily divided segments of the choroid and the results were presented in tabular form (Table 11). These arbitrary segments (Figure 2) included: a segment near the ora serrata (Segment A), an equatorial segment (Segment B), and a segment near the posterior pole of the bulbus oculi (Segment C).

Lipid deposition was not found in any age group prior to Age Group IV (1.5 - 4.4 years of age). The youngest dog (Dog No. B75) in which choroidal lipid deposition was observed was 3.2 years of

age. In Age Groups IV, V, and VI (1.5 - 13.1 years of age), the percentage incidence of lipid deposition was variable but generally included from one-third to one-half of the dogs in each age group. Regionally, a moderate predilection was noted in Age Group VI (10.0 - 13.1 years of age) for deposition in the segment near the ora serrata (Segment A, Table 11).

Lipid deposition in the choroid was characterized by either diffuse permeation (Figure 67) or focal globular accumulations (Figure 68) in the vascular walls, the connective tissue framework, and the tapetum. Occasionally, homogeneous depositions were present in the nodular intimal plaques of the larger vessels in the posterior choroid (Figure 69). The intensity of lipid deposition was generally increased with age. Invariably, in cases of prolific choroidal deposition dense, diffuse lipid infiltration was noted in the adjacent portion of the sclera (Figure 68).

Hog Choroidal deposition of lipids existed in only two of 40 hogs (Table 12). In both hogs deposition was not extensive and appeared as a slight diffuse infiltration of the vascular wall. In one hog (Hog No. 3093-259; 7.0 years of age) there was mild thickening of the tunica media in the area of deposition. In the other

hog (Hog No. 4512, 2.03 years of age), except for the meager lipid infiltration of the tunica media, there was no alteration in the vascular wall.

Mineralization

Dog Choroidal mineralization in the dog was characterized by a progressive accumulation with age of diffuse and focal depositions of mineral salts in the choroidal stroma and choroidal vasculature. In sections stained with the alizarin red S technique, focal mineral deposits appeared bright to dark red and often obscured the internal structure of the choroid (Figures 70-73).

The incidence of choroidal mineralization was determined for each age group in the three arbitrary choroidal segments (Figure 2) designated for lipid evaluation, and the results were recorded in tabular form (Table 11). The total percentage incidence was found to be slightly greater in segment "C" than in either segments "A" or "B".

In the younger dogs of Age Group I (0.1 - 4.0 months of age) mineral salts were present in a very mild, diffuse form in all segments of the choroid. However, in three of the older dogs in this age group mineral salts were slightly concentrated in the choroidal stroma, especially in the segment adjacent to the posterior pole (Segment C).

In Age Group II (5.4 - 9.9 months of age) the incidence (Table 11) and the intensity of mineralization was increased in all segments of the choroid. In this age group the incidence was noticeably greater in segment "C". At this site, dense mineral accumulations were characteristically found in all layers of the choroid and the tapetum.

In Age Groups III - V (11.0 months - 9.9 years of age) the incidence of choroidal mineralization increased progressively with age in each of the choroidal segments (Table 11), and the percentage incidence was nearly equal in the various segments of the choroid. The intensity of mineralization, although variable among individual specimens, tended to increase with age in Age Groups III - V. There was a reduction in the intensity of mineralization in the majority of the dogs in Age Group VI (10.0 - 13.1 years of age). A slight reduction in the incidence of mineralization was noted in segments "B" and "C" in the latter age group (Table 11).

As the intensity of mineralization increased in the choroid, mineral deposits tended to be extruded through the chorioretinal barrier (Bruch's membrane and the pigment epithelium of the retina) into the retina (Figures 71-73). Mineral extrusions were also noted from the choroid into the scleral tissues. Briefly, the alterations in the chorioretinal barrier which accompanied

increased choroidal mineralization consisted of thickening and breaks in Bruch's membrane, hypertrophy and hyperplasia of the retinal pigment epithelium, and the formation of nodular, mineralized excrescences which impinged upon the retina. Explicit details of the alterations in the chorioretinal barrier were presented in this dissertation in conjunction with descriptions of chorioretinal degenerative changes in the retina.

Hog The manifestations of choroidal mineralization were similar in the hog and dog. Extrusions of mineral accumulations from the choroid into the retina and sclera were also similar in the two species.

In hogs up to two months of age in Age Group I (0.1 - 6.0 months of age) mineral salts in a mild diffuse form were present in the three arbitrary segments of the choroid. In older hogs in this age group mineral concentration was intensified, especially in the segment near the ora serrata (Segment A) and the equatorial segment (Segment B).

The incidence of mineral deposition was greatly increased in hogs in Age Group II (6.2 - 11.9 months of age), and the incidence was approximately equal in each of the three choroidal segments (Table 12).

A corresponding increase was noted in the incidence of intracellular accumulation and hypertrophy of the retinal pigment epithelium (Table 16).

The incidence (Table 11) of choroidal mineralization remained high in hogs in Age Groups III - V (1.2 - 8.0 years of age). In hogs in these age groups over four and one-half years of age, focal areas of mineralization were often present which obscured the internal structure of the choroid.

Fibrosis

Dog Collagenous fibers were initially visible in the choroid at one week of age, after which time they progressively increased with age.

The choroid was found to be essentially a vascular structure, and the increase in fibrous connective tissue with age was primarily in the form of perivascular and intervascular accumulations (Figures 74, 75). These forms of fibrosis increased the size of the intervascular spaces and tended to decrease the dimensions of the blood vessels. The latter effect was partially counteracted by a concomitant increase in the fibrous content of the medial portion of the vascular wall.

The criteria utilized to determine the percentage incidence of choroidal fibrosis were primarily the increase in size and compactness of the intervascular spaces and the amount of perivascular fibrous

connective tissue. Animals possessing slight to moderate accumulations at these sites were not included in the calculation of the percentage incidence.

The total incidence (Table 11) of choroidal fibrosis was greatest in the segment near the posterior pole (Segment C), next greatest in the equatorial segment (Segment B), and least in the segment near the ora serrata (Segment A). In dogs older than six years of age choroidal fibrosis was found to be almost universal in the three segments (Table 11).

Hog In the hog choroidal fibrosis attendant with aging was characterized more by perivascular than intervascular accumulation of collagenous fibers (Figures 76, 77). Consequently, fibrotic changes with age appeared less dense in the choroid of the hog than in the dog; both perivascular and intervascular fibrosis were quite prominent in the dog.

The collagenous fiber content of the choroid was not excessive, except in the segment near the ora serrata, (Segment A), in hogs in Age Groups I and II (0.1 - 11.9 months of age). The incidence (Table 12) and intensity of fibrosis was increased in all segments of the choroid in Age Group III (1.2 - 2.9 years of age). In subsequent age groups, a progressive increase was observed in the degree of choroidal fibrosis, particularly, in the segments

adjacent to the equator (Segment B) and the posterior pole (Segment C). The total incidence of choroidal fibrosis was greatest in segment "C" and least in segment "A".

Vascular changes

Dog Alteration with age in the structure of the choroidal arteries was manifested by spontaneous intimal and medial sclerosis.

Intimal sclerosis was restricted to the larger arteries in the posterior segment of the choroid (Segment C) and was characterized by nodular proliferations on the intimal surface (Figure 75). The proliferations were composed of cellular and fibrous elements, and occasionally lipid deposition was observed within the nodular plaques (Figure 69). Mild intimal proliferation was observed in one dog (Dog No. 068, 2.5 months of age) in Age Group I (0.1 - 5.9 months of age). The incidence of intimal sclerosis was greatest in Age Group III (11.0 - 12.9 months of age) and gradually declined in subsequent age groups (Table 11). Although a reduction was noted in the incidence of intimal sclerosis in the older age groups, nodular proliferations were numerous and extensive in the older dogs in which they were found.

Medial sclerosis was characterized by a progressive increase with age of collagenous fibers and a reduction in the number of smooth muscle cells in the tunica media. Enlargement of the vascular wall

tended to diminish the vascular lumen. In the peripheral portion of the choroid the lumens of the smaller arterioles and venules were extremely narrowed in areas of dense fibrosis.

Hog Arteriosclerotic changes in the choroid of the hog were characterized almost exclusively by alterations in the tunica media. Alterations in the tunica intima of the choroidal arteries were not apparent in the hogs utilized in this investigation.

The earliest manifestations of medial sclerosis were observed in hogs in Age Group II (6.2 - 11.9 months of age) and consisted of a slight accumulation of collagenous fibers in the tunica media as well as a modest increase in perivascular fibrosis. In hogs in Age Group III (1.2 - 2.9 years of age), in addition to an intensification of the fibrotic changes noted in hogs in Age Group II, degenerative changes were found in the smooth muscle cells of the media. A definite increase in the thickness of the arterial wall, progressive increase in medial fibrosis, and a decrease of muscular nuclei were apparent in hogs in Age Groups IV and V (3.1 - 8.0 years of age). The incidence (Table 12) of medial sclerosis was almost universal in hogs in Age Group V (6.0 - 8.0 years of age). In the latter age group, hyalinization of large portions of the vascular wall occurred as the result of the progressive sclerotic changes in the tunica media (Figures 76-78).

Lens

Statistical evaluation of dimensional change with age

Thickness of the lens capsule at the anterior pole

Dog The thickness of the lens capsule at the anterior pole increased linearly with age in the 46 dogs in the Maturation Age Group (Graph 33). The regression coefficient and the correlation between capsular thickness and age were significant. The increase in thickness was at the rate of 2.39 microns per month and ranged from 5.19 microns in the one-day old puppy to 36.18 microns at 18 months of age.

In the 32 dogs in the Postmaturation Age Group, the thickness of the anterior lens capsule also followed a significant linear increase with age (Graph 34). Increase in capsular thickness was in yearly increments of 6.34 microns. At 1.5 years of age the thickness was 38.92 microns, and at 13.1 years it was 112.47 microns. The correlation between anterior capsular thickness and age was significant.

Hog A curvilinear relationship existed between the thickness of the anterior lens capsule and age in the 22 hogs in the Maturation Age Group (Graph 35). Capsular thickness increased from 6.58 microns in the three-day old pig to 37.23 microns at

12 months of age. Approximately 79 per cent of this increase occurred during the first six months of life.

In the 86 hogs in the Postmaturation Age Group, the thickness of the anterior lens capsule increased linearly with age from 36.55 microns at 1.2 years to 138.60 microns at 8.0 years of age (Graph 36). This increase in thickness represented an increase of 15.01 microns per year. Both the regression and correlation coefficients were significant.

Thickness of the lens capsule at the posterior pole

Dog The posterior lens capsule increased in thickness from 3.67 microns at 0.1 month to 5.25 microns at 13.0 months of age (Graph 33). This increase in thickness was linear with respect to age, and the regression coefficient was significant. The correlation between posterior capsular thickness and age was significant.

In the Postmaturation Age Group, the thickness of the posterior lens capsule increased linearly with age (Graph 34). The slope of the regression line indicated the thickness to be 4.27 microns at 1.5 years and 6.37 microns at 13.1 years of age. Both the regression and correlation coefficients were significant.

Hog The thickness of the posterior lens capsule increased linearly with age, and the regression coefficient was significant in the Maturation Age Group (Graph 35). The average

thickness of the posterior lens capsule in the 22 hogs in this age group was 5.77 microns. The correlation between posterior capsular thickness and age was significant.

In the age group which ranged from 1.2 years to 8.0 years of age, posterior capsular thickness increased from 5.02 microns to 7.91 microns (Graph 36). The increase was linear with age, and the regression coefficient was significant as was the correlation between age and capsular thickness. The mean thickness for the 86 hogs in this age group was 5.93 microns.

Sagittal thickness of the lens epithelium

Dog In the Maturation Age Group, a curvilinear relationship existed between the sagittal thickness of the lens epithelium, measured at the geometric axis of the lens, and age (Graph 33). Curvilinear analysis revealed that the epithelial thickness decreased from 8.48 microns at 0.1 month to 6.11 microns at the seventh and eighth months of age. From eight months of age the thickness increased to 7.39 microns at 13.0 months of age. The mean epithelial thickness for the 46 dogs in this age group was 6.93 microns.

The lens epithelial thickness increased linearly with age in the Postmaturation Age Group, and the regression coefficient was significant (Graph 34). The increase in thickness ranged from 4.63

microns at 1.5 years to 6.88 microns at 13.1 years. The average epithelial thickness for the 32 dogs in this age group was 5.96 microns.

Hog The sagittal thickness of the lens epithelium was curvilinear in relation to age in the 22 hogs in the Maturation Age Group (Graph 35). Epithelial thickness increased from 7.60 microns in the three-day old pig to 12.95 microns at six months of age, and was followed by a decrease to 8.68 microns at 12 months of age.

There was no significant change in the thickness of the lens epithelium in hogs in the Postmaturation Age Group (Graph 36). The mean sagittal thickness of the lens epithelium for this age group was 9.18 microns.

Equatorial diameter of the lens

Dog The equatorial diameter of the lens increased curvilinearly with age in the Maturation Age Group (Graph 37). The curvilinear increase ranged from 4.510 mm. at 0.1 month to a maximum of 9.147 mm. at 11 months of age. The mean equatorial diameter of 46 dogs in the Maturation Age Group was 7.891 mm.

There was a nonsignificant linear decrease of the equatorial diameter dependent on age in the Postmaturation Age Group (Graph 38). The equatorial diameter was 9.548 mm. at 1.5 years and 8.727 mm. at 13.1 years of age, with a mean of 9.060 mm. for the 32 dogs in this age group.

Hog In the Maturation Age Group a curvilinear relationship existed between the size of the equatorial diameter of the lens and age (Graph 39). The curvilinear increase ranged from 5.890 mm. in the neonatal pig to 8.202 mm. at 12 months of age. The mean equatorial diameter for the 22 hogs in the Maturation Age Group was 7.575 mm.

The equatorial lens diameter increased linearly with age in the Postmaturation Age Group, and the regression coefficient was significant (Graph 40). The correlation between equatorial diameter and age was also significant. The equatorial diameter was 8.458 mm. at 1.2 years and 9.972 mm. at 8.0 years of age.

Polar diameter of the lens

Dog The polar diameter of the lens increased from 3.630 mm. in the one-day old puppy to a maximum of 5.392 mm. at nine months of age (Graph 37). The increase in the size of the polar diameter was curvilinear with respect to age. The mean polar diameter for the 22 dogs in the Maturation Age Group was 4.902 mm.

In the Postmaturation Age Group the polar diameter decreased from 5.705 mm. at 1.5 years to 5.298 mm. at 13.1 years of age (Graph 38). The regression coefficient was not significant.

Hog The polar diameter of the lens was curvilinear with respect to age in the Maturation Age Group (Graph 39). The polar diameter was 4.139 mm. at 0.1 month, 5.575 mm. at the seventh and eighth months, and 4.979 mm. at 12.0 months of age. The average polar diameter for the 22 hogs in this age group was 5.15 mm.

In the Postmaturation Age Group the polar diameter of the lens was also curvilinear with respect to age (Graph 40). The polar diameter increased from 5.175 mm. at 1.2 years to 6.469 mm. at 6.0 years and was followed by a slight decrease to 6.165 mm. at 8.0 years of age. The mean polar diameter for the 86 hogs in this age group was 5.902.

Histological and histochemical changes with age

Maturation changes

Dog In puppies between two and seven days of age, the lens was spherical in shape and either adherent or in close proximity to the cornea and iris (Figures 5, 6). Remnants of the fetal vasculature (Tunica vasculosa lentis) were observed on the lens surfaces in specimens in which separation of the lens and the adjacent structures was complete or partially complete. Cellular debris indicative of recent dehiscence was also observed on the anterior lens surface and in the anterior chamber (Camera anterior bulbi). The anterior and posterior lens capsules (Capsula lentis) were visible at this

age but were inconspicuous. At this age the subcapsular epithelial cells were cuboidal in the region of the anterior pole (Polus anterior lentis) but were low columnar in the region of the equator (Equator lentis). A lenticular bow resulting from an inward migration of the equatorial subcapsular epithelial cells was observed at both equatorial extremities of the lens. The cells of the bow coursed at various levels deep to the anterior subcapsular epithelial layer. The deeper or older cells extended almost to the polar axis of the lens. A definitive lens nucleus (Nucleus lentis) and cortex (Cortex lentis) were not apparent at this age. The central portion of the lens appeared homogeneous, however, small individual fibers (Fibrae lentis) were discernible near the periphery.

By two weeks of age the equatorial subcapsular epithelial cells were increased in height, and cells in the lenticular bow were increased in number. As the result of the peripheral addition of new cells from the lenticular bow, the cells which originated from the lenticular bow earlier in development were compressed centrally and were in various stages of degeneration. The anterior capsule was approximately the size of the subcapsular epithelium at this age.

At one month of age, the first distinction between lens nucleus and cortex was apparent, and by two and one-half months of age cortical and nuclear regions of the lens were both microscopically

and macroscopically discernible. Microscopically, adjacent fibers in the lens nucleus appeared to be joined by means of surface serrations. In the cortical region the fibers were more homogeneous and smaller than nuclear fibers, and surface serrations were not visible. In transverse section, fibers in both regions were hexagonal in shape.

At two and one-half months of age, all the mature histological features of the mature lens were present, although maximum growth of the lens was not attained until a later age.

Hog In the three-day old pig the lens was completely separated from the iris and cornea, and relatively spacious anterior and posterior chambers were formed. A distinctly visible capsule, devoid of remnants of the fetal vasculature, covered both surfaces of the lens. Subcapsular epithelial cells were cuboidal at the anterior pole and columnar at the equator. The lenticular bow of the pig contained a greater number of epithelial cells than did the dog at a comparable stage, and the deeper cells of the bow were more degenerate in the pig than in the dog. Distinction between the lens cortex and nucleus was possible at this age. The central nuclear fibers were compressed into a dense laminated mass, whereas, the peripheral cortical fibers were more homogeneous in appearance.

Nuclear sclerosis

Dog Histochemical changes in the central fibers of the lens were observed in dogs as young as two weeks of age. The early changes were manifested by the initial appearance of acid mucopolysaccharides in the ground substance and an alteration in the proteinogenous constituents of the lenticular fibers. Less intensely stained acid mucopolysaccharides were observed in the subcapsular region of the lens. In sections stained with the colloidal iron technique of Rinehart and Abul-Haj acid mucopolysaccharides appeared as an amorphous, blue staining material (Figures 109, 112). In Weigert's resorcin-fuchsin stained sections, the central lenticular fibers appeared reddish-brown as opposed to pale yellow in areas of the lens where histochemical changes were not evident (Figures 108, 111, 114).

By the age at which a definitive lens nucleus and cortex were visible (2.5 months of age), the aforementioned histochemical alterations were increased in intensity and occupied a large portion of the nucleus. The initial accumulation of mineral salts in the nucleus was evident by this age. Areas of mineralization were bright red in sections stained with the alizarin red S technique for calcium salts (Figure 113) and gray to light blue in hematoxylin and eosin stained sections (Figure 110). Varying degrees of

mineralization, protein changes, and accumulations of acid mucopolysaccharides, were present in the lens nucleus (Table 13) of all dogs over 2.5 months of age. These histochemical alterations were generally increased in intensity and occupied an increasingly larger proportion of the nucleus as age increased (Figures 107-114).

Two forms of degrees of mineralization were noted: one characterized by a gradual, progressive increase in mineralization with age; the other, by marked mineralization occurring predominantly at an early age.

In the slow progressive form of mineralization, deposits were mainly concentrated along the serrated borders of the lens fibers and gave the nucleus a striped appearance (Figure 115). Fine granular deposits were present within the fibers, and small focal deposits were frequently scattered throughout the nucleus. Concentrations of minerals and acid mucopolysaccharides were particularly evident at the lens sutures.

The more extensive and intense form of mineralization was characterized by multiple focal mineral aggregates which occupied large portions of the nucleus and occasionally extended into the lens cortex and lens capsule. The focal aggregates were composed of varying numbers of rhomboid crystalline structures and were surrounded by a homogeneous accumulation of mineral salts which

gradually blended with the lenticular fibers (Figure 117). This form of mineralization was observed in 29.6 per cent of 81 dogs (Table 13). In the dogs in which this form of mineralization occurred, 71.8 per cent were in Age Groups I - II (0.1 - 12.9 months of age). Due to extensive shattering, attributed to the sectioning process, the lenses of five dogs were not sufficiently intact to accurately evaluate the histological and histochemical changes.

Hog In the three-day old pig the lens nucleus and cortex were uniformly stained with the colloidal iron, alizarin red S, Weigert's resorcin-fuchsin, and hematoxylin and eosin techniques. Sections stained with these techniques revealed no evidence of histochemical alteration at this age.

By two months of age, the presence of slight amounts of acid mucopolysaccharides and mineral salts, and an alteration in the protein content of the nuclear fibers was demonstrated in the lens nucleus with the previously mentioned techniques. The area of histochemical alteration was restricted to the more central portion of the lens nucleus. Varying degrees of these concomitantly occurring histochemical alterations were found in all hogs over two months of age (Table 14). As in the dog, the extent and intensity of the alterations generally increased with age.

The two forms of nuclear mineralization, observed in the dog, were also noted in the hog. However, the incidence (Tables 13, 14) and the intensity of the form characterized by multiple focal aggregates were not as great in the hog as in the dog. The mineral aggregates were typically much smaller in the hog.

Cortical and capsular sclerosis

Dog The lens cortex and capsule of dogs in Age Groups I - III (0.1 - 12.9 months of age) were homogeneously stained with the hematoxylin and eosin and Weigert's resorcin-fuchsin techniques. In colloidal iron stained sections, there was a slight accumulation of acid mucopolysaccharides beneath the subcapsular epithelium and at the lens sutures. In sections stained with the alizarin red S technique, fine granular mineral deposits, when present, were sparsely scattered throughout the cortex and to an even lesser extent in the lens capsule and subcapsular epithelium. Occasionally in dogs in Age Groups I - III, small focal mineral deposits were usually observed in cases in which multiple focal mineral aggregates were present in the lens nucleus.

In dogs in Age Groups IV - VI (1.5 - 13.1 years of age) the intensity and extent of cortical and capsular mineralization were progressively increased with age. Small focal mineral deposits, although, never as great in intensity and extent as in the lens

nucleus, were frequent in both the cortex and capsule (Figure 116). Mild intracellular accumulation of mineral salts and acid mucopolysaccharides existed in the subcapsular epithelium, and the epithelial cells of the lenticular bow.

Weigert's resorcin-fuchsin stained sections from dogs in Age Groups V - VI (6.0 - 13.1 years of age) revealed proteinogenous changes, similar to those observed in the lens nucleus, in a small number of the cortical fibers. The altered fibers were predominantly located near the lens nucleus and were interspersed among the more numerous unaltered cortical fibers.

The incidence (Table 13) of mineralization in the cortex and capsule was low in dogs in Age Group I (0.1 - 4.0 months of age). In dogs in Age Group II (5.4 - 9.9 months of age), the incidence of cortical mineralization was greatly increased and was universal in dogs in Age Groups IV - VI (1.5 - 13.1 years of age). The incidence of capsular mineralization was not significantly increased in dogs in age groups prior to Age Group V (6.0 - 9.9 years of age). Capsular mineralization was present in all dogs in Age Group VI (10.0 - 13.1 years of age).

Hog Mineralization was found to be the most prominent histochemical alteration in the lens cortex and capsule of the hog.

Cortical mineralization occurred in hogs in all age groups, with the maximum incidence (Table 14) being in Age Group II (5.4 - 9.9 months of age). Mineralization in the cortex was in the form of fine granules and small, widely scattered, focal deposits located in and among the cortical fibers. As in the dog, the extent and intensity of these deposits increased with age. In the older hogs (Age Groups IV and V, 3.1 - 8.0 years of age), the deposits tended to be concentrated beneath the subcapsular epithelium, particularly in hogs in which capsular mineralization was extensive. Concentrations of mineral salts were also observed in the subcapsular epithelium, the epithelial cells of the lenticular bow, and at the lens sutures.

The total incidence (Tables 13, 14) and the intensity of mineralization of the anterior capsule of the lens were greater in the hog than in the dog. In the hog, capsular mineralization was characterized by fine granular, multiple focal and diffuse homogeneous accumulations of mineral salts in the capsule. Mineralized excrescences which projected into the anterior chamber of the eye, were occasionally present on the anterior surface of the lens capsule (Figure 118). These excrescences were continuous with focal deposits in the capsule and were morphologically and histochemically similar to mineralized excrescences observed on the posterior surface of the cornea. Mineralization of the anterior capsule, in one or more

of the described forms, was present in 93.8 per cent of the hogs in Age Group V (6.0 - 8.0 years of age).

Variable quantities of acid mucopolysaccharides were present in the subcapsular epithelium, in the cortex beneath the subcapsular epithelium, and in the epithelial cells of the lenticular bow. More constant accumulations occurred at the lenticular sutures. As age increased, acid mucopolysaccharides tended to be increased at each of these sites.

Retina

Statistical evaluation of dimensional change with age

Thickness at the geometric axis of the bulbus oculi

Dog Retinal thickness at the geometric axis of the bulbus oculi was curvilinear in relation to age in the 46 dogs in the Maturation Age Group (Graph 41). Retinal thickness declined linearly from 0.243 mm. at 1.2 years to 0.227 mm. at 8.0 years of age (Graph 44). The regression coefficient was not significant. The mean retinal thickness was 0.238 mm. for the 86 hogs in the Postmaturation Age Group.

Thickness at the ora serrata

Dog A curvilinear relationship existed between the thickness of the retina, measured near the ora serrata, and age

in dogs in the Maturation Age Group (Graph 41). Retinal thickness, at this site, was 0.150 mm. at 0.1 month, 0.088 mm. at 8.0 months, and 0.114 mm. at 13.0 months of age.

In the Postmaturation Age Group, retinal thickness near the ora serrata increased linearly from 0.148 mm. at 1.5 years to 0.168 mm. at 8.0 years of age (Graph 42). The regression coefficient was not significant.

Hog There was a nonsignificant linear increase in the thickness of the retina measured near the ora serrata in hogs in the Maturation Age Group (Graph 43). The linear increase ranged from 0.105 mm. at 0.1 month to 0.127 mm. at 12.0 months of age. The mean retinal thickness for the 22 hogs was 0.116 mm.

No significant change occurred in the retinal thickness near the ora serrata in 86 hogs ranging in age from 1.2 years to 8.0 years of age (Graph 44). The mean retinal thickness for the 86 hogs in the Postmaturation Age Group was 0.104 mm.

Histological and histochemical changes with age

Maturation changes

Dog The sensory portion of the retina was relatively undifferentiated at one day of age. The most prominent feature of the retina at this age was the extensive combined inner and outer nuclear layers; an outer plexiform layer was not present separating

these two nuclear layers. Numerous neuroblastic and spongioblastic cells, which were less intensely stained with the basic dyes than in the mature retina, were present in the area of the future ganglion cell and nerve fiber layers. Many small blood vessels of capillary size were intermingled with these embryonal appearing neural cells. Although a distinct nerve fiber layer was not present in the one-day old puppy, a few neuroblastic cells in the posterior segment of the retina (Segment C) were enlarged and short dendritic and axonic processes existed on their surfaces. A narrow inner plexiform layer separated the neuroblastic ganglion cells and the combined inner and outer nuclear layers. The rods and cones (predominantly rods in the dog) were approximately one-half their mature length. At the ora serrata a semicircular fold of the retina (Lange's fold), which projected into the vitreous body, constituted another manifestation of retinal immaturity in the one-day old puppy (Figure 79).

At one week of age, slight cleavage occurred in the center of the previously combined inner and outer nuclear layers to initiate the formation of the outer plexiform layer (Figure 80). There was a marked decrease in the cellularity of the ganglion cell and nerve fiber areas, and individual ganglion cells and neuroglial cells were more prominent. The retinal vasculature was more organized into definitive arterioles and venules than in the one-day old puppy.

The nerve fiber layer, although not extensive in thickness, was visible at two weeks of age. The outer plexiform layer was increased in thickness, and the rods and cones were approximately two-thirds their mature length. The affinity for the basic stains was increased in the ganglion cells. At two weeks of age this affinity appeared greater in the nucleus than in the cytoplasm of the ganglion cell. The semicircular fold at the ora serrata was absent at this age.

At one month of age, the cytoplasmic chromidial substance of the ganglion cells was stained intensely with the basic stains, and all layers typical of the mature retina were distinctly visible. In essence, the retina appeared histologically mature in dogs one month of age.

Hog All layers usually seen in the mature retina were present in the retina of the three-day old pig. In arbitrary retinal segments "A" and "B" (Figure 2) the rods and cones were approximately three-fourths their mature length, and the outer plexiform layer was about one-half its mature thickness. In arbitrary retinal segment "C" both the rods and cones and outer plexiform layer were dimensionally mature. At this age, the retinal blood supply was organized into a system of relatively well developed arteries, arterioles, capillaries, and their satellite venous structures. Ganglion cells stained lightly with the basic dyes.

Histologically, all segments of the retina of the hog appeared mature at two months of age. Both the nucleus and the cytoplasmic chromidial substance of the ganglion cells were deeply stained with the basic dyes in hogs two months of age.

Spontaneous retinal atrophy

Dog With increased age there was a gradual attrition to the neural components of the retina. The loss of neural elements was most evident in the inner and outer nuclear layers (Figures 81-84). The decrease in nuclear thickness of these two layers was quantified by utilizing the photographic reticle of the microscope eyepiece to establish a perpendicular line across both nuclear layers. Subsequently, the nuclear count for each layer was computed by determining the number of nuclei which contacted the perpendicular line. Separate nuclear counts were made from each dog in the peripheral, middle, and central segments of the retina (Segments A, B, and C, respectively; Figure 2). The means of these individual observations were ascertained for each age group and presented in tabular form (Table 17).

Comparison of the means in successive age groups revealed a progressive loss of nuclei with age in both the inner and outer nuclear layers of each of the arbitrary retinal segments. Comparing the mean nuclear counts of Age Groups I and VI, the percentage

loss of nuclei between these two age groups was found to be greatest in the peripheral segment (Segment A), least in the central segment (Segment C), and consistently greater in the inner nuclear than in the outer nuclear layer (Table 17).

The progressive loss of nuclear elements appeared to be accentuated when other degenerative or atrophic processes were present. In the segment of the retina adjacent to the ora serrata (Segment A), the inner nuclear layer was occasionally absent or the nuclei were extremely dispersed in dogs in which peripheral cystic degeneration of the retina was coexistent with spontaneous retinal atrophy (Figure 82). Loss of nuclei in the outer nuclear layer as well as the layer of rods and cones was accentuated by degenerative changes in the chorioretinal barrier (Figure 82).

The ganglion cells were also reduced in number with age, and varying degrees of neuronal degeneration were observed in a large number of the remaining ganglion cells. In dogs over six years of age, ganglion cells were sparse in segment "A" and the peripheral portion of segment "B". Small cytoplasmic vacuoles and a loss or absence of chromidial substance characterized the degenerate ganglion cell of the aged dog (Figures 83-84).

A loss of nerve fibers, proliferation of neuroglial cells, thickening of Müllers fibers, and alterations in the retinal vessels accompanied the loss of neuronal elements in the nuclear and synaptic layers (Figure 82).

Hog A progressive decrease of the neural components also occurred with increased age in the retina of the hog. As in the dog, the loss was most evident and easily quantified in the inner and outer nuclear layers. In these layers, the mean nuclear count (Table 18) was gradually reduced from a maximum in Age Group I (0.1 - 6.0 months of age) to a minimum in Age Group V (6.0 - 8.0 years of age). In the age group which included the oldest hogs, Age Group V, the mean nuclear count was greatest in the central segment (Segment C) and least in the peripheral segment (Segment A). However, the percentage loss of nuclei, which occurred between Age Groups I and V, was greatest in the central segment and approximately equal in the peripheral and middle segments (Table 18). This finding was in contrast to the dog in which the greatest percentage loss of nuclei occurred in the peripheral segment of the retina (Table 17). The percentage loss of nuclei was always greater in the inner nuclear than in the outer nuclear layer in each of the retinal segments of the hog.

Peripheral cystic degeneration

Dog Peripheral cystic degeneration of the retina was present in 61.6 per cent of the dogs utilized in this investigation (Table 15). The earliest manifestations of this apparently spontaneous degenerative process were present in 31.3 per cent of the dogs in Age Group II (5.4 - 9.9 months of age). In this age group the alteration in the retinal architecture was characterized by the development of small cystic spaces in close proximity to the ora serrata. These cystic spaces were most frequently located in the outer plexiform layer, however, in some dogs in Age Group II they were also present in the adjacent nuclear layers and the inner plexiform layer.

The incidence (Table 15) of peripheral cystic degeneration was progressively increased in the subsequent older age groups and was universal in Age Groups V and VI (6.0 - 13.1 years of age). The number and size of the cystic spaces were also increased with age and resulted in a gradual central extension of the area of cystic degeneration. In dogs over six years of age, cystic degeneration frequently extended from one to two mm. from the ora serrata (Figure 85). The cystic spaces adjacent to the ora serrata usually occupied the entire area between the limiting membranes of the retina, whereas the more central cysts were smaller and were restricted to the middle layers of the retina (Figure 85). Occasionally, greatly

enlarged cysts were present near the ora serrata. The larger cysts at this site measured up to 500 microns at their greatest dimension and protruded extensively into the vitreous body (Figure 86). Sections stained with the colloidal iron technique of Rinehart and Abul-Haj revealed the presence of an unorganized mucoid debris within the cystic spaces which was positively stained for acid mucopolysaccharides (Figure 87).

The gradual enlargement and central extension of the cystic spaces resulted in a progressive disruption and oftentimes extinction of the neural components of the peripheral retina. Thickened Müllers fibers and compressed neuroglial cells formed the walls of the distended cystic cavities. Proliferative neuroglial cells, macrophages, and invasive pigmentary deposits surrounded the enlarged cysts and blood vessels of the degenerate peripheral retina (Figure 82).

Pigment invasion of the peripheral retina was not present in dogs in Age Groups I - III (0.1 - 12.9 months of age). However, in Age Groups III - VI (1.5 - 13.1 years of age), the incidence was markedly increased (Table 15). In the latter age groups, peripheral pigmentary invasion (Figure 88) was characterized by the presence of both free and phagocytized pigment granules and aggregates of pigment granules in the segment of the retina adjacent to the ora

serrata (Segment A). Invariably degenerative changes in the peripheral retina were noted in the areas of pigmentary invasion. The morphology and staining qualities of the invasive pigment were similar to the pigment existing beneath the Pars ciliaris retinae rather than to the lanceolate pigment granules contained within the pigmented epithelial cells associated with the Pars optica retinae.

Hog The total incidence of peripheral cystic degeneration was found to be greater in the hog than in the dog (Tables 15, 16), and the initial manifestations were present at a younger age in the hog. However, the individual cystic spaces were, as a rule, much smaller in the hog than in the dog. Small vacuolar spaces (microcysts), near the ora serrata, were present in the outer plexiform layer of 66.6 per cent of the hogs in Age Group I (0.1 - 6.0 months of age). The youngest hog (Hog No. 5330), in which microcysts were present, was 2.3 months of age. Varying degrees of peripheral cystic degeneration existed in all hogs in Age Groups II - V (6.2 months - 8.0 years of age).

The progressive nature of the degenerative process was manifested in hogs in Age Groups II and III(6.2 months - 2.9 years of age) by the presence of microcysts in the outer nuclear and inner nuclear layers as well as in the outer plexiform layer. The progressiveness was further denoted by a gradual spread with

increased age of the area of microcystoid degeneration to include all of segment "A" and the peripheral portion of segment "B".

Continued central extension resulted in the area of degeneration frequently occupying all of retinal segments "A" and "B" in hogs in Age Groups IV and V (3.1 - 8.0 years of age). In these age groups larger cysts, which typically occupied the middle layers of the retina, were formed by coalescence of preexisting microcysts (Figure 89). The formation of these enlarged cysts produced a marked decrease in the neural components of the peripheral retina and a disruption of its layered structure. Neurogliosis, thickened Mullers fibers, and peripheral pigmentation commonly accompanied the reduction in neural elements and the enlargement of the cysts. The incidence (Tables 15, 16) and extent of peripheral retinal pigmentation was not as great in the hog as in the dog.

The enlarged cysts occasionally occupied the entire area between the limiting membranes of the retina, but in contrast to the dog, were seldom sufficiently distended to protrude into the vitreous body. In fact, marked thinning of the peripheral retina, rather than distension, was characteristic of advanced peripheral cystic degeneration in the hog.

Chorioretinal degeneration

Dog A degenerative and atrophic process which primarily involved the rod and cone and outer nuclear layers was present in 27.9 per cent of the dogs utilized in this investigation (Table 15). The degenerative and atrophic lesions were found in all segments of the retina. In addition to tabulating the total incidence of chorioretinal degeneration, the lesions were classified according to location in the retina as either central lesions (Segment C) or peripheral lesions (Segments A and B). The incidence (Table 15) of central and peripheral lesions was approximately equal in all age groups up to Age Group VI (10.0 - 13.1 years of age). In Age Group VI, the incidence of peripheral lesions was greater than central lesions.

In dogs in Age Groups III and IV (11.0 months - 4.4 years of age), chorioretinal degeneration was characterized by a moderate focal loss of rods and cones and nuclei of the outer nuclear layer. The severity of the focal atrophic lesions was generally increased in dogs in Age Groups V and VI (6.0 - 13.1 years of age). The more severe lesions were characterized by an almost complete loss of the sensory components of the retina and a marked reduction in the thickness of the retina (Figures 90-92). Sclerotic changes in the retinal and choroidal arteries frequently accompanied the atrophic changes (Figure 91).

Chorioretinal degeneration was usually preceded by and associated with alterations in the selectively permeable chorioretinal blood-barrier. Alterations in the blood-barrier were characterized by sclerotic changes in the choroidal vessels and stroma, thickening of Bruch's membrane (Lamina basalis), degenerative and proliferative changes in the pigment epithelial cells, and by mineralized excrescences existing between the choroid and retina.

The age-related sclerosis of the choroidal stroma and vasculature was described previously in this dissertation in reporting the findings pertaining to age changes in the choroid.

Hypertrophy of the pigment epithelial cell was the most obvious and consistent alteration in the chorioretinal blood-barrier. This change was present in dogs in all age groups, and the incidence increased progressively with age (Table 15). The hypertrophic changes were more pronounced in the relatively less pigmented cells adjacent to the tapetum than in the heavily pigmented cells of the non-tapetal retina. In the tapetal area, the hypertrophic pigment epithelial cells measured up to 40 microns in thickness (normal thickness = 10 microns) and their rounded or convex inner borders protruded deeply into the layer of rods and cones. The cytoplasm of these enlarged cells was granular and often vacuolated (Figure 93). Occasionally, binucleate cells were observed (Figure 93), and in

the older dogs foci of hyperplastic pigment epithelial cells existed between the choroid and retina (Figure 92). The degenerative and proliferative processes were characterized histochemically by increased intracellular accumulation of mineral salts (Figure 94), acid mucopolysaccharides (Figures 95, 96), and lipids (Figure 97).

In addition to the previously designated histochemical alterations, depigmentation followed hypertrophy and hyperplasia of the pigment epithelial cell. Depigmentation was particularly noticeable in the nontapetal portion of the retina (Figure 94). Upon liberation, the rod-shaped pigment granules tended to migrate into the layer of rods and cones.

Another alteration in the blood-retinal barrier, commonly associated with chorioretinal degeneration, was manifested by focal and multiple focal mineralized excrescences in the outer layers of the retina. Morphologically, two types of excrescences were distinguishable. One type was characterized by its dome-shaped appearance, smooth outline, and flattened area of attachment to the pigment epithelial cell (Figures 73 and 98-101). The inner cell membrane of the latter cell enclosed the dome-shaped portion of the excrescence. The other type excrescence was typified by its cauliflower-like appearance and narrow basal stalk, which was usually continuous with diffuse mineral deposits in the choroid (Figures 71, 72).

Continuity between the choroidal deposits and the retinal excrescence was effected by means of small discrete fissures in the lamina basalis (Figure 71). Therefore, the irregularly shaped retinal excrescence appeared to originate from choroidal mineralization rather than from the pigment epithelial cell. The extent of protrusion into the outer retinal layers ranged from 15 to 100 microns. Mineralized excrescences reacted positively for mineral salts in sections stained with the alizarin-red-S (Figures 71-73) and Von Kossa's (Figure 100) staining techniques and were also positively stained for acid mucopolysaccharides with the colloidal iron technique of Rinehart and Abul-Haj (Figure 101).

Mineralized chorioretinal excrescences were observed initially in dogs in Age Group II (5.4 - 9.9 months of age), and the incidence (Table 15) was greatest in Age Group III (11.0 - 12.9 months of age). In the subsequent older age groups, the incidence was decreased, and the size and number of excrescences in individual dogs were, generally less than dogs in Age Groups II and III.

Hog Early manifestations of chorioretinal degeneration were present near the ora serrata in 25.0 per cent of the hogs in Age Group I (0.1 - 6.0 months of age). The incidence (Table 16) and usually the severity of the lesions increased progressively with age. With one exception (Hog No. 119-259, 7.0 years of age), the

degenerative lesions were peripherally located in all hogs. Degeneration was predominantly restricted to segment "A" of the retina, however, in animals over three years of age degeneration frequently extended into segment "B". In the one hog in which central (Segment C) chorioretinal atrophy existed, lesions typical of multiple focal embolic retinitis were also present in the inner layers of the retina.

Spontaneous chorioretinal degeneration in the hog was characterized by focal and multiple focal atrophy of the rod and cone and outer nuclear layers. In the older animals (Age Groups IV and V, 3.1 - 8.0 years of age), enlargement and coalescence of the peripheral atrophic foci produced larger areas of atrophy which resulted in marked thinning of the peripheral retina (Figure 102). As in the dog, hypertrophy of the pigment epithelial cell, mineralized excrescences located between the choroid and retina, and thickening of the lamina basalis usually preceded or accompanied chorioretinal degeneration in the hog.

The incidence of pigment epithelial cell hypertrophy in the hog was found to increase with age (Table 16). Hypertrophy was accompanied by intracellular accumulation of mineral salts (Figure 103). Neither hyperplasia nor lipid accumulation was observed in the retinal pigment epithelium of the hog.

The more peripheral pigment epithelial cells near the ora serrata were often obscured by the presence of compact aggregates of melanin granules which were continuous with pigment beneath the Pars ciliaris retinae (Figure 102). In hematoxylin and eosin stained sections the round melanin granules were stained a deep black, whereas, the rod-shaped pigment granules of the pigment epithelial cell stained a yellowish-brown. Invariably, some degree of peripheral chorioretinal degeneration, as evidenced by atrophy of the rods and cones and outer layer, existed adjacent to the melanin aggregates (Figure 102).

The frequency distribution within age groups of chorioretinal mineralized excrescences in the hog was relatively comparable to the dog; e. g., the incidence increased in the younger and decreased in the older age groups (Tables 15, 16). The formation of mineralized excrescences was preceded by increased intracellular mineralization, depigmentation, and hypertrophy of the pigment epithelial cell. These changes were followed by effusion of mineralized transudates from the choroidal vasculature, through the chorioretinal blood barrier and into the retina proper. The resulting retinal excrescences were rounded to pedunculate in shape, with a very irregular internal structure (Figure 104). The mineralized excrescences observed in the hog were, generally, not as large as in the dog.

Vascular changes with age

Dog Age-related changes in the retinal vessels of the dog were characterized by a moderate, usually uniform thickening of the vessel walls of the retinal arterial network. Mural thickening was first apparent in dogs in Age Group III (11.0 - 12.9 months of age) and was restricted in this age group to the larger retinal arteries near the optic nerve. In the succeeding age groups, the thickness of the vascular wall of the larger retinal arteries was gradually increased with age. The walls of the more peripheral medium size arteries and arterioles, also became thickened with age.

Histochemically, mural thickening was characterized in dogs in Age Group III by an increase in the thickness and prominence of a PAS-positive, subendothelial basement membrane and a slight deposition of fibrocollagenous connective tissue in the medial portion of the vascular wall. In subsequent age groups, the PAS-positive basement membrane, upon progressive enlargement, tended to fragment and reduplicate (Figure 105). This fragmentation and reduplication resulted in a network of PAS-positive fibrils which were dispersed concentrically throughout the media. Progressive increase in the fibrocollagenous connective tissue produced initially hypertrophy and eventually fibrous replacement of the smooth muscle cells of the

retinal arteries and arterioles (Figure 106). Focal accumulations of an amorphous material, which stained positively for acid mucopolysaccharides, accompanied the increase in fibrous tissue in the vascular wall.

Marked perivascular edema and slight perivascular gliosis (Figures 81, 82, 91) were usually concomitant with retinal arteriosclerosis in dogs in Age Groups V and VI (6.0 - 13.1 years of age). Fibrous intimal sclerosis or atheromatous intimal plaques in the retinal vessels were not observed in any of the dogs utilized in this investigation. However, diffuse lipid deposition was present in the thickened arteriolar wall of one dog 12.9 years of age (Dog No. M33). Little alteration was observed in the retinal venous system except for an almost imperceptible increase in the thickness of the venous walls in dogs in Age Groups V and VI. Generally, the lumens of these vessels were greatly dilated. Pigmentary deposits, glial cells, and macrophages often surrounded the prominent retinal vein located near the ora serrata.

Hog Changes with age in the retinal vessels of the hog were, generally, similar to the age-related alterations observed in the dog. Initial thickening of the walls of the retinal arteries occurred in hogs in Age Group III (1.2 - 2.9 years of age). As in the dog, the early changes consisted of an increased prominence of the PAS-

positive, subendothelial basement membrane and a slight deposition of fibrocollagenous connective tissue in the media of the larger retinal vessels near the optic nerve. These early changes were followed by gradual enlargement and reduplication of the basement membrane, increased intramural fibrocollagenous connective tissue and medial accumulation of acid mucopolysaccharides. Perivascular edema and perivascular gliosis usually accompanied the increase in thickness of the arterial walls.

DISCUSSION

Dimensional Change with Age

The growth pattern of the bulbus oculi of the dog was found to be essentially similar to the pattern described by Scammon and Wilmer (1950) in man. Scammon and Wilmer detected little change in the dimensional aspects of the eyeball in man after puberty and none after the early twenties. In dogs less than 13 months of age (maturation period), the maximum size of the transverse, vertical, and anteroposterior diameters of the bulbus oculi was attained at approximately ten months of age. During this period all diameters of the bulbus oculi were curvilinear with respect to age. It was interesting to note that these regression curves were similar to regression curves established by workers at the Gaines Dog Research Center (1965) pertaining to an increase in body weight in Beagle dogs in the same age range. In dogs over 13 months of age (postmaturation period), the only significant change in the dimensional aspects of the eyeball occurred in the anteroposterior diameter.

In contrast to the dog, all diameters of the bulbus oculi of the hog continued to increase in size during the postmaturation period. The transverse and vertical diameters reached a maximum size

at six years and declined slightly between six and eight years of age; whereas, the anteroposterior diameter increased linearly with age throughout the postmaturation period. A likely factor responsible for this continued increase in diameter sizes of the bulbus oculi was the tremendous increase with age in body weight of hogs in the Postmaturation Age Group. Cursory evaluation revealed that the average body weight of the 86 hogs in the Postmaturation Age Group was more than double the average body weight of the 22 hogs in the Maturation Age Group. Postmaturation increase in body weight was found to be much less in the dog than in the hog.

Distortion created by the standardization of the intraocular pressure with intraocular injections of formalin prior to measurement could not be discounted as a possible factor in accentuating the dimensions of the bulbus oculi. However, since all eyes were subjected to the same standardization technique, individual measurements should have reflected an equal amount of distortion.

In the dog, the central thickness of the cornea, the substantia propria, and the corneal epithelium, as well as the transverse and vertical diameters of the cornea reached their approximate mature dimensions during the first thirteen months of life. In the postmaturation period there was no significant dimensional change in these structures. These findings in the dog were comparable to

measurements made in man by Smith (1890) and Berliner (1949) which indicated that the total thickness and transverse diameter of the cornea were more or less independent of adult age.

In keeping with the generally more advanced development of most ocular structures in the neonatal pig than in the newborn puppy, the corneal epithelium was found to be essentially mature dimensionally in the former species at birth. Furthermore, there was no significant change in the thickness of the corneal epithelium of hogs in either the Maturation or Postmaturation Age Groups. However, other corneal dimensions of the hog continued to increase in size during the postmaturation period. The transverse and vertical diameters of the cornea increased linearly with age throughout the postmaturation period. The central thickness of the cornea and the substantia propria attained maximum dimensions at approximately four years of age and declined slightly in subsequent years.

Apart from changes associated with normal growth, the most consistent and statistically significant age-related dimensional change in the cornea of both species consisted of a progressive increase in the thickness of Descemet's membrane. During the postmaturation period, Descemet's membrane increased linearly with age in increments of one micron per year in the dog and almost four microns per year in the hog. These findings were comparable

to observations in the rabbit by Prince (1964) who noted an increase in the thickness of Descemet's membrane from 7 - 8 microns in the young up to 15 microns in older rabbits. Wislocki (1952) pointed out the generally held opinion thatDescemet's membrane represented a hypertrophied basement membrane of the endothelial cell. Ultra-structural studies by Jakus (1956) further substantiated this opinion by demonstrating an abundance of endoplasmic reticulum in the endothelial cell which according to Jakus was related to the manufacture and maintenance of Descemet's membrane.

The fallacy of ascertaining the curvature of the anterior surface of the cornea by keratometric measurements and extrapolating such determinations as being precisely indicative of the curvature in the vital state was recognized prior to undertaking this specific portion of this investigation. Furthermore, it was recognized that the artificially induced intraocular pressure of 120 mm. Hg , which was needed to eliminate all undulations in the fixed corneal surface prior to performing a keratometric reading, far exceeded the range of 16 - 30 mm. Hg ascribed by Magrane (1965) as being normal for the dog. In spite of these existing technical difficulties, the findings of this investigation revealed an age-related flattening of the anterior surface of the cornea in both the dog and hog. These findings were remarkably similar to observations pertaining to living human subjects by Fischer

(1948), Marin-Amat (1956), Wolff (1961), Hogan and Zimmerman (1962) and Weale (1963) as well as to measurements made on living rabbits by Stone and Leary (1957).

The decrease in corneal curvature with age occurred predominantly in the younger years in both species. In fact, approximately 75 per cent of the decrease took place during the first 12 months of life, and although planation continued throughout the remainder of life, it was relatively minimal after one year of age.

In accord with the findings of Prince et al. (1960), the canine sclera was found to be thickest in the ciliary region, slightly thinner at the posterior pole, and thinnest in the equatorial region of the bulbus oculi. The mature dimensions in each of these three regions were attained during the first year of life, and a significant alteration either in total thickness or in the relative size of the three measured zones did not occur in subsequent years.

However, the sclera of the hog increased in thickness up to approximately five years of age. After five years of age, a decrease in thickness was noted in all regions of the sclera. A similar decrease in scleral thickness in aged human subjects was reported by Friedenwald (1952) and Vannas and Teir (1960). Contrary to the findings of Friedenwald and Vannas and Teir in man and the findings of the present investigation with reference to the hog, Melanowski

and Stachow (1958) reported a progressive increase with age in the scleral thickness in man. The findings of the present study also revealed a change in the relative thickness of the various scleral segments of the hog as age increased. The alteration in relative thickness resulted from a greater increase in the thickness of the sclera at the posterior pole than in the ciliary and equatorial regions.

Species comparison of scleral and corneal thickness in the dog and hog disclosed almost identical patterns of dimensional change with age for these two fibrous tunics of the eye. Correspondingly, the sclera and cornea were also correlated with changes in the dimensional aspects of the bulbus oculi. The anteroposterior diameter of the latter structure was a notable exception to this general observation.

Histologically and histochemically several factors appeared to contribute to the change in thickness of the sclera with age. Foremost among the factors responsible for an increase in total scleral thickness was an increase with age in the thickness of the individual scleral fibers. Other frequently observed contributing factors consisted of intrascleral deposition of lipids and minerals. In later years the accumulation of extraneous material and the increase in fiber size were compensated by a reduction in the loose and elastic

connective tissue components of the sclera. Reduction in these connective tissue elements resulted in many cases in an increased density of the sclera and a subsequent reduction in scleral thickness in the aged animals.

In the dog, the central and basal thickness of the iris and the thickness of the basal lamina of the ciliary crown followed similar curvilinear growth patterns during the maturation period. In contrast to the cornea and sclera in which a postmaturation increase in thickness was not noted, the iris and basal lamina of the ciliary crown continued to increase in thickness throughout the remainder of life. Intuitively, it appeared logical to explain such an increase in the iris and ciliary crown upon the basis of the inherent muscular functions of the iris and ciliary body or possibly on the basis of a greater degree of metabolic activity in these structures than in the essentially fibrous structures of the eye. However, subsequent findings with regard to the dimensional aspects of the porcine iris and ciliary body tended to negate such a simple explanation.

Dimensional change with age in the iris and ciliary body of the hog proved to be considerably more complex than in the dog. Surprisingly, the central iridal thickness was found to be slightly larger in the newborn pig than at 12 months of age. The slight insignificant decrease in this dimension during the maturation period was

succeeded by a significant increase during the postmaturation period. The complexity of the dimensional changes with age in the iris of the hog was accentuated by the fact that the basal thickness increased during the maturation period; whereas, a significant change in size was not detected during the postmaturation period. Since comparable changes to those observed at the base of the iris were noted in the basal lamina of the ciliary body there appeared to be some degree of interrelationship between the size of these segments of the iris and ciliary body. Considering the close proximity of the two segments as well as the similar stress to which these segments were normally subjected, such an assumption seemed quite plausible.

Histological and histochemical factors which appeared to be accountable for the increased thickness of the iris with age were increased perivascular and stromal fibrosis, mineral deposition, and increased pigmentation. In addition to the aforementioned changes found in the iris, lipid accumulation contributed to the increase in thickness of the basal lamina of the ciliary crown.

The investigations of Collins (1890), and Dub (1891), and Raeder (1922) established that the human lens increased in thickness throughout life. In this respect, the findings of the present investigation revealed that the lens of the hog was similar to the human lens.

In contrast, the lenticular thickness of the dog, after following a typical curvilinear growth pattern during the maturation period, did not increase in either the equatorial or polar planes during the postmaturation period. In fact, during the latter period, a non-significant linear decrease with age occurred in both planes. These findings in the dog substantiated a general statement made by Weale (1963) which maintained that animal lenses ceased their growth at a relatively young age. However, the diametrically opposed findings with regard to postmaturation growth of the lens in the dog and hog pointed out the existence of species differences in lenticular growth and necessitated that a species specification be attached to Weale's general statement.

The most striking age-related dimensional change in the lens of the dog and hog occurred in the anterior capsule. In the Postmaturation Age Groups, the thickness of the anterior capsule, measured at the geometric axis of the bulbus oculi, increased at the rate of 6.43 microns per year in the hog. Although statistically significant linear increases were noted in the thickness of the posterior lens capsule in both species, these increases were relatively insignificant when compared to the astounding increases found in the anterior capsule.

Prince (1964) considered the anterior capsule as probably a secretory product of the underlying lens epithelium and likened its

structure and formation to Descemet's membrane of the cornea. The similar age-related linear increase in thickness of the two structures, as unveiled by the present study, pointed out another similarity and justification for comparison of Descemet's membrane and the anterior lens capsule.

According to Hogan and Zimmerman (1962), the anterior capsule of the lens served to assist the lens in absorbing nutrients from the aqueous fluid and to provide insertion for the zonular fibers and thereby to mould the shape of the lens in accommodation. The increased thickness with age of the anterior capsule as determined in the present study appeared to reflect the mechanical influence of the capsule's accommodative function, the influence of nutritive diffusion from the anterior chamber, and the postulated secretory influence of the underlying lens epithelium.

Variable data with regard to the sagittal thickness of the lens epithelium offered no conclusive evidence as to a correlation between epithelial thickness and anterior capsular thickness.

The histological immaturity of the canine retina at birth was manifested dimensionally by a curvilinear decrease in both central and peripheral thickness during the first eight months of life. During this period the retina progressed developmentally from a highly undifferentiated structure composed almost entirely of enlarged

primitive appearing nuclei to a multilayered structure with extremely specialized functions. The slope of the regression line which indicated retinal thickness inclined slightly from eight to thirteen months of age. Increase in thickness during this period likely denoted the initiation of various cystic and proliferative processes, which became more apparent in dogs in the Postmaturation Age Group.

Although there was a slight linear increase in central retinal thickness and a linear decrease in peripheral retinal thickness in the 32 dogs in the Postmaturation Age Group, these changes were not statistically significant. The counter effects of cystic and proliferative as opposed to atrophic processes apparently accounted for the insignificant alterations in total retinal thickness during this period.

In general, central and peripheral choroidal thicknesses in the dog followed almost identical patterns of regression with age as did corresponding segments of the retina; e. g., change in thickness of one structure was accompanied by a change in thickness of the other structure. Therefore, in keeping with this general observation, significant changes in choroidal thickness occurred only during the maturation period in the dog.

In the hog there was no significant alteration in central or peripheral retinal thickness in either the maturation or postmaturation

periods. The absence in this species of a significant decrease in retinal thickness during the early portion of the maturation period was indicative of the advanced developmental and histological maturity of the porcine retina at birth. In addition, choroidal thickness in the 22 hogs in the Maturation Age Group was not significantly altered with increased age. However, in the 86 hogs in the Postmaturation Age Group both the central and peripheral choroidal thicknesses followed a significant linear increase with age. Since retinal thickness remained essentially unchanged in the post-maturation period there appeared to be little correlation between choroidal and retinal thickness in this particular age group of hogs. Consequently, continued increase with age in choroidal thickness of the hogs in the Postmaturation Age Group was more likely related to the previously described increase in the dimensions of the bulbus oculi of this species than to retinal thickness. In explanation, the increased dimensions of the bulbus oculi during the postmaturation period appeared to be accompanied by an increased vascular supply to the constituent parts of the globe.

Fibrotic Changes with Age

Casarett (1964) emphasized that in "normal" aging of mammals, the most general, universal, and deleterious change consisted of a

progressive increase in the "histohematic barrier". Casarett defined this appropriate term as the connective tissue barrier which developed with age between blood and dependent parenchymal cells. The development of the "histohematic barrier" was characterized by an increase of collagenous fibers and fibrillar density along with a relative decrease of ground substance in the interstitial connective tissue and basement membranes.

Apart from vascular sclerosis and an increase in the thickness of the scleral fibers, fibrotic changes with age in the ocular tissues of the dog and hog were restricted to the constituent parts of the uvea. Considering the important nutritional functions of the choroid and the muscular functions of the ciliary body and iris, the age-related increase of collagenous fibers in the uvea was deemed extremely significant.

The decrease in the diameter of the pupil with age was documented by numerous investigators (Birren, Casperson, and Botwinick, 1950; Kumnick, 1956; Kadlecova, Peleska, and Vasko, 1958; Leinhos, 1959). In spite of its unquestioned occurrence, the cause of senile miosis engendered considerable diversity of opinion. Fischer (1948) attributed senile miosis to sclerosis of the iridal tissue and vascular sclerosis; whereas, Kornzweig (1954) postulated that dilator muscle atrophy in addition to vascular sclerosis were accountable for senile

miosis. Atrophy of both the dilator and sphincter muscles, vascular rigidity, and calcification were found in cases of senile miosis by Larsson and Österlind (1943). Rones (1938) detected hyalinization of the dilator muscle and an increase of collagenous fibers between the fibers of the sphincter muscle. Rones further noted that atrophy of the sphincter muscle fibers did not occur in spite of the partitioning effect created by increased fibrosis.

Various combinations of all the forenamed alterations were observed in the irides of dogs and hogs. However, the only histologic alteration consistently found in all irides was an increase in the collagenous fibers in the iridal stroma. Increased fibrous elements, and in many instances increased pigments, impinged upon and were interspersed among the smooth muscle fibers of the sphincter and dilator muscles. In contrast to the observations of Rones (1938) atrophy of the sphincter muscle was found to occur in the dog and hog as a result of the partitioning effect created by interstitial fibrosis. Weale (1963) was of the opinion that neither senile increase in the rigidity of the tissue nor atrophy of iridal muscles explained the reduced ability of the iris to constrict with age. In contrast to Weale's first assumption, the findings of this investigation offered strong evidence in favor of attributing senile miosis primarily to increased sclerosis of the iridal stroma. Furthermore, these

findings indicated that muscular atrophy was secondary to iridal fibrosis and/or increased pigmentation of the iris, and except for possibly dilator atrophy, muscular atrophy contributed little to the production of senile miosis. In fact, simple sphincter atrophy would likely produce a state of mydriasis rather than miosis. On this basis, senile miosis accompanied by atrophy of the dominant sphincter muscle was explainable only by an overriding influence of iridal fibrosis and rigidity upon the loss of constrictor response.

The most outstanding example of increased fibrosis with age in the eye of the dog and hog occurred in the ciliary body. In this structure a progressive increase with age of fibrous connective tissue was observed in the basal lamina and ciliary processes of the corona ciliaris and in the ciliary muscle. The earliest manifestations of increased fibrous accumulation were detected between the fibers of the ciliary muscle and in the basal lamina. Subsequent increase at the latter site was followed by an increase of collagenous fibers in the ciliary processes. Extensive fibrosis resulted in marked distension and hyalinization of the connective tissue core of the processes and a diminution of the previously extensive vascular network. It was considered appropriate to emphasize the existence of mineral and lipid deposits at these sites of increased fibrosis and hyalinization.

In the dog and hog hyperplasia of the pigmented and nonpigmented epithelial cells of the ciliary processes was frequently concomitant with increased fibrosis and hyalinization of the underlying connective tissue cores of the ciliary processes. Rones (1938) attached great significance to this progressive phenomenon of fibrosis, hyalinization, and hyperplasia in regard to the effective functioning of the ciliary epithelium in the formation of aqueous humor.

Various reports in the literature (Van der Hoeve and Flieringa, 1924; Rones, 1938; Friedenwald, 1952; Schofield, 1961) attested to an age-related increase in ciliary muscle fibrosis and atrophy in man. The description of these senile alterations in man were, for the most part, similar to changes noted in the dog and hog. Van her Hoeve and Flieringa (1924) found no decrease in the functional ability of the ciliary muscle in spite of increased muscular fibrosis and atrophy. These authors attributed the decline in accommodative powers of the aged to lenticular changes. However, Rones (1938) observed fatty droplets in the degenerative muscular fibers and asserted that these droplets likely impaired the function of the ciliary muscle and were important in the production of presbyopia in man. Lipid deposition was infrequent in the ciliary muscle of the dog and hog and in this respect the findings of the present investigation did not correspond to the findings of Rones. However, the extent

of fibrosis and atrophy of the ciliary muscle in the dog and hog indicated a likely reduction in accommodative powers in these animals.

Kerschbaumer (1892) proclaimed that an increase in the interstitial fibrillar material and arteriosclerotic lesions were important features in the aging process of the choroid. In recent years primary emphasis was focused upon the sclerotic changes which occurred with age in the choroidal vessels with little mention of the fibrotic changes in the choroidal stroma. Considering the highly vascular structure of the choroid and the important nutritional function of the choroid in nourishing the outer layers of the retina, this emphasis appeared largely justified.

In accord with the findings of Kerschbaumer in man, stromal fibrosis increased progressively with age in the choroid of the dog and hog. Collagenous fibers were increased in the intervascular connective tissue, and the increase was accentuated around the choroidal vessels. In the case of perivascular accumulations, stromal fibrosis often blended with fibrillar alterations in the vascular wall. The blending effect was most evident in the choroidal arterioles and choroidocapillaris.

Stromal and perivascular fibrosis coupled with vascular sclerosis quite likely exerted a significant alteration in the semipermeable capabilities of the choroid as part of the blood-retinal

barrier. Furthermore, stromal fibrosis produced an environment which likely promoted the accumulation of extraneous substances within the choroid and hindered their removal by the choroidal circulation. The accumulation of both minerals and lipids in the fibrosed choroidal stroma of the dog and hog substantiated the validity of this observation.

Schwarz (1953) determined that the thickness of the embryonal fibers of the cornea and sclera was approximately equal. Scleral fibers were found to increase progressively in thickness with age, while the thickness of corneal fibers remained essentially unchanged. In support of these findings by Schwarz, average scleral fiber thickness in the dog and hog more than doubled during the span of time represented by the youngest and oldest age groups. As the scleral fibers thickened with age, connective tissue became less abundant, and lipid and mineral deposition was increased in the sclera. These factors were likely instrumental in producing an age-related increase in ocular rigidity.

Pigmentary Changes with Age

Pigmentary changes with age in the eye of the dog and hog were associated with melanin-producing cells in the surface epithelium, the uvea, and the pigmented epithelial cells of the retina, ciliary

body, and the iris. According to Mann (1950), cutaneous and uveal pigments increased after birth and pigments within the pigmented epithelia were not increased. In regard to the pigment epithelial cell of the retina, Mann's statement was essentially in accord with the findings of this investigation, since an increase with age in the pigmentation of this particular cell was not observed in either species. In fact, depigmentation typically accompanied the hypertrophic and degenerative processes so frequently observed with aging of the retinal pigment epithelial cell. Contrary to observations in man made by Tower (1955) and Kaczurowski (1962) neither clumping nor clustering of the pigment granules were observed in the retinal pigment epithelial cell of the dog and hog.

With increased age, the pigment epithelial cells of the iris and ciliary body tended to undergo hypertrophy and hyperplasia. In contrast to the pigment epithelial cells of the retina, pigment granules increased with age in the pigmented epithelia of the ciliary body and iris. Hypertrophy and pigment accumulation in the pigment epithelial cell of the iris resulted in the formation of pigmented excrescences on the posterior surface of the iris. Pigment granules, apparently liberated from these excrescences, were found in the dog and hog on the posterior surface of the cornea, the anterior surface of the lens, at the chamber angle, and in the trabecula

meshwork. Similar observations in the human eye were made by Schofield (1961) and Hogan and Zimmerman (1962). Schofield pointed out that iridal pigment, fragments of lens capsule, and other cellular debris carried by the aqueous fluid into the trabecula meshwork were undoubtedly contributing factors in the etiology of chronic glaucoma.

Pigment invasion at the limbal region of the cornea was detected in both species utilized in this investigation. However, distinct species differences were observed in regard to the portion of the peripheral cornea invaded by these pigments and in the origin of the invasive pigments. In the hog, pigment invasion of the cornea was restricted to the middle portion of the substantia propria and appeared to originate from melanocytes dispersed along the corneo-scleral junction in the sclera. In the dog, corneal pigmentation was found in the portion of the substantia propria adjacent to Descemet's membrane and in some cases within the membrane proper. In agreement with the work of Roberts (1954), the origin of these pigmentary particles appeared to be from melanocytes in the ciliary body.

Pigment invasion of the superficial stromal lamellae of the cornea was not observed in either species. Neither was a significant increase noted in the pigmentation of the germinal cells of the corneal epithelium.

A lucid explanation as to the basic cause of corneal pigmentation in the two species was not apparent on account of several conflicting observations. In the dog, deep corneal pigmentation was possibly explainable upon the basis of a reactionary response to alterations in the peripheral portion of the corneal endothelium and in Descemet's membrane; e. g., mineralized excrescences, colloid excrescences (Hassal-Henle bodies), and lipid deposition. The presence of histiocytes, fibrocytes and occasionally monocytes in conjunction with pigment invasion gave some credence to such an explanation. In contention with this explanation was the fact that in the hog posterior corneal alterations, except for lipid deposition, were as prevalent and intense as in the dog. Yet deep corneal pigmentation was rarely observed in the hog. The lesser degree of lipid deposition at this site in the hog was the only evidence uncovered which possibly explained the relative lack of deep corneal pigmentation in this species.

Furthermore, the incidence of scleral pigmentation at the corneoscleral junction was approximately equal in both species with the intensity of pigmentation generally being greater in the dog. From this observation one would logically expect at least a proportional degree of pigment invasion into the middle portion of the substantia propria to occur in both species. These conflicting observations presented more questions than answers in regard to the basic

factors responsible for pigmentary invasion of the cornea and offered an interesting direction for further investigation.

Although extreme variations were observed between breeds of dogs and hogs and between animals of the same breed, melanocytes were generally increased with age in the stroma of the iris, ciliary body, and the choroid. The age-related increase in uveal pigmentation was consistent with the findings of Mann (1950) in the human eye.

Peripheral retinal pigmentation was observed in both species, with the incidence and intensity of pigmentation being greater in the dog than in the hog. The staining qualities and morphology of the invasive pigment granules were similar to melanin granules in the pigment epithelial cell of the orbiculus ciliaris and in the melanocytes of the choroidal stroma, rather than to the typical rod-shaped granules of the pigment epithelial cell of the retina. Therefore, the origin of the invasive pigments of the peripheral retina appeared to be from either choroidal melanocytes or from the pigmented epithelial cells of the portion of the orbiculus ciliaris located near the ora serrata. Dense pigmentation which was continuous with and similar to pigment granules in the latter cells extended centrally between the choroid and retina for a distance usually comparable to the extent of retinal pigment invasion.

In the older dogs and hogs, peripheral retinal pigmentation was most often concomitant with age-related degenerations of the peripheral retina; e. g., peripheral cystic degeneration and peripheral chorioretinal degeneration. Since these degenerative processes were observed in younger animals, prior to the intitiation of pigment invasion, peripheral pigment invasion appeared to be secondary to the degenerative processes.

Lipid Deposition

The principal sites of spontaneous lipid deposition in the eye of the dog and hog were the cornea, sclera, ciliary body, and the choroid. In these sites, there was a progressive increase with age in the incidence and intensity of lipid deposition. In the iris, retina, and lens, lipid deposition was either infrequent or nonexistent in both species.

In comparison, the incidence and intensity of deposition was found to be much greater in the dog than in the hog, and the initial ocular deposition of lipids occurred at a younger age in the dog. These comparative findings were quite unexpected, since other investigators, utilizing a large number of the same dogs and hogs included in this study, demonstrated spontaneously occurring atherosclerotic plaques and/or intimal thickening in the coronary

arteries, the cerebral arteries, the abdominal and thoracic aorta, and at the bifurcation of many of the other major blood vessels (Skold and Getty, 1961; Getty and Skold, 1962; Getty, 1965; Getty, 1966). Cardiovascular lesions, as reported by these investigators, were characterized, in part, by fatty intimal streaks which contained fine droplets of sudanophilic material in foam cells and extracellularly. Getty (1966) observed lipid containing plaques in the wall of the abdominal aorta of hogs as young as six months of age and in all hogs over one year of age; whereas, lipids were not detected in the blood vessels of dogs until the animals reached five years of age.

A difference in the genesis of ocular and cardiovascular lipid deposition was considered probable, inasmuch as, Getty (1966) demonstrated an inherent predisposition for early occurring, lipid containing, vascular lesions in the hog, and this investigator found a partial resistance to ocular deposition in the same species. In reference to the dog, the findings of the two investigations were also reversed. The present study indicated a specificity for ocular deposition in the dog; whereas, Getty found a partial resistance to atheromatous lesions of the cardiovascular system.

Additional evidence of a dissimilarity in the genesis of lesions in the two sites was manifested by a difference in the histological appearance of lipid deposits in the eye and in the cardiovascular

system. In the cornea, sclera, ciliary body, and the choroid, lipids were predominantly present in a diffuse, homogeneous form or as small extracellular droplets. The diffuse ocular depositions imparted a "paint brush" effect to the infiltrated tissues and were not associated with a particular cell, such as the macrophage (foam cell).

A determination of the complex nature of lipid deposition in the ocular structures has been the objective of numerous investigators (Attias, 1912; Verse, 1916, 1925; Cogan and Kuwabara, 1955, 1957a, 1957b, 1959a; Kuwabara and Cogan, 1957; Schofield, 1961; Janes, 1964). Various, probably interrelated, factors were considered by these investigators as contributory to the increased deposition of lipids in the eye with age. Among the chief factors considered were vascular ischemia (Schofield, 1961), hypercholesteremia (Attias, 1912; Verse, 1916, 1925; and Janes, 1964), and local fat synthesis by corneal cells, fibrocytes, and macrophages in the presence of a suitable substrate (oleic acid or a derivative of oleic acid) and a species nonspecific serum factor (Cogan and Kuwabara, 1955, 1957a, 1957b; Kuwabara and Cogan, 1957).

The presence of vascular sclerosis and increased connective tissue fibrosis in the areas of lipid deposition in the ciliary body, sclera and choroid supported the contention of Schofield (1961) that a diminished blood supply to the tissues and the subsequent faulty

oxidation of fatty acids were important factors in the age-related deposition of lipids in the structures of the eye.

Factors other than vascular ischemia must be considered in order to explain the deposition of lipids found in the avascular cornea. Admittedly, the initial depositions were restricted to the substantia propria and were present in close proximity to the marginal network of scleral vessels. However, as age increased, depositions were progressively extended axially beneath the corneal epithelium and adjacent to Descemet's membrane. The lipogenic capacity of the corneal stromal cells, as clearly demonstrated by Cogan and Kuwabara could satisfactorily explain lipid deposition in the deeper portions of the cornea.

Additional support for the lipogenic theory of Cogan and Kuwabara was unveiled by this study, in that other histochemical alterations which likely promoted lipogenesis were detected in the cornea of the dog and hog. These alterations, which were most prominent at the corneal periphery, consisted of diffuse and focal accumulations of acid mucopolysaccharides and minerals in the corneal endothelium and epithelium, and Descemet's membrane. The presence of these entities likely affected the barrier and transport functions of these corneal structures and consequently, permitted the inward transport of factors favorable for lipid

deposition. Cogan and Kuwabara (1957a) established that a serum factor, necessary for lipogenesis by the corneal cell, must contain primarily calcium and to a lesser degree magnesium ions. These authors further noted that excess calcium diminished subsequent lipogenesis. The latter fact possibly clarified the lesser degree of lipid deposition in the cornea of the hog, since the intensity of mineralization and acid mucopolysaccharide accumulation was far greater in the cornea of the hog than in the dog.

Cholesterol deposits per se were infrequent and weakly demonstrable in lipid deposits of the ocular tissues of the dog and hog. This finding was compatible with those of Janes (1964) in experimental lesions in rabbits and Attias (1912) in spontaneous lesions in man. Janes (1964) postulated that serum cholesterol was oxidized prior to deposition in the ocular tissues and was present in tissue in a degraded form. Serum cholesterol determinations carried out by Getty (1966) on a portion of the dogs and hogs utilized in this investigation revealed a progressive increase in serum cholesterol with age in both species.

Mineralization

Mineralization in one or more forms was found in all structures of the eye of the dog and hog. A sequential pattern of progressive

mineralization was detected which led to the development of various changes in the normal histological and histochemical structure of the ocular tissues as age increased. The initial accumulation of mineral was observed in both species during the first two months following birth and was usually present at this age in an intracellular form. Intracellular accumulations were found in the stromal cells of the cornea, sclera, iris, ciliary body, and choroid; in the epithelia of the iris, ciliary body, and cornea; the corneal endothelial cells; and the ganglion and pigment epithelial cells of the retina. The vascular endothelium was not immune to intracellular accumulation of minerals, particularly in the vessels of the scleral venous plexuses and the vortices veins.

Subsequent increase in intracellular mineralization in the fore-named stromal cells resulted in extracellular deposition in the tissues, first in a diffuse form, and eventually, as focal and multiple deposits. Mineral accumulation in the epithelial and endothelial cells tended to form mineralized excrescences which projected from the surface of the usually hypertrophic cell.

Although mineralization was characterized by a high incidence and a progressive increase in intensity during the maturation period, both the incidence and the intensity tended to be stabilized in dogs and hogs over two years of age. Actually, a slight reduction in

incidence and intensity was noted in most forms of mineralization, especially extracellular depositions, in the older dogs and hogs (Dog, Age Group VI, 10.0 - 13.1 years of age; Hog, Age Group V, 6.0 - 8.0 years of age). Of more than casual interest was the fact that mineralization was initiated early in the maturation period, at a time when mineral metabolism within the body was probably greatest and was stabilized or reduced in later years when mineral metabolism was likely decreased.

According to Zeiter (1962), calcium deposition within the eye, as in other tissues of the body, was the natural consequence of degenerative processes. In view of the occurrence of intracellular and extracellular mineralization in both dogs and hogs as young as two months of age, mineralization, as observed in this study, appeared to be a precursor rather than a sequel to degeneration.

Various investigators (Boyd and Neuman, 1951; Zimmerman, 1961) described a distinct relationship between the accumulation of minerals and mucopolysaccharides in the tissues. Boyd and Neuman (1951) demonstrated the ability of chondroitin sulfate to bind calcium and phosphorus by a process of ion exchange; whereas, Zimmerman (1961) observed that mineral deposits in many tissues of the eye appeared to lie in a matrix of hyaluronidase-resistant acid mucopolysaccharides. Zimmerman postulated that such mucoid material accumulated first

and served as mineral-binding resins which led to mineralization. In the dog and hog, mineral deposits were consistently accompanied by accumulations of acid mucopolysaccharides. These concomitant accumulations were found in the cornea, sclera, ciliary body, iris, lens, choroid, and retina of both species.

Acid mucopolysaccharides, without mineralization, were frequently observed in the mucoid debris present within cysts found at the periphery of the retina and in the orbiculus ciliaris (pars plana).

Due to the possible clinical and functional implications, mineralization as found in certain ocular tissues of the dog and hog was considered worthy of additional comment.

Magrane (1965) described superficial (epithelial) and deep (endothelial) dystrophies in the dog and considered both conditions to be obscure in origin. Although mineralization was not specifically implicated in the genesis of the lesion, Magrane characterized superficial corneal dystrophy in the dog as being noninflammatory, slowly progressive, and usually unilateral in nature. Similar corneal lesions in apparently normal eyes of man were classified by Duke-Elder (1938) as idiopathic or primary band keratopathy. The earliest histologic change in band keratopathy in man was manifested by basophilic stippling in Bowman's membrane, which, according to Hogan and Zimmerman (1962), represented the deposition of calcium

salts. An interesting explanation pertaining to the initiation of band keratopathy was presented by Radnot (1948). Radnot explained that the greatest amount of evaporation from the corneal surface occurred at the palpebral aperture, and that with evaporation the fluid permeating the cornea became oversaturated with calcium which then precipitated in the corneal stroma. The relevance of sub-epithelial mineralization as observed in the present investigation as an early manifestation of the superficial corneal dystrophies in man and dog was considered plausible.

In contrast to epithelial dystrophy in which only the superficial corneal structures were involved, endothelial dystrophy in the dog produced a diffuse corneal involvement (Magrane, 1965). Clinically, Magrane found this form of dystrophy to be uncommon in the dog and attributed its underlying cause to aging of the tissues and subsequent loss of the ability of the mesenchyme to prevent passage of the aqueous fluid into the corneal stroma. The incidence of posterior corneal alterations, as evaluated histologically in this study, was expectedly much greater than clinically diagnosed changes. Magrane's belief relating to the basic cause and functional effects of these alterations was entirely compatible with the findings of this investigation.

Mineral excrescences, which were found distributed irregularly along the posterior surface of the cornea in both species, likely

affected the barrier and transport functions of the corneal endothelium. In support of this view, focal areas containing acid mucopolysaccharides in a distended form commonly existed in the portion of the substantia propria adjacent to the mineralized excrescence. Acid mucopolysaccharides, usually in a less distended form, were also found in the substantia propria near the limbus and beneath the corneal epithelium. The edematous appearance of acid mucopolysaccharides at these sites was considered as indicative of increased permeability of the corneal endothelium and epithelium and increased fluid transport from the pericorneal network of vessels.

These observations supported certain facets of a hypothesis presented by Hedbys (1961) regarding the importance of acid mucopolysaccharides in corneal edema. In brief, Hedbys proposed that acid mucopolysaccharides existed normally in the corneal stroma as long-chain, negatively charged macromolecules which resisted swelling, or as loose polymers which encouraged swelling. Conceivably, the accumulation of excess mineral in the cornea, as observed in this investigation, exerted an opposing attraction to the negatively charged acid mucopolysaccharides, thereby negating the tendency for the latter to retain their usual tight structure, and diminishing their function as a bonding substance for contiguous stromal lamellae. Therefore, corneal edema as viewed in this

study appeared to be promoted by the following sequence of events: 1) alteration in the "barrier structures" of the cornea; 2) an influx of fluid, enhanced by a high concentration of cationic elements in the corneal stroma via these alterations; 3) and the acceptance of these fluids by anionic elements which were predisposed to swelling by their electroionic environment.

Hypertrophy of the pigment epithelial cell of the retina constituted one of the most constant and progressive changes with age in the eye of the dog and hog. Intracellular accumulation of minerals and acid mucopolysaccharides frequently accompanied hypertrophy, and as a consequence, produced small (10 - 50 microns) excrescences situated between the choroid and the sensory portion of the retina. Diverse opinions existed in the literature as to the etiology of similar excrescences, referred to as drusen, colloid bodies, or hyaline excrescences, in the eye of man.

Most investigators implicated the pigment epithelial cell in the production of the excrescences and attributed their formation either to passive degeneration and transformation of the cell into hyaline masses (Donders, 1855; Rones, 1937; Wolter, 1957), or to active secretion and deposition by the cell (Müller, 1856; Coats, 1905; Verhoeff and Sisson, 1926). More recently, Freidman, Smith, and Kuwabara (1963) introduced evidence which indicated that in many

instances senile drusen were "deposited" or "transformed", as the case may be, in relationship to the capillaries associated with the collecting venules in the choroid. These authors pointed out that the earliest manifestations of drusen formation, even prior to the involvement of the lamina basalis and the pigment epithelial cell, occurred in the choroidal stroma between capillaries associated with the venules. In reconciling this observation with other known facts implicating the pigment epithelial cell in drusen formation, Friedman et al. suggested that the metabolic environment of the pigment epithelial cells in the neighborhood of the capillaries was so altered that the pigment epithelial cells were stimulated to secrete or be transformed into drusen. These authors also suggested the possibility of a preferential passage through the wall of the choroidal capillaries of some component of the circulating blood which accumulated first between the capillaries and then beneath the pigment epithelium.

Mineralized pigment epithelial cells and excrescences, as viewed in the dog and hog, were invariably accompanied by mineral deposits in the adjacent portion of the choroid and in the lamina basalis. This finding supported the conclusions of Freidman et al. (1963) that the microcirculation of the choroid was an important factor in the process leading to the formation of some drusen, and

indicated that a mineral component of the serum might be the unknown serum factor referred to by these investigators. In addition, mineralized excrescences were also observed in the outer retinal layers of the dog and hog which were not associated with the pigment epithelial cell. These chorioretinal excrescences were continuous with focal or diffuse mineral deposits in the choroidal stroma and served to implicate further the choroid as the source of mineralized chorioretinal excrescences.

Prince (1965) pointed out the dependence of the rods and cones, and the outer and inner nuclear layers of the retina upon the choroidal circulation for nutrition. Furthermore, Prince emphasized the important function of the choroid, the lamina basalis and the pigment epithelial cell as a selectively permeable blood-retinal barrier. Alterations in these three structures followed by anoxia and/or chemical imbalance resulted in detrimental effects upon the retinal structures nourished by the choroidocapillaris. In support of these observations by Prince, mineralized excrescences which involved the pigment epithelial cell and/or the lamina basalis and choroid in the dog and hog were accompanied by focal degeneration of the outer retinal layers.

Focal mineral deposits were occasionally observed in both species in the middle and inner layers of the retina. Since a

morphological connection was not demonstrated between these focal deposits and deposits related to the blood-retinal barrier, their origin remained questionable. The significance of intracellular mineralization in the ganglion cell of the retina also remained unclear.

Quantitative studies related to the inorganic constituents of the lenses of man and animals denoted a tendency for calcium to accumulate with age in the lens (Mackay, Stewart, and Robertson, 1932; Fischer, 1933). In support of these studies, lenticular mineralization, preceded by accumulation of acid mucopolysaccharides, was initiated in the dog and hog at approximately two months of age and slowly increased in intensity as age advanced. Lansing (1951) advocated that the accumulation of calcium in tissues frequently accompanied a reduction in cell permeability. Accordingly, progressive nuclear, cortical and capsular sclerosis attendant with aging in the dog and hog quite likely produced a state of decreased cell permeability and an environment capable of fomenting the slow progressive form of mineral accumulation.

In contrast to the slow progressive form of mineralization, another form of lenticular mineralization, characterized by multiple focal mineral aggregates and by a maximum incidence and intensity at approximately one year of age, was observed in the lens of both the dog and hog. The basic factor or factors inciting this exaggerated

form of mineralization in the lens, as well as in other ocular tissues, was not apparent. Inasmuch as calcium and phosphate levels of the blood and the media immediately surrounding the lens were not determined, specific classification of this form of mineralization was considered imprudent at this time.

Mackay et al. (1932) demonstrated a tendency for calcium to accumulate in cataractous lenses. However, Weale (1963) commented that calcium as a causative factor in cataracts was not established. In support of the latter comment, only one case of cortical cataract was observed, histologically, in the 88 dogs and 108 hogs examined.

Vascular Changes with Age

Anatomical studies by Prince et al. (1960) revealed that the principal blood supply to the posterior intraocular structures of the dog and hog were derived from the medial and lateral long posterior ciliary arteries. Both of these arteries, prior to entering the sclera, were found to give rise to numerous branches, the true retinal arteries of the dog and hog, which entered the globe immediately adjacent to the optic nerve. The retinal arteries after traversing the sclera emerged around the optic disc and nourished the inner layers of the retina. Prince et al. further noted that the long posterior ciliary arteries entered the sclera in close proximity to the optic

nerve and gave origin to the short posterior ciliary arteries which supplied the choroid. After giving origin to the latter arteries, the long posterior ciliary arteries continued anteriorly within the sclera on the medial and lateral aspects of the globe and anastomosed with the anterior ciliary artery in the vicinity of the corneoscleral junction. These authors found no evidence of a central retinal artery within the optic nerve, as characteristic in the human eye, in either the dog or hog. Extensive histological examinations performed during the course of this study verified the absence of a central retinal artery in these two species.

The most prominent histomorphological alterations in the ocular vessels of the dog and hog occurred near the optic nerve in the intrascleral segments of the long posterior ciliary arteries, the retinal arteries, and the short posterior ciliary arteries. Hemodynamic stress resulting from the flow of blood into a relatively dense tissue environment, the sclera, and from resistance created by the extensive branching of the arteries at this site was considered a likely factor in the genesis of lesions at this site.

In both species, alterations in the intrascleral segments of the forenamed arteries were characterized by fibrous intimal and medial sclerosis. Less marked alterations occurred in the choroidal, iridal and the anterior ciliary arteries. Since lipid accumulations

were rarely observed in the vascular lesions, and then only in the aged animals, atherosclerosis was not considered to be a significant feature of the generalized arteriosclerotic process in the eye of either species.

Getty (1966) utilized many of the same dogs and hogs included in this investigation in studying age-related arteriosclerotic and atherosclerotic lesions in the aorta, the coronary and cerebral arteries, and many of the other major arteries; the arteries of the eye were not included in Getty's study. In the dog, Getty found intimal plaques to be devoid of lipid in dogs younger than five years of age and further observed that lipid accumulation appeared to be a secondary phenomenon in older dogs. This finding was compatible with the observations made in the present study in regard to the lipid nature of arteriosclerotic lesions in the ocular vessels. The absence or minimal occurrence of spontaneous atherosclerotic lesions as well as the predominant fibrous nature of intimal plaques in the ocular arteries of dogs was also consistent with the findings of Luginbühl et al. (1965), Waters (1965), Lindsey et al. (1952), and Gonzalez and Furman (1965) regarding spontaneous arteriosclerotic lesions in various arteries other than in the eye.

In hogs over two years of age, Getty (1966), detected atherosclerotic lesions to one degree or another in most of the major blood

vessels. This proclivity for lipid accumulation was not observed in arteriosclerotic lesions found in the ocular arteries of the same hogs utilized by Getty.

Straus and Roberts (1965) proposed in summary of numerous papers presented at a recent symposium pertaining to the morphology of spontaneous and induced atherosclerotic lesions in animals and the relation of these changes to human disease, that intimal fibrous thickening of arteries appeared to be a progressive age-related process and not a precursor of atherosclerosis. In support of this premise by Straus and Roberts, early lesions of fibrous intimal plaquation were observed in the ocular vessels of dogs as young as two months of age, and the incidence and the number of plaques within a cross section of an artery increased progressively with age. The finding of intimal sclerosis at such a young age in the ocular vessels was not entirely unexpected since Morehead and Little (1945) demonstrated intimal thickening with splitting and reduplication of the internal elastic lamina in the aorta of ten-day old puppies.

Alterations in the intima of ocular vessels were not demonstrable in hogs younger than 1. 5 years of age. In the hog intimal elevations were more laminated and less nodular than in the dog. In spite of the difference in the shape of the intimal elevations, the basic

histomorphological and histochemical alterations leading to or accompanying intimal plaquation were similar in the two species. These alterations typically consisted of the following changes in the normal structure of the intima: 1) thickening, splitting and disruption of the internal elastic membrane, 2) the appearance in the intima of numerous pleomorphic cells, and 3) an increase of acid mucopolysaccharides, collagenous fibers, and elastic fibers within the intimal plaque.

In the older animals as collagenous and elastic fibers increased within the intimal plaques, the cellularity of the plaques was decreased, acid mucopolysaccharides appeared to diminish, and mineralization was observed more frequently. At this stage of plaquation, endothelial cells were either absent or quite pyknotic. In the older dogs multiple fibrous nodules appeared to coalesce and form more crescentric intimal plaques. Basically, these histochemical and histomorphological alterations concurred with the findings of Gonzalez and Furman (1965) in spontaneous fibrous lesions in the vessels of the dog and rabbit.

Getty (1966) proposed that progressive age-related alterations of the vascular walls which consisted of altered collagenous and elastic fibers, smooth muscle cells, and lipid and calcium deposits

contributed to the deleterious effects of the connective tissue "histohematic" barrier as described by Casarett (1964).

In the present investigation, a progressive increase with age of collagenous fibers was observed in the tunica media of ocular vessels of the dog and hog. Medial sclerosis was more clearly visualized and delineated in the larger arteries of the sclera, iris, ciliary body and the choroid, however, an increase of fibrous connective tissue was discernible in the media of the smaller vessels of these structures. For instance, in the smaller choroidal arteries distinction between fibrous medial sclerosis and stromal fibrosis was most difficult. In keeping with the conviction of Getty (1966), alterations in the smaller arteries appeared to be more important, functionally, than alterations in the larger arteries.

In comparison, medial sclerosis was more extensive in the dog than in the hog. However, in both species, as collagenous fibers increased, the quantity of acid mucopolysaccharides and the number of smooth muscle cells were decreased. Distinctive "collagenous nests" of degenerate smooth muscle cells surrounded by proliferations of fibrous connective tissue were observed in the tunica media of the older dogs. In the older hogs, senile hyalinization of the tunica media was occasionally observed in both the small and large

ocular arteries. Comparable alterations were found by Freidman et al. (1963) in the choroidal arteries of man.

In accord with Getty (1966), mineral deposition frequently accompanied medial sclerosis, particularly in the older animals. Lipid deposition, although infrequently found in the tunica media of the larger vessels, quite often occurred in the tunica media of the smaller choroidal arteries. Lipid accumulations in the latter vessels were consistently associated with extensive lipid deposition in the choroidal stroma and in the sclera, and consequently, appeared to be the results of lipid diffusion from these sites rather than an inherent atheromatous process of the choroidal vessels.

Although changes were minimal and progressed slowly with age, distinct differences were ascertainable between the histomorphology of the intraretinal arteries of the young and the old dogs and hogs. The slow progressiveness and minimal nature of the changes with age probably led Tower (1955) to question, on the basis of knowledge at that time, the existence of truly physiologic aging of the retinal vessels in man.

The most consistent alteration in the retinal vessels of the dog and hog consisted of an increase with age in the thickness of a PAS-positive subendothelial basement membrane. Friedenwald (1949) originally described this membrane as being a distinguishing

feature of the retinal arterioles in man and also observed an increase in its thickness with age. As observed in the present investigation this membrane tended to split and reduplicate as it increased in thickness. It was interesting to note that Blumenthal et al. (1961) found reduplication of this membrane in hemodynamic vascular lesions of human patients with diabetus mellitus and non-diabetic patients. However, the frequency distribution of hemodynamic retinal vascular lesions was not significantly higher in diabetic patients than in non-diabetic subjects.

Blumenthal et al. (1961) also described an intramural increase of fibrocollagenous tissue and acid mucopolysaccharides in the hemodynamic lesions of the small retinal arteries and arterioles. In such lesions fibrocollagenous tissue was deposited in concentric rings which produced marked narrowing of the vessel lumen. The hemodynamic lesions in man, as described by Blumenthal et al., were remarkably similar to the senile changes observed in the retinal vessels of the dog and hog. The major difference apparently consisted of a lesser degree of fibrocollagenous and acid mucopolysaccharide deposition in the dog and hog, since marked narrowing of the lumen was not observed in these two species.

Lipid deposition in the retinal arteries was found in only one dog and in no hogs utilized in this investigation. This finding tended

to substantiate Schofield's (1961) observation that atheromatous degeneration, although frequently accompanying or following diffuse hyperplastic sclerosis in the body, was less common in the retina.

There were relatively few alterations with age in the venous vasculature of the ocular structures in the dog and hog. The major exception existed in the scleral venous plexuses and the vortices veins of both species. Intracellular accumulation of minerals in the endothelial cells and the subsequent formation of mineralized plaques were not uncommon findings in these vascular structures. The existence of mineral deposits in these venous structures was conceivably linked with the outflow of aqueous fluid from areas bounded by structures in which mineral deposition was prevalent; namely, those structures bounding the anterior and posterior chambers of the eye.

SUMMARY

In order to evaluate the changes which occurred in the eye of the dog and hog from birth to senility, dimensional, histological, and histochemical studies were conducted on eyes from 86 dogs ranging in age from 0.1 month to 13.1 years of age and on 108 hogs ranging in age from 0.1 month to 8.0 years of age.

In both the dog and hog, the external dimensions of the bulbus oculi and cornea were greatly increased during the first year of life. In the dog, there was little change in these dimensions after 13 months of age; whereas in the hog a continued increase was observed in animals up to four to six years of age. In general, the microscopic dimensions of the cornea, sclera, and lens of both species followed a pattern similar to the external dimensional changes with age. In the dog a significant increase in thickness of Descemet's membrane and the anterior capsule of the lens during the postmaturation period constituted a notable exception to the latter observation. In both species, the thickness of Descemet's membrane and the anterior lens capsule increased linearly with age throughout the postmaturation period. Postmaturation increases were also noted in the thickness of the ciliary body and iris of the dog. Dimensional changes with age in the latter two structures were observed in the hog but were much

more complex than in the dog. Choroidal and retinal thicknesses were highly correlated throughout the life span of the dog. The thickness of these two structures was also correlated in hogs less than one year of age; however, in older hogs the choroid increased in thickness, and retinal thickness remained essentially unchanged. The curvatures of the anterior surface of the cornea were markedly decreased in both the dog and hog during the first year of life, and although the decrease continued throughout life, it was relatively minimal after one year of age.

Changes with age in the histological and histochemical constituency of the eye of the dog and hog were predominantly characterized by an increase in fibrous connective tissue, pigment proliferation, lipid and mineral deposition, and alterations in the ocular vasculature.

Apart from vascular sclerosis, proteinogenous alteration in the lenticular fibers, and an increase in thickness of the scleral fibers, fibrotic changes with age were predominantly found in the uvea. Progressive stromal fibrosis of the choroid, ciliary body, and iris resulted in the creation of a histohematic barrier between the uveal blood supply and dependent tissues and cells. Stromal fibrosis appeared to be a dominant factor in the production of senile atrophy of the ciliary muscle and the dilator and sphincter muscles of the

iris as well as a contributing factor in the initiation of proliferative changes in the superficial epithelia of the iris and ciliary body.

Although extreme variations were observed among breeds of dogs and hogs, and among animals of the same breed, pigmentation was generally increased with age in the stroma of the iris, ciliary body, and choroid. Pigmentation was also commonly increased with age in the pigmented epithelia of the iris and ciliary body. However, depigmentation usually preceded by hypertrophy and hyperplasia characterized pigmentary changes with age in the pigment epithelial cells of the retina. In the dog, invasive pigments which appeared to originate from the uvea were observed in the deep layers of the cornea and in the peripheral retina. In the hog, retinal pigment invasion was similar to the invasion observed in the dog; whereas, corneal pigmentation occurred in the middle layers of the substantia propria and appeared to originate from existing melanocytes on the scleral side of the corneoscleral junction.

There was a progressive increase with age in the incidence and intensity of spontaneous lipid deposition in the stroma of the cornea, sclera, ciliary body and choroid of the dog and hog. In the iris, retina, and lens, lipid deposition was either infrequent or nonexistent in both species. In comparison, the incidence and intensity of

lipid deposition was much greater in the dog than in the hog, and the initial deposition of lipids was found to occur at a younger age in the dog.

In the eye of the dog and hog, a sequential pattern of progressive mineralization was detected which led to the development of various changes in the normal histological and histochemical structure of the ocular tissues as age increased. Prominent intracellular accumulation of mineral was observed in dogs and hogs as young as two months of age in the stromal cells of the cornea, sclera, iris, ciliary body, and choroid; the epithelia of the iris, ciliary body and cornea; the corneal endothelium and the ganglion and pigment epithelial cells of the retina. Increased intracellular mineralization in the stromal cells resulted in extracellular deposition of mineral in the tissues. Extracellular depositions were present in either a diffuse form or as focal or multiple focal deposits. Increased mineral accumulation in the epithelial and endothelial cells tended to form mineralized excrescences which projected from the surface of the usually hypertrophic cells. Generally the incidence and intensity of lenticular mineralization increased with age in dogs up to ten years of age and in hogs up to six years of age. In older animals both the incidence and intensity of mineralization was moderately decreased in the lens, as well as in the other ocular structures. Prominent accumulations

of acid mucopolysaccharides were found at all sites of increased mineralization as in the ocular tissues.

The most severe histomorphological alterations in the ocular vessels of the dog and hog occurred near the optic nerve in the intrascleral segments of the long posterior ciliary, retinal, and short posterior ciliary arteries. Less severe alterations were present in the choroidal, iridal, and anterior ciliary arteries. The incidence and the severity of the vascular lesions were progressively increased with age. Alterations in the intrascleral vessels of both species were characterized by fibrous intimal and medial sclerosis. Nodular intimal plaques were typical in the dog; whereas, in the hog plaques tended to be crescentric in shape. The basic histological and histochemical alterations leading to or accompanying intimal plaquation were similar in the two species and included: 1) thickening, splitting, and disruption of the internal elastic membrane, 2) the appearance in the intima of variable numbers of spindle-shaped cells, and 3) an increase of acid mucopolysaccharides, collagenous fibers, and elastic fibers in the intimal plaque. Medial sclerosis, although generally more extensive in the dog than in the hog, was typified in both species by a progressive increase of collagenous fibers and a decrease in the cellularity of the tunica media. Changes with age in the intraretinal vessels were manifested by an increase in thickness

of a PAS-positive basement membrane, and an intramural increase in fibrocollagenous connective tissue and acid mucopolysaccharides. Since lipid accumulations were rarely observed in the vascular lesions of the eye, and then only in the aged animals, atherosclerosis was not considered to be an important feature of the generalized arteriosclerotic process in the eye of the dog and hog.

LITERATURE CITED

Adams, D. R. 1929. The role of calcium in senile cataract. Biochem. J. 23: 902-912.

Archer, J. N. 1963. Age changes in the gastric mucosa of the pig. Unpublished M.S. thesis. Ames, Iowa, Library, Iowa State University of Science and Technology.

Armed Forces Institute of Pathology. 1960. Manual of histologic and special staining technics. 2nd ed. New York, New York, McGraw-Hill Book Company, Incorporated.

Attias, G. 1912. Über Altersveränderungen des menschlichen Auges. Albrecht v. Graefes Arch. Ophthal. 81: 405-485.

Barnett, K. C. 1965a. Canine retinopathies. I. History and review of the literature. J. Sm. An. Pract. 6: 41-55.

Barnett, K. C. 1965b. Canine retinopathies. II. The miniature and toy poodle. J. Sm. An. Pract. 6: 93-109.

Barnett, K. C. 1965c. Canine retinopathies. III. The other breeds. J. Sm. An. Pract. 6: 185-196.

Bell, J. T. 1959. Polyoxyethylene sorbitan monopalmitate (Tween 40) as a vehicle for oil red o fat stain. Stain Techn. 34: 219-221.

Benedict, W. L. and Wagener, H. P. 1961. Retinal arterial and arteriolar lesions associated with systemic vascular hypertension. A review of some recent opinions. Amer. J. Med. Sci. 241: 240-250.

Berliner, M. L. 1949. Biomicroscopy of the eye. Vol. II. New York, New York, Paul B. Hoeber, Incorporated.

Birren, J. E., Casperson, R. C., and Botwinick, J. 1950. Age changes in pupil size. J. Gerontol. 5: 216-221.

Blumenthal, H. T., Alex, M., and Goldenberg, S. 1961. A non-atheromatous proliferative vascular lesion of the retina in diabetes mellitus. Amer. J. Med. 31: 382-396.

Boyd, E. S. and Neuman, W. F. 1951. The surface chemistry of bone. V. The ion binding properties of cartilage. J. Biol. Chem. 193: 243-251.

Brown, E. V. L. and Evans, E. I. 1935. Studies on the crystalline lens. Amer. Ophthal. Soc. Trans. 33: 220-236.

Bürger, M. 1958. Das Altern des Auges. Acta XVIII Int. Cong. Ophthal., Bruxelles 1: 280-301.

Bürger, M. 1963. Biomorphosis of mammalian lens (abstract). Excerpta medica 6: 565.

Burn, R. A. 1951. Senile changes in the eye. In Sorsby, A., ed. Systemic ophthalmology. Pp. 699-710. St. Louis, Missouri, The C. V. Mosby Company.

Casarett, G. W. 1964. Similarities and contrasts between radiation and time pathology. In Strehler, B. L., ed. Advances in gerontological research. Vol. 1. Pp. 109-163. New York, New York, Academic Press.

Catcott, E. J. and Magrane, W. G. 1959. The crystalline lens. In Hoskins, H. P., Lacroix, J. V., Mayer, K., Bone, J. F., and Golich, P. F., eds. Canine medicine. 2nd ed. Pp. 532-535. Santa Barbara, California, American Veterinary Publications, Incorporated.

Coats, G. 1905. The structure of the membrane of Bruch, and its relation to the formation of colloid excrescences. Roy. London Ophthal. Hosp. Report 16: 164-178.

Cogan, D. G. and Kuwabara, T. 1955. Lipogenesis by cells of the cornea. A. M. A. Arch. Path. 59: 453-456.

Cogan, D. G. and Kuwabara, T. 1957a. Experimental aberrent lipogenesis. I. Serum factor. A. M. A. Arch. Path. 63: 381-386.

Cogan, D. G. and Kuwabara, T. 1957b. Experimental aberrent lipogenesis. III. Tissue factor. A. M. A. Arch. Path. 64: 22-33.

Cogan, D. G. and Kuwabara, T. 1959a. Ocular changes in experimental hypercholesteremia. A. M. A. Arch. Ophthal. 61: 219-226.

Cogan, D. G. and Kuwabara, T. 1959b. Focal senile transluncency of the sclera. A. M. A. Arch. Ophthal. 62: 604-610.

Collins, E. T. 1890. On the development and abnormalities of the zonule of Zinn. Roy. Lond. Ophthal. Hosp. Report 13: 81-96.

Donders, F. C. 1855. Beiträge zur pathologischen Anatomie des Auges. Albrecht v. Graefes Arch. Ophthal. 1: 106-118.

Donn, A. 1966. Cornea and sclera. A. M. A. Arch. Ophthal. 75: 261-288.

Dub, B. 1891. Beiträge zur Kenntnis der Cataracta zonularis. Albrecht v. Graefes Arch. Ophthal. 37: 26-38.

Duke-Elder, W. S. 1938. Textbook of ophthalmology. Vol. 2. St. Louis, Missouri, The C. V. Mosby Company.

Everett, W. G. 1957. Peripheral cystic degeneration of the retina. Amer. J. Ophthal. 43: 472.

Feeney, M. L. and Garron, L. K. 1961. Descemet's membrane in the human peripheral cornea a study by light and electron microscopy. In Smelser, G. K., ed. The structure of the eye. Pp. 367-377. New York, New York, Academic Press.

Few, A. and Getty, R. 1967. Occurrence of lipofuscin as related to aging in the canine and porcine nervous system. J. Gerontol. 22: 357-368.

Fischer, F. P. 1933. Der Mineralbestand des Auges. Arch. Augenheilk. 107: 295-313.

Fischer, F. P. 1948. Senescence in the eye. In Sorsby, A., ed. Modern trends in ophthalmology. Vol. 2. Pp. 612-656. London, England, Butterworth and Company.

Forsius, H. 1954. Acta Ophthal., Kbh. 32: 78. Original not available; cited in Schofield, P. B. 1961. Aging changes in the eye. In Bourne, G. H., ed. Structural aspects of aging. Pp. 281-288. New York, New York, Hafner Publishing Company, Incorporated.

Forsius, H. 1958. Sensitivity of the cornea in arcus senilis. Acta Ophthal. Kbh. 36: 43-49.

Francois, J. 1958. Contribution a l'etude de la senescence en ophthalmologia. Acta XVIII Int. Cong. Ophthal., Bruxelles 1: 302-326.

Friedenwald, J. S. 1949. A new approach to some problems of retinal vascular diseases. Amer. J. Ophthal. 32: 487-498.

Friedenwald, J. S. 1952. The eye. In Lansing, A. I., ed. Cowdry's problems of aging. 3rd ed. Pp. 239-259. Baltimore, Maryland, The Williams and Wilkins Company.

Friedman, E., Smith, T. R., and Kuwabara, T. 1963. Senile choroidal vascular patterns and drusen. A. M. A. Arch. Ophthal. 69: 220-230.

Fuchs, E. 1924. Textbook of ophthalmology. 8th ed. Philadelphia, Pennsylvania, J. B. Lippincott Company.

Gaines Dog Research Center. 1965. Basic guide to canine nutrition. New York, New York, author.

Getty, R. 1962. Gerontologic studies in domestic animals - their implications and applications. J. A. V. M. A. 140: 1323-1324.

Getty, R. 1965. The gross and microscopic occurrence and distribution of spontaneous atherosclerosis in the arteries of swine. In Roberts, J. C., Straus, R., and Cooper, M. S., eds. Comparative atherosclerosis. Pp. 11-20. New York, New York, Harper and Row, Publishers.

Getty, R. 1966. Histomorphological studies in the dog and hog as related to aging. In Lindop, P. J. and Sacher, G. A., eds. Radiation and aging. Pp. 245-276. London, England, Taylor and Francis, Limited.

Getty, R. and Skold, B. H. 1962. Cardiovascular studies in the hog. J. Gerontol. 17: 451.

Goldmann, H. 1964. Senile changes of the lens and vitreous. Amer. J. Ophthal. 57: 1-13.

Gonzalez, I. E. and Furman, R. H. 1965. Histochemistry of spontaneous and experimental arterial lesions. In Roberts, J. C., Straus, R., and Cooper, M. S., eds. Comparative atherosclerosis. Pp. 329-341. New York, New York, Harper and Row, Publishers.

Grabar, P. and Nordmann, J. C. R. 1933. La teneur en calcium du cristallin normal et pathologique. Soc. Biol., Paris 112: 1534-1536.

Hadek, R. and Getty, R. 1959. Age changes of the ovary of the domesticated pig. Am. J. Vet. Res. 20: 578-584.

Haensly, W. E. and Getty, R. 1965. Age changes in the weight of the adrenal glands of the dog. J. Gerontol. 20: 544-547.

Haensly, W. E. and Getty, R. 1968. Age changes in the weight of the adrenal glands of swine from birth to eight years. J. Gerontol. 23: 53-57.

Haensly, W. E., Jermier, J. A., and Getty, R. 1964. Age changes in the weight of the thyroid gland of the dog from birth to senescence. J. Gerontol. 19: 54-56.

Hedbys, B. 1961. The role of polysaccharides in corneal swelling. Exp. Eye Res. 1: 81-91.

Herbert, H. 1923. The pectinate ligament in its relation to chronic glaucoma. Brit. J. Ophthal. 7: 469-477.

Hodgman, S. F. J., Parry, H. B., Rasbridge, W. J., and Steel, J. D. 1949. Progressive retinal atrophy in dogs. Vet. Rec. 61: 185-189.

Hogan, M. J. and Zimmerman, L. E. 1962. Ophthalmic pathology. 2nd ed. Philadelphia, Pennsylvania, W. B. Saunders Company.

Jakus, M. 1956. Studies on the cornea. II. The fine structure of the Descemet's membrane. J. Biophys. Biochem. 2: 243-255.

Janes, R. G. 1964. Changes in the rabbit's eye caused by cholesterol feeding. A. M. A. Arch. Ophthal. 58: 819-828.

Kaczurowski, M. I. 1962. The pigment epithelium of the human eye. Amer. J. Ophthal. 53: 79-92.

Kadlecova, V., Peleska, M., and Vasko, A. 1958. Dependence on age of the diameter of the pupil in the dark. Nature, London 182: 1520-1521.

Kerschbaumer, R. 1888. Ueber Altersveränderungen der Uvea. Albrecht v. Graefes Arch. Ophthal. 34: 16-34.

Kerschbaumer, R. 1892. Ueber Altersveränderungen der Uvea. Albrecht v. Graefes Arch. Ophthal. 38: 127-148.

Kornzweig, A. L. 1951. Pathology of eye in old age. III. Changes attributed to the aging process. Amer. Acad. Ophthal. Otolaryng. Trans. 55: 261-276.

Kornzweig, A. L. 1954. Physiological effects of age on the visual process. Sight-Sav. Rev. 24: 130-138.

Kornzweig, A. L., Feldstein, M., and Schneider, J. 1959. The pathogenesis of senile macular degeneration. Amer. J. Ophthal. 48: 22-28.

Krause, A. C. 1934. The biochemistry of the eye. Baltimore, Maryland, The Johns Hopkins Press.

Krotova, S. I. 1963. Age changes in the organ of vision in dogs. Exp. Biol. Med. Bull. 45-47.

Kumnick, L. S. 1956. Aging and decay of pupillary psychosensory restitution. J. Gerontol. 11: 46-52.

Kuwabara, T., Carroll, J. M., and Cogan, D. G. 1961. Retinal vascular patterns. III. Age, hypertension, absolute glaucoma, injury. A. M. A. Arch. Ophthal. 65: 708-716.

Kuwabara, T. and Cogan, D. G. 1957. Experimental aberrent lipogenesis. II. Substrate factor. A. M. A. Arch. Path. 63: 496-501.

Lansing, A. I. 1951. Some physiological aspects of aging. Physiol. Rev. 31: 274-284.

Larsson, S. and Österlind, G. 1943. Studies in the causes of senile miosis and rigidity of the pupil. Acta Ophthal., Kbh. 21: 1-25.

Leinhos, R. 1959. Die Altersabhängigkeit des Augenpupillendurchmessers. Optik 16: 669-671.

Lindsay, S., Chaikoff, I. L., and Gilmore, J. W. 1952. Arteriosclerosis in the dog. I. Spontaneous lesions in the aorta and the coronary arteries. A. M. A. Arch. Path. 53: 281-300.

Luginbühl, H., Jones, J. E. T., and Detweiler, D. K. 1965. The morphology of spontaneous arteriosclerotic lesions in the dog. In Roberts, J. C., Straus, R., and Cooper, M. S., eds. Comparative atherosclerosis. Pp. 161-169. New York, Harper and Row, Publishers.

Mackay, G., Stewart, C. P., and Robertson, J. D. 1932. A note on the inorganic constituents of normal and cataractous human crystalline lenses. Brit. J. Ophthal. 16: 193-201.

Magrane, W. G. 1959. The eye. In Hoskins, H. P., Lacroix, J. V., Mayer, K., Bone, J. F., and Golich, P. F., eds. Canine medicine. 2nd ed. Pp. 517-527. Santa Barbara, California, American Veterinary Publications, Incorporated.

Magrane, W. G. 1965. Canine ophthalmology. Philadelphia, Pennsylvania, Lea and Febiger.

Mallory, F. B. 1938. Pathological technique. Philadelphia, Pennsylvania, W. B. Saunders Company.

Mann, I. 1950. The development of the human eye. New York, New York, Grune and Stratton, Incorporated.

Marin-Amat, M. 1956. Les variations physiologiques de la courbure de la cornee pendant la vie: Leur importance et transcendance dans la refraction oculaire. Soc. Belge Ophthal. Bull. 113: 251-293.

Maurice, D. M. 1962. Distribution and movement of plasma protein in the cornea. J. Physiol. 162: P2.

Melanowski, W. H. and Stachow. A. 1958. Recherches sur la structure chimique de la sclerotique de l'oeil humain selon l'age. Acta XVIII Int. Cong. Ophthal., Bruxelles 1: 397-408.

McGee-Russell, S. M. 1958. Histochemical methods for calcium. J. Histochem. and Cytochem. 6: 22-42.

Morehead, R. P. and Little, J. M. 1945. Changes in the blood vessels of apparently healthy mongrel dogs. Amer. J. Path. 21: 339-345.

Müller, H. 1856. Untersuchungen über die Glashäute des Auges insbesondere die Glaslamelle der Choroidea und ihre senilen Veränderungen. Albrecht v. Arch. Ophthal. 2: 1-65.

Munnell, J. F. and Getty, R. 1968a. Rate of accumulation of cardiac lipofuscin in the aging canine. J. Gerontol. 23: 154-158.

Munnell, J. F. and Getty, R. 1968b. Nuclear lobulation and amitotic division associated with increasing cell size in aging canine myocardium. J. Gerontol. 23: 363-369.

Nicolas, E. 1925. Veterinary and comparative ophthalmology. London, England, H. and W. Brown.

Okun, E. 1960. Gross and microscopic pathology in autopsy eyes. II. Peripheral chorioretinal atrophy. Amer. J. Ophthal. 50: 574-583.

Okun, E., Rubin, L. F., and Collins, E. M. 1961. Retinal breaks in the senile dog eye. A. M. A. Arch. Ophthal. 66: 702-707.

Parry, H. B. 1953a. Degenerations of the dog retina. I. Structure and development of the retina of the normal dog. Brit. J. Ophthal. 37: 385-404.

Parry, H. B. 1953b. Degenerations of the dog retina. II. Generalized progressive atrophy of hereditary origin. Brit. J. Ophthal. 37: 487-502.

Parry, H. B. 1954. Degenerations of the dog retina. VI. Central progressive atrophy with pigment epithelial dystrophy. Brit. J. Ophthal. 38: 653-668.

Prince, J. H. 1964. The rabbit in eye research. Springfield, Illinois, Charles C. Thomas, Publisher.

Prince, J. H. 1965. Introduction to aging and pathology of the retina. Springfield, Illinois, Charles C. Thomas, Publisher.

Prince, J. H., Diesem, C. D., Eglitis, I., and Ruskell, G. L. 1960. Anatomy and histology of the eye and orbit in domestic animals. Springfield, Illinois, Charles C. Thomas, Publisher.

Radnot, M. 1948. Data on the occurrence of calcification in the eye tissues. Brit. J. Ophthal. 32: 47-54.

Raeder, J. G. 1922. Untersuchungen über Dicke und Lage der Linse. Albrecht v. Graefes Arch. Ophthal. 110: 73-108.

Rice, V. A. and Andrews, F. N. 1951. Breeding and improvement of farm animals. New York, New York, McGraw-Hill Book Company, Incorporated.

Rinehart, J. F. and Abul-Haj, S. K. 1951. An improved method for histologic demonstration of acid mucopolysaccharides in tissues. A. M. A. Arch. Path. 52: 189-194.

Roberts, S. R. 1954. The nature of corneal pigmentation in the dog. J. A. V. M. A. 124: 208-211.

Rodstein, M. and Zeman, F. D. 1961. Interrelationships of arcus senilis and cardiovascular indices of arteriosclerosis in the aged (abstract). J. Gerontol. 16: 398.

Rone, B. 1937. Formation of drusen of the lamina vitrea. A. M. A. Arch. Ophthal. 18: 388-402.

Rones, B. 1938. Senile changes and degenerations in the human eye. Amer. J. Ophthal. 21: 239-255.

Sallmann, L., Caravaggio. L. L., and Grimes, P. 1961. Studies on the corneal endothelium of the rabbit. I. Cell division and growth. Amer. J. Ophthal. 51: 955-966.

Scammon, R. E. and Wilmer, H. A. 1950. Growth of the components of the human eyeball. II. Comparison of the calculated volumes of the eyes of the newborn and of adults and their components. A. M. A. Arch. Ophthal. 43: 620-637.

Schofield, P. B. 1961. Aging changes in the eye. In Bourne, G. H., ed. Structural aspects of aging. Pp. 277-286. New York, New York, Hafner Publishing Company, Incorporated.

Schwarz, W. 1953. Elektronenmikroskopische Untersuchungen uber die Differenzierung der Cornea and Sklerafibrillen des Menschen. Z. Zellforsch. 38: 78-86.

Skold, B. H. and Getty, R. 1961. Spontaneous atherosclerosis of swine. J. A. V. M. A. 139: 655-660.

Skold, B. H., Getty, R., and Ramsey, F. K. 1966. Spontaneous atherosclerosis in the arterial system of aging swine. Am. J. Vet. Res. 27: 257-273.

Smith, P. 1890. On the size of the cornea in relation to age, sex, refraction and primary glaucoma. Ophthal. Soc. Trans. U. K. 10: 68-78.

Smythe, R. H. 1958. Veterinary ophthalmology. 2nd ed. Baltimore, Maryland, The Williams and Wilkins Company.

Snedecor, G. W. 1967. Statistical methods. 6th ed. Ames, Iowa, Iowa State University Press.

Sommers, I. G. 1949. Histology and histopathology of the eye and its adnexa. New York, New York, Grune and Stratton, Incorporated.

Stocker, F. W. 1953. The endothelium of the cornea and its clinical applications. Amer. Ophthal. Soc. Trans. 51: 669-786.

Stone, J. and Leary, G. 1957. Brit. J. Physiol. Optics 14: 90. Original not available; cited in Prince, J. H. 1964. Cornea, trabecular region, and sclera. In Prince, J. H., ed. The rabbit in eye research. Pp. 86-139. Springfield, Illinois, Charles C. Thomas, Publisher.

Straus, R. and Roberts, J. C. 1965. Summary of conference discussions and editorial comment. In Roberts, J. C., Straus, R., and Cooper, M. S., eds. Comparative atherosclerosis. Pp. 365-379. New York, New York, Harper and Row, Publishers.

Tassman, I. S. 1951. The eye manifestations of internal diseases. 3rd ed. St. Louis, Missouri, The C. V. Mosby Company.

Tassman, I. S. 1956. Significance of ocular changes occurring after middle age. Geriatrics 11: 493-502.

Teng, C. C. and Katzin, H. M. 1953. An anatomic study of the peripheral retina. II. Peripheral cystoid degeneration of the retina; formation of cysts and holes. Amer. J. Ophthal. 36: 29-39.

Tower, P. 1955. The aging retina. Geriatrics 10: 12-16.

Van der Hoeve, J. and Flieringa, H. J. 1924. Accommodation. Brit. J. Ophthal. 8: 97-106.

Vannas, S. and Teir, H. 1960. Observations on structures and age changes in the human sclera. Acta Ophthal., Kbh. 38: 268-269.

Verhoeff, F. H. and Sisson, R. J. 1926. Basophilic staining of Bruch's membrane. A. M. A. Arch. Ophthal. 55: 125-127.

Verse, M. 1916. Ueber die Blut-und Augenveränderungen bei experimenteller Cholesterinämine. Muchen. Med. Wchnschr. 63: 1074-1076.

Verse, M. 1925. Ueber den Cholesteringehalt des Blutes bein Arcus lipoides corneae senilis des Menschen. Klin. Mbl. Augenheilk. 74: 110-112.

Waters, L. L. 1965. Spontaneous and experimental atherosclerosis in the dog. In Roberts, J. C., Straus, R., and Cooper, M. S., eds. Comparative atherosclerosis. Pp. 196-207. New York, New York, Harper and Row, Publishers.

Weale, R. A. 1963. The aging eye. New York, New York, Harper and Row, Publishers.

Whiteford, R. D. 1956. Macroscopic and microscopic anatomy of the canine eye from birth to two years of age. Unpublished M. S. thesis. Ames, Iowa, Library, Iowa State University of Science and Technology.

Whiteford, R. and Getty, R. 1966. Distribution of lipofuscin in the canine and porcine brain as related to aging. J. Gerontol. 21: 31-44.

Wislocki, G. 1952. The anterior segment of the rhesus monkey investigated by histochemical means. Amer. J. Anat. 91: 233-255.

Wolff, E. 1961. Anatomy of the eye and orbit. 5th ed. Philadelphia, Pennsylvania, W. B. Saunders Company.

Wolter, J. R. 1957. Die Histogenese der Drusen im Pigmentepithel der Netzhaut des menschlichen Auges. Klin. Mbl. Augenheilk. 130: 86-95.

Wood, C. G. R. 1915. Choroidal sclerosis. Ophthalmoscope 13: 373-376.

Zeiter, H. J. 1962. Calcification and ossification in ocular tissue. Amer. J. Ophthal. 53: 265-274.

Zimmerman, L. E. 1961. Acid mucopolysaccharides in ocular histology and pathology. Inst. Med. Chicago Proc. 23: 267-277.

ACKNOWLEDGEMENTS

Sincere appreciation is expressed to Dr. Robert Getty for making available to the author the facilities of the Department of Veterinary Anatomy, Iowa State University and for entrusting the invaluable collection of ocular specimens to the purposes of this investigation. The excellent supervision, guidance, and encouragement rendered by Dr. Getty throughout the course of this study is gratefully acknowledged.

The superb training in pathology, the assistance in evaluating subtle changes in the ocular tissues, and the constant inspiration offered by Dr. Frank K. Ramsey is gratefully recognized.

Appreciation is also extended to the following: Dr. William E. Haensly, for valuable advice and assistance with the statistical analyses; Dr. K. S. Sun M. D., ophthalmologist, McFarland Clinic, Ames, Iowa for assistance in performing the keratometric measurements; Dr. Bernard H. Skold and Dr. Ray J. Bryan for review and evaluation of the manuscript; Mr. Ralph Lanz, for the difficult task of processing, sectioning, and staining the ocular tissues; Dr. Daniel J. Hillman, for guidance with the photomicrographic procedures; Mr. Ronald Hamm and Mrs. Judith Guenther for preparing the

diagrammatic illustrations; Mrs. Marianne Dennis for proofreading the manuscript; and Mrs. Farrys Hillestad for typing the manuscript.

This work was supported in part by Special Fellowship No. 2 F11 NB 1475-03 VSN from the National Institute of Neurological Diseases and Blindness, Public Health Service and by grants No. H 4487 and No. HD 00041-08 from the National Institutes of Health, Department of Health, Education, and Welfare. The author acknowledges with gratitude this financial support and is deeply appreciative of the many courtesies extended by the personnel of these agencies.

APPENDIX A

GRAPHS OF DIMENSIONAL CHANGE WITH AGE

Graph 1. Transverse, vertical, and anteroposterior diameters of the bulbus oculi in 46 dogs ranging in age from 0.1 month to 13.0 months.

A. Transverse diameter; Data for curvilinear regression, where Y = transverse diameter in mm and X = age in months.

$N = 46$
$Y = 11.1959 + 2.2602\ X_1 - 0.1161\ X_2$; $s_y = 1.1107$ mm
$b_y1.2 = 2.2602 \pm 0.1472$ mm/month, $P<0.01$
$b_y2.1 = 0.1161 \pm 0.0196$ mm/month, $P<0.01$
$\bar{Y} = 19.3228 \pm 0.1638$ mm , $P<0.01$

B. Vertical diameter; Data for curvilinear regression, where Y = vertical diameter in mm and X = age in months.

$N = 46$
$Y = 10.2804 + 2.2930\ X_1 - 0.1171\ X_2$; $s_y = 1.1678$ mm
$b_y1.2 = 2.2930 \pm 0.1578$ mm/month, $P<0.01$
$b_y2.1 = 0.1171 \pm 0.0115$ mm/month, $P<0.01$
$\bar{Y} = 18.5739 \pm 0.1719$ mm , $P<0.01$

C. Anteroposterior diameter; Data for curvilinear regression, where Y = anteroposterior diameter in mm and X = age in months.

$N = 46$
$Y = 10.1923 + 2.1962\ X_1 - 0.1138\ X_2$; $s_y = 1.0757$ mm
$b_y1.2 = 2.1962 \pm 0.1462$ mm/month, $P<0.01$
$b_y2.1 = 0.1139 \pm 0.0106$ mm/month, $P<0.01$
$\bar{Y} = 18.0141 \pm 0.1586$ mm , $P<0.01$

DIAMETER OF THE BULBUS OCULI (MILLIMETERS)
10.50
13.00
15.50
18.00
20.50
23.00
AGE (MONTHS)
0.1
2
4
6
8
10
12
13.0
A
B
C

Graph 2. Transverse, vertical, and anteroposterior diameters of the bulbus oculi of 32 dogs ranging in age from 1.5 years to 13.1 years.

A. Transverse diameter; Data for linear regression, where Y = transverse diameter in mm and X = age in years.

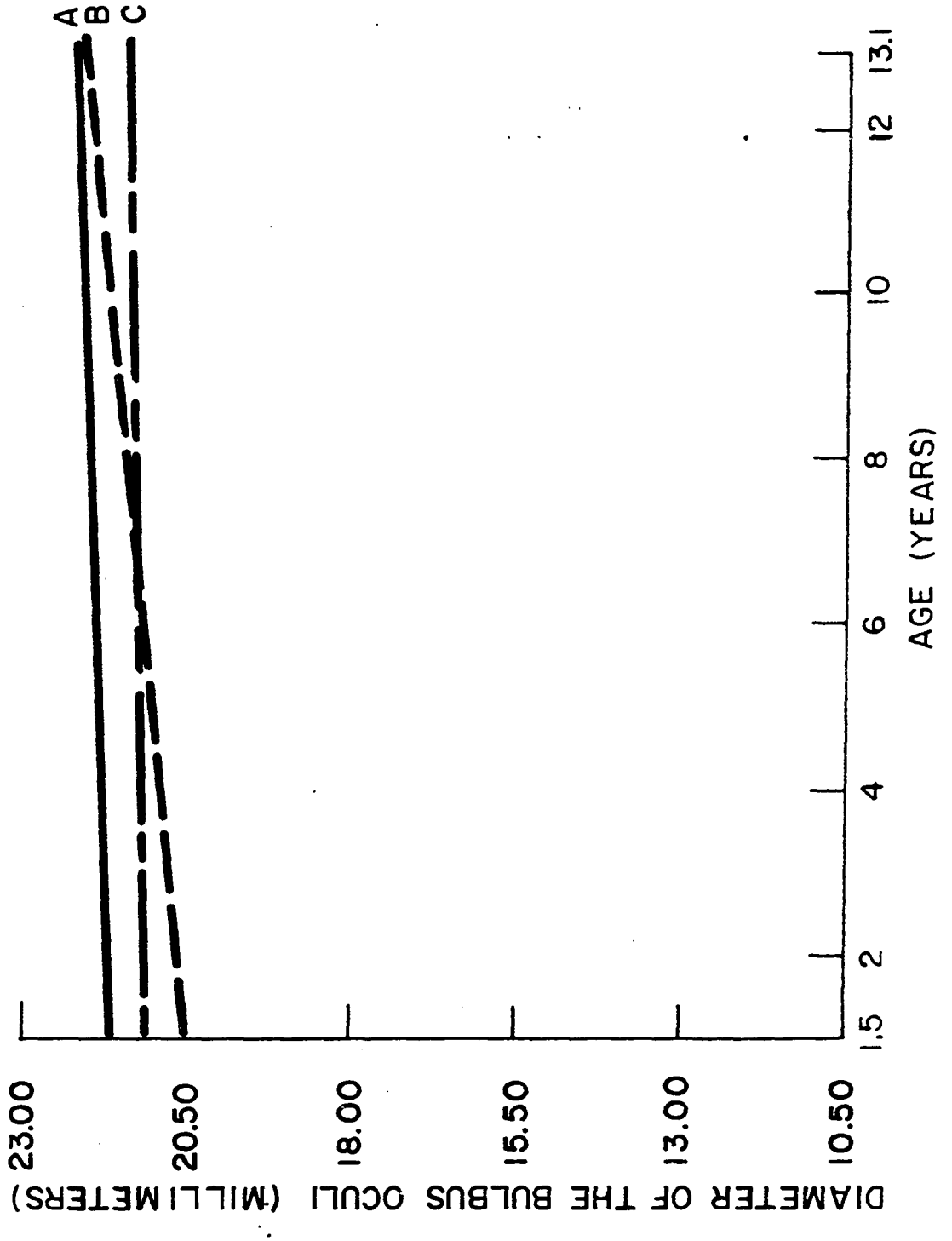
N = 32
Y = 21.6097 + 0.0543 X ; s_y = 0.7539 mm
b = 0.0543 ± 0.0373 mm/year, P NS
$\bar{Y}$ = 22.0656 ± 0.1357 mm , P <0.01
r = 0.26 , P NS

B. Vertical diameter; Data for linear regression, where Y = vertical diameter in mm and X = age in years.

N = 32
Y = 21.1130 + 0.0294 X ; s_y = 0.6922 mm
b = 0.0294 ± 0.0342 mm/year, P NS
$\bar{Y}$ = 21.3594 ± 0.1218 mm , P <0.01
r = 0.15 , P NS

C. Anteroposterior diameter; Data for linear regression, where Y = anteroposterior diameter in mm and X = age in years.

N = 32
Y = 20.5128 + 0.1295 X ; s_y = 0.6764 mm
b = 0.1295 ± 0.0335 mm/year, P <0.01
$\bar{Y}$ = 21.6000 ± 0.1196 mm , P <0.01
r = 0.58 , P <0.01


A
B
C
23.00
20.50
18.00
15.50
13.00
10.50
DIAMETER OF THE BULBUS OCULI (MILLIMETERS)
1.5
2
4
6
8
10
12
13.1
AGE (YEARS)

Graph 3. Transverse, vertical, and anteroposterior diameters of the bulbus oculi in 22 hogs ranging in age from 0.1 month to 12.0 months.

A. Transverse diameter; Data for curvilinear regression, where Y = transverse diameter in mm and X = age in months.

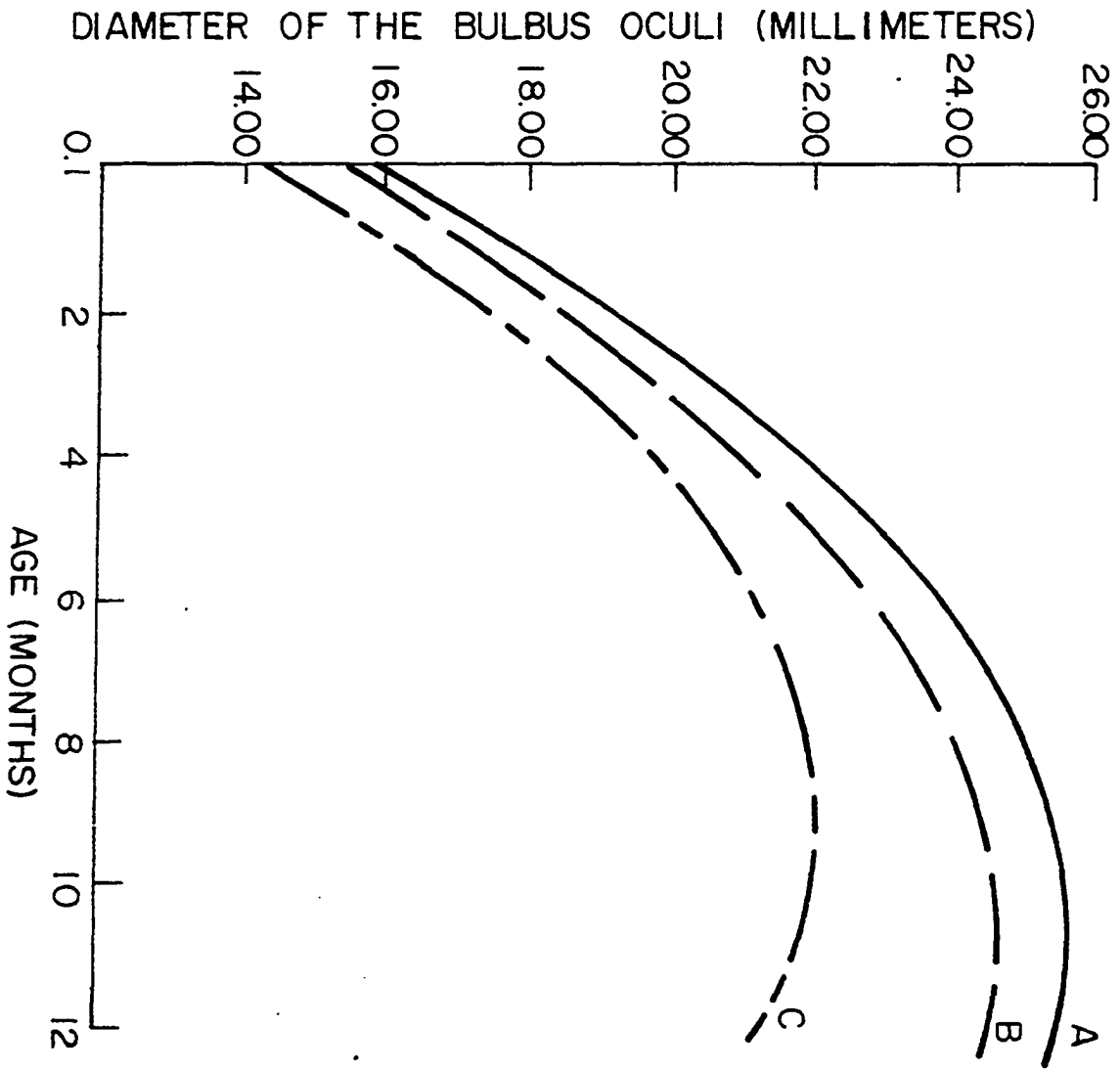
$N = 22$
$Y = 15.6864 + 1.8946\ X_1 - 0.0899\ X_2$; $s_y = 0.6570$ mm
$b_y1.2 = 1.8946 \pm 0.1540$ mm/month, $P<0.01$
$b_y2.1 = 0.0899 \pm 0.0124$ mm/month, $P<0.01$
$\bar{Y} = 22.4500 \pm 0.1400$ mm/month, $P<0.01$

B. Vertical diameter; Data for curvilinear regression, where Y = vertical diameter in mm and X = age in months.

$N = 22$
$Y = 15.2708 + 1.6952\ X_1 - 0.0765\ X_2$; $s_y = 0.7543$ mm
$b_y1.2 = 1.6952 \pm 0.1768$ mm/month, $P<0.01$
$b_y2.1 = 0.0765 \pm 0.0142$ mm/month, $P<0.01$
$\bar{Y} = 21.5068 \pm 0.1608$ mm , $P<0.01$

C. Anteroposterior diameter; Data for curvilinear regression, where Y = anteroposterior diameter in mm and X = age in months.

$N = 22$
$Y = 14.0272 + 1.7941\ X_1 - 0.0990\ X_2$; 0.8512 mm
$b_y1.2 = 1.7941 \pm 0.1996$ mm/month, $P<0.01$
$b_y2.1 = 0.0990 \pm 0.0160$ mm/month, $P<0.01$
$\bar{Y} = 19.8136 \pm 0.1815$ mm , $P<0.01$


DIAMETER OF THE BULBUS OCULI (MILLIMETERS)
14.00
16.00
18.00
20.00
22.00
24.00
26.00
AGE (MONTHS)
0.1
2
4
6
8
10
12
A
B
C

Graph 4. Transverse, vertical, and anteroposterior diameters of the bulbus oculi in 86 hogs ranging in age from 1.2 years to 8.0 years.

A. Transverse diameter; Data for curvilinear regression, where Y = transverse diameter in mm and X = age in years.

$N = 86$

$Y = 25.1888 + 1.1766\ X_1 - 0.0968\ X_2$; $s_y = 0.7875$ mm

$b_y1.2 = 1.1766 \pm 0.2739$ mm/year, $P<0.01$

$b_y2.1 = 0.0968 \pm 0.0322$ mm/year, $P<0.01$

$\bar{Y} = 27.7233 \pm 0.0849$ mm , $P<0.01$

B. Vertical diameter; Data for curvilinear regression, where Y = vertical diameter in mm and X = age in years.

$N = 86$

$Y = 24.7436 + 0.9467\ X_1 - 0.0751\ X_2$; $s_y = 0.7182$ mm

$b_y1.2 = 0.9467 \pm 0.2498$ mm/year, $P<0.01$

$b_y2.1 = 0.0751 \pm 0.0294$ mm/year, $P<0.05$

$\bar{Y} = 26,8233 \pm 0.0245$ mm , $P<0.01$

C. Anteroposterior diameter; Data for linear regression, where Y = anteroposterior diameter in mm and X = age in years.

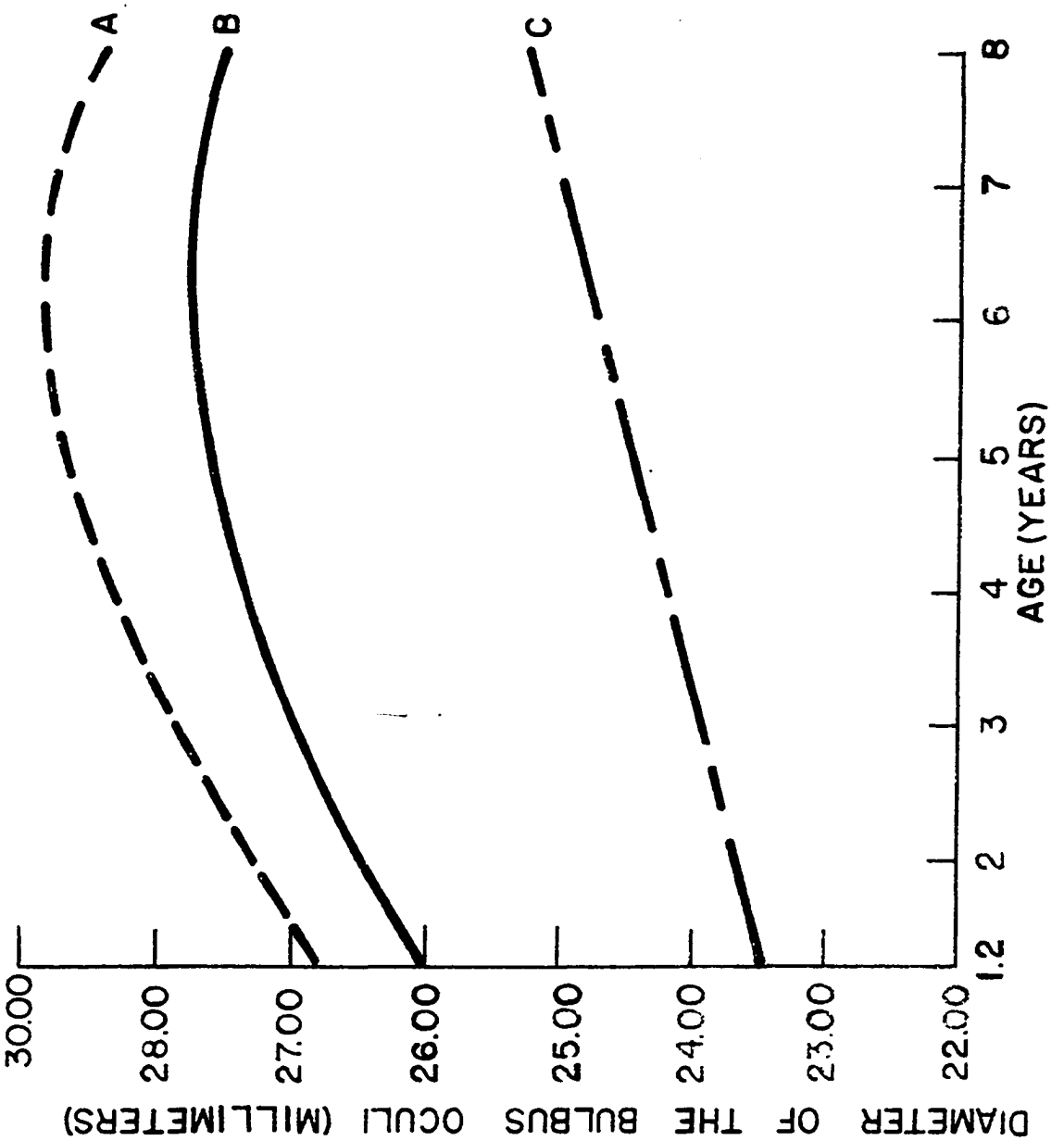
$N = 86$

$Y = 23.1850 + 0.2664\ X$; $s_y = 0.8010$ mm

$b = 0.2664 \pm 0.0481$ mm/year, $P<0.01$

$\bar{Y} = 24.0762 \pm 0.0873$ mm , $P<0.01$

$r = 0.52$, $P<0.01$


A
B
C
30.00
28.00
27.00
26.00
25.00
24.00
23.00
22.00
DIAMETER OF THE BULBUS OCULI (MILLIMETERS)
1.2
2
3
4
5
6
7
8
AGE (YEARS)

Graph 5. Transverse and vertical diameters of the cornea in 46 dogs ranging in age from 0.1 month to 13.0 months.

A. Transverse diameter; Data for curvilinear regression, where Y = transverse diameter in mm and X = age in months.

$N = 46$

$Y = 7.8935 + 1.7907\ X_1 - 0.0908\ X_2\ ;\ s_y = 0.9350$ mm

$b_y1.2 = 1.7907 \pm 0.1239$ mm/month, $P<0.01$

$b_y2.1 = 0.0908 \pm 0.0092$ mm/month, $P<0.01$

$\bar{Y} = 14.4239 \pm 0.1378$ mm , $P<0.01$

B. Vertical diameter; Data for curvilinear regression, where Y = vertical diameter in mm and X = age in months.

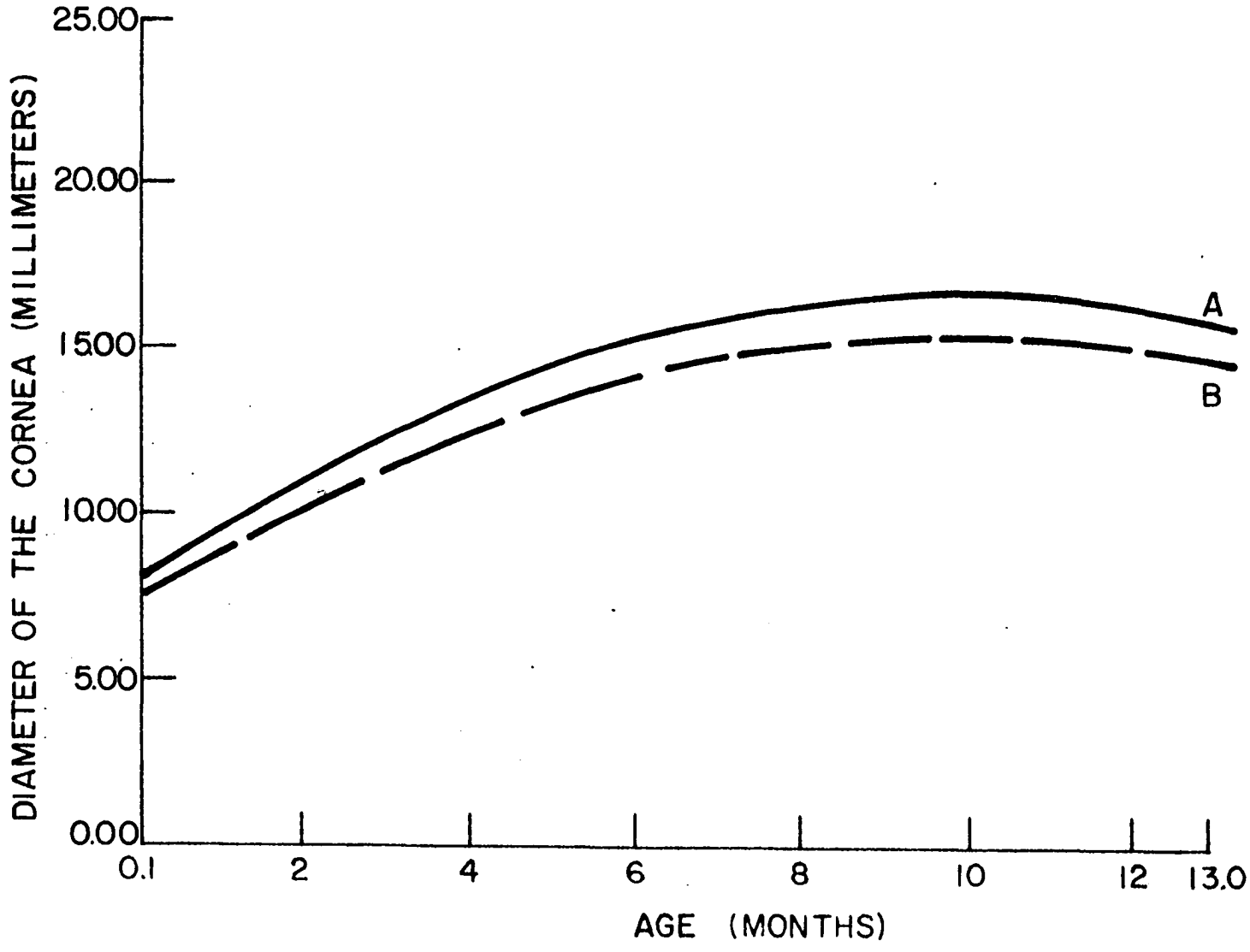
$N = 46$

$Y = 7.3479 + 1.5862\ X_1 - 0.0785\ X_2\ ;\ s_y = 0.8950$ mm

$b_y1.2 = 1.5862 \pm 0.1186$ mm/month, $P<0.01$

$b_y2.1 = 0.0785 \pm 0.0088$ mm/month, $P<0.01$

$\bar{Y} = 13.2696 \pm 0.1320$ mm , $P<0.01$


25.00
20.00
15.00
10.00
5.00
0.00
DIAMETER OF THE CORNEA (MILLIMETERS)
A
B
0.1
2
4
6
8
10
12
13.0
AGE (MONTHS)

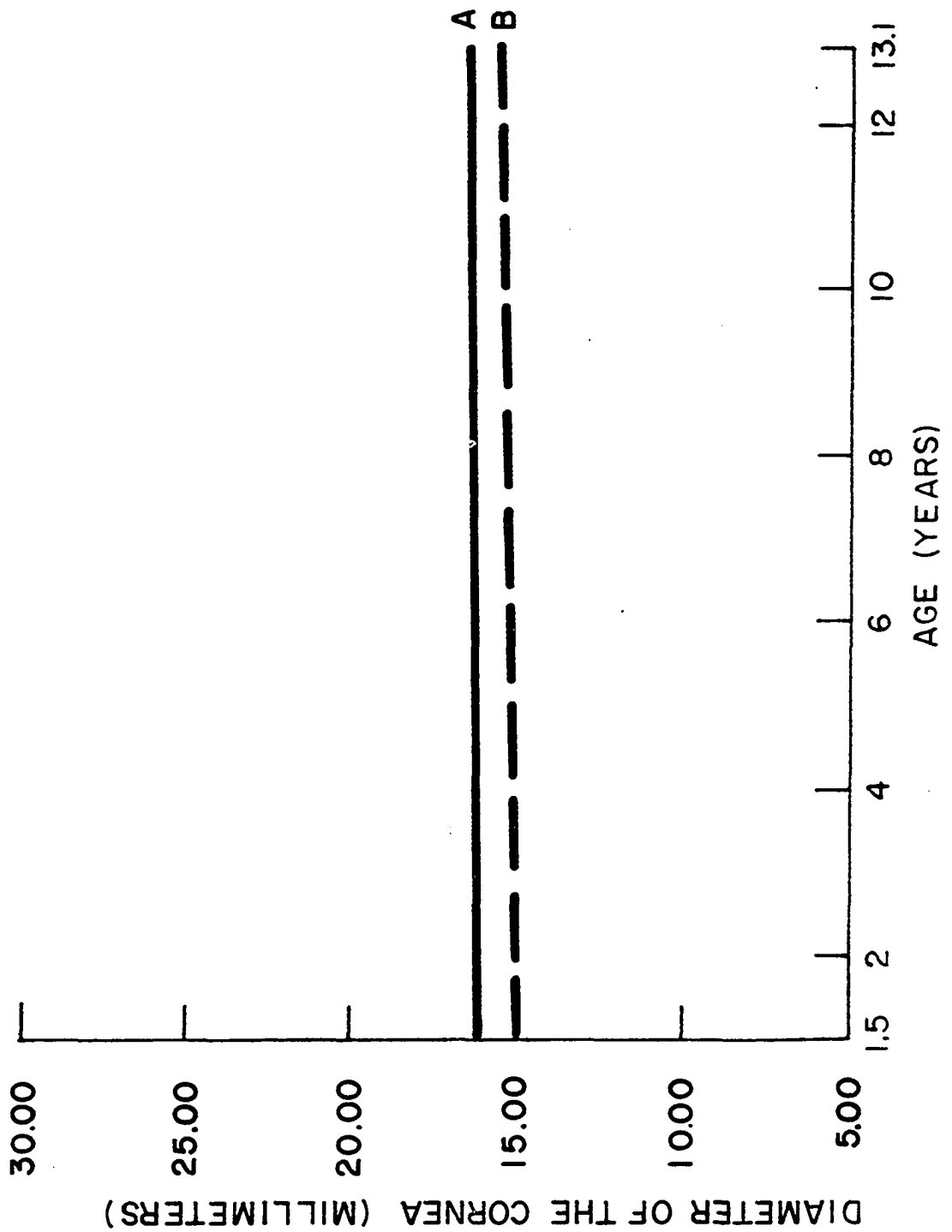
Graph 6. Transverse and vertical diameters of the cornea in 32 dogs ranging in age from 1.5 years to 13.1 years.

A. Transverse diameter; Data for linear regression, where Y = transverse diameter in mm and X = age in years.

$N = 32$
$Y = 16.2249 + 0.0186\ X$; $s_y = 0.4628$ mm
$b = 0.0186 \pm 0.0229$ mm/year , P NS
$\bar{Y} = 16.3813 \pm 0.0814$ mm , $P < 0.01$
$r = 0.15$, P NS

B. Vertical diameter; Data for linear regression, where Y = vertical diameter in mm and X = age in years.

$N = 32$
$Y = 14.9867 + 0.0489\ X$; $s_y = 0.5162$ mm
$b = 0.0489 \pm 0.0255$ mm/year, P NS
$\bar{Y} = 15.3969 \pm 0.0951$ mm , $P < 0.01$
$r = 0.33$, P NS


A
B
1.5
2
4
6
8
10
12
13.1
AGE (YEARS)
30.00
25.00
20.00
15.00
10.00
5.00
DIAMETER OF THE CORNEA (MILLIMETERS)

Graph 7. Transverse and vertical diameters of the cornea in 22 hogs ranging in age from 0.1 month to 12.0 months.

A. Transverse diameter; Data for curvilinear regression, where Y = transverse diameter in mm and X = age in months.

$N = 22$

$Y = 10.7563 + 1.1216\ X_1 - 0.0509\ X_2$; $s_y = 0.5215$ mm

$b_y1.2 = 1.1216 \pm 0.1223$ mm/month, $P<0.01$

$b_y2.1 = 0.0509 \pm 0.0098$ mm/month, $P<0.01$

$\bar{Y} = 14.8659 \pm 0.3426$ mm , $P<0.01$

B. Vertical diameter; Data for curvilinear regression, where Y = vertical diameter in mm and X = age in months.

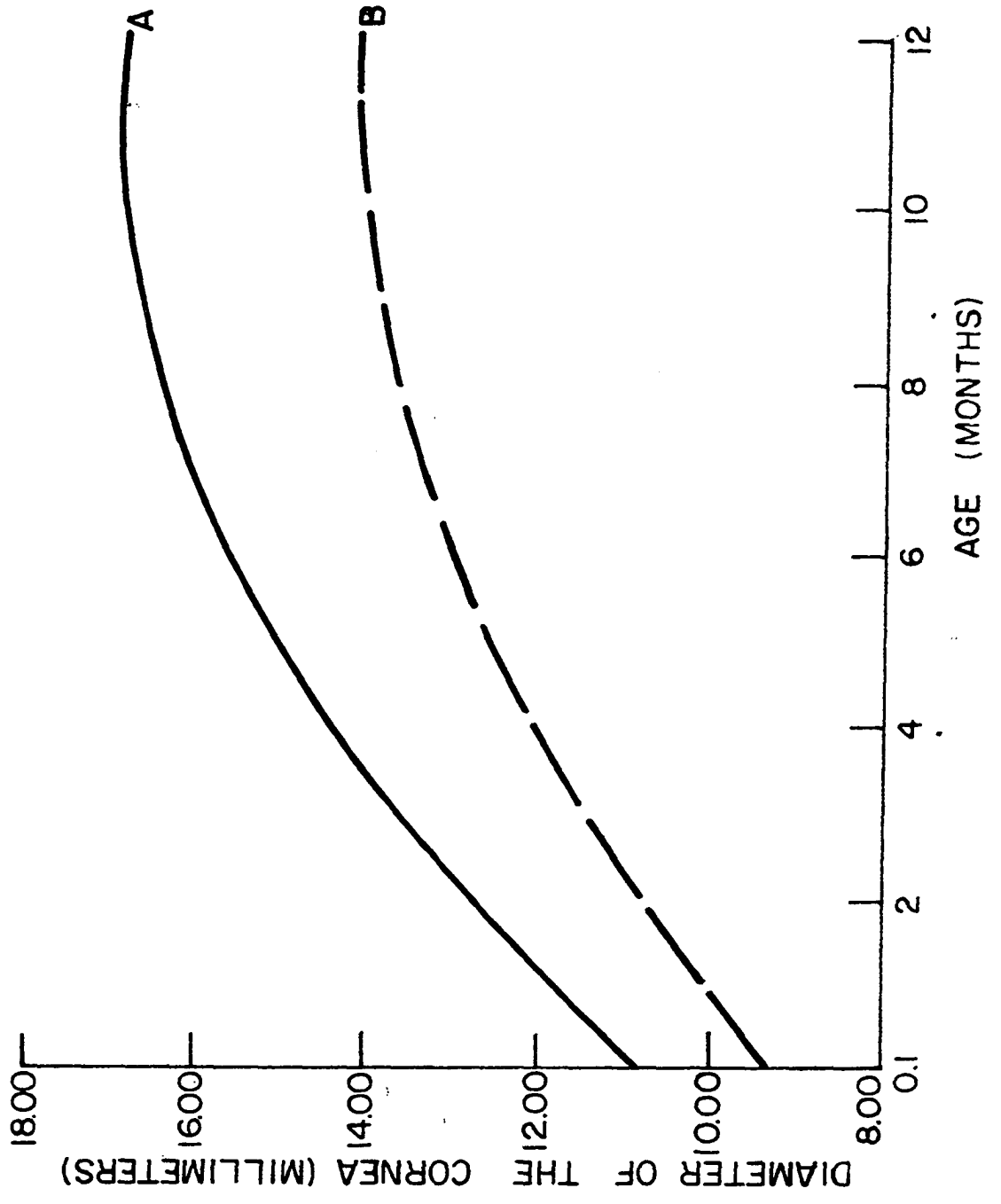
$N = 22$

$Y = 9.2663 + 0.8304\ X_1 - 0.0355\ X_2$; $s_y = 0.5636$ mm

$b_y1.2 = 0.8304 \pm 0.1321$ mm/month, $P<0.01$

$b_y2.1 = 0.0355 \pm 0.0106$ mm/month, $P<0.01$

$\bar{Y} = 12.4136 \pm 0.1202$ mm , $P<0.01$


A
B
18.00
16.00
14.00
12.00
10.00
8.00
0.1
2
4
6
8
10
12
AGE (MONTHS)
DIAMETER OF THE CORNEA (MILLIMETERS)

Graph 8. Transverse and vertical diameters of the cornea in 86 hogs ranging in age from 1.2 years to 8.0 years.

A. Transverse diameter; Data for linear regression, where Y = transverse diameter in mm and X = age in years.

$N = 86$

$Y = 17.5679 + 0.3647\ X\ ;\ s_y = 0.7682$

$b = 0.3647 \pm 0.0475$ mm/year, $P < 0.01$

$\bar{Y} = 18.7880 \pm 0.0828$ mm , $P < 0.01$

$r = 0.66$, $P < 0.01$

B. Vertical diameter; Data for curvilinear regression, where Y = vertical diameter in mm and X = age in years.

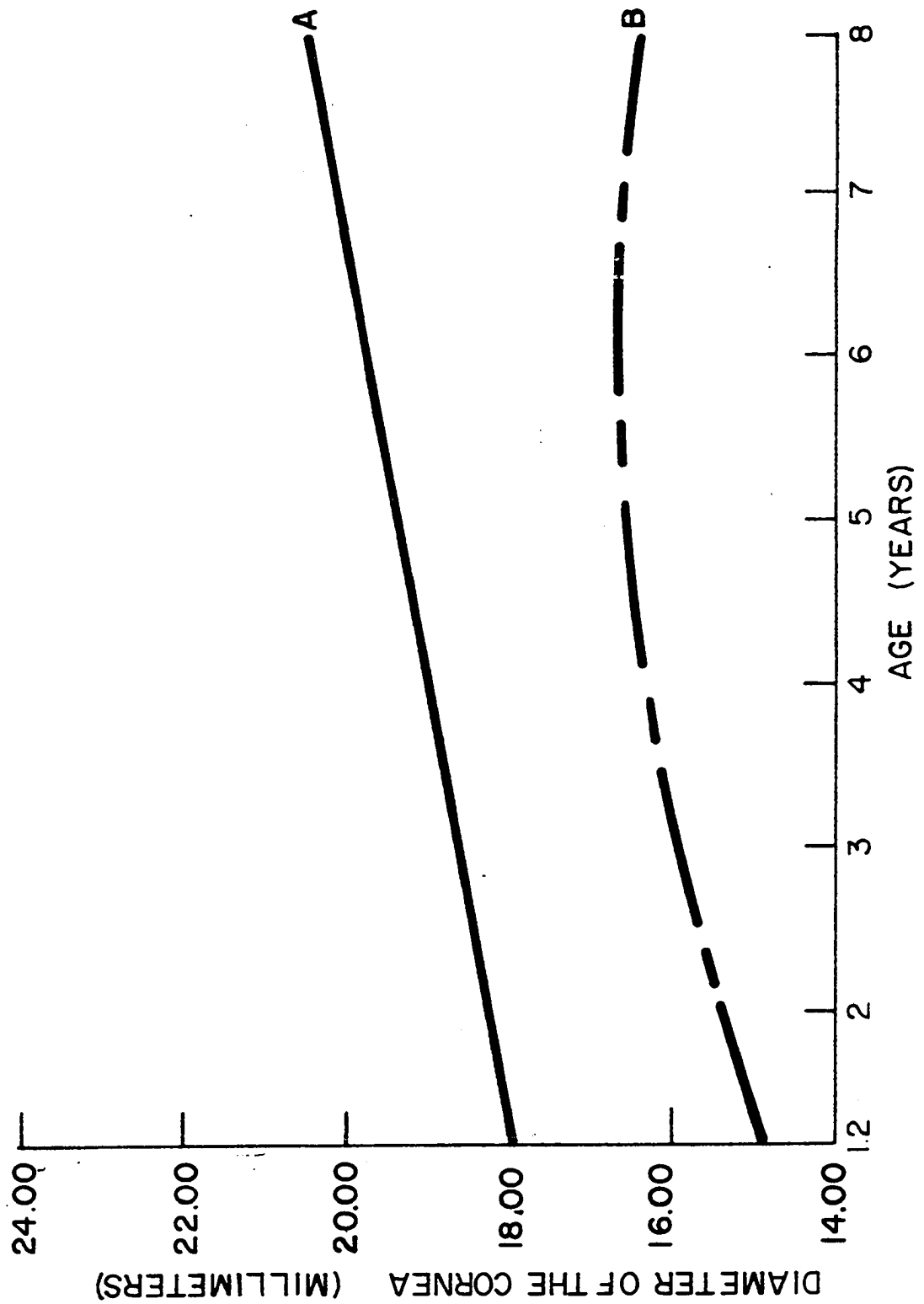
$N = 86$

$Y = 13.9293 + 0.8924\ X_1 - 0.0720\ X_2\ ;\ s_y = .0.6571$ mm

$b_y1.2 = 0.8924 \pm 0.2286$ mm/year, $P < 0.01$

$b_y2.1 = 0.0720 \pm 0.0269$ mm/year, $P < 0.01$

$\bar{Y} = 15.8727 \pm 0.0709$ mm , $P < 0.01$


A
B
24.00
22.00
20.00
18.00
16.00
14.00
1.2
2
3
4
5
6
7
8
AGE (YEARS)
DIAMETER OF THE CORNEA (MILLIMETERS)

Graph 9. Transverse and vertical curvatures of the anterior surface of the cornea in 46 dogs ranging in age from 0.1 month to 13.0 months.

A. Transverse curvature; Data for curvilinear regression, where Y = transverse curvature in diopters and X = age in months.

$N = 46$

$Y = 56.9069 - 2.4899\ X_1 + 0.1005\ X_2$; $s_y = 2.7837$ diopters

$b_y1.2 = 2.4899 \pm 0.3689$ diopters/month, $P<0.01$

$b_y2.1 = 0.1005 \pm 0.0275$ diopters/month, $P<0.01$

$\bar{Y} = 45.9393 \pm 0.4104$ diopters , $P<0.01$

B. Vertical curvature; Data for curvilinear regression, where Y = vertical curvature in diopters and X = age in months.

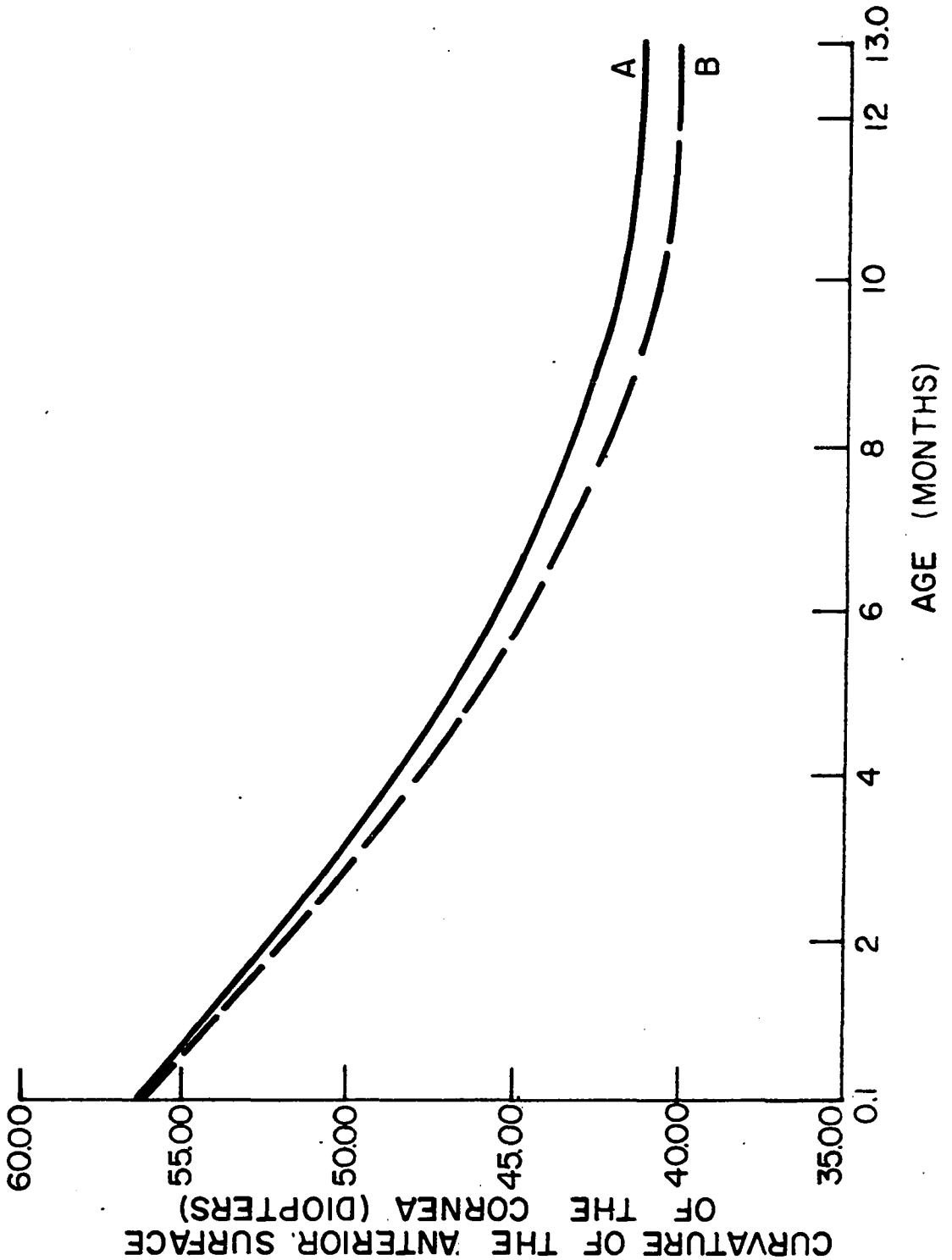
$N = 46$

$Y = 56.7225 - 2.6294\ X_1 + 0.1050\ X_2$; $s_y = 2.8391$ diopters

$b_y1.2 = 2.6294 \pm 0.3763$ diopters/month, $P<0.01$

$b_y2.1 = 0.1050 \pm 0.0280$ diopters/month, $P<0.01$

$\bar{Y} = 45.0509 \pm 0.4186$ diopters , $P<0.01$


CURVATURE OF THE ANTERIOR SURFACE OF THE CORNEA (DIOPTERS)
60.00
55.00
50.00
45.00
40.00
35.00
0.1
2
4
6
8
10
12
13.0
AGE (MONTHS)
A
B

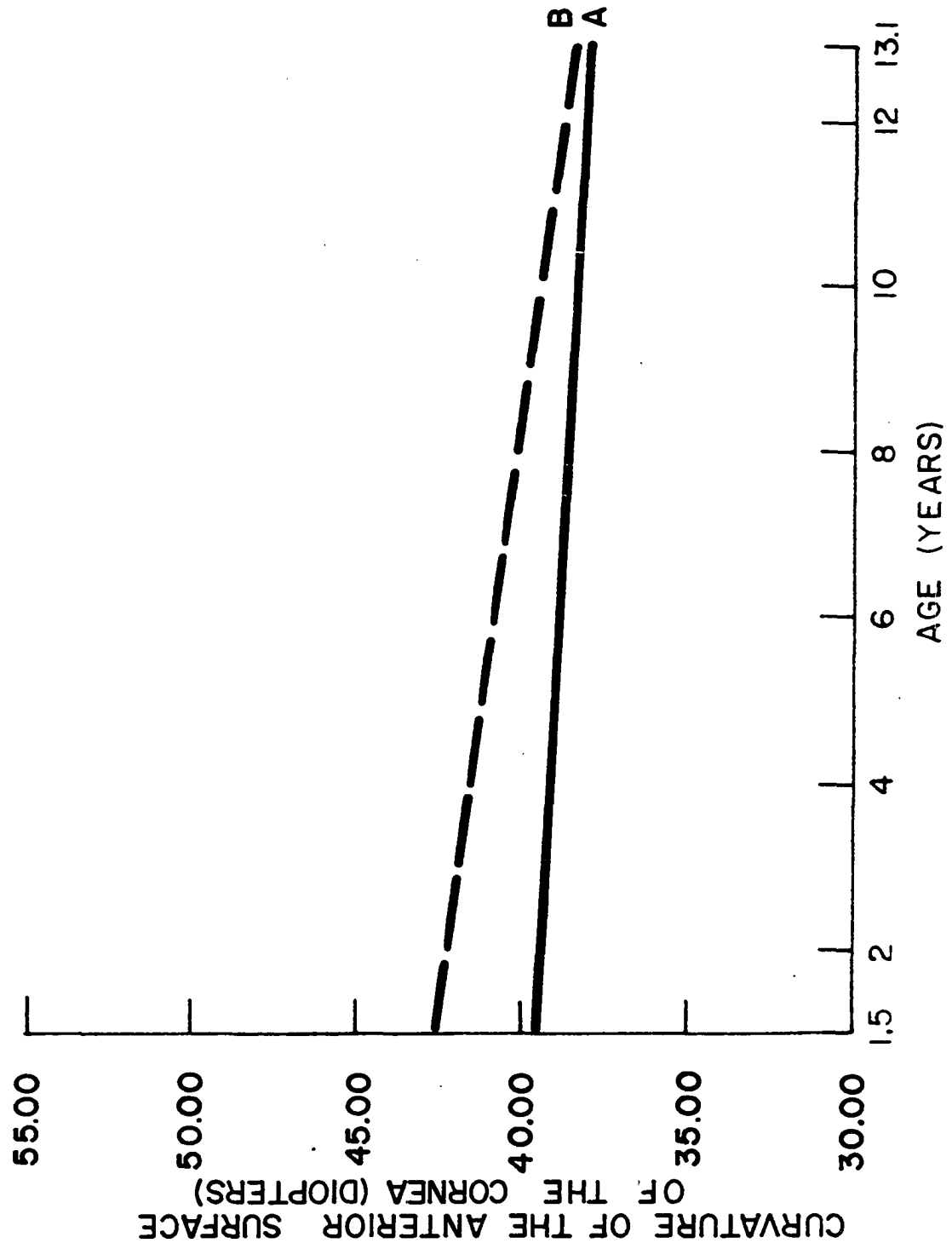
Graph 10. Transverse and vertical curvatures of the anterior surface of the cornea in 32 dogs ranging in age from 1.5 years to 13.1 years.

A. Transverse curvature; Data for linear regression, where Y = transverse curvature in diopters and X = age in years.

N	= 32	
Y	= 39.7127 - 0.1228 X ; s_y = 2.6092 diopters	
b	= 0.1228 ± 0.1291 diopters/year	, P NS
$\bar{Y}$	= 38.6882 ± 0.4605 diopters	, P<0.01
r	= 0.17	, P NS

B. Vertical curvature; Data for linear regression, where Y = vertical curvature in diopters and X = age in years.

N	= 32	
Y	= 43.2638 - 0.3667 X ; s_y = 2.6913 diopters	
b	= 0.3667 ± 0.1331 diopters/year	, P<0.01
$\bar{Y}$	= 40.1863 ± 0.1504 diopters	, P<0.01
r	= 0.45	, P<0.01


B
A
1.5
2
4
6
8
10
12
13.1
AGE (YEARS)
55.00
50.00
45.00
40.00
35.00
30.00
CURVATURE OF THE ANTERIOR SURFACE
OF THE CORNEA (DIOPTERS)

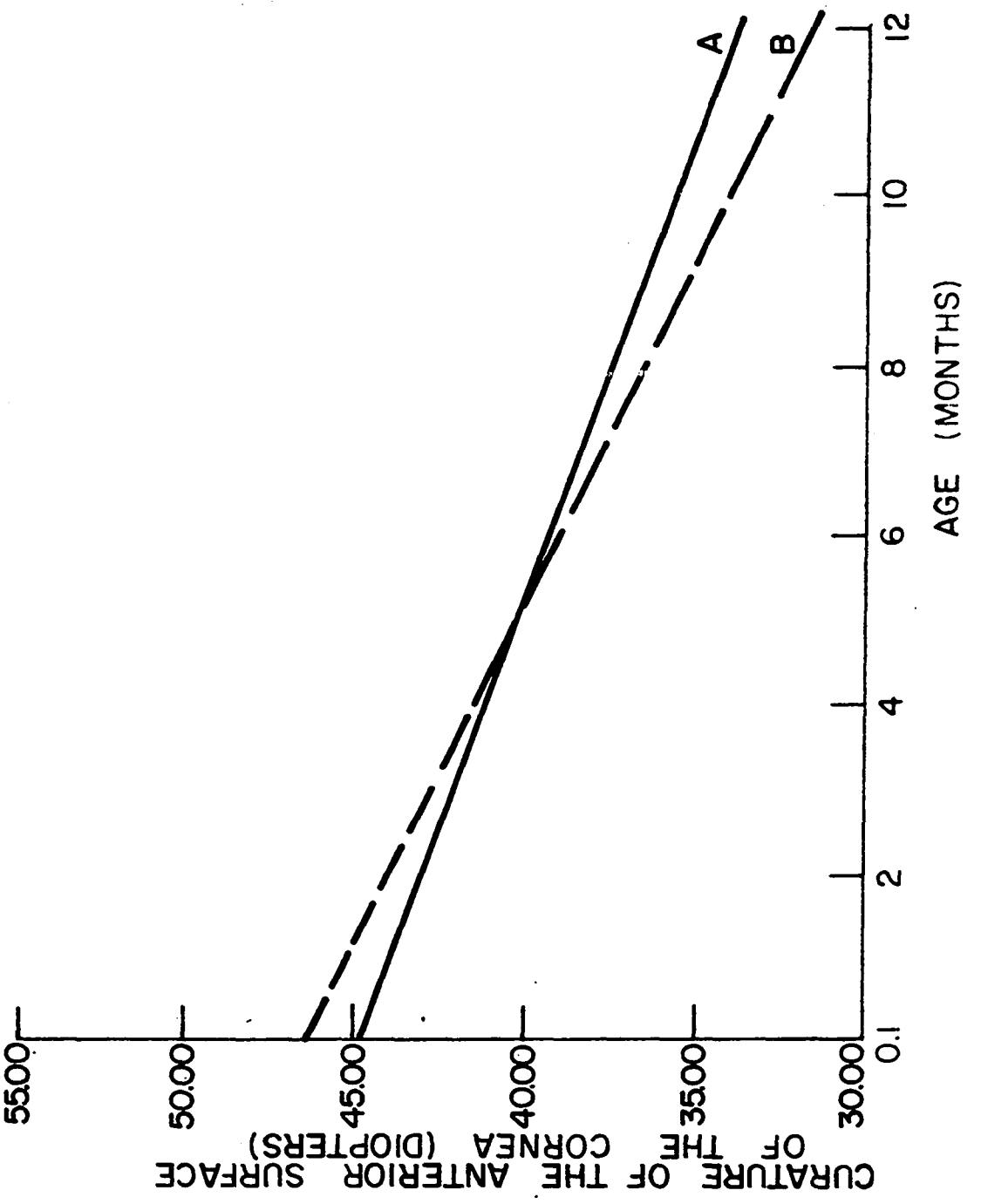
Graph 11. Transverse and vertical curvatures of the anterior surface of the cornea in 22 hogs ranging in age from 0.1 month to 12.0 months.

A. Transverse curvature; Data for linear regression, where Y = transverse curvature in diopters and X = age in months.

$N = 22$
$Y = 49.8017 - 0.9137\ X$; $s_y = 3.2230$ diopters
$b = 0.9137 \pm 0.1905$ diopters/month, $P<0.01$
$\bar{Y} = 44.5340 \pm 0.6871$ diopters , $P<0.01$
$r = 0.73$, $P<0.01$

B. Vertical curvature; Data for linear regression, where Y = vertical curvature in diopters and X = age in months.

$N = 22$
$Y = 51.4336 - 1.2437\ X$; $s_y = 2.2073$ diopters
$b = 1.2437 \pm 0.1304$ diopters/month, $P<0.01$
$\bar{Y} = 44.2632 \pm 0.4705$ diopters , $P<0.01$
$r = 0.90$, $P<0.01$


CURATURE OF THE ANTERIOR SURFACE OF THE CORNEA (DIOPTERS)
55.00
50.00
45.00
40.00
35.00
30.00
0.1
2
4
6
8
10
12
AGE (MONTHS)
A
B

Graph 12. Transverse and vertical curvatures of the anterior surface of the cornea in 86 hogs ranging in age from 1.2 years to 8.0 years.

A. Transverse curvature; Data for linear regression, where Y = transverse curvature in diopters and X = age in years.

$N = 86$
$Y = 37.4288 - 0.2055\ X$; $s_y = 1.4051$ diopters
$b = 0.2055 \pm 0.0835$ diopters/year, $P<0.05$
$\bar{Y} = 36.7413 \pm 0.1515$ diopters , $P<0.01$
$r = 0.26$, $P<0.05$

B. Vertical curvature; Data for curvilinear regression, where Y = vertical curvature in diopters and X = age in years.

$N = 86$
$Y = 39.5329 - 1.4647\ X_1 + 0.1400\ X_2$; $s_y = 1.4875$ diopters
$b_y1.2 = 1.4647 \pm 0.5174$ diopters/year, $P<0.01$
$b_y2.1 = 0.1400 \pm 0.0608$ diopters/year, $P<0.05$
$\bar{Y} = 36.6601 \pm 0.1604$ diopters , $P<0.01$

CURVATURE OF THE ANTERIOR SURFACE
OF THE CORNEA (DIOPTERS)
30.00
35.00
40.00
45.00
50.00
55.00
AGE (YEARS)
1.2
2
3
4
5
6
7
8
A
B

Graph 13. Thickness of the corneal epithelium, total cornea, substantia propria, Descemet's membrane, and the corneal endothelium in 46 dogs ranging in age from 0.1 month to 13.0 months.

A. Corneal epithelial thickness; Data for curvilinear regression, where Y = the corneal epithelial thickness in microns and X = age in months.

$N = 46$

$Y = 15.5260 + 9.9446\ X_1 - 0.5368\ X_2$; $s_y = 9.3924$ microns

$b_y1.2 = 9.9446 \pm 1.2448$ microns/month, $P<0.01$

$b_y2.1 = 0.5368 \pm 0.0927$ microns/month, $P<0.01$

$\bar{Y} = 49.3743 \pm 1.3812$ microns , $P<0.01$

B. Total corneal thickness; Data for curvilinear regression, where Y = total corneal thickness in mm and X = age in months.

$N = 46$

$Y = 0.3413 + 0.0705\ X_1 - 0.0028\ X_2$; $s_y = 0.1130$ mm

$b_y1.2 = 0.0705 \pm 0.0150$ mm/month, $P<0.01$

$b_y2.1 = 0.0028 \pm 0.0011$ mm/month, $P<0.01$

$\bar{Y} = 0.6559 \pm 0.0166$ mm , $P<0.01$

C. Substantia propria thickness; Data for curvilinear regression, where Y = the thickness of the substantia propria in mm and X = age in months.

$N = 46$

$Y = 0.3384 + 0.0624\ X_1 - 0.0026\ X_2$; $s_y = 0.0094$ mm

$b_y1.2 = 0.0624 \pm 0.0012$ mm/month, $P<0.01$

$b_y2.1 = 0.0026 \pm 0.0009$ mm/month, $P<0.01$

$\bar{Y} = 0.6104 \pm 0.0297$ mm , $P<0.01$

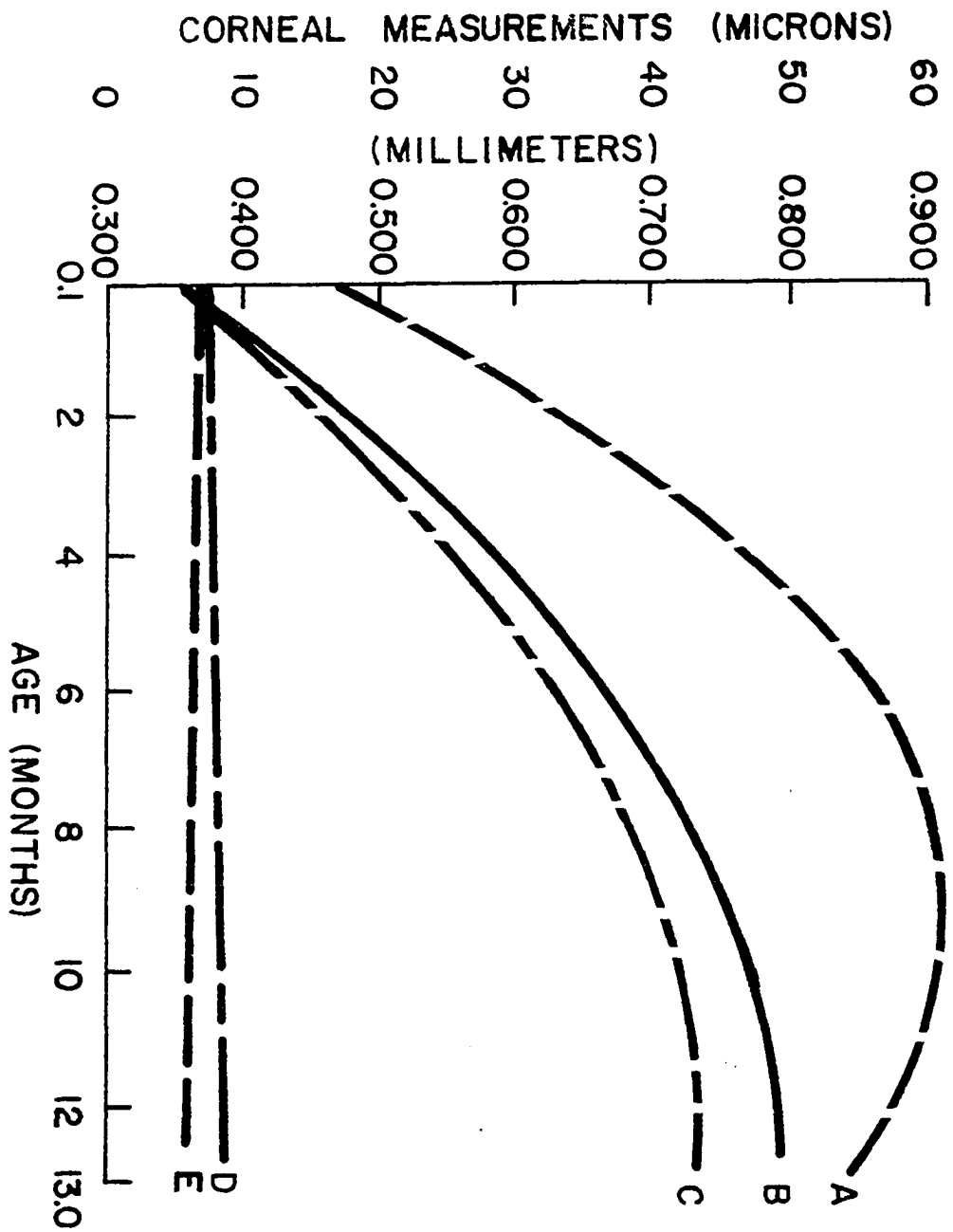
Graph 13. (Continued)

D. Descemet's membrane thickness; Data for linear regression, where Y = the thickness of Descemet's membrane in microns and X = age in months.

$N = 46$
$Y = 7.9153 + 0.0892\ X$; $s_y = 2.9533$ microns
$b = 0.0892 \pm 0.0995$ microns/month, P NS
$\bar{Y} = 8.5733 \pm 0.4345$ microns , $P<0.01$
$r = 0.13$, P NS

E. Corneal endothelial thickness; Data for linear regression, where Y = the corneal endothelial thickness in microns and X = age in months.

$N = 46$
$Y = 6.2960 - 0.0532\ X$; $s_y = 2.2362$ microns
$b = 0.0532 \pm 0.0753$ microns/month, P NS
$\bar{Y} = 5.9039 \pm 0.3279$ microns , $P<0.01$
$r = 0.11$, P NS


CORNEAL MEASUREMENTS (MICRONS)
0
10
20
30
40
50
60
(MILLIMETERS)
0.300
0.400
0.500
0.600
0.700
0.800
0.900
AGE (MONTHS)
0.1
2
4
6
8
10
12
13.0
A
B
C
D
E

Graph 14. Thickness of the corneal epithelium, total cornea, substantia propria, Descemet's membrane, and the corneal endothelium in 32 dogs ranging in age from 1.5 years to 13.1 years.

A. Corneal epithelial thickness; Data for linear regression, where Y = corneal epithelial thickness in microns and X = age in years.

N = 32
Y = 49.5746 + 1.1377 X ; s_y = 13.0097 microns
b = 1.1377 ± 0.6435 microns/year, P NS
$\bar{Y}$ = 59.1234 ± 2.3773 microns , P<0.01
r = 0.31 , P NS

B. Total corneal thickness; Data for linear regression, where Y =total corneal thickness in mm and X = age in years.

N = 32
Y = 0.8377 + 0.0092 X ; s_y = 0.1492 mm
b = 0.0092 ± 0.0074 mm/year, P NS
$\bar{Y}$ = 0.9150 ± 0.0266 mm , P<0.01
r = 0.22 , P NS

C. Substantia propria thickness; Data for linear regression, where Y = the thickness of the substantia propria in mm and X = age in years.

N = 32
Y = 0.7778 + 0.0077 X ; s_y = 0.1439 mm
b = 0.0077 ± 0.0071 mm/year, P NS
$\bar{Y}$ = 0.8420 ± 0.0255 mm , P<0.01
r = 0.19 , P NS

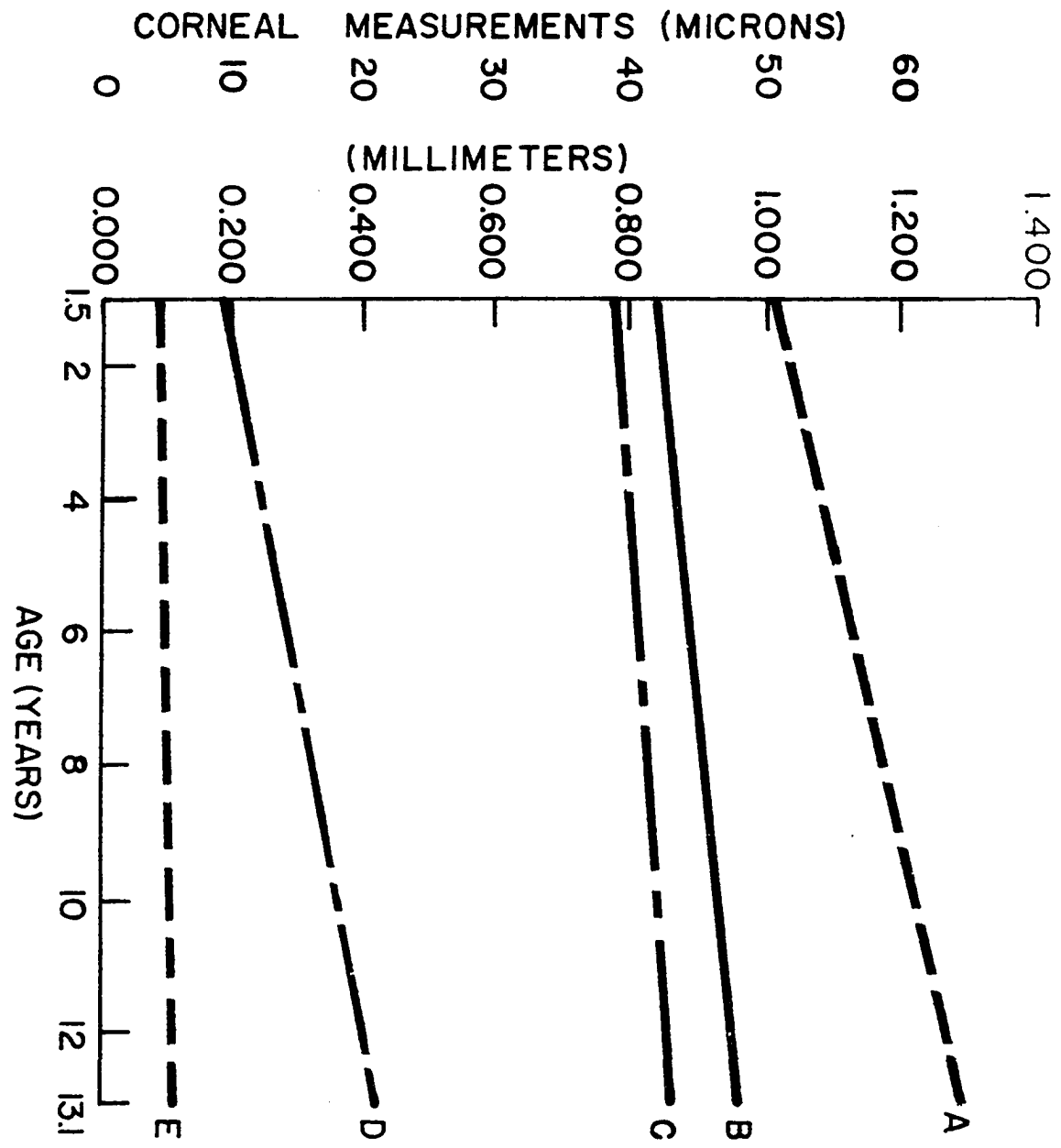
Graph 14. (Continued)

D. Descemet's membrane thickness; Data for linear regression, where Y = the thickness of Descemet's membrane in microns and X = age in years.

N = 32
Y = 7.3459 + 1.0062 X ; s_y = 4.9812 microns
b = 1.0062 ± 0.2464 microns/year, P<0.01
$\bar{Y}$ = 15.7909 ± 0.8806 microns , P<0.01
r = 0.60 , P<0.01

E. Corneal endothelial thickness; Data for linear regression, where Y = the thickness of the corneal endothelium in microns and X = age in years.

N = 32
Y = 4.1410 + 0.0330 X ; s_y = 0.9159 microns
b = 0.0330 ± 0.0453 microns/year, P NS
$\bar{Y}$ = 4.4184 ± 0.1607 microns , P<0.01
r = 0.13 , P NS


CORNEAL MEASUREMENTS (MICRONS)
0
10
20
30
40
50
60
(MILLIMETERS)
0.000
0.200
0.400
0.600
0.800
1.000
1.200
1.400
AGE (YEARS)
1.5
2
4
6
8
10
12
13.1
A
B
C
D
E

Graph 15. Thickness of the corneal epithelium, total cornea, substantia propria, Descemet's membrane, and the corneal endothelium in 22 hogs ranging in age from 0.1 month to 12.0 months.

A. Corneal epithelial thickness; Data for linear regression, where Y = corneal epithelial thickness in microns and X = age in months.

N = 22
Y = 61.2132 + 1.3684 X ; s_y = 1.1406 microns
b = 1.3684 ± 0.6740 microns/month, P NS
$\bar{Y}$ = 64.2132 ± 6.7923 microns , P<0.01
r = 0.41 , P NS

B. Total corneal thickness; Data for linear regression, where Y = total corneal thickness in mm and X = age in months.

N = 22
Y = 0.9223 + 0.0326 X ; s_y = 0.1362 mm
b = 0.0326 ± 0.0080 mm/month, P<0.01
$\bar{Y}$ = 1.1100 ± 0.0290 mm , P<0.01
r = 0.67 , P<0.01

C. Substantia propria thickness; Data for linear regression, where Y = the thickness of the substantia propria in mm and X = age in months.

N = 22
Y = 0.8485 + 0.0316 X ; s_y = 0.1297 mm
b = 0.0316 ± 0.0077 mm/month, P<0.01
$\bar{Y}$ = 1.0308 ± 0.0276 mm , P<0.01
r = 0.68 , P<0.01

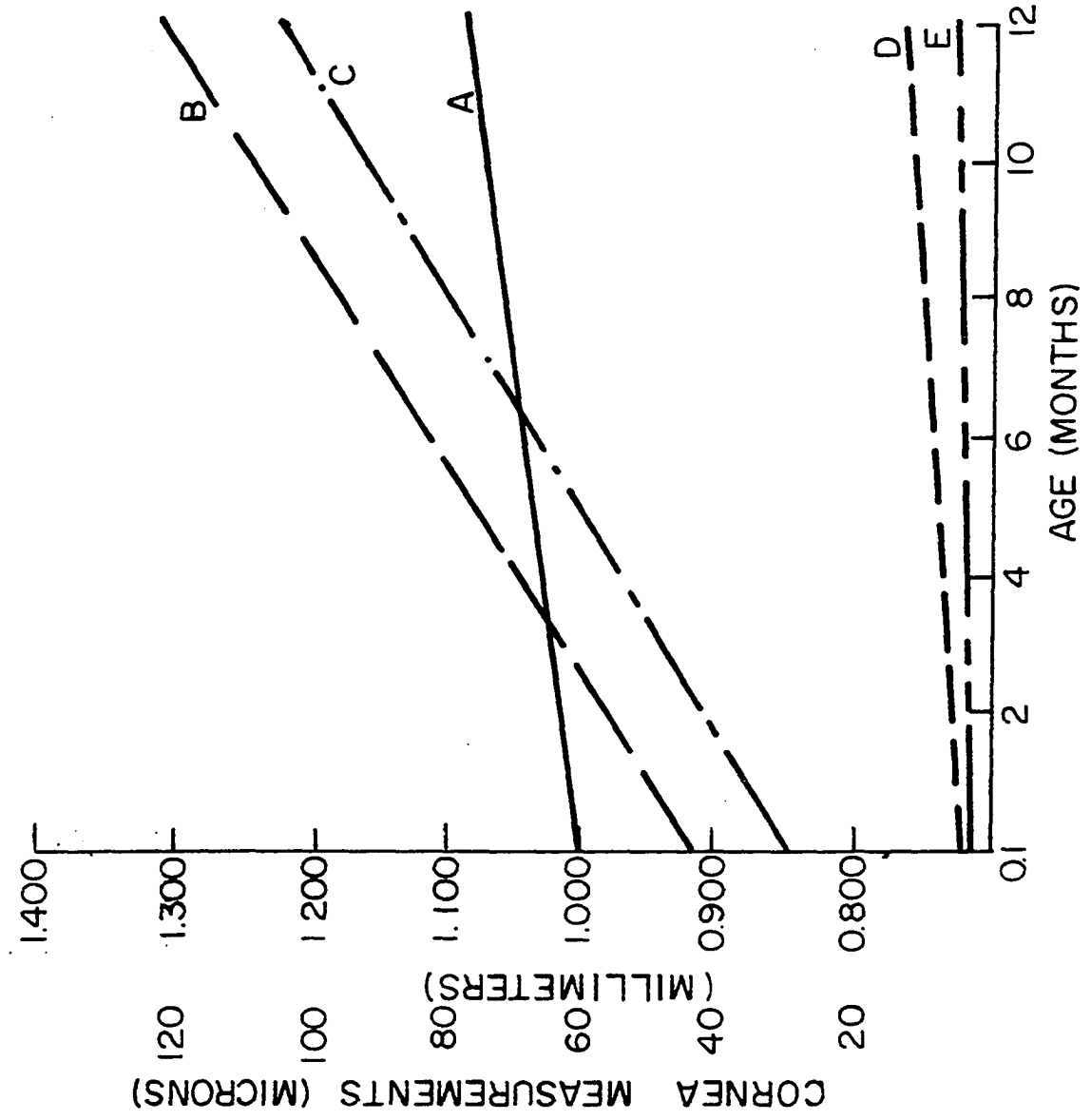
Graph 15. (Continued)

D. Descemet's membrane thickness; Data for linear regression, where Y = the thickness of Descemet's membrane in microns and X = age in months.

N	= 22	
Y	= 4.0705 + 0.7427 X ; s_y = 2.4359 microns	
b	= 0.7427 $\pm$ 0.1440 microns/month,	$P<0.01$
$\bar{Y}$	= 8.3523 $\pm$ 1.9228 microns ,	$P<0.01$
r	= 0.76 ,	$P<0.01$

E. Corneal endothelial thickness; Data for linear regression, where Y = the thickness of the corneal endothelium in microns and X = age in months.

N	= 22	
Y	= 3.5935 + 0.2026 X ; s_y = 1.4153 microns	
b	= 0.2026 $\pm$ 0.0836 microns/month,	$P<0.05$
$\bar{Y}$	= 4.7614 $\pm$ 0.3017 microns ,	$P<0.01$
r	= 0.48 ,	$P<0.05$


CORNEA MEASUREMENTS (MICRONS)
120
100
80
60
40
20
(MILLIMETERS)
1.400
1.300
1.200
1.100
1.000
0.900
0.800
0.1
2
4
6
8
10
12
AGE (MONTHS)
A
B
C
D
E

Graph 16. Thickness of the corneal epithelium, total cornea, substantia propria, Descemet's membrane, and the corneal endothelium in 86 hogs ranging in age from 1.2 years to 8.0 years.

A. Corneal epithelial thickness; Data for linear regression, where Y = corneal epithelial thickness in microns and X = age in years.

$N = 86$
$Y = 78.6948 - 0.9194\ X$; $s_y = 11.9789$ microns
$b = 0.9194 \pm 0.7120$ microns/year, P NS
$\bar{Y} = 75.6192 \pm 1.2968$ microns , $P<0.01$
$r = 0.14$, P NS

B. Total corneal thickness; Data for curvilinear regression, where Y = total corneal thickness in mm and X = age in years.

$N = 86$
$Y = 0.9688 + 0.1818\ X_1 - 0.0215\ X_2$; $s_y = 0.0911$ mm
$b_y1.2 = 0.1818 \pm 0.0529$ mm/year, $P<0.01$
$b_y2.1 = 0.0215 \pm 0.0062$ mm/year, $P<0.01$
$\bar{Y} = 1.2662 \pm 0.0621$ mm , $P<0.01$

C. Substantia propria thickness; Data for curvilinear regression, where Y = thickness of the substantia propria in mm and X = age in years.

$N = 86$
$Y = 0.8907 + 0.1725\ X_1 - 0.0210\ X_2$; $s_y = 0.1482$ mm
$b_y1.2 = 0.1725 \pm 0.0516$ mm/year, $P<0.01$
$b_y2.1 = 0.0210 \pm 0.0061$ mm/year, $P<0.01$
$\bar{Y} = 1.1633 \pm 0.0160$ mm/year, $P<0.01$

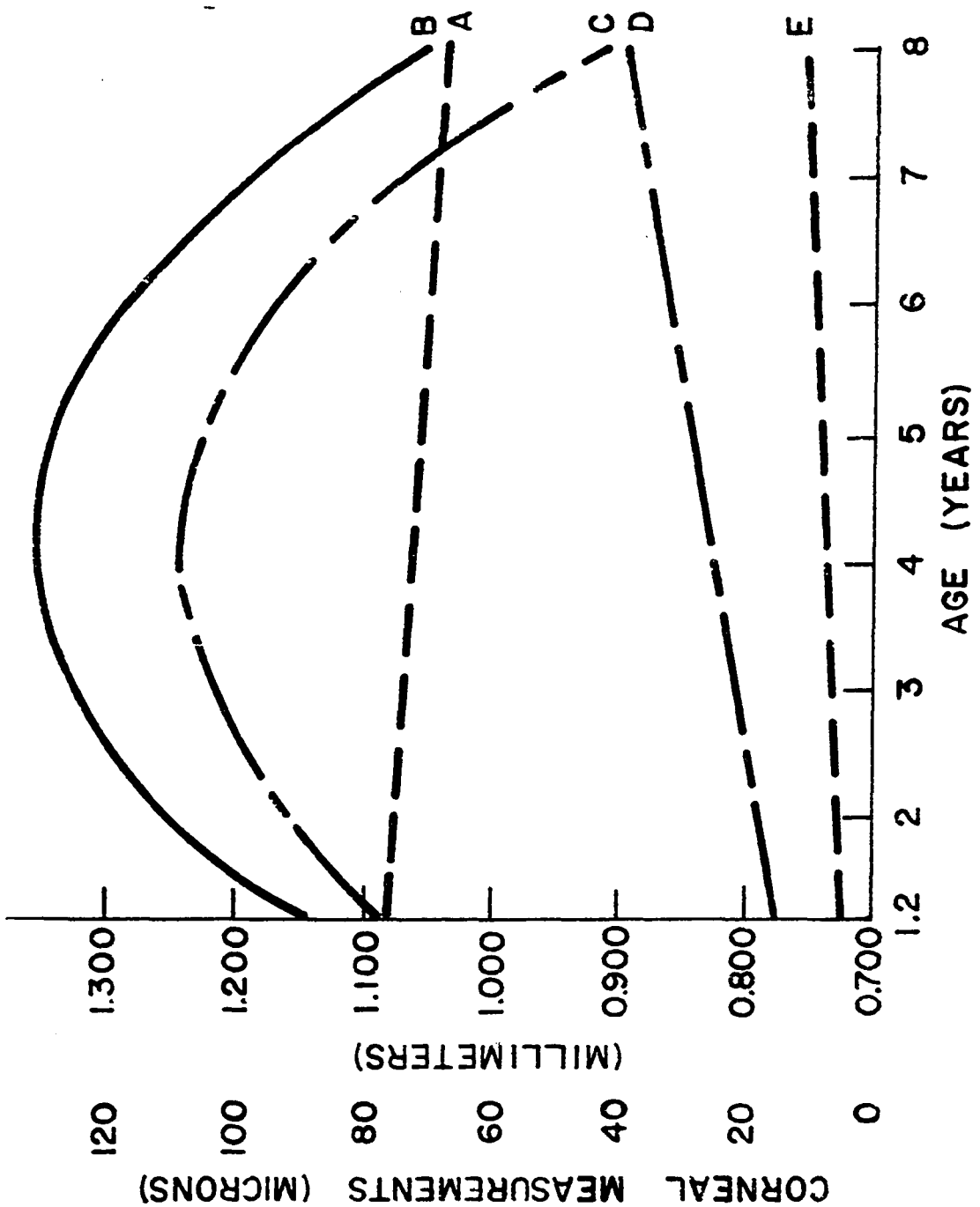
Graph 16. (Continued)

D. Descemet's membrane thickness; Data for linear regression, where Y = the thickness of Descemet's membrane in microns and X = age in years.

N	= 86	
Y	= 8.6686 + 3.9887 X ; s_y = 5.8779 microns	
b	= 3.9887 ± 0.3494 microns/year,	$P<0.01$
$\bar{Y}$	= 22.0116 ± 0.6338 microns ,	$P<0.01$
r	= 0.78 ,	$P<0.01$

E. Corneal endothelial thickness; Data for linear regression, where Y = the thickness of the corneal endothelium in microns and X = age in years.

N	= 86	
Y	= 5.4170 + 0.0587 X ; s_y = 1.5867 microns	
b	= 0.0587 ± 0.0943 microns/year,	P NS
$\bar{Y}$	= 5.6134 ± 1.7048 microns ,	$P<0.01$
r	= 0.06 ,	P NS


CORNEAL MEASUREMENTS (MICRONS)
120
100
80
60
40
20
0
(MILLIMETERS)
1.300
1.200
1.100
1.000
0.900
0.800
0.700
AGE (YEARS)
1.2
2
3
4
5
6
7
8
A
B
C
D
E

Graph 17. Thickness of the sclera at the corneo-scleral junction, the geometric axis of the bulbus oculi, and the equator of the eye in 46 dogs ranging in age from 0.1 month to 13.0 months.

A. Thickness of the sclera at the corneo-scleral junction; Data for curvilinear regression, where Y = the thickness of the sclera in mm and X = age in months.

$N = 46$

$Y = 0.3036 + 0.1272\ X_1 - 0.0063\ X_2$; $s_y = 0.1366$ mm

$b_y1.2 = 0.1272 \pm 0.0181$ mm/month, $P<0.01$

$b_y2.1 = 0.0063 \pm 0.0013$ mm/month, $P<0.01$

$\bar{Y} = 0.7773 \pm 0.0201$ mm , $P<0.01$

B. Thickness of the sclera at the geometric axis of the bulbus oculi; Data for curvilinear regression, where Y = the scleral thickness in mm and X = age in months.

$N = 46$

$Y = 0.1573 + 0.0576\ X_1 - 0.0030\ X_2$; $s_y = 0.0878$ mm

$b_y1.2 = 0.0576 \pm 0.0164$ mm/month, $P<0.01$

$b_y2.1 = 0.0030 \pm 0.0009$ mm/month, $P<0.01$

$\bar{Y} = 0.3647 \pm 0.0129$ mm , $P<0.01$

C. Thickness of the sclera at the equator of the eye; Data for linear regression, where Y = the thickness of the sclera in mm and X = age in months.

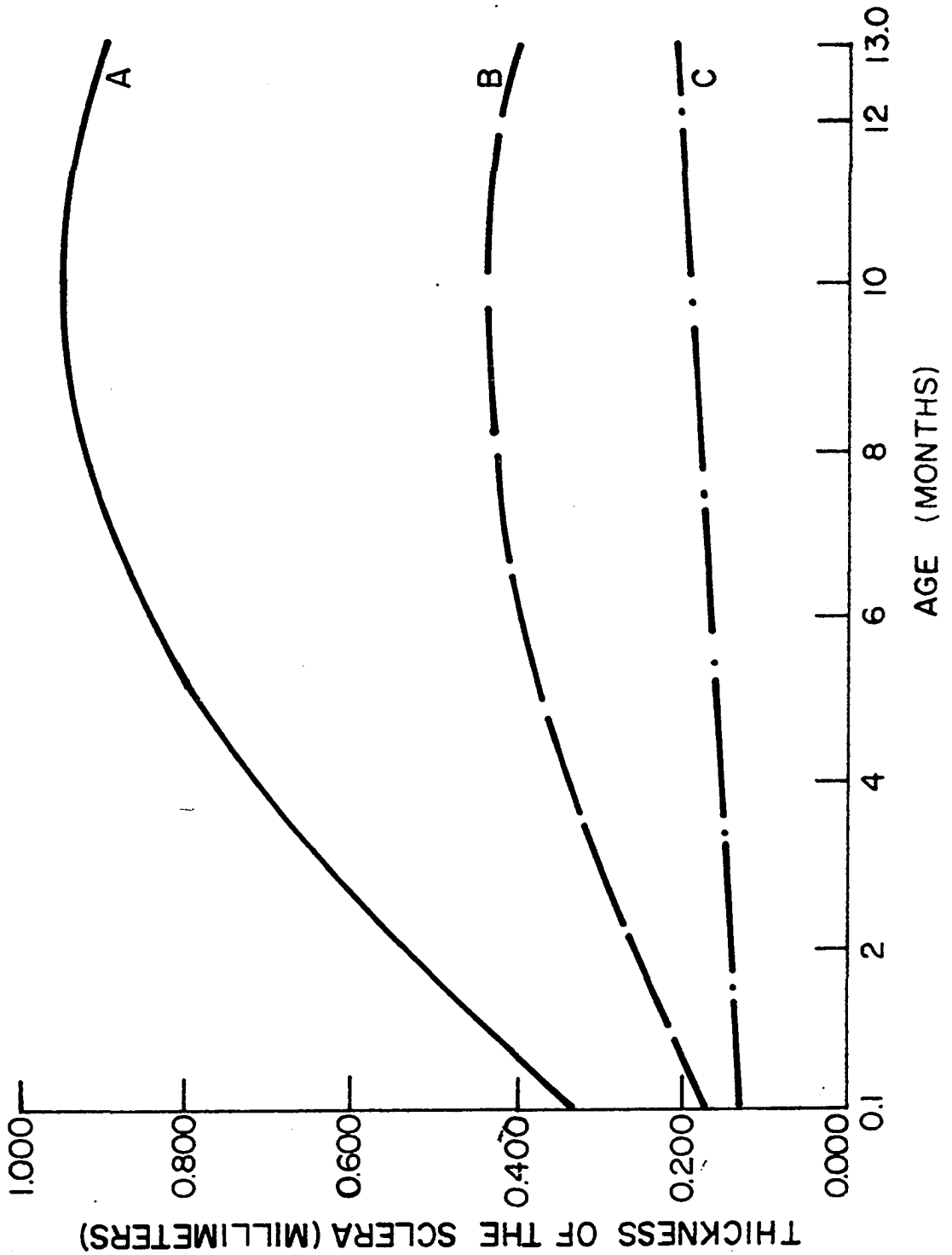
$N = 46$

$Y = 0.1260 + 0.0063\ X$; $s_y = 0.0727$ mm

$b = 0.0063 \pm 0.0024$ mm/month, $P<0.05$

$\bar{Y} = 0.1728 \pm 0.0107$ mm , $P<0.01$

$r = 0.36$, $P<0.05$


A
B
C
1.000
0.800
0.600
0.400
0.200
0.000
0.1
2
4
6
8
10
12
13.0
AGE (MONTHS)
THICKNESS OF THE SCLERA (MILLIMETERS)

Graph 18. Thickness of the sclera at the corneo-scleral junction, the geometric axis of the bulbus oculi, and the equator of the eye in 32 dogs ranging in age from 1.5 years to 13.1 years.

A. Thickness of the sclera at the corneo-scleral junction; Data for linear regression, where Y = scleral thickness and X = age in years.

N = 32
Y = 0.8731 + 0.0064 X ; s_y = 0.1055 mm
b = 0.0064 ± 0.0052 mm/year, P NS
$\bar{Y}$ = 0.9267 ± 0.0188 mm , P<0.01
r = 0.22 , P NS

B. Thickness of the sclera at the geometric axis of the bulbus oculi; Data for linear regression, where Y = scleral thickness in mm and X = age in years.

N = 32
Y = 0.3326 + 0.0043 X ; s_y = 0.1194 mm
b = 0.0043 ± 0.0059 mm/year, P NS
$\bar{Y}$ = 0.3689 ± 0.0168 mm , P<0.01
r = 0.13 , P NS

C. Thickness of the sclera at the equator of the eye; Data for linear regression, Y = scleral thickness in mm and X = age in years.

N = 32
Y = 0.1328 + 0.0040 X ; s_y = 0.0451 mm
b = 0.0040 ± 0.0023 mm/year, P NS
$\bar{Y}$ = 0.1662 ± 0.0082 mm , P<0.01
r = 0.31 , P NS

THICKNESS OF THE SCLERA (MILLIMETERS)
0.000
0.200
0.400
0.600
0.800
1.000
AGE (YEARS)
1.5
2
4
6
8
10
12
13.1
A
B
C

Graph 19. Thickness of the sclera at the corneo-scleral junction, the geometric axis of the bulbus oculi, and the equator of the eye in 22 hogs ranging in age from 0.1 month to 12.0 months.

A. Thickness of the sclera at the corneo-scleral junction; Data for linear regression where Y = scleral thickness in mm and X = age in months.

$N = 22$

$Y = 0.9105 + 0.0424\ X\ ;\ s_y = 0.2121$ mm

$b = 0.0424 \pm 0.0125$ mm/month, $P<0.01$

$\bar{Y} = 1.1549 \pm 0.0452$ mm , $P<0.01$

$r = 0.60$, $P<0.01$

B. Thickness of the sclera at the geometric axis of the bulbus oculi; Data for curvilinear regression, where Y = scleral thickness in mm and X = age in months.

$N = 22$

$Y = 0.5613 + 0.2001\ X_1 - 0.0123\ X_2\ ;\ s_y = 0.2174$ mm

$b_y1.2 = 0.2001 \pm 0.0508$ mm/month, $P<0.01$

$b_y2.1 = 0.0123 \pm 0.0041$ mm/month, $P<0.01$

$\bar{Y} = 1.1471 \pm 0.0464$ mm , $P<0.01$

C. Thickness of the sclera at the equator of the eye; Data for curvilinear regression, where Y = scleral thickness in mm and X = age in months.

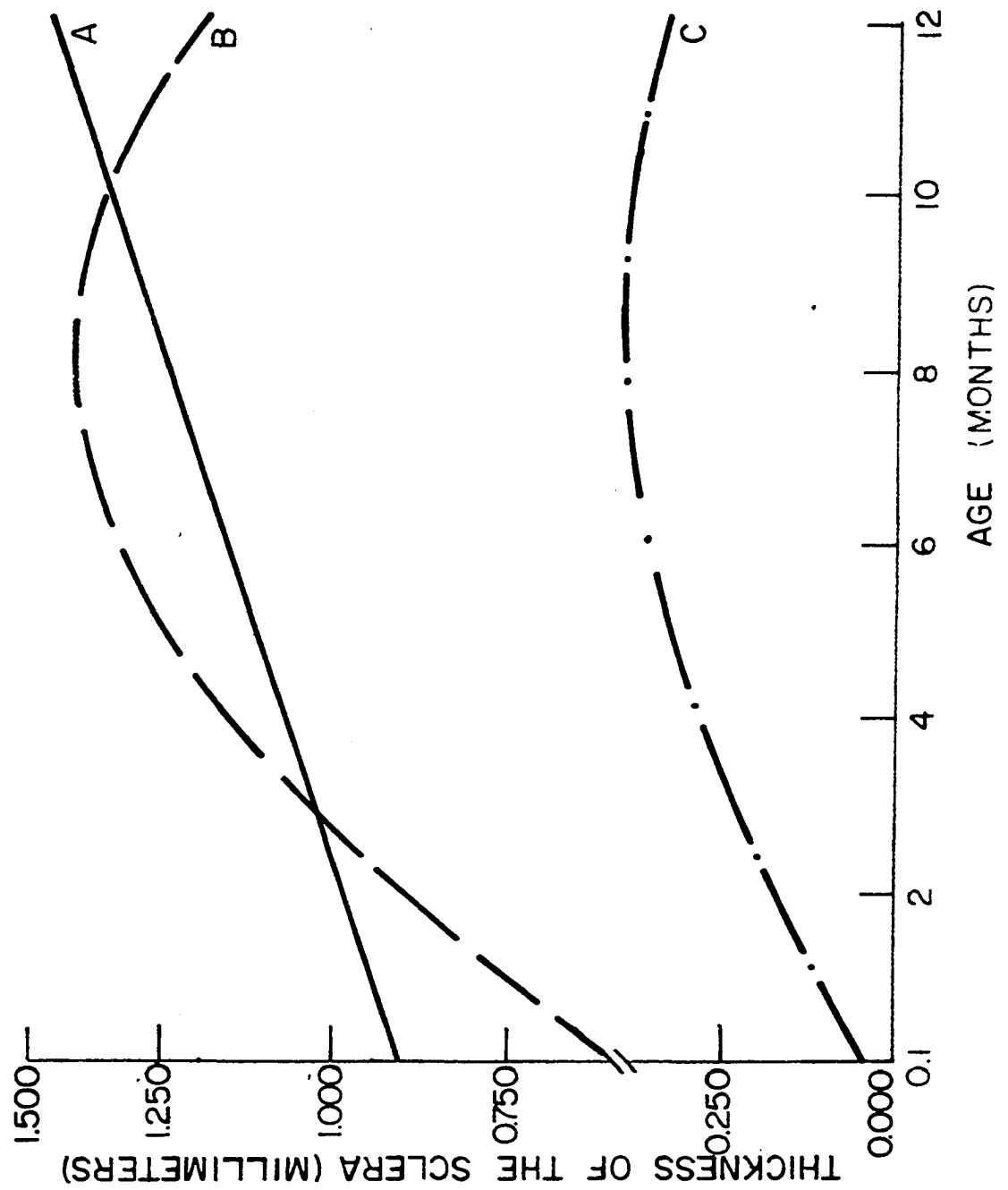
$N = 22$

$Y = 0.0330 + 0.0820\ X_1 - 0.0047\ X_2\ ;\ s_y = 0.0915$ mm

$b_y1.2 = 0.0820 \pm 0.0215$ mm/month, $P<0.01$

$b_y2.1 = 0.0047 \pm 0.0017$ mm/month, $P<0.05$

$\bar{Y} = 0.2903 \pm 0.0195$ mm , $P<0.01$


A
B
C
1.500
1.250
1.000
0.750
0.250
0.000
0.1
2
4
6
8
10
12
AGE (MONTHS)
THICKNESS OF THE SCLERA (MILLIMETERS)

Graph 20. Thickness of the sclera at the corneo-scleral junction, the geometric axis of the bulbus oculi, and the equator of the eye in 86 hogs ranging in age from 1.2 years to 8.0 years.

A. Thickness of the sclera at the corneo-scleral junction; Data for curvilinear regression, where Y = scleral thickness in mm and X = age in years.

$N = 86$

$Y = 0.9709 + 0.1969\ X_1 - 0.0199\ X_2$; $s_y = 0.2343$ mm

$b_y1.2 = 0.1969 \pm 0.0815$ mm/year, $P<0.05$

$b_y2.1 = 0.0199 \pm 0.0096$ mm/year, $P<0.05$

$\bar{Y} = 1.3413 \pm 0.0253$ mm , $P<0.01$

B. Thickness of the sclera at the geometric axis of the bulbus oculi; Data for curvilinear regression, where Y = scleral thickness in mm and X = age in years.

$N = 86$

$Y = 1.0952 + 0.2279\ X_1 - 0.0305\ X_2$; $s_y = 0.1410$ mm

$b_y1.2 = 0.2279 \pm 0.0819$ mm/year, $P<0.01$

$b_y2.1 = 0.0305 \pm 0.0096$ mm/year, $P<0.01$

$\bar{Y} = 1.4166 \pm 0.0254$ mm , $P<0.01$

C. Thickness of the sclera at the equator of the eye; Data for curvilinear regression, where Y = scleral thickness in mm and X = age in years.

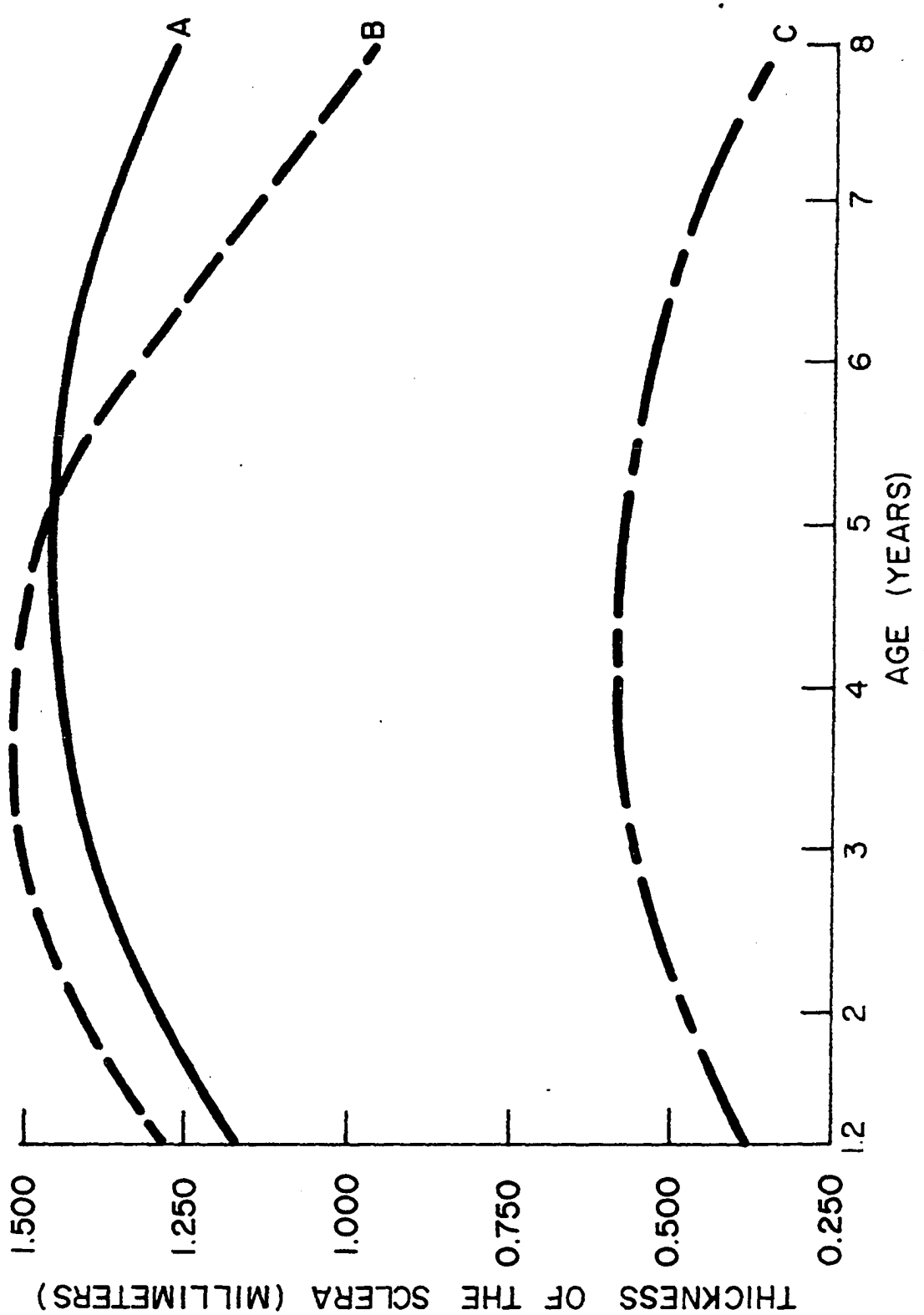
$N = 86$

$Y = 0.2049 + 0.1660\ X_1 - 0.0185\ X_2$; $s_y = 0.1643$ mm

$b_y1.2 = 0.1660 \pm 0.0572$ mm/year, $P<0.01$

$b_y2.1 = 0.0185 \pm 0.0067$ mm/year, $P<0.01$

$\bar{Y} = 0.4925 \pm 0.0177$ mm , $P<0.01$


A
B
C
1.500
1.250
1.000
0.750
0.500
0.250
THICKNESS OF THE SCLERA (MILLIMETERS)
1.2
2
3
4
5
6
7
8
AGE (YEARS)

Graph 21. Central and basal thickness of the iris in 46 dogs ranging in age from 0.1 month to 13.0 months.

A. Central thickness of the iris; Data for curvilinear regression, where Y = the central thickness in mm and X = age in months.

$N = 46$

$Y = 0.1398 + 0.0715\ X_1 - 0.0038\ X_2$; $s_y = 0.1049$ mm

$b_y1.2 = 0.0715 \pm 0.0139$ mm/month, $P<0.01$

$b_y2.1 = 0.0038 \pm 0.0010$ mm/month, $P<0.01$

$\bar{Y} = 0.3902 \pm 0.0155$ mm , $P<0.01$

B. Basal thickness of the iris; Data for curvilinear regression, where Y = the basal thickness in mm and X = age in months.

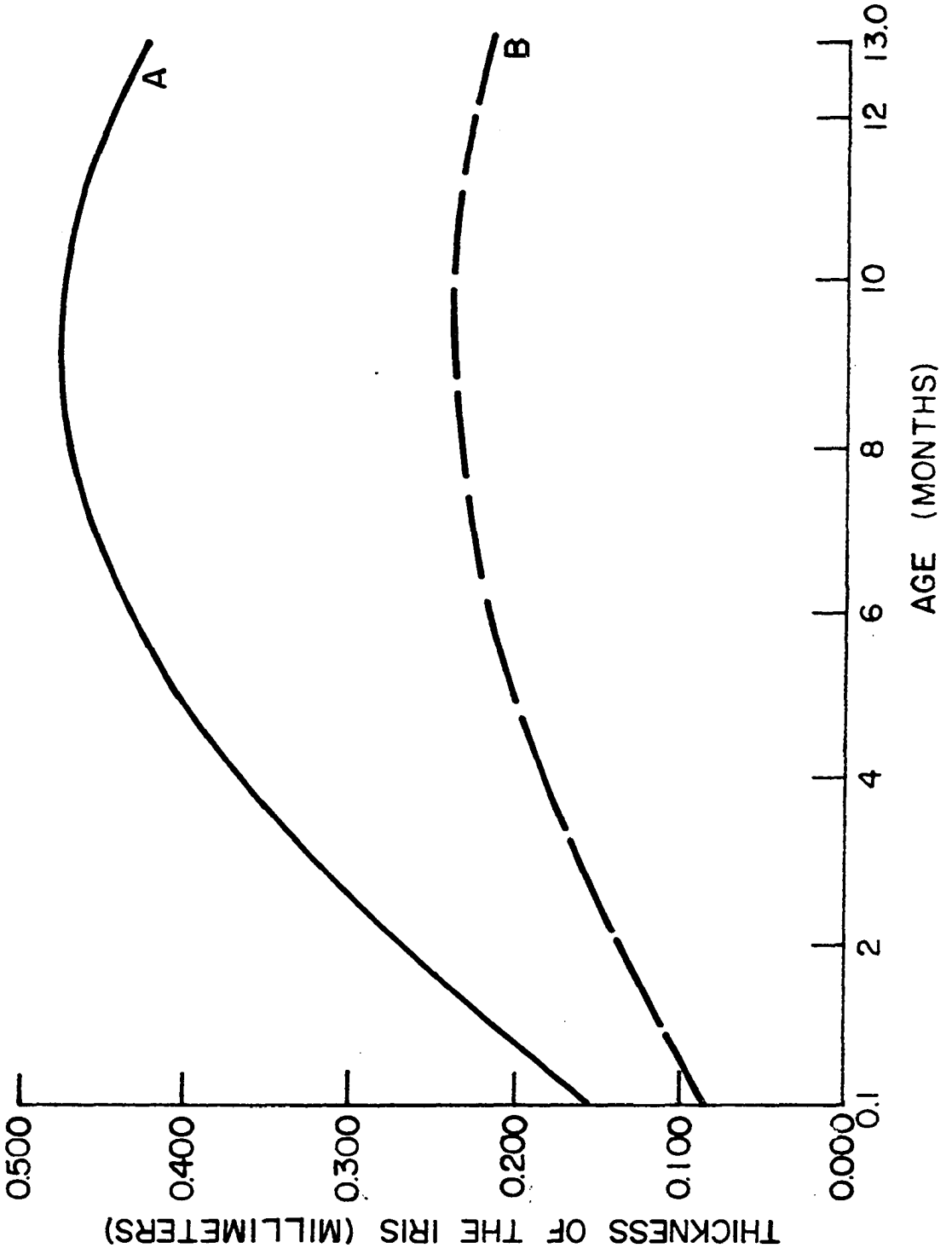
$N = 46$

$Y = 0.0791 + 0.0328\ X_1 - 0.0017\ X_2$; $s_y = 0.0510$ mm

$b_y1.2 = 0.0328 \pm 0.0068$ mm/month, $P<0.01$

$b_y2.1 = 0.0017 \pm 0.0005$ mm/month, $P<0.01$

$\bar{Y} = 0.1956 \pm 0.0075$ mm , $P<0.01$


A
B
0.500
0.400
0.300
0.200
0.100
0.000
0.1
2
4
6
8
10
12
13.0
AGE (MONTHS)
THICKNESS OF THE IRIS (MILLIMETERS)

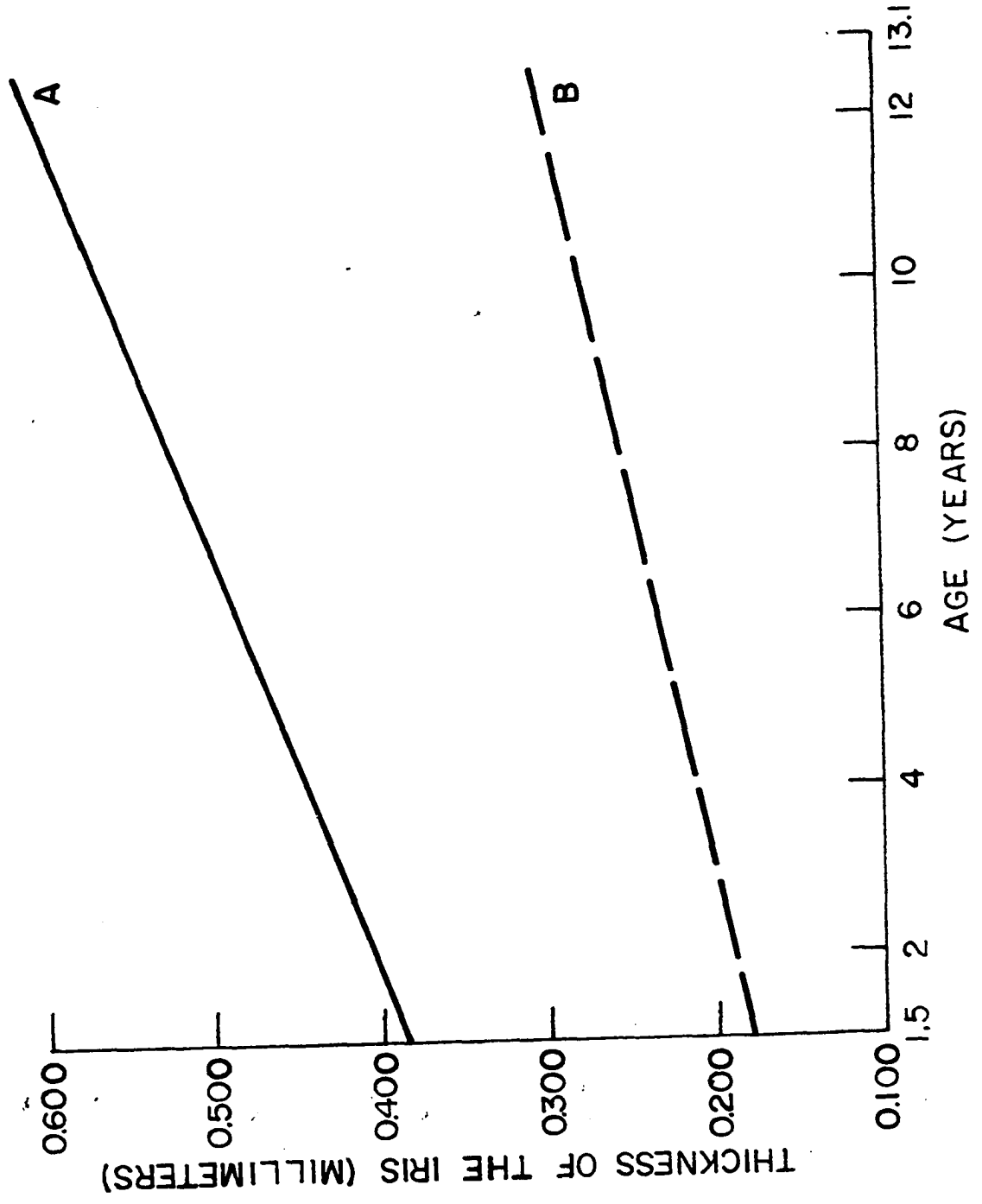
Graph 22. Central and basal thickness of the iris in 32 dogs ranging in age from 1.5 years to 13.1 years.

A. Central thickness of the iris; Data for linear regression, where Y = the central thickness of the iris in mm and X = age in years.

N	= 32		
Y	= 0.3562 + 0.0198 X ; s_y = 0.1261 mm		
b	= 0.0198 ± 0.0062 mm/year	,	$P<0.01$
$\bar{Y}$	= 0.5225 ± 0.0223 mm	,	$P<0.01$
r	= 0.50	,	$P<0.01$

B. Basal thickness of the iris; Data for linear regression, where Y = basal thickness of the iris in mm and X = age in years.

N	= 32		
Y	= 0.1648 + 0.0106 X ; s_y = 0.0818 mm		
b	= 0.0106 ± 0.0040 mm/year	,	$P<0.05$
$\bar{Y}$	= 0.2539 ± 0.0145 mm	,	$P<0.01$
r	= 0.43	,	$P<0.05$


A
B
0.600
0.500
0.400
0.300
0.200
0.100
THICKNESS OF THE IRIS (MILLIMETERS)
1.5
2
4
6
8
10
12
13.1
AGE (YEARS)

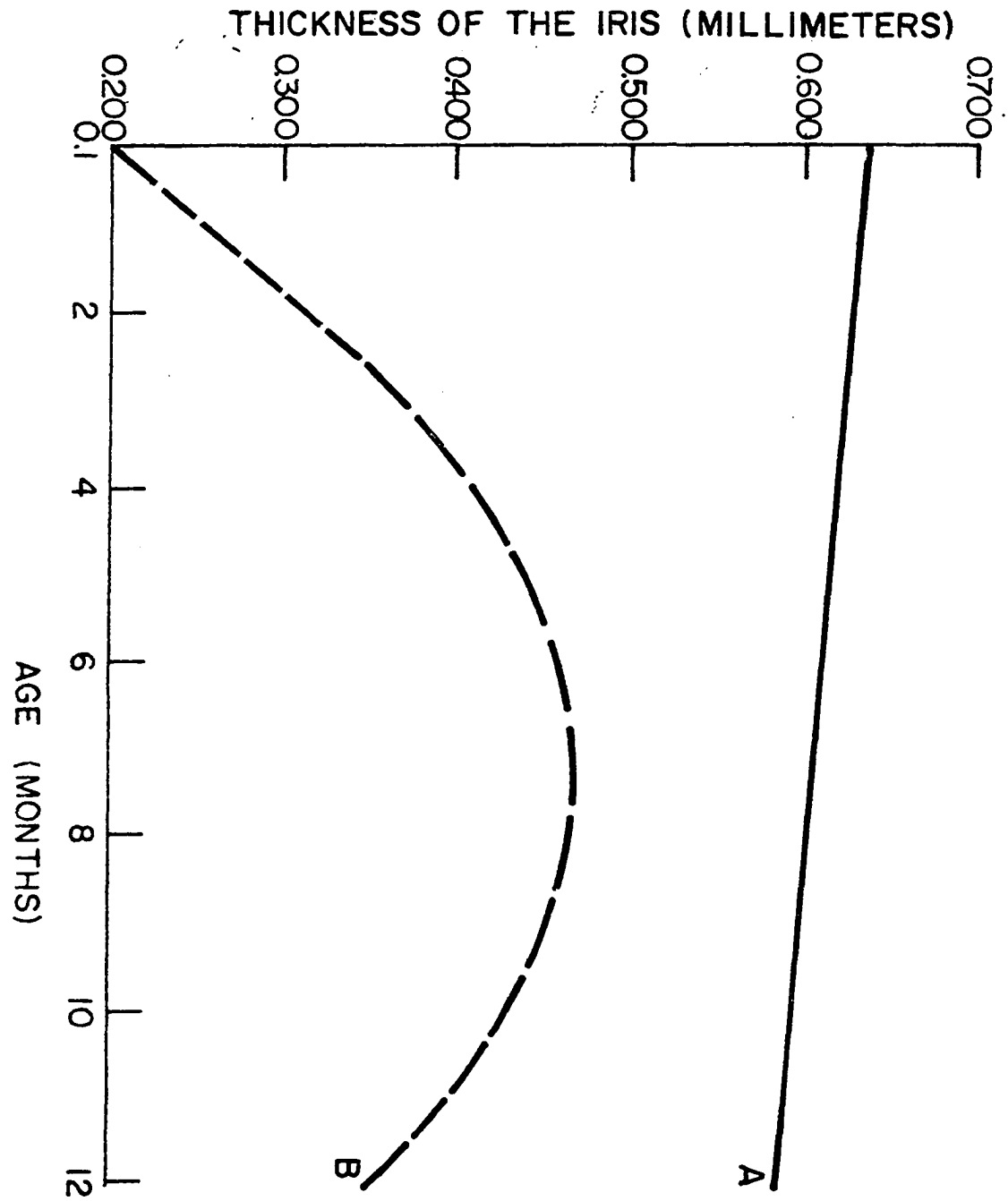
Graph 23. Central and basal thickness of the iris in 22 hogs ranging in age from 0.1 month to 12.0 months.

A. Central thickness of the iris; Data for linear regression, where Y = the central thickness of the iris in mm and X = age in months.

$N = 22$
$Y = 0.6348 - 0.0044\ X$; $s_y = 0.1486$ mm
$b = 0.0044 \pm 0.0088$ mm/month, P NS
$\bar{Y} = 0.6097 \pm 0.0190$ mm , $P<0.01$
$r = 0.11$, P NS

B. Basal thickness of the iris; Data for curvilinear regression, where Y = the basal thickness of the iris in mm and X = age in months.

$N = 22$
$Y = 0.1843 + 0.0772\ X_1 - 0.0053\ X_2$; $s_y = 0.0769$ mm
$b_y1.2 = 0.0772 \pm 0.0180$ mm/month, $P<0.01$
$b_y2.1 = 0.0053 \pm 0.0014$ mm/month, $P<0.01$
$\bar{Y} = 0.3860 \pm 0.0164$ mm/month, $P<0.01$


THICKNESS OF THE IRIS (MILLIMETERS)
0.200
0.300
0.400
0.500
0.600
0.700
AGE (MONTHS)
0.1
2
4
6
8
10
12
A
B

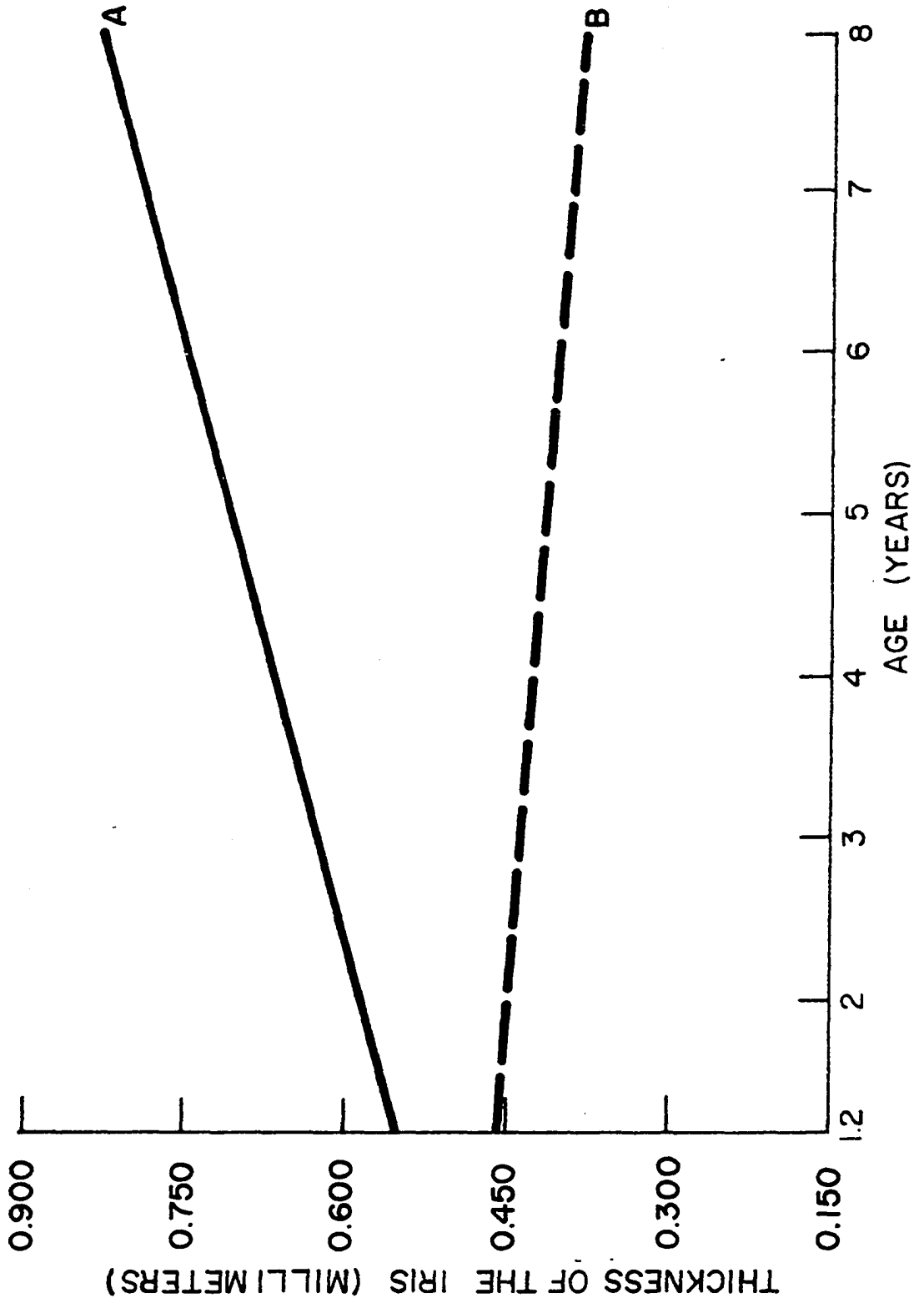
Graph 24. Central and basal thickness of the iris in 86 hogs ranging in age from 1.2 years to 8.0 years.

A. Central thickness of the iris; Data for linear regression, where Y = the central thickness of the iris in mm and X = age in years.

$N = 86$
$Y = 0.5328 + 0.0375\ X\ ;\ s_y = 0.1247$ mm
$b = 0.0375 \pm 0.0074$ mm/year, $P<0.01$
$\bar{Y} = 0.6583 \pm 0.0134$ mm , $P<0.01$
$r = 0.48$, $P<0.01$

B. Basal thickness of the iris; Data for linear regression, where Y = the basal thickness of the iris in mm and X = age in years.

$N = 86$
$Y = 0.4423 - 0.0073\ X\ ;\ s_y = 0.0997$ mm
$b = 0.0073 \pm 0.0059$ mm/year, P NS
$\bar{Y} = 0.4180 \pm 0.0108$ mm , $P<0.01$
$r = 0.13$, P NS


A
B
0.900
0.750
0.600
0.450
0.300
0.150
THICKNESS OF THE IRIS (MILLIMETERS)
1.2
2
3
4
5
6
7
8
AGE (YEARS)

Graph 25. Thickness of the ciliary body in the proximity of the anterior chamber angle of the eye in 46 dogs ranging in age from 0.1 month to 13.0 months.

A. Data for curvilinear regression, where Y = the thickness of the ciliary body in mm and X = age in months.

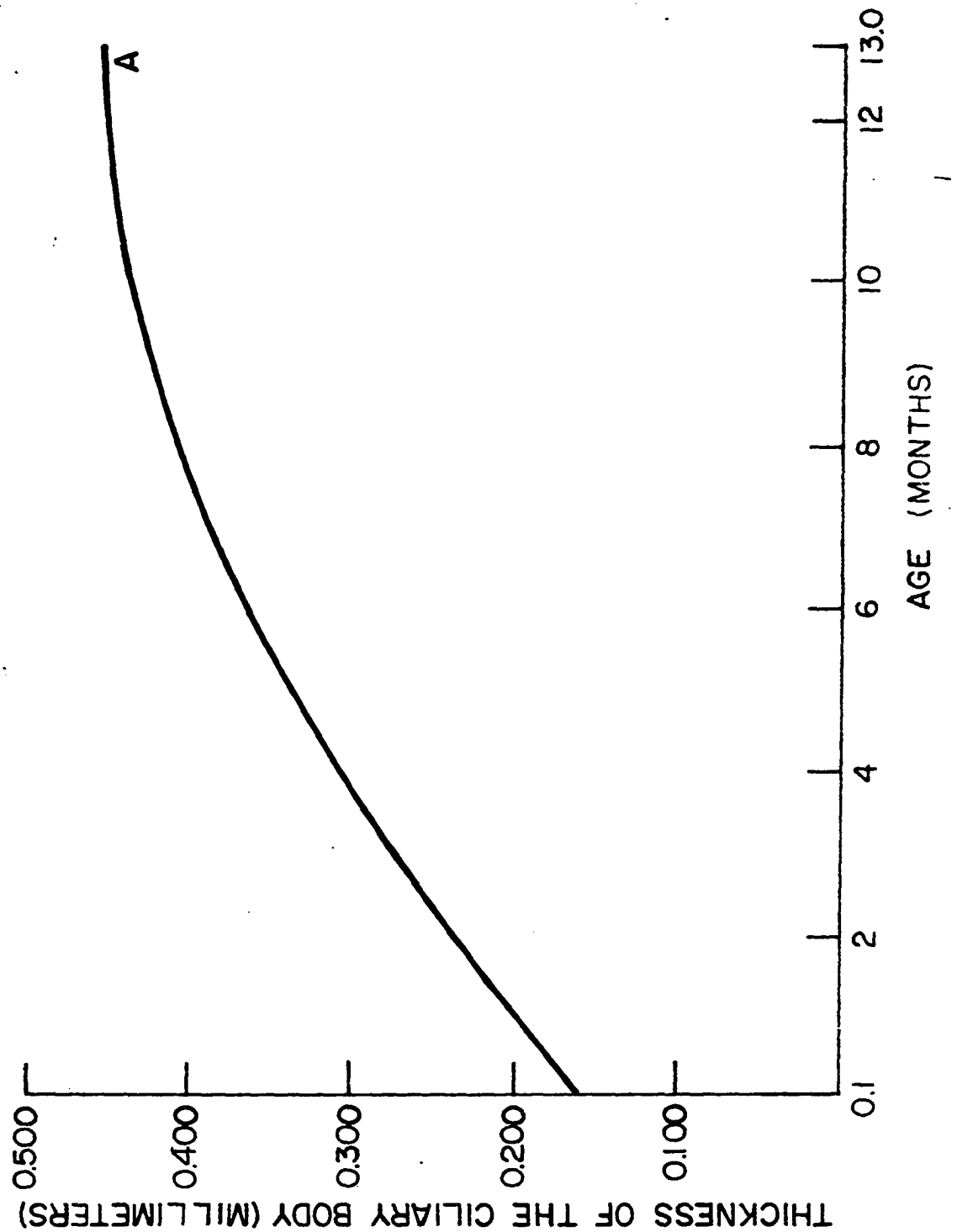
$N = 46$

$Y = 0.1505 + 0.0454\ X_1 - 0.0017\ X_2$; $s_y = 0.0749$ mm

$b_y1.2 = 0.0454 \pm 0.0099$ mm/month, $P<0.01$

$b_y2.1 = 0.0017 \pm 0.0007$ mm/month, P NS

$\bar{Y} = 0.3620 \pm 0.0110$ mm , $P<0.01$


A
0.500
0.400
0.300
0.200
0.100
THICKNESS OF THE CILIARY BODY (MILLIMETERS)
0.1
2
4
6
8
10
12
13.0
AGE (MONTHS)

Graph 26. Thickness of the ciliary body in the proximity of the anterior chamber angle of the eye in 32 dogs ranging in age from 1.5 years to 13.1 years.

A. Data for linear regression, where Y = the thickness of the ciliary body in mm and X = age in years.

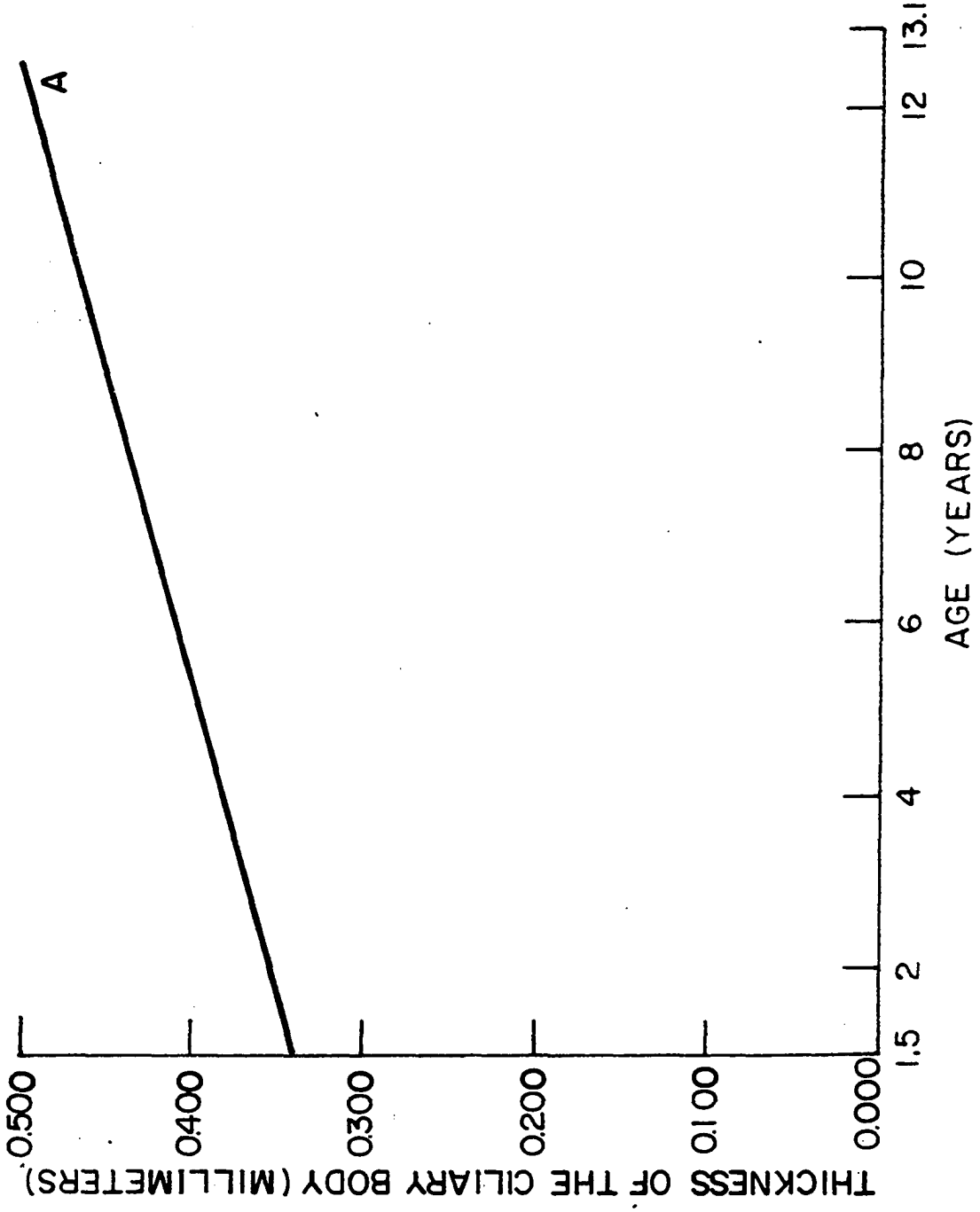
$N = 32$

$Y = 0.3283 + 0.0137\ X$; $s_y = 0.1202$ mm

$b = 0.0137 \pm 0.0059$ mm/year, $P < 0.05$

$\bar{Y} = 0.4435 \pm 0.0212$ mm , $P < 0.01$

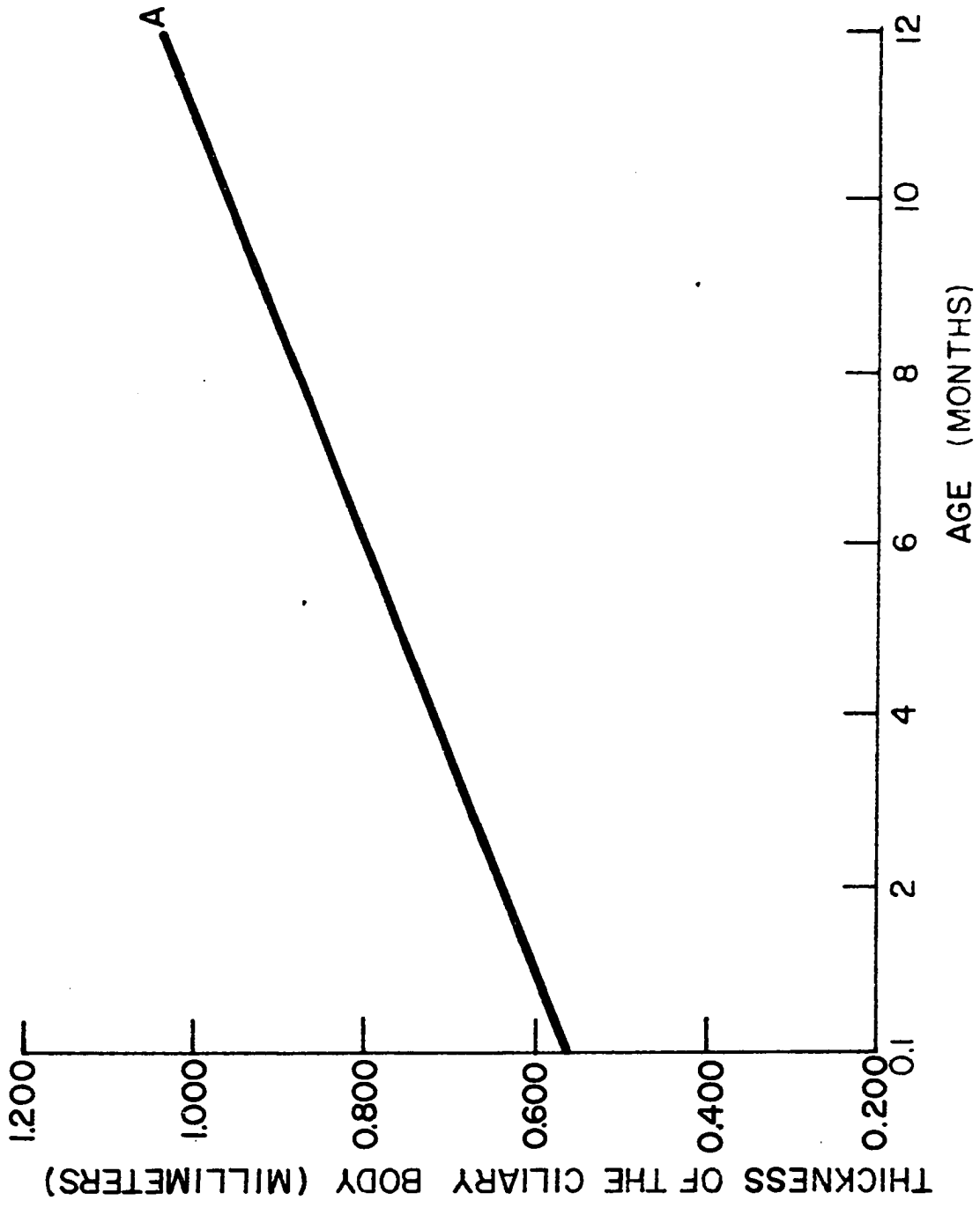
$r = 0.39$, $P < 0.05$


A
0.500
0.400
0.300
0.200
0.100
0.000
THICKNESS OF THE CILIARY BODY (MILLIMETERS)
1.5
2
4
6
8
10
12
13.1
AGE (YEARS)

Graph 27. Thickness of the ciliary body in the proximity of the anterior chamber angle of the eye in 22 hogs ranging in age from 0.1 month to 12.0 months.

A. Data for linear regression, where Y = the thickness of the ciliary body in mm and X = age in months.

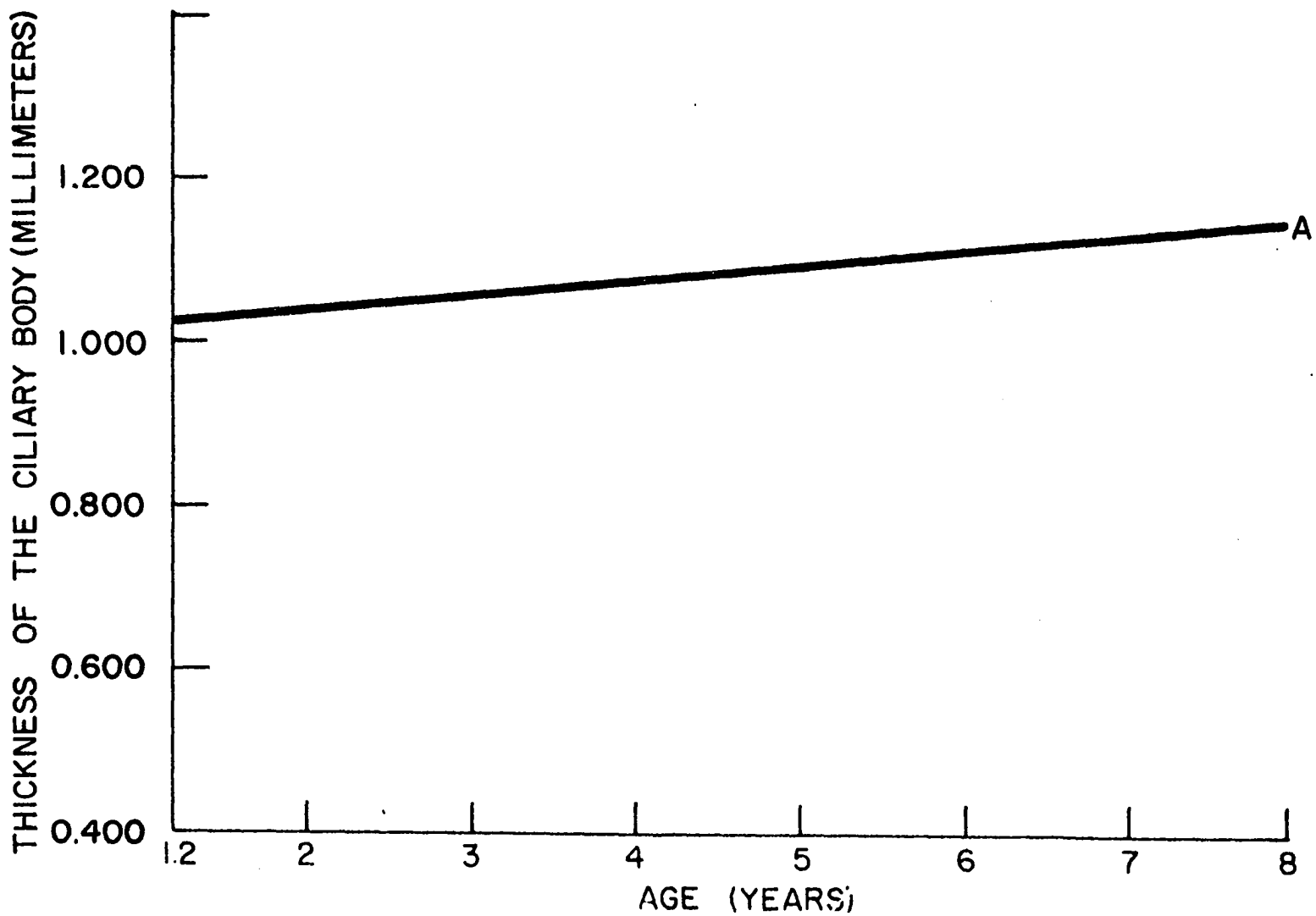
N	= 22		
Y	= 0.5412 + 0.0417 X ; s_y = 0.2164 mm		
b	= 0.0417 $\pm$ 0.0128 mm/month	,	$P<0.01$
$\bar{Y}$	= 0.7816 $\pm$ 0.1459 mm	,	$P<0.01$
r	= 0.59	,	$P<0.01$


A
1.200
1.000
0.800
0.600
0.400
0.200
0.1
2
4
6
8
10
12
AGE (MONTHS)
THICKNESS OF THE CILIARY BODY (MILLIMETERS)

Graph 28. Thickness of the ciliary body in the proximity of the anterior chamber angle of the eye in 86 hogs ranging in age from 1.2 years to 8.0 years.

A. Data for linear regression, where Y = the thickness of the ciliary body in mm and X = age in years.

N = 86
Y = 1.0092 + 0.0175 X ; s_y = 0.2221 mm
b = 0.0175 ± 0.0132 mm/year, P NS
$\bar{Y}$ = 1.0678 ± 0.0240 mm , P<0.01
r = 0.14 , P NS


THICKNESS OF THE CILIARY BODY (MILLIMETERS)
1.200
1.000
0.800
0.600
0.400
A
1.2
2
3
4
5
6
7
8
AGE (YEARS)

Graph 29. Choroidal thickness at the geometric axis of the bulbus oculi, and near the ora serrata in 46 dogs ranging in age from 0.1 month to 13.0 months.

A. Choroidal thickness at the geometric axis of the bulbus oculi; Data for curvilinear regression, where Y = choroidal thickness in mm and X = age in months.

$N = 46$

$Y = 0.0849 - 0.0050\ X_1 + 0.0007\ X_2$; $s_y = 0.0284$ mm

$b_y1.2 = 0.0050 \pm 0.0038$ mm/month, P NS

$b_y2.1 = 0.0007 \pm 0.0003$ mm/month, $P<0.05$

$\bar{Y} = 0.0987 \pm 0.0041$ mm , $P<0.01$

B. Choroidal thickness at the ora serrata; Data for linear regression, where Y = the choroidal thickness in mm and X = age in months.

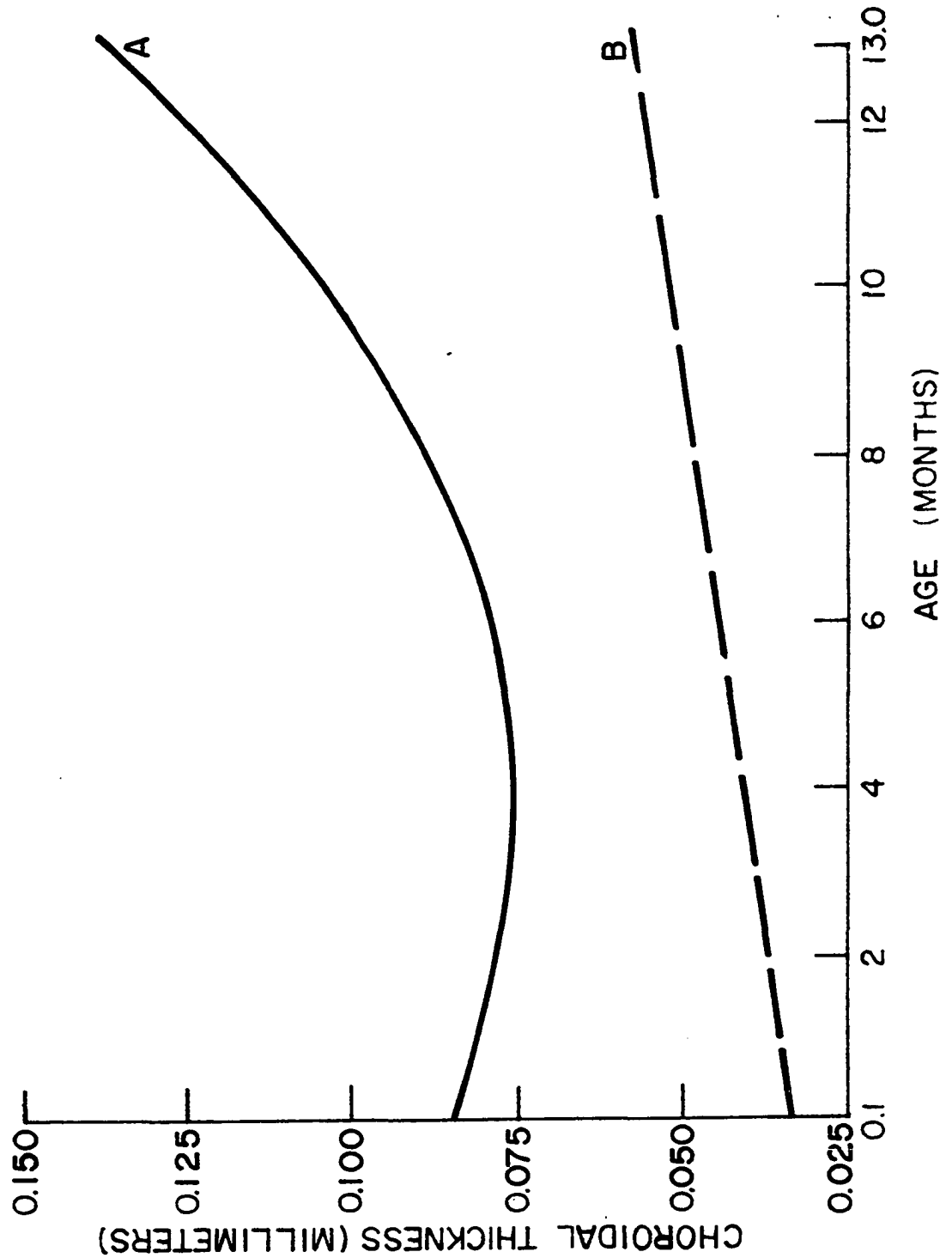
$N = 46$

$Y = 0.0331 + 0.0019\ X$; $s_y = 0.0117$ mm

$\underline{b} = 0.0019 \pm 0.0004$ mm/month, $P<0.01$

$\bar{Y} = 0.0469 \pm 0.0017$ mm , $P<0.01$

$r = 0.58$, $P<0.01$


A
B
0.150
0.125
0.100
0.075
0.050
0.025
CHOROIDAL THICKNESS (MILLIMETERS)
0.1
2
4
6
8
10
12
13.0
AGE (MONTHS)

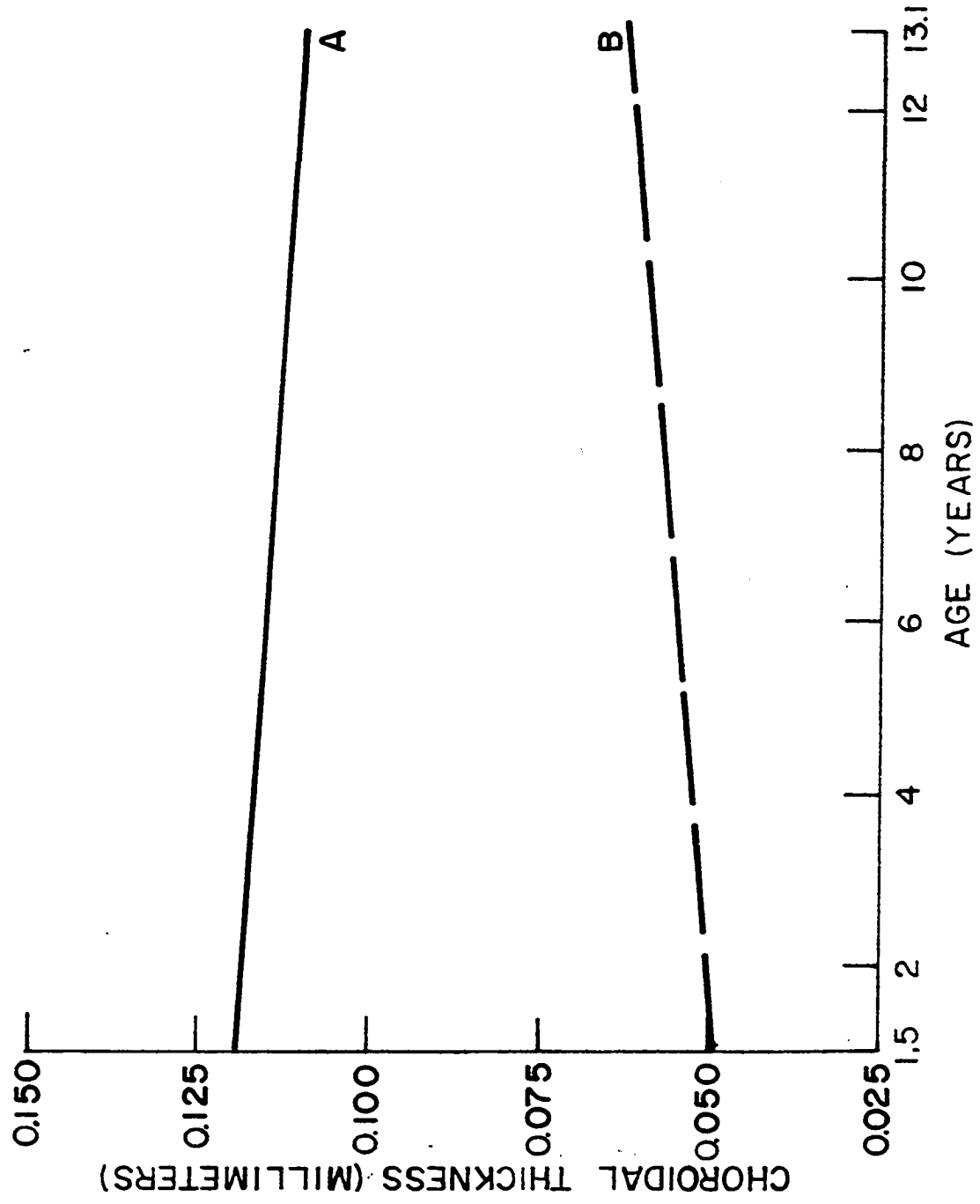
Graph 30. Choroidal thickness at the geometric axis of the bulbus oculi, and near the ora serrata in 32 dogs ranging in age from 1.5 years to 13.1 years.

A. Choroidal thickness at the geometric axis of the bulbus oculi; Data for linear regression, where Y = choroidal thickness in mm and X = age in years.

N = 32
Y = 0.1199 - 0.0007 X ; s_y = 0.0491 mm
b = 0.0007 ± 0.0024 mm/year, P NS
$\bar{Y}$ = 0.1138 ± 0.0085 mm , P<0.01
r = 0.05 , P NS

B. Choroidal thickness near the ora serrata; Data for linear regression, where Y = choroidal thickness in mm and X = age in years.

N = 32
Y = 0.0480 + 0.0012 X ; s_y = 0.0157 mm
b = 0.0012 ± 0.0007 mm/year, P NS
$\bar{Y}$ = 0.0577 ± 0.0028 mm , P<0.01
r = 0.26 , P NS


A
B
0.150
0.125
0.100
0.075
0.050
0.025
CHOROIDAL THICKNESS (MILLIMETERS)
1.5
2
4
6
8
10
12
13.1
AGE (YEARS)

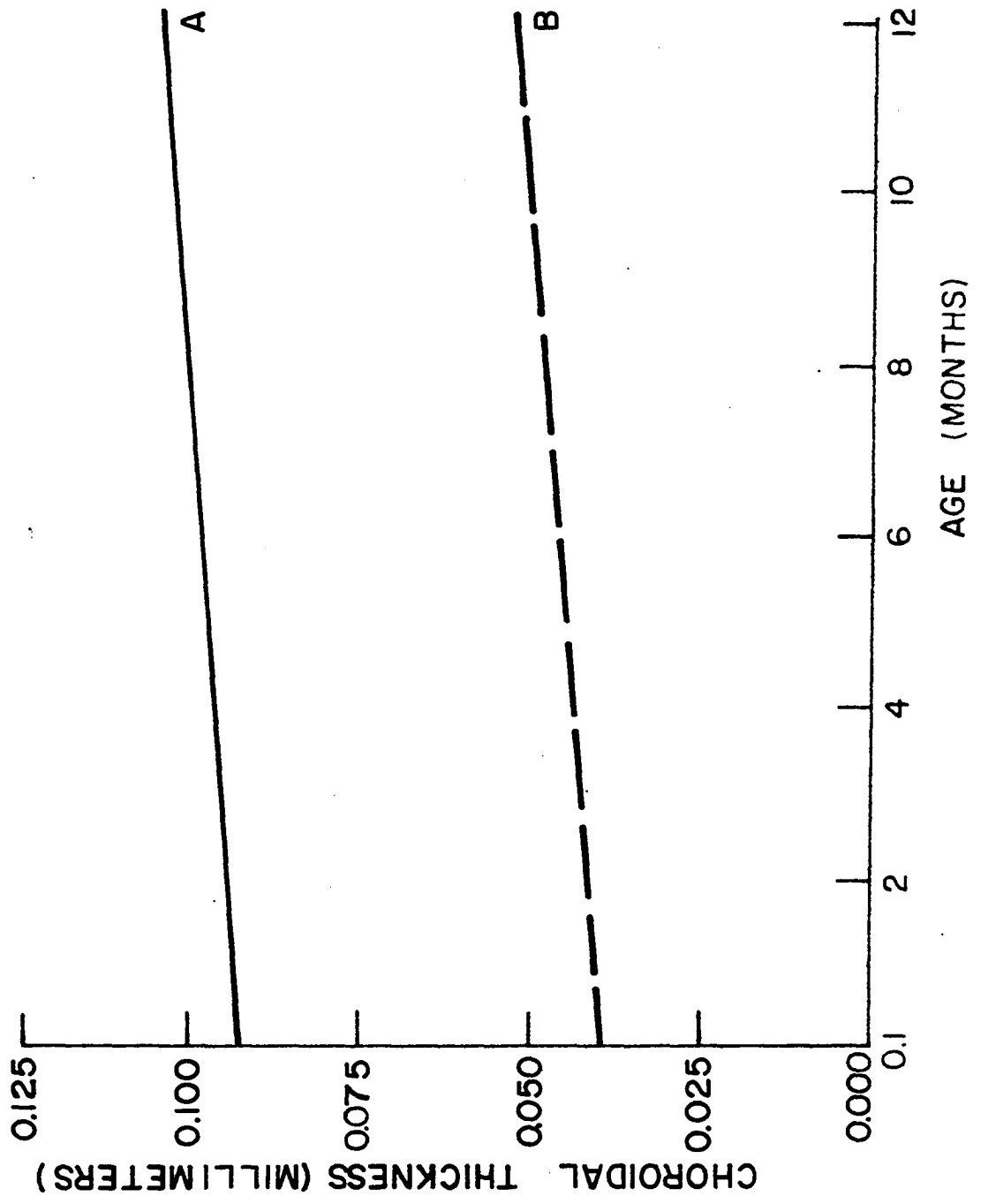
Graph 31. Choroidal thickness at the geometric axis of the bulbus oculi, and near the ora serrata in 22 hogs ranging in age from 0.1 month to 12.0 months.

A. Choroidal thickness at the geometric axis of the bulbus oculi; Data for linear regression, where Y = choroidal thickness in mm and X = age in months.

N = 22
Y = 0.0926 + 0.0010 X ; s_y = 0.0299
b = 0.0011 ± 0.0018 mm/month, P NS
$\bar{Y}$ = 0.0983 ± 0.0062 mm , P<0.01
r = 0.12 , P NS

B. Choroidal thickness near the ora serrata; Data for linear regression, where Y = choroidal thickness in mm and X = age in months.

N = 22
Y = 0.0393 + 0.0011 X ; s_y = 0.0136
b = 0.0011 ± 0.0008 mm/month, P NS
$\bar{Y}$ = 0.0455 ± 0.0089 mm , P<0.01
r = 0.28 , P NS


A
B
0.125
0.100
0.075
0.050
0.025
0.000
0.1
2
4
6
8
10
12
AGE (MONTHS)
CHOROIDAL THICKNESS (MILLIMETERS)

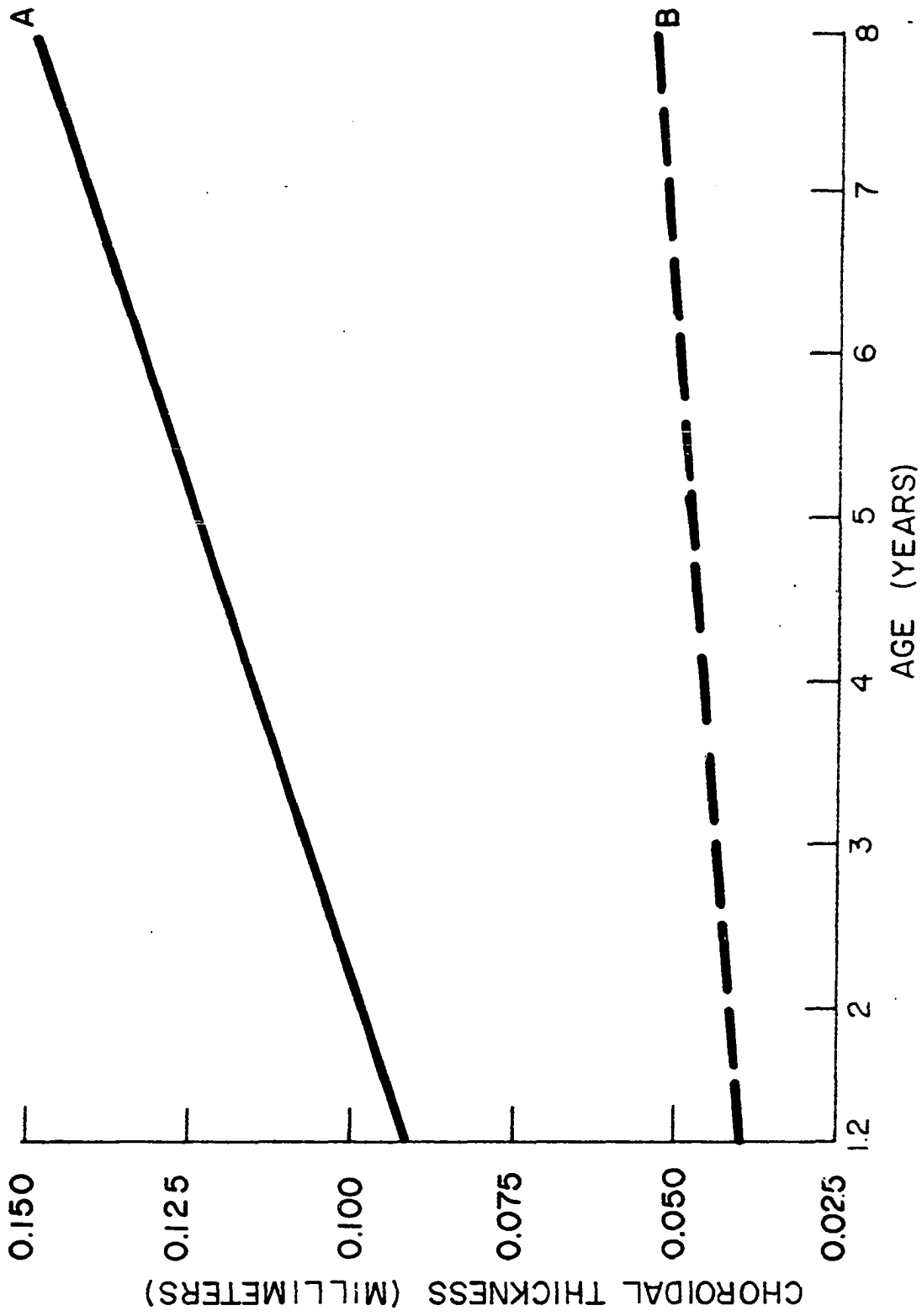
Graph 32. Choroidal thickness of the geometric axis of the bulbus oculi, and near the ora serrata in 86 hogs ranging in age from 1.2 years to 8.0 years.

A. Choroidal thickness at the geometric axis of the bulbus oculi; Data for linear regression, where Y = choroidal thickness in mm and X = age in years.

$N = 86$
$Y = 0.0836 + 0.0083\ X\ ;\ s_y = 0.0411$ mm
$b = 0.0083 \pm 0.0024$ mm/year, $P<0.01$
$\bar{Y} = 0.1115 \pm 0.0047$ mm , $P<0.01$
$r = 0.35$, $P<0.01$

B. Choroidal thickness near the ora serrata; Data for linear regression, where Y = choroidal thickness in mm and X = age in years.

$N = 86$
$Y = 0.0377 \pm 0.0020\ X\ ;\ s_y = 0.0110$ mm
$b = 0.0020 \pm 0.0006$ mm/year, $P<0.01$
$\bar{Y} = 0.0442 \pm 0.0012$ mm , $P<0.01$
$r = 0.32$, $P<0.01$


A
B
0.150
0.125
0.100
0.075
0.050
0.025
CHOROIDAL THICKNESS (MILLIMETERS)
1.2
2
3
4
5
6
7
8
AGE (YEARS)

Graph 33. Thickness of the anterior lens capsule, the lens epithelium, and the posterior lens capsule at the geometric axis of the lens, in 46 dogs ranging in age from 0.1 months to 13.0 months.

A. Thickness of the anterior lens capsule; Data for linear regression, where Y = the capsular thickness in microns and X = age in months.

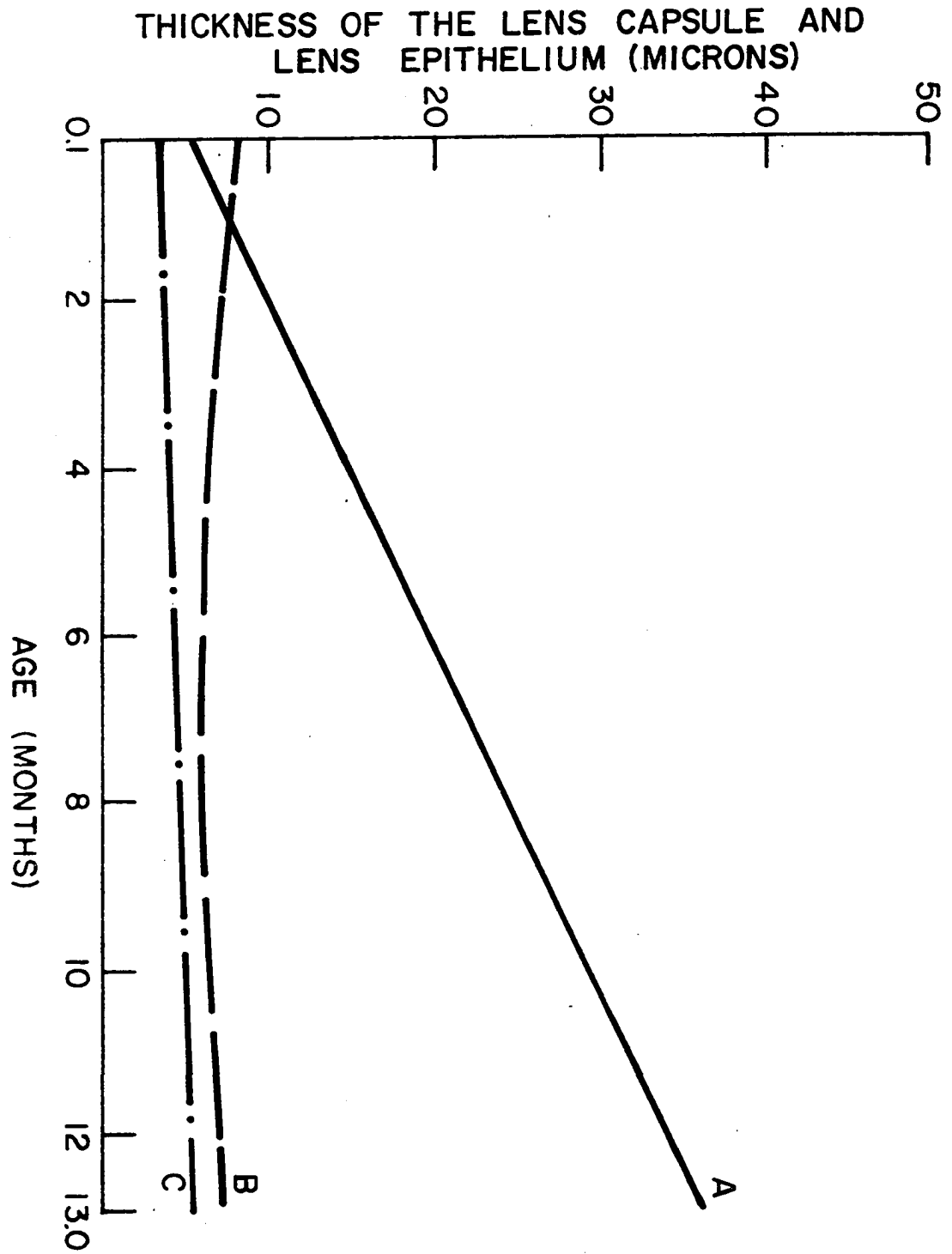
$N = 46$
$Y = 5.1680 + 2.3857\ X$; $s_y = 4.4708$ microns
$b = 2.3857 \pm 0.1506$ microns/month, $P<0.01$
$\bar{Y} = 22.7635 \pm 0.6592$ microns , $P<0.01$
$r = 0.92$, $P<0.01$

B. Thickness of the lens epithelium; Data for curvilinear regression, where Y = the sagittal thickness of the lens epithelium in microns and X = age in months.

$N = 46$
$Y = 8.5418 - 0.6490\ X_1 + 0.0431\ X_2$; $s_y = 1.7119$ microns
$b_y1.2 = 0.6490 \pm 0.2269$ microns/month, $P<0.01$
$b_y2.1 = 0.0431 \pm 0.0169$ microns/month, $P<0.05$
$\bar{Y} = 6.9289 \pm 0.2524$ microns , $P<0.01$

C. Thickness of the posterior lens capsule; Data for linear regression, where Y = the capsular thickness in microns and X = age in months.

$N = 46$
$Y = 3.6722 + 0.1213\ X$; $s_y = 1.3491$ microns
$b = 0.1213 \pm 0.0454$ microns/month, $P<0.05$
$\bar{Y} = 4.5667 \pm 0.1989$ microns , $P<0.01$
$r = 0.37$, $P<0.05$


THICKNESS OF THE LENS CAPSULE AND LENS EPITHELIUM (MICRONS)
10
20
30
40
50
0.1
2
4
6
8
10
12
13.0
AGE (MONTHS)
A
B
C

Graph 34. Thickness of the anterior lens capsule, the lens epithelium, and the posterior lens capsule at the geometric axis of the lens in 32 dogs ranging in age from 1.5 years to 13.1 years.

A. Thickness of the anterior lens capsule; Data for linear regression, where Y = capsular thickness in microns and X = age in years.

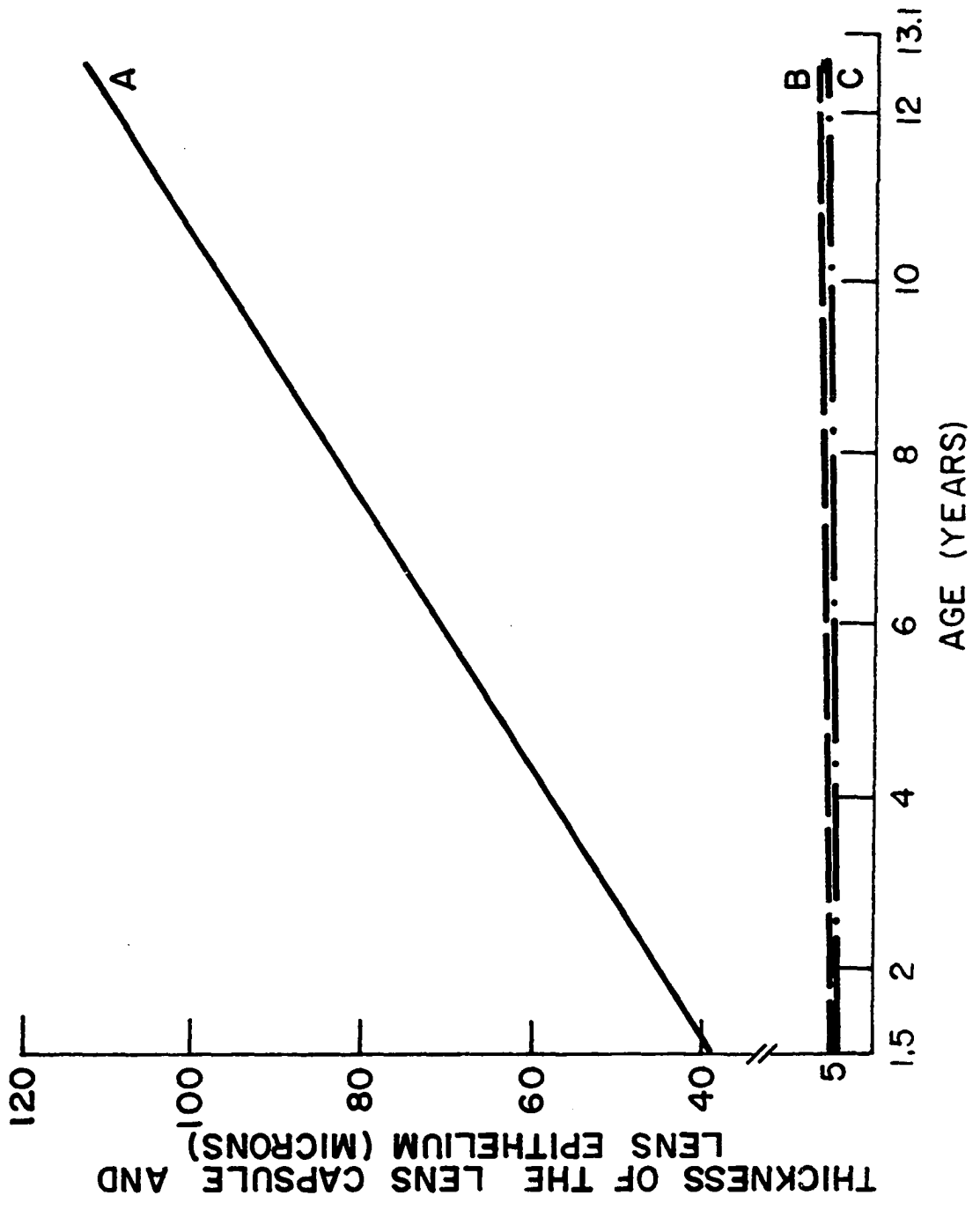
$N = 32$
$Y = 29.4133 + 6.4300\ X\ ;\ s_y = 16.4295$
$b = 6.4300 \pm 0.8127$ microns/year, $P<0.01$
$\bar{Y} = 82.6253 \pm 2.9043$ microns/year, $P<0.01$
$r = 0.82$, $P<0.01$

B. Thickness of the lens epithelium; Data for linear regression, where Y = the sagittal thickness of the lens epithelium in microns and X = age in years.

$N = 32$
$Y = 4.3402 + 0.1935\ X\ ;\ s_y = 1.2723$ microns
$b = 0.1935 \pm 0.0693$ microns/year, $P<0.01$
$\bar{Y} = 5.9641 \pm 0.2249$ microns, $P<0.01$
$r = 0.49$, $P<0.01$

C. Thickness of the posterior lens capsule; Data for linear regression, where Y = capsular thickness in microns and X = age in years.

$N = 32$
$Y = 3.9977 + 0.1808\ X\ ;\ s_y = 1.0756$ microns
$b = 0.1808 \pm 0.0532$ microns/year, $P<0.01$
$\bar{Y} = 5.5150 + 0.1901$ microns, $P<0.01$
$r = 0.53$, $P<0.01$


A
B
C
120
100
80
60
40
5
1.5
2
4
6
8
10
12
13.1
AGE (YEARS)
THICKNESS OF THE LENS CAPSULE AND
LENS EPITHELIUM (MICRONS)

Graph 35. Thickness of the anterior lens capsule, the lens epithelium, and the posterior lens capsule at the geometric axis of the lens in 22 hogs ranging in age from 0.1 month to 12.0 months.

A. Thickness of the anterior lens capsule; Data for curvilinear regression, where Y = capsular thickness in microns and X = age in months.

$N = 22$

$Y = 6.0213 + 5.6558\ X_1 - 0.2546\ X_2$; $s_y = 6.2170$ microns

$b_y1.2 = 5.6558 \pm 1.4575$ microns/month, $P<0.01$

$b_y2.1 = 0.2546 \pm 0.1170$ microns/month, $P<0.05$

$\bar{Y} = 26.8523 \pm 1.3255$ microns , $P<0.01$

B. Thickness of the lens epithelium; Data for curvilinear regression, where Y = the sagittal thickness of the epithelium in microns and X = age in months.

$N = 22$

$Y = 7.4278 + 1.7362\ X_1 - 0.1360\ X_2$; $s_y = 2.5242$ microns

$b_y1.2 = 1.7362 \pm 0.5918$ microns/month, $P<0.01$

$b_y2.1 = 0.1360 \pm 0.0475$ microns/month, $P<0.01$

$\bar{Y} = 11.1477 \pm 0.5382$ microns , $P<0.01$

C. Thickness of the posterior lens capsule; Data for linear regression, where Y = capsular thickness in microns and X = age in months.

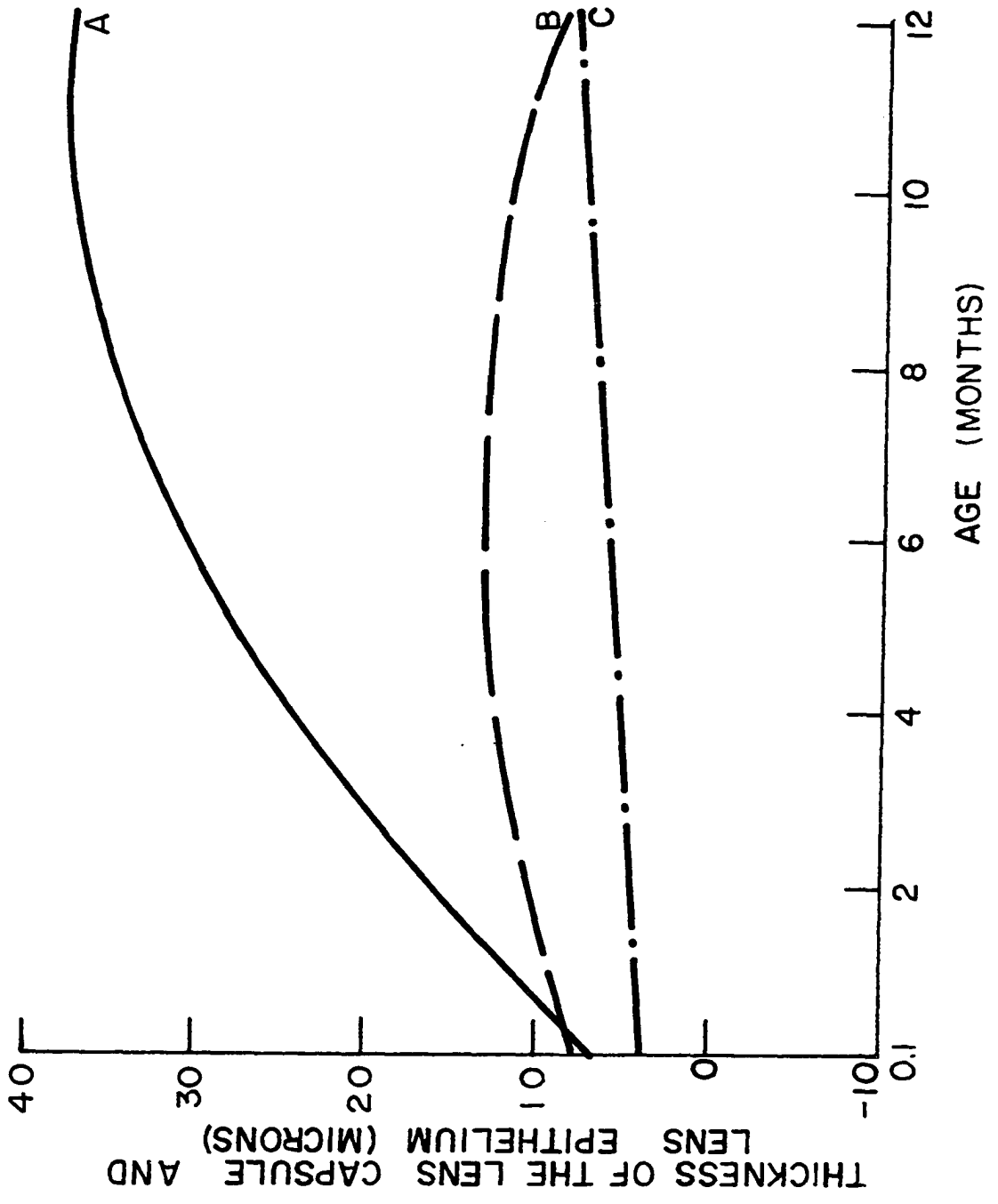
$N = 22$

$Y = 3.6838 + 0.3631\ X$; $s_y = 2.0717$ microns

$b = 0.3631 \pm 0.1224$ microns/month, $P<0.01$

$\bar{Y} = 5.7773 \pm 0.4417$ microns , $P<0.01$

$r = 0.55$, $P<0.01$


A
B
C
40
30
20
10
0
-10
0.1
2
4
6
8
10
12
AGE (MONTHS)
THICKNESS OF THE LENS CAPSULE AND
LENS EPITHELIUM (MICRONS)

Graph 36. Thickness of the anterior lens capsule, the lens epithelium, and the posterior lens capsule at the geometric axis of the lens in 86 hogs ranging in age from 1.2 years to 8.0 years.

A. Thickness of the anterior lens capsule; Data for linear regression, where Y = the capsular thickness in microns and X = age in years.

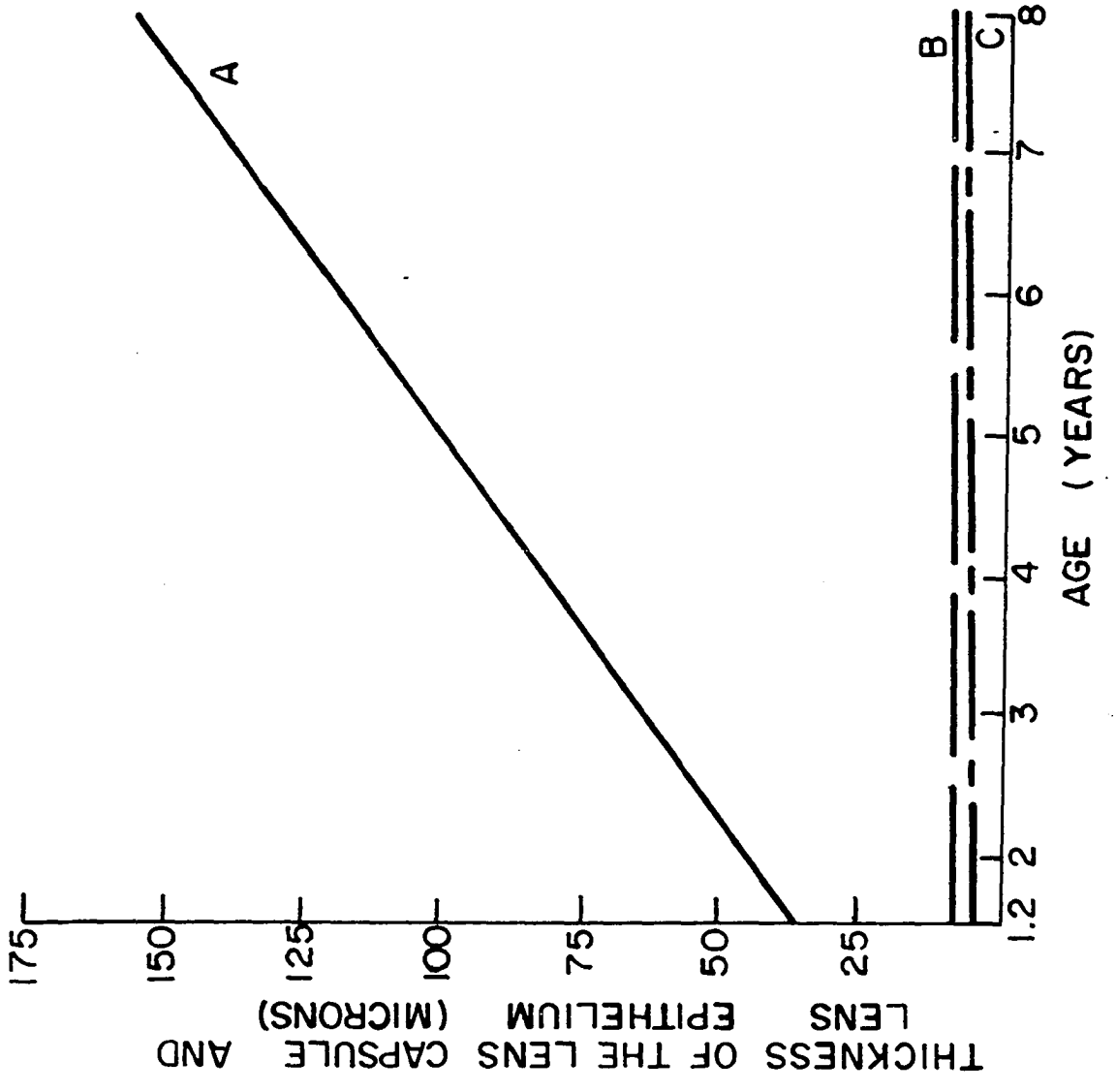
N = 86
Y = 18.5457 + 15.0069 X ; s_y = 15.3072 microns
b = 15.0069 ± 0.0910 microns/year, P<0.01
$\bar{Y}$ = 68.7471 ± 1.6506 microns , P<0.01
r = 0.87 , P<0.01

B. Thickness of the lens epithelium; Data for linear regression, where Y = the sagittal thickness of the epithelium in microns and X = age in years.

N = 86
Y = 9.0780 + 0.0306 X ; s_y = 1.7115 microns
b = 0.0306 ± 0.1017 microns/year, P NS
$\bar{Y}$ = 9.1802 ± 0.1846 microns , P<0.01
r = 0.03 , P NS

C. Thickness of the posterior lens capsule; Data for linear regression, where Y = the capsular thickness in microns and X = age in years.

N = 86
Y = 4.5109 + 0.4243 X ; s_y = 1.6726 microns
b = 0.4243 ± 0.0994 microns/year, P<0.01
$\bar{Y}$ = 5.9302 ± 0.1804 microns , P<0.01
r = 0.42 , P<0.01


A
B
C
AGE (YEARS)
1.2
2
3
4
5
6
7
8
25
50
75
100
125
150
175
THICKNESS OF THE LENS EPITHELIUM AND LENS CAPSULE (MICRONS)

Graph 37. Equatorial and polar diameters of the lens in 46 dogs ranging in age from 0.1 month to 13.0 months.

A. Equatorial diameter of the lens; Data for curvilinear regression, where Y = the equatorial diameter in mm and X = age in months.

$N = 46$

$Y = 4.4234 + 0.8672\ X_1 - 0.0398\ X_2$; $s_y = 0.5388$ mm

$b_y1.2 = 0.8672 \pm 0.0714$ mm/month, $P<0.01$

$b_y2.1 = 0.0398 \pm 0.0053$ mm/month, $P<0.01$

$\bar{Y} = 7.8907 \pm 0.0794$ mm , $P<0.01$

B. Polar diameter of the lens; Data for curvilinear regression, where Y = the polar diameter in mm and X = age in months.

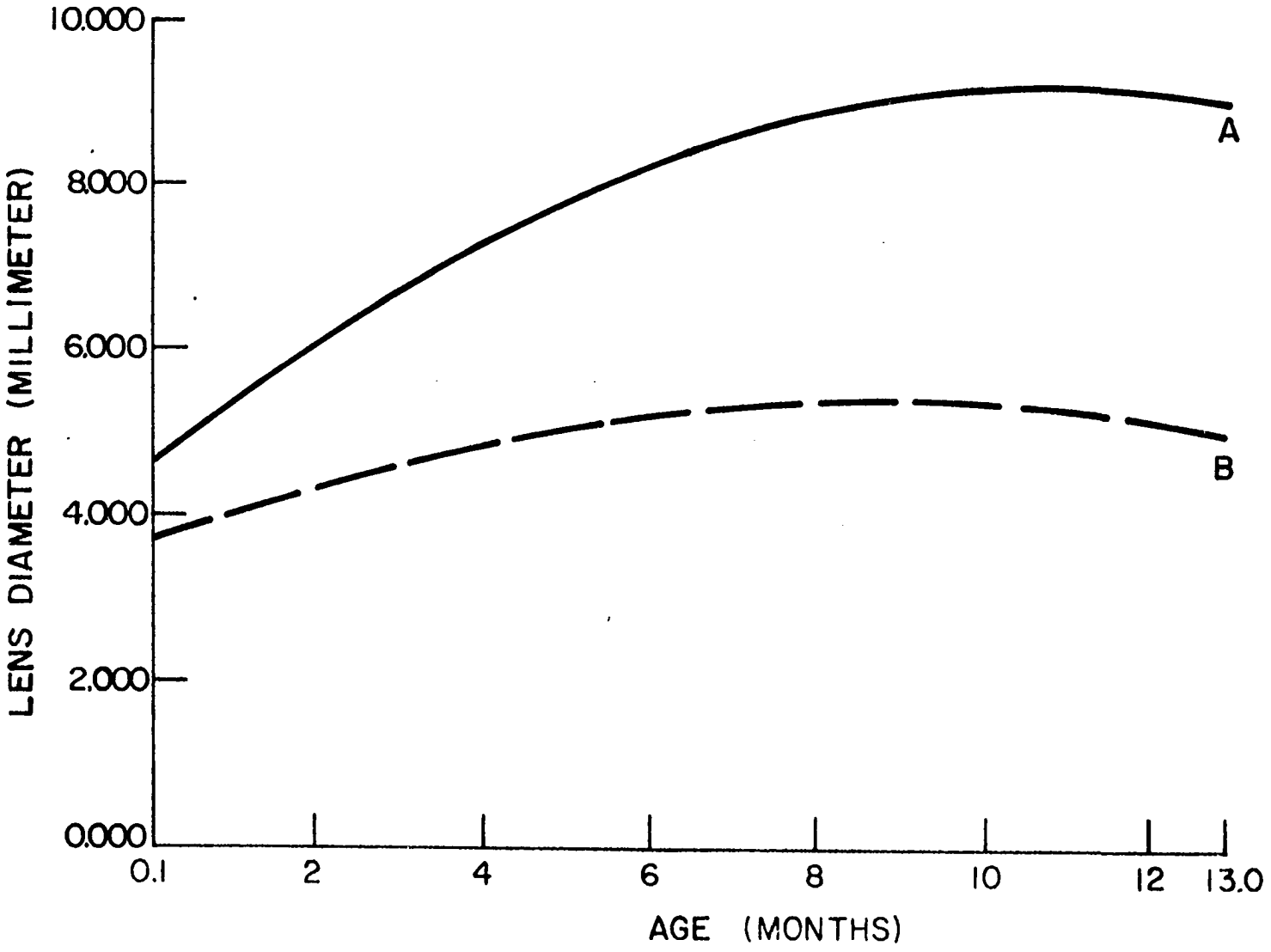
$N = 46$

$Y = 3.5852 + 0.4044\ X_1 - 0.0227\ X_2$; $s_y = 0.3821$ mm

$b_y1.2 = 0.4044 \pm 0.0506$ mm/month, $P<0.01$

$b_y2.1 = 0.0227 \pm 0.0038$ mm/month, $P<0.01$

$\bar{Y} = 4.9017 \pm 0.0563$ mm , $P<0.01$


10.000
8.000
6.000
4.000
2.000
0.000
LENS DIAMETER (MILLIMETER)
A
B
0.1
2
4
6
8
10
12
13.0
AGE (MONTHS)

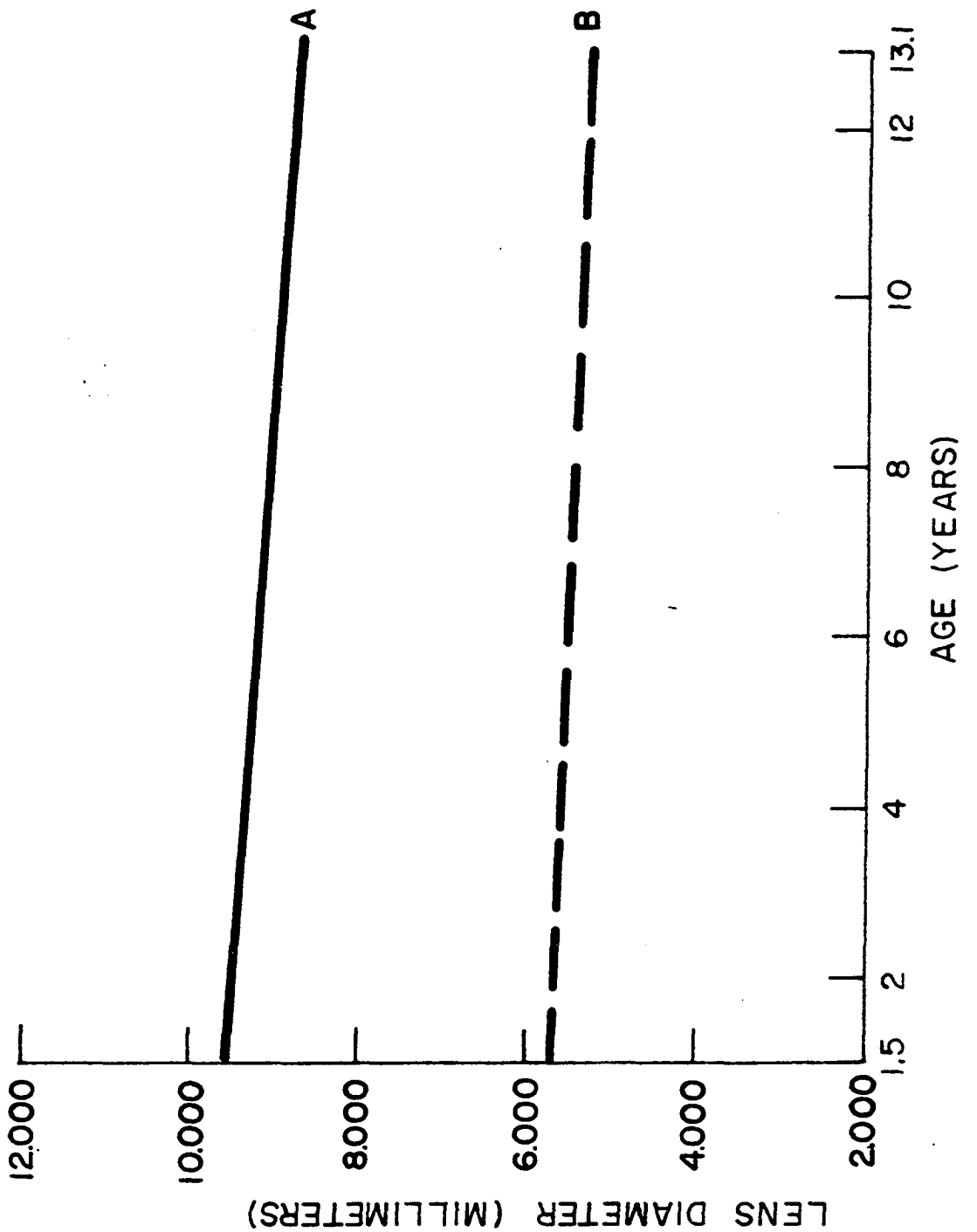
Graph 38. Equatorial and polar diameters of the lens in 32 dogs ranging in age from 1.5 years to 13.1 years.

A. Equatorial diameter of the lens; Data for linear regression, where Y = equatorial diameter in mm and X = age in years.

N	= 32		
Y	= 9.6540 - 0.0708 X ; s_y	= 0.7822	mm
b	= 0.0708 ± 0.0387	mm/year,	P NS
$\bar{Y}$	= 9.0597 ± 0.1434	mm ,	P<0.01
r	= 0.32	,	P NS

B. Polar diameter of the lens; Data for linear regression, where Y = polar diameter in mm and X = age in years.

N	= 32		
Y	= 5.7579 - 0.0351 X ; s_y	= 0.7025	mm
b	= 0.0351 ± 0.0347	mm/year,	P NS
$\bar{Y}$	= 5.4631 ± 0.1242	mm ,	P<0.01
r	= 0.18	,	P NS


A
B
12.000
10.000
8.000
6.000
4.000
2.000
LENS DIAMETER (MILLIMETERS)
1.5
2
4
6
8
10
12
13.1
AGE (YEARS)

Graph 39. Equatorial and polar diameters of the lens in 22 hogs ranging in age from 0.1 month to 12.0 months.

A. Equatorial diameter of the lens; Data for curvilinear regression, where Y = equatorial diameter in mm and X = age in months.

$N = 22$

$Y = 5.8392 + 0.5101\ X_1 - 0.0261\ X_2$; $s_y = 0.5662$ mm

$b_y1.2 = 0.5101 \pm 0.1327$ mm/month, $P<0.01$

$b_y2.1 = 0.0261 \pm 0.0107$ mm/month, $P<0.05$

$\bar{Y} = 7.5750 \pm 0.1207$ mm , $P<0.01$

B. Polar diameter of the lens; Data for curvilinear regression, where Y = polar diameter of the lens in mm and X = age in months.

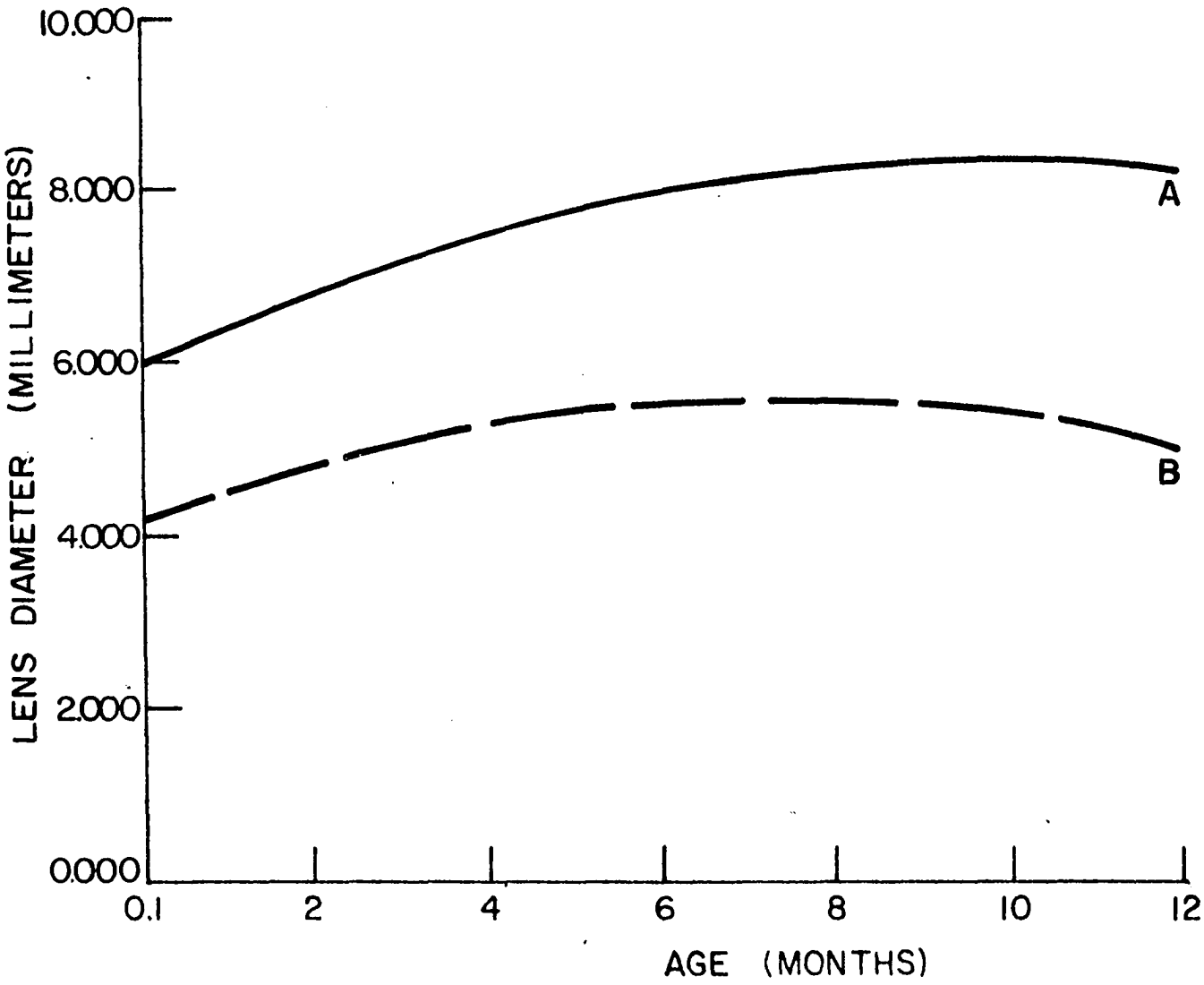
$N = 22$

$Y = 4.0993 + 0.4033\ X_1 - 0.0275\ X_2$; $s_y = 0.4765$ mm

$b_y1.2 = 0.4033 \pm 0.1117$ mm/month, $P<0.01$

$b_y2.1 = 0.0275 \pm 0.0090$ mm/month, $P<0.01$

$\bar{Y} = 5.1509 \pm 0.1016$ mm , $P<0.01$


10.000
8.000
6.000
4.000
2.000
0.000
LENS DIAMETER (MILLIMETERS)
A
B
0.1
2
4
6
8
10
12
AGE (MONTHS)

Graph 40. Equatorial and polar diameters of the lens in 86 hogs ranging in age from 1.2 years to 8.0 years.

A. Equatorial diameter of the lens; Data for linear regression, where Y = the equatorial diameter in mm and X = age in years.

$N = 86$

$Y = 8.1911 + 0.2227\ X$; $s_y = 0.5753$

$b = 0.2227 \pm 0.0342$ mm/year, $P<0.01$

$\bar{Y} = 8.9359 \pm 0.0196$ mm , $P<0.01$

$r = 0.58$, $P<0.01$

B. Polar diameter of the lens; Data for curvilinear regression, where Y = the polar diameter of the lens in mm and X = age in years.

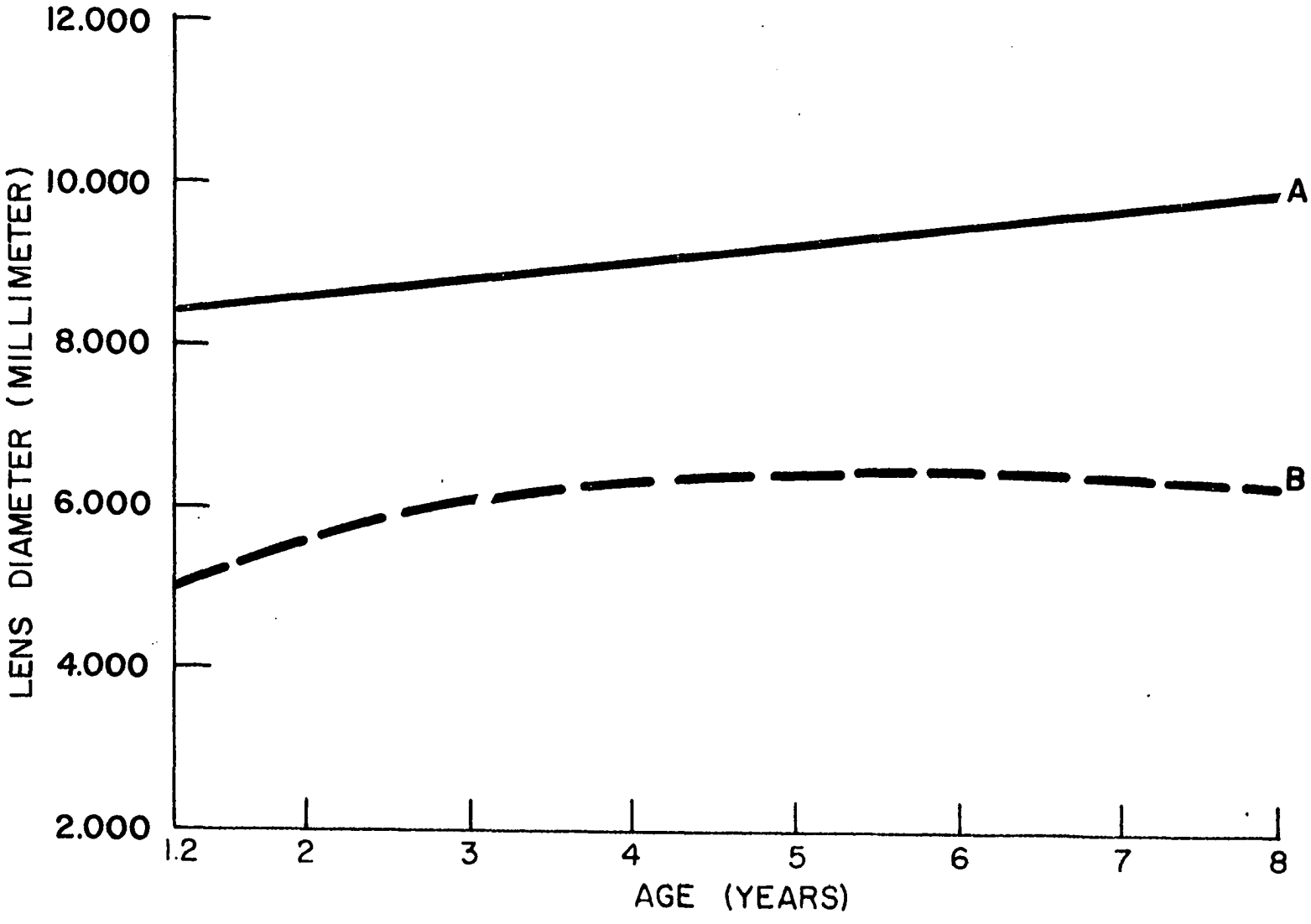
$N = 86$

$Y = 4.4046 + 0.7161\ X_1 - 0.0620\ X_2$; $s_y = 0.6657$ mm

$b_y1.2 = 0.7176 \pm 0.2315$ mm/year, $P<0.01$

$b_y2.1 = 0.0620 \pm 0.0272$ mm/year, $P<0.05$

$\bar{Y} = 5.9026 \pm 0.0718$ mm , $P<0.01$


12.000
10.000
8.000
6.000
4.000
2.000
LENS DIAMETER (MILLIMETER)
A
B
1.2
2
3
4
5
6
7
8
AGE (YEARS)

Graph 41. Retinal thickness at the geometric axis of the bulbus oculi, and near the ora serrata in 46 dogs ranging in age from 0.1 month to 13.0 months.

A. Retinal thickness at the geometric axis of the bulbus oculi; Data for curvilinear regression, where Y = retinal thickness in mm and X = age in months.

$N = 46$

$Y = 0.2205 - 0.0140\ X_1 + 0.0008\ X_2$; $s_y = 0.0325$ mm

$b_y1.2 = 0.0140 \pm 0.0043$ mm/month, $P<0.01$

$b_y2.1 = 0.0008 \pm 0.0003$ mm/month, $P<0.05$

$\bar{Y} = 0.1796 \pm 0.0065$ mm , $P<0.01$

B. Retinal thickness near the ora serrata; Data for curvilinear regression, where Y = the retinal thickness in mm and X = age in months.

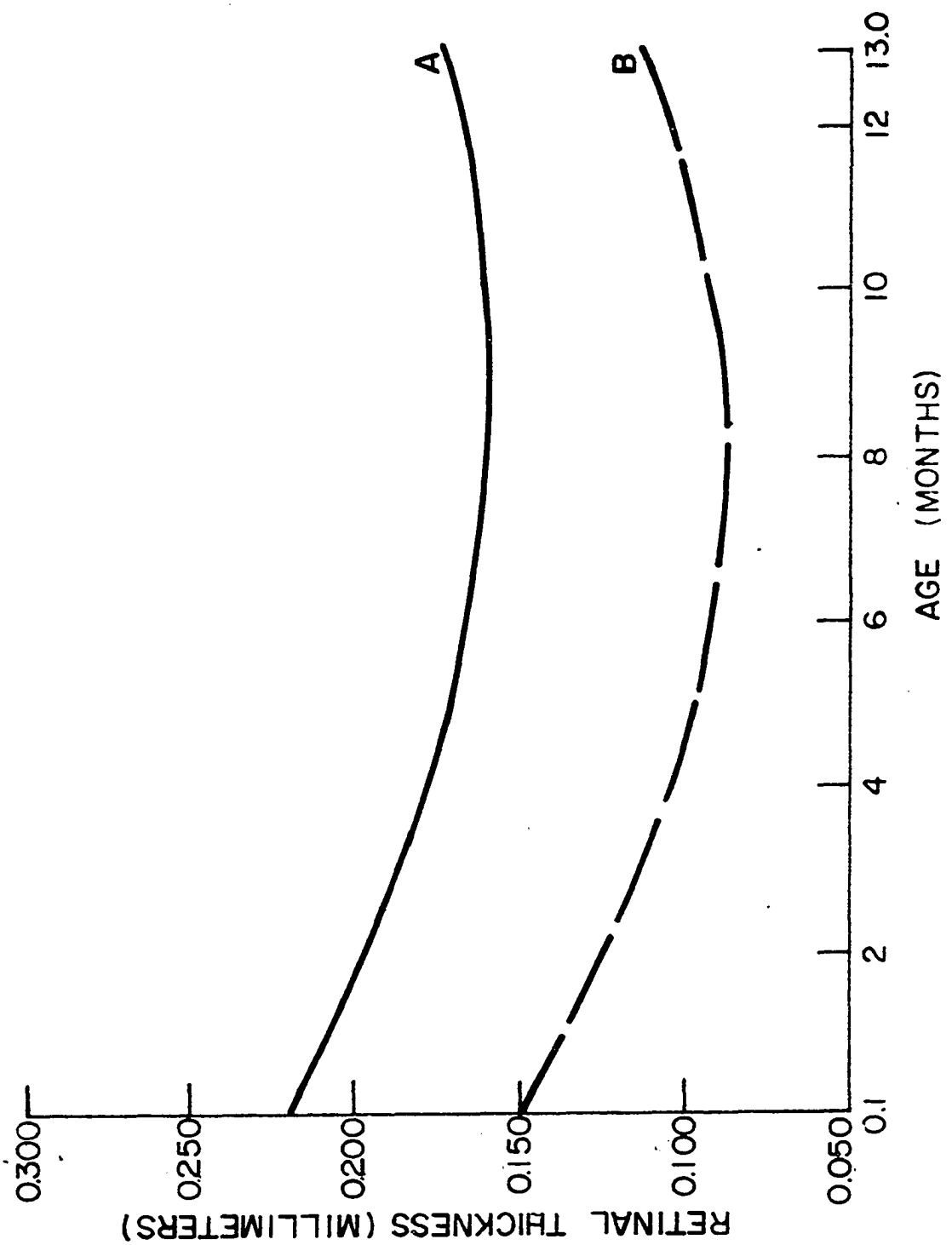
$N = 46$

$Y = 0.1515 - 0.0159\ X_1 + 0.0010\ X_2$; $s_y = 0.0190$ mm

$b_y1.2 = 0.0159 \pm 0.0248$ mm/month, $P<0.01$

$b_y2.1 = 0.0010 \pm 0.0001$ mm/month, $P<0.01$

$\bar{Y} = 0.1057 \pm 0.0055$ mm , $P<0.01$


A
B
0.300
0.250
0.200
0.150
0.100
0.050
0.1
2
4
6
8
10
12
13.0
AGE (MONTHS)
RETINAL THICKNESS (MILLIMETERS)

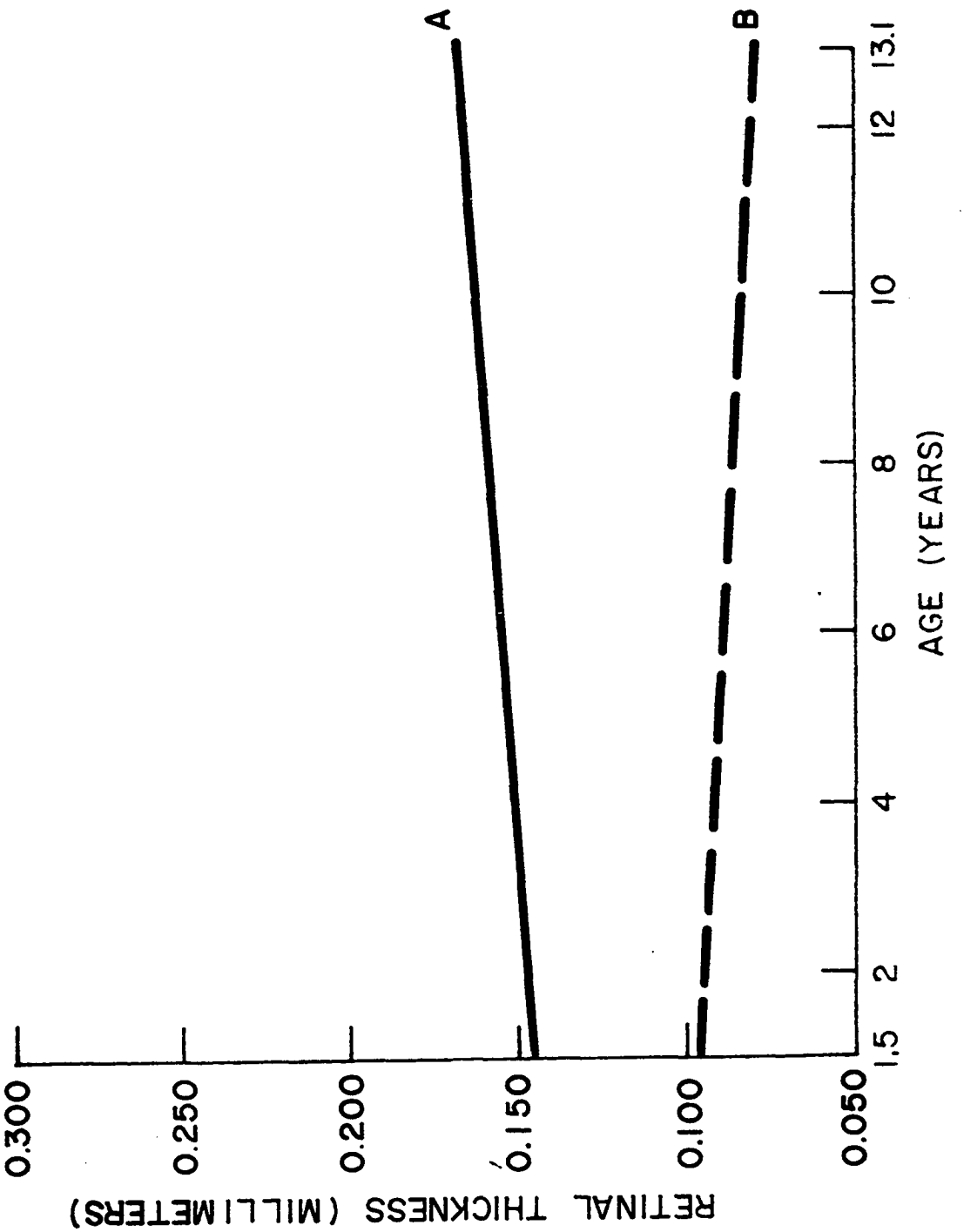
Graph 42. Retinal thickness at the geometric axis of the bulbus oculi, and near the ora serrata in 32 dogs ranging in age from 1.5 years to 13.1 years.

A. Retinal thickness at the geometric axis of the bulbus oculi; Data for linear regression, where Y = retinal thickness in mm and X = age in years.

N = 32
Y = 0.1448 + 0.0018 X ; s_y = 0.0365 mm
b = 0.0018 ± 0.0018 mm/year, P NS
$\bar{Y}$ = 0.1599 ± 0.0064 mm , P<0.01
r = 0.18 , P NS

B. Retinal thickness near the ora serrata; Data for linear regression, where Y = retinal thickness in mm and X = age in years.

N = 32
Y = 0.0977 - 0.0013 X ; s_y = 0.0207 mm
b = 0.0013 ± 0.0010 mm/year, P NS
$\bar{Y}$ = 0.0872 ± 0.0036 mm , P<0.01
r = 0.22 , P NS


A
B
0.300
0.250
0.200
0.150
0.100
0.050
RETINAL THICKNESS (MILLIMETERS)
1.5
2
4
6
8
10
12
13.1
AGE (YEARS)

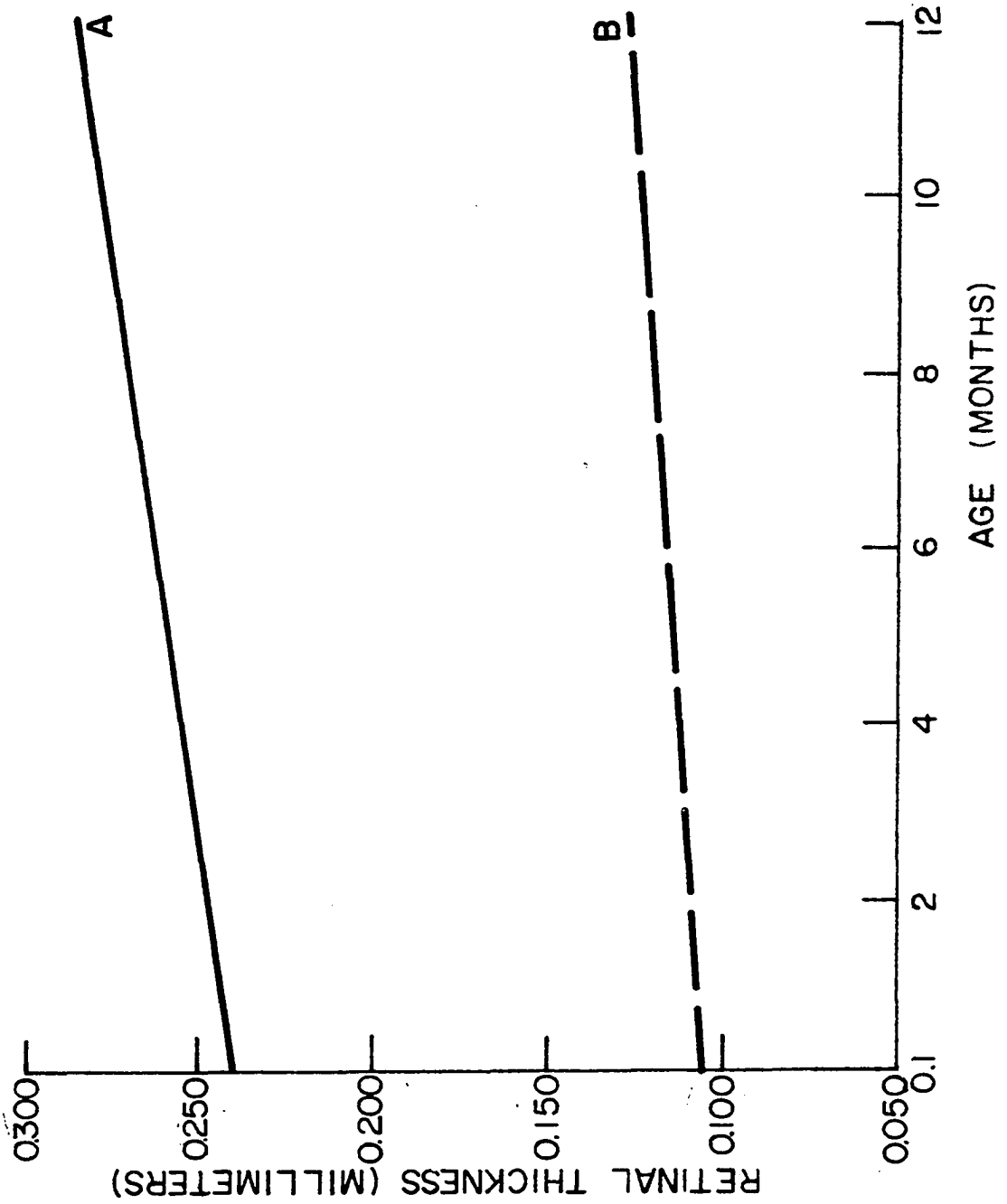
Graph 43. Retinal thickness at the geometric axis of the bulbus oculi, and near the ora serrata in 22 hogs ranging in age from 0.1 month to 12.0 months.

A. Retinal thickness at the geometric axis of the bulbus oculi; Data for linear regression, where Y = retinal thickness in mm and X = age in years.

$N = 22$
$Y = 0.2414 + 0.0037\ X$; $s_y = 0.0459$ mm
$b = 0.0037 \pm 0.0027$ mm/month, P NS
$\bar{Y} = 0.2626 \pm 0.0099$ mm , $P<0.01$
$r = 0.29$, P NS

B. Retinal thickness at the ora serrata; Data for linear regression, where Y = retinal thickness in mm and X = age in months.

$N = 22$
$Y = 0.1054 + 0.0018\ X$; $s_y = 0.0226$ mm
$b = 0.0018 \pm 0.0013$ mm/month, P NS
$\bar{Y} = 0.1158 \pm 0.0049$ mm , $P<0.01$
$r = 0.29$, P NS


A
B
0.300
0.250
0.200
0.150
0.100
0.050
0.1
2
4
6
8
10
12
RETINAL THICKNESS (MILLIMETERS)
AGE (MONTHS)

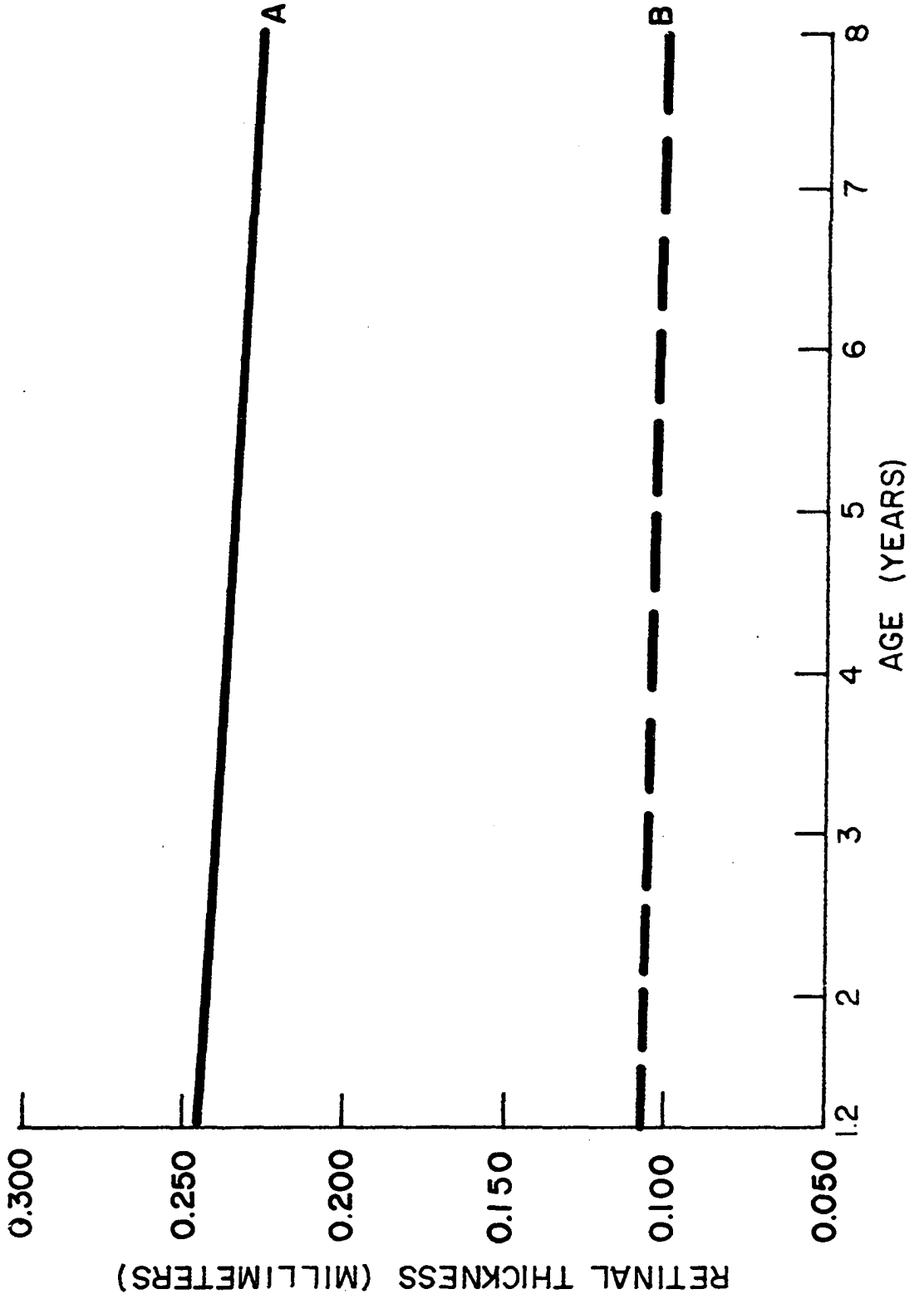
Graph 44. Retinal thickness at the geometric axis of the bulbus oculi, and near the ora serrata in 86 hogs ranging in age from 1.2 years to 8.0 years.

A. Retinal thickness at the geometric axis of the bulbus oculi; Data for linear regression, where Y = retinal thickness in mm and X = age in years.

N	= 86		
Y	= 0.2457 - 0.0024 X ; s_y = 0.0418 mm		
b	= 0.0024 ± 0.0025 mm/year	, p	NS
$\bar{Y}$	= 0.2376 ± 0.0045 mm	, p	<0.01
r	= 0.11	, p	NS

B. Retinal thickness near the ora serrata; Data for linear regression, where Y = retinal thickness in mm and X = age in years.

N	= 86		
Y	= 0.1066 - 0.0007 X ; s_y = 0.0169 mm		
b	= 0.0007 ± 0.0010 mm/year	, p	NS
$\bar{Y}$	= 0.1042 ± 0.0017 mm	, p	<0.01
r	= 0.08	, p	NS


A
B
0.300
0.250
0.200
0.150
0.100
0.050
RETINAL THICKNESS (MILLIMETERS)
1.2
2
3
4
5
6
7
8
AGE (YEARS)

APPENDIX B

TABLES OF INCIDENCE OF VARIOUS HISTOLOGICAL AND HISTOCHEMICAL CHANGES WITH AGE

Table 1. Age, sex, breed, weight, diet, and source of dogs studied; Designation of dogs utilized for lipid and statistical evaluation

Dog number	Age[a]	Sex	Breed[b]	Weight[c]	Diet[d]	Source[e]	Lipid evaluation	Statistical evaluation
Age Group I								
A52	0.1	M	B	0.2	LP	AC		X
056	0.1	M	B	0.2	LP	AC	X	X
060	0.1	FM	B	0.2	LP	AC		X
061	0.2	M	B	0.2	LP	AC	X	X
065	0.2	FM	B	0.1	LP	AC	X	X
B50 (1A)	0.5	M	B	0.5	C	AC		X
B45 (1DAA)	1.0	M	B	1.4	C	AC	X	X
B46 (1DAC)	1.0	FM	B	1.0	C	AC	X	X
B47 (1DAB)	1.9	M	B	1.6	C	AC	X	X
068	2.5	M	B	2.7	MP	AC	X	X
072	2.6	FM	B	2.5	MP	AC	X	X
059	2.8	FM	B	2.1	LP	AC	X	X
B69 (A26)	4.0	FM	B	7.0	C	AC	X	X

[a]Age Groups I-III in months; Age Groups IV-VI in years.

[b]B = Beagle; BA = Basenji; CS = Cocker Spaniel; D = Dachshund; FT = Smooth-haired Fox Terrier; GR = Golden Retriever; IS = Irish Setter; LR = Labrador Retriever; WC = Welsh Corgi; WT = Welsh Terrier.

[c]Weight in kilograms.

[d]C = Control diet; HP = High protein diet; MP = Medium protein diet; LP = Low protein diet.

[e]AC = Animal Colony, Department of Veterinary Anatomy, Iowa State University, Ames, Iowa; GRK = Gaines Research Kennels, Saint Anne, Illinois.

Table 1. (Continued)

Dog number	Age[a]	Sex	Breed[b]	Weight[c]	Diet[d]	Source[e]	Lipid evaluation	Statistical evaluation
Age Group II								
049	5.4	FM	B	6.9	MP	AC	X	X
B76 (C38)	5.9	M	B	5.7	C	AC		X
C35	6.0	M	B	10.5	MP	AC	X	X
B66 (034)	6.5	FM	B	6.8	C	AC	X	X
B60 (1D1)	6.8	M	B	9.2	C	AC	X	X
B59 (1D3)	6.8	FM	B	5.8	C	AC		X
B61 (1D4)	6.8	FM	B	4.8	C	AC		X
A41	7.6	M	B	7.3	M	AC	X	X
B72 (A37)	7.8	M	B	8.2	C	AC		X
B48 (361)	7.9	FM	B	8.8	C	AC	X	X
B70 (A22)	8.1	M	B	8.4	C	AC		X
B71 (A23)	8.1	M	B	7.4	C	AC	X	X
B49 (354)	8.1	FM	B	12.7	C	AC		X
A46	9.0	FM	B	7.3	MP	AC	X	X
B74 (A39)	9.1	FM	B	6.4	C	AC		X
B67 (009)	9.3	FM	B	6.1	C	AC	X	X
B53 (352)	9.9	M	B	11.6	C	AC	X	X

Table 1. (Continued)

Dog number	Age[a]	Sex	Breed[b]	Weight[c]	Diet[d]	Source[e]	Lipid evaluation	Statistical evaluation
Age Group III								
B55 (353K)	11.1	M	B	13.5	C	AC	X	X
B54 (1DD)	12.0	M	B	9.3	C	AC	X	X
B58 (355)	12.0	M	B	15.2	MP	AC	X	X
B57 (1DC)	12.0	M	B	9.9	MP	AC	X	X
B56 (1DB)	12.0	M	B	11.9	C	AC		X
1FB	12.0	M	B	8.9	LP	AC	X	X
B62 (1D6)	12.0	FM	B	7.3	C	AC		X
7BAA	12.1	FM	B	8.4	HP	AC	X	X
2BC	12.1	M	B	6.1	MP	AC		X
5FF	12.1	FM	B	8.1	MP	AC	X	X
5FD	12.1	M	B	5.2	MP	AC		X
2BB	12.2	M	B	6.7	MP	AC		X
7BAB	12.2	FM	B	9.8	HP	AC	X	X
7BAC	12.2	FM	B	10.1	HP	AC		X
5FC	12.2	M	B	7.2	MP	AC	X	X
2BD	12.9	FM	B	5.6	MP	AC	X	X

Table 1. (Continued)

Dog number	Age[a]	Sex	Breed[b]	Weight[c]	Diet[d]	Source[e]	Lipid evaluation	Statistical evaluation
Age Group IV								
B77 (A08)	1.5	M	B	8.4	C	AC	X	X
B41 (13D)	1.7	FM	B	4.6	C	AC	X	X
21	2.0	M	B	8.9	HP	AC	X	X
B68 (1B)	2.7	FM	B	6.4	C	AC	X	X
053	2.8	FM	B	8.2	HP	AC	X	
B88 (029)	3.1	M	B	10.5	C	AC	X	
B75 (1D5)	3.2	FM	B	7.5	C	AC	X	X
B89 (008)	3.2	M	B	12.7	C	AC	X	
B82 (017)	3.2	FM	B	8.2	C	AC	X	
B65 (1D)	3.6	FM	B	14.7	C	AC	X	X
B51 (13C)	4.1	FM	B	10.2	C	AC	X	X

Table 1. (Continued)

Dog number	Age[a]	Sex	Breed[b]	Weight[c]	Diet[d]	Source[e]	Lipid evaluation	Statistical evaluation
Age Group V								
B18	6.0	FM	B	12.7	C	AC		X
7BA	6.4	FM	B	14.8	HP	AC	X	X
1F	6.6	FM	B	10.5	LP	AC	X	X
M52 (272)	7.5	M	BA	17.3	C	GRK	X	
B43 (4)	7.8	FM	B	10.7	C	AC	X	X
B44 (7)	7.8	FM	B	11.1	C	AC	X	X
M47	8.3	FM	GR	38.2	C	GRK	X	X
B42 (2)	8.6	FM	B	10.9	C	AC	X	X
M35 (190-M)	8.6	M	FT	9.8	C	GRK	X	X
9	8.7	M	B	8.6	HP	AC	X	X
B63 (10)	9.2	M	B	12.1	C	AC	X	X
M51 (115)	9.3	FM	IS	26.8	C	GRK	X	
M40 (120)	9.7	FM	D	13.3	C	GRK		X
M46 (266)	9.9	FM	IS	29.5	C	GRK	X	X

Table 1. (Continued)

Dog number	Age[a]	Sex	Breed[b]	Weight[c]	Diet[d]	Source[e]	Lipid evaluation	Statistical evaluation
Age Group VI								
B64 (1)	10.1	FM	B	11.3	C	AC	X	X
M49 (73)	10.3	M	LR	42.7	C	GRK	X	
M50 (72)	10.3	FM	LR	30.5	C	GRK	X	
M38 (231)	10.4	FM	LR	30.7	C	GRK	X	X
M21 (212)	10.5	FM	WT	9.5	C	GRK		X
M48 (238)	10.5	M	CS	17.3	C	GRK	X	X
M42 (194)	11.2	FM	FT	8.2	C	GRK	X	X
M43 (233)	11.4	FM	FT	27.5	C	GRK	X	X
B73 (5)	11.9	FM	B	9.8	C	AC	X	X
M44 (203)	12.0	FM	WC	13.0	C	GRK	X	X
M45 (172)	12.0	FM	FT	8.3	C	GRK	X	X
M33 (191)	12.9	M	GR	30.0	C	GRK	X	X
M34 (221)	13.1	FM	WC	8.6	C	GRK	X	X
M37 (132)	13.1	FM	GR	39.1	C	GRK	X	X
M39 (211)	13.1	M	WC	12.7	C	GRK	X	X

Table 2. Age, sex, breed, and weight of hogs studied; Designation of hogs utilized for lipid evaluation

Hog number	Age[a]	Sex	Breed[b]	Weight[c]	Lipid evaluation
Age Group I					
1448B	0.1	M	Y-L	1.0	X
1449B	0.1	M	Y-L	1.1	
627	2.2	FM	PC-Y-L	14.5	X
592	2.2	FM	PC-Y-L	16.4	
5330	2.3	FM	PC-Y-L	18.2	X
5353	2.5	FM	PC-Y-L	20.0	X
5250	2.5	FM	PC-Y-L	25.0	
5262	3.7	FM	PC-Y-L	42.3	X
9753	4.2	FM	PC-Y-L	61.4	X
2250	4.2	FM	PC-Y-L	66.8	X
9713	4.2	FM	PC-Y-L	52.3	
9310	5.9	FM	PC-Y-L	104.5	X
Age Group II					
1292	6.2	FM	PC-Y-L	92.7	X
6022	8.1	FM	PC-Y-L	111.4	X
634	8.2	FM	PC-L	121.8	
2210	8.2	FM	Y-L	126.0	
3920	8.5	FM	Y	125.4	X
5093	9.1	FM	Y-L	115.9	X
2211	10.0	FM	Y-L	180.0	X
9442	11.2	FM	Y-L	156.8	X
3923	11.3	FM	Y	175.5	X
7973	11.9	FM	Y-L	163.6	X
Age Group III					
3430	1.2	FM	Y-L	171.4	X
29445	1.2	FM	Y-L	204.5	
5930	1.3	FM	Y-L	186.4	
2360	1.3	FM	Y-L	176.8	
2021	1.4	FM	Y-L	200.9	X

[a]Age Groups I and II in months; Age Groups III-V in years.

[b]Y = Yorkshire; L = Landrace; PC = Poland China; H = Hampshire; D = Duroc.

[c]Weight in kilograms.

Table 2. (Continued)

Hog number	Age[a]	Sex	Breed[b]	Weight[c]	Lipid evaluation
4461	1.5	FM	PC-Y-L	196.4	
4460	1.5	FM	PC-Y-L	153.6	
4471	1.5	FM	PC-Y-L	178.6	
4475	1.5	FM	PC-Y-L	188.2	
6333	1.6	FM	Y-L	159.1	X
3521	1.7	FM	Y	156.8	
3204	1.7	FM	Y	193.2	X
4491	2.0	FM	L	230.0	
4513	2.0	FM	PC-Y-L	166.8	
4512	2.0	FM	PC-Y-L	185.5	X
6154	2.0	FM	Y-L	167.3	
6153	2.1	FM	Y-L	168.2	
5912	2.1	FM	Y-L	177.3	
3420	2.1	FM	Y-L	252.7	
3523	2.1	FM	Y-L	260.9	
5931	2.2	FM	Y-L	190.9	
2363	2.2	FM	Y-L	243.2	
5913	2.2	FM	Y-L	201.8	
5911	2.2	FM	Y-L	195.5	
2362	2.2	FM	Y-L	225.0	
2443	2.2	FM	Y-L	195.5	
2943	2.2	FM	Y-L	247.3	
2442	2.2	FM	Y-L	220.9	
6020	2.2	FM	Y-L	193.2	
2440	2.2	FM	Y-L	206.4	
5933	2.2	FM	Y-L	190.9	
6024	2.3	FM	Y-L	188.6	
5910	2.3	FM	Y-L	190.9	
2941	2.3	FM	Y-L	199.1	
4741	2.3	FM	PC-Y-L	254.5	
4740	2.3	FM	PC-Y-L	209.1	
2654	2.3	FM	Y-L	202.7	
4640	2.3	FM	PC-Y-L	239.1	
4641	2.3	FM	PC-Y-L	239.1	
2651	2.3	FM	Y-L	190.9	
2653	2.3	FM	Y-L	229.1	
1470	2.4	FM	Y-L	159.1	X
1790	2.4	FM	Y-L	230.0	
1472	2.4	FM	Y-L	210.0	
1610	2.4	FM	Y-L	215.9	
1573	2.4	FM	Y-L	190.0	
1424	2.4	FM	Y-L	159.1	
3202	2.6	FM	Y-L	175.5	
3203	2.6	FM	Y-L	117.7	

Table 2. (Continued)

Hog number	Age[a]	Sex	Breed[b]	Weight[c]	Lipid evaluation
3195	2.8	FM	Y-L	209.1	
3196	2.8	FM	Y-L	190.9	X
7122	2.9	FM	Y-L	229.5	
1362	2.9	FM	Y-L	185.9	
Age Group IV					
3633 PC29	3.1	M	PC	236.4	X
1361	3.1	FM	Y-L	168.2	
4383	3.4	M	PC	290.9	X
4870	3.4	M	PC	290.9	
3652	3.7	M	PC	254.5	
2324-58F	3.7	M	PC	350.0	
2260	3.8	FM	L	208.2	
4631 PC17	3.8	M	PC	281.8	X
4192	4.1	M	PC	252.3	X
190-10	4.5	FM	Y	250.0	X
7710	4.5	FM	L	254.5	
4110	4.6	M	PC	275.0	
392	4.6	FM	L	211.4	X
966 PC20	5.0	M	PC	327.3	
4734	5.1	M	PC	330.9	
24	5.2	M	D	336.4	X
22-160	5.9	M	H	260.9	X
Age Group V					
5895	6.0	FM	L	252.3	
6043	6.0	FM	L	220.5	X
29-260	6.0	M	D	227.3	
4583	6.1	FM	Y-L	240.9	
323-160	6.1	FM	D	255.9	
1350	6.1	FM	L	175.0	
5815	6.2	FM	L	204.5	X
903-259	6.3	M	H	390.9	
19-259	6.3	M	H	367.3	
221	6.4	FM	L	268.2	X
312	6.8	FM	Y-L	229.1	X
119-259	7.0	FM	D	268.6	X
9014-259	7.0	FM	D	335.5	
3093-259	7.0	FM	D	281.8	X
26-258	7.2	FM	H	287.3	X
13-258	8.0	FM	H	231.8	X

Table 3. Per cent incidence of various histological and histochemical changes in the cornea of 86 dogs ranging in age from 0.1 month (1 day) to 13.1 years

Histological and histochemical changes	Age Groups I (0.1-4.0 mo) N = 13[a]	II (5.4-9.9 mo) N = 17[a]	III (11.0-12.9 mo) N = 16[a]	IV (1.5-4.4 yr) N = 11[a]	V (6.0-9.9 yr) N = 14[a]	VI (10.0-13.1 yr) N = 15[a]	Total (0.1 mo-13.1 yr) N = 86[a]
Lipid deposition	0	0	60.0	90.9	91.7	100.0	59.7
Pigment invasion	7.7	47.1	68.8	100.0	100.0	93.3	68.6
Mineralization	100.0	88.2	87.5	87.5	92.9	100.0	93.0
Intracellular	100.0	88.2	87.5	90.9	92.9	100.0	93.0
Stromal cell	100.0	88.2	87.5	90.9	92.9	93.9	91.9
Endothelial cell	92.3	88.2	87.5	90.9	92.9	100.0	91.9
Epithelial cell	92.3	52.9	75.0	72.7	64.3	80.0	72.1
Extracellular	69.2	64.7	68.8	90.9	92.9	66.7	74.4
Diffuse	69.2	47.1	68.8	63.6	71.4	60.0	62.8
Focal	30.8	29.4	37.5	9.1	35.7	13.3	26.7
Excrescences	30.8	47.1	50.0	72.7	78.6	60.0	56.9
[a]Lipid deposition N =	10	10	10	11	12	14	67

Table 4. Per cent incidence of various histological and histochemical changes in the cornea of 108 hogs ranging in age from 0.1 month (3 days) to 8.0 years

Histological and histochemical changes	Age Groups I (0.1-6.0 mo) N = 12[a]	II (6.2-11.9 mo) N = 10[a]	III (1.2-2.9 yr) N = 53[a]	IV (3.1-5.9 yr) N = 17[a]	V (6.0-8.0 yr) N = 16[a]	Total (0.1 mo-8.0 yr) N = 108[a]
Lipid deposition	0.0	0.0	0.0	12.5	37.5	10.0
Pigment invasion	8.3	0.0	49.1	76.5	58.8	46.3
Mineralization	100.0	100.0	98.1	94.1	100.0	98.1
Intracellular	100.0	100.0	94.3	94.1	93.8	95.4
Stromal cell	100.0	100.0	90.6	88.2	87.5	91.7
Endothelial cell	100.0	100.0	90.6	94.1	87.5	92.6
Epithelial cell	91.6	90.0	56.6	64.7	62.5	65.7
Extracellular	91.6	100.0	73.6	70.6	75.0	77.8
Diffuse	83.3	80.0	64.2	52.9	56.3	64.8
Focal	33.3	70.0	56.6	64.7	43.8	54.6
Excrescences	8.3	40.0	49.1	47.1	37.5	41.7
[a]Lipid deposition N =	8	8	8	8	8	40

Table 5. Per cent incidence of various histological and histochemical changes and the individual fiber size of the sclera in 86 dogs ranging in age from 0.1 month (1 day) to 13.1 years

Histological and histochemical changes	Age Groups I (0.1-4.0 mo) N = 13[a]	II (5.4-9.9 mo) N = 17[a]	III (11.0-12.9 mo) N = 16[a]	IV (1.5-4.4 yr) N = 11[a]	V (6.0-9.9 yr) N = 14[a]	VI (10.0-13.1 yr) N = 15[a]	Total (0.1 mo-13.1 yr) N = 86[a]
Lipid deposition							
Ciliary segment	0.0	0.0	30.0	81.8	91.7	100.0	55.2
Equatorial segment	0.0	0.0	0.0	63.6	91.7	100.0	47.8
Posterior segment	20.0	60.0	80.0	90.9	91.7	100.0	76.1
Vascular changes							
Scleral venous plexus							
Endothelial mineral	69.2	88.2	87.5	100.0	92.9	93.3	88.4
Mineral plaques	38.5	70.6	75.0	63.6	78.6	66.7	66.3
Arterial changes							
Intimal sclerosis	7.7	35.3	75.0	72.7	71.4	93.3	59.3
Medial sclerosis	0.0	5.9	12.5	18.2	71.4	93.3	33.7
Mineralization							
Ciliary segment							
Intracellular	69.2	64.7	93.8	90.9	92.9	93.3	83.7
Extracellular	15.4	41.2	43.8	63.6	85.7	80.0	54.7
Focal	46.2	64.7	68.8	72.7	64.3	26.7	57.0
Equatorial segment							
Intracellular	0.0	23.5	87.5	72.7	57.1	80.0	53.5
Extracellular	7.7	35.3	56.3	72.7	78.6	93.3	57.0
Focal	15.4	41.2	43.8	63.6	42.9	33.3	39.5
Posterior segment							
Intracellular	7.7	17.6	93.8	81.8	92.9	66.7	59.3
Extracellular	30.8	29.4	62.5	90.9	92.9	73.3	61.6
Focal	53.8	11.8	56.3	72.7	71.4	26.7	46.5
Corneoscleral pigment	38.5	76.5	87.5	90.9	85.7	93.3	79.1
Scleral fiber size(microns)[b]	2.6	4.0	4.1	4.3	4.8	5.6	4.2
[a]Lipid deposition N =	10	10	10	11	12	14	64

[b]Mean scleral fiber thickness in 5 dogs per age group; 10 randomly selected fibers per dog.

Table 6. Per cent incidence of various histological and histochemical changes and the individual fiber size of the sclera in 108 hogs ranging in age from 0.1 month (3 days) to 8.0 years

Histological and histochemical changes	Age Groups I (0.1-6.0 mo) N = 12[a]	II (6.2-11.9 mo) N = 10[a]	III (1.2-2.9 yr) N = 53[a]	IV (3.1-5.9 yr) N = 17[a]	V 6.0-8.0 yr) N = 16[a]	Total (0.1 mo-8.0 yr) N = 108
Lipid deposition						
Ciliary segment	0.0	0.0	12.5	12.5	12.5	7.5
Equatorial segment	0.0	0.0	0.0	25.0	0.0	5.0
Posterior segment	0.0	0.0	0.0	25.0	25.0	10.0
Vascular changes						
Scleral veins						
Endothelial mineral	58.3	100.0	92.5	88.2	93.8	88.9
Mineral plaques	16.7	40.0	90.6	82.4	81.3	75.0
Arterial changes						
Intimal sclerosis	0.0	0.0	24.5	47.1	87.5	32.4
Medial sclerosis	0.0	0.0	5.7	82.4	100.0	30.1
Mineralization						
Ciliary segment						
Intracellular	91.7	100.0	100.0	94.1	100.0	98.1
Extracellular	66.7	70.0	60.4	76.5	87.5	68.5
Focal	41.7	50.0	60.4	64.7	56.3	57.4
Equatorial segment						
Intracellular	91.7	90.0	100.0	94.1	100.0	97.2
Extracellular	75.0	80.0	60.4	88.2	100.0	74.1
Focal	25.0	60.0	49.1	41.2	56.3	47.2
Posterior segment						
Intracellular	75.0	90.0	90.6	94.1	100.0	90.1
Extracellular	41.7	50.0	39.6	52.9	75.0	48.1
Focal	41.7	50.0	39.6	35.3	81.3	46.3
Corneoscleral pigment	50.0	90.0	69.8	82.4	81.3	73.1
Scleral fiber size (microns)[b]	2.9	3.2	4.6	5.7	6.9	4.7
[a]Lipid deposition N =	8	8	8	8	8	40

[b]Mean scleral fiber thickness in 5 hogs per age group; 10 randomly selected fibers per hog.

Table 7. Per cent incidence of various histological and histochemical changes in the iris of 86 dogs ranging from 0.1 (1 day) to 13.1 years of age

Histological and histochemical changes	Age Groups I (0.1-4.0 mo) N = 13[a]	II (5.4-9.9 mo) N = 17[a]	III (11.0-12.9 mo) N = 16[a]	IV (1.5-4.4 yr) N = 11[a]	V (6.0-9.9 yr) N = 14[a]	VI (10.0-13.1 yr) N = 15[a]	Total (0.1 mo-13.1 yr) N = 86[a]
Lipid deposition	0.0	0.0	0.0	0.0	8.3	14.3	4.7
Mineralization	90.0	94.1	87.5	54.5	78.6	80.0	81.4
Fibrosis	53.8	88.2	93.8	81.8	100.0	100.0	87.2
Muscular changes							
Dilator atrophy	0.0	0.0	6.3	9.1	57.1	46.7	19.8
Hypertrophy of dilator	0.0	0.0	0.0	0.0	21.4	26.7	8.1
Sphincter atrophy	0.0	0.0	0.0	45.5	85.7	73.3	32.6
Vascular changes							
Intimal sclerosis	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Medial sclerosis	0.0	0.0	27.5	63.6	85.7	100.0	62.5
[a]Lipid deposition N =	10	10	10	11	12	14	64

Table 8. Per cent incidence of various histological and histochemical changes in the iris of 108 hogs ranging from 0.1 (3 days) to 8.0 years of age

Histological and histochemical changes	Age Groups I (0.1-6.0 mo) N = 12[a]	II (6.2-11.9 mo) N = 10[a]	III (1.2-2.9 yr) N = 53[a]	IV (3.1-5.9 yr) N = 17[a]	V (6.0-8.0 yr) N = 16[a]	Total (0.1 mo-8.0 yr) N = 108[a]
Lipid deposition	0.0	0.0	0.0	0.0	0.0	0.0
Mineralization	50.0	90.0	90.6	88.2	87.5	85.2
Fibrosis	75.0	100.0	100.0	76.5	100.0	93.5
Muscular changes						
Dilator atrophy	0.0	40.0	84.9	82.4	93.8	73.1
Hypertrophy of dilator	0.0	0.0	0.0	17.6	25.0	6.5
Sphincter atrophy	0.0	30.0	30.2	35.3	56.3	31.5
Vascular changes						
Intimal sclerosis	0.0	0.0	0.0	5.9	0.0	0.9
Medial sclerosis	0.0	0.0	35.8	52.9	68.8	36.1
[a]Lipid deposition N =	8	8	8	8	8	40

Table 9. Per cent incidence of various histological and histochemical changes in the ciliary body of 86 dogs ranging from 0.1 month (1 day) 13.1 years of age

Histological and histochemical changes	Age Groups I (0.1-4.0 mo) N = 13[a]	II (5.4-9.9 mo) N = 17[a]	III (11.0-12.9 mo) N = 16[a]	IV (1.5-4.4 yr) N = 11[a]	V (6.0-9.9 yr) N = 14[a]	VI (10.0-13.1 yr) N = 15[a]	Total (0.1 mo-13.1 yr) N = 86[a]
Lipid deposition							
Corona ciliaris							
Basal lamina	0.0	0.0	0.0	63.6	100.0	100.0	51.6
Ciliary process	0.0	0.0	0.0	54.5	83.3	85.7	43.8
Ciliary muscle	0.0	0.0	0.0	0.0	8.3	0.0	1.6
Mineralization							
Corona ciliaris							
Basal lamina	15.4	29.4	6.3	27.3	57.1	73.3	34.9
Ciliary process	38.5	41.2	56.3	72.7	35.7	20.0	43.0
Chamber angle	30.8	35.3	68.8	45.5	78.6	33.3	48.8
Orbiculus ciliaris (pars plana)	23.1	41.2	68.8	63.6	57.1	73.3	54.7
Ciliary muscle	38.5	41.2	75.0	63.6	64.3	13.3	48.8
Fibrosis							
Corona ciliaris							
Basal lamina	7.7	52.9	68.8	90.9	100.0	100.0	69.8
Ciliary process	0.0	5.9	6.3	9.1	57.1	66.7	24.4
Ciliary muscle	15.4	5.9	37.5	72.7	85.7	100.0	51.2
Atrophy of ciliary muscle	23.1	23.5	56.3	72.7	71.4	100.0	57.0
Epithelial hyperplasia	15.4	52.9	68.8	81.8	100.0	100.0	69.8
Hyalinized ciliary processes	0.0	5.9	25.0	54.5	71.4	93.3	40.7
Pars plana cysts	0.0	23.5	12.5	81.8	78.6	66.7	41.9
[a]Lipid deposition N =	10	10	10	11	12	14	64

Table 10. Per cent incidence of various histological and histochemical changes in the ciliary body of 108 hogs ranging from 0.1 month (3 days) to 8.0 years of age

Histological and histochemical changes	Age Groups I (0.1-6.0 mo) N = 12[a]	II (6.2-11.9 mo) N = 10[a]	III (1.2-2.9 yr) N = 53[a]	IV (3.1-5.9 yr) N = 17[a]	V (6.0-8.0 yr) N = 16[a]	Total (0.1 mo-8.0 yr) N = 108[a]
Lipid deposition						
Corona ciliaris						
Basal lamina	0.0	0.0	11.3	37.5	50.0	20.0
Ciliary process	0.0	0.0	0.0	50.0	37.5	17.5
Ciliary muscle	0.0	0.0	0.0	0.0	12.5	2.5
Mineralization						
Corona ciliaris						
Basal lamina	50.0	60.0	90.6	88.2	50.0	76.9
Ciliary process	41.7	70.0	69.8	52.9	62.5	63.0
Chamber angle	50.0	80.0	94.3	58.8	56.3	76.9
Orbicularis ciliaris (pars plana)	25.0	60.0	64.2	58.8	62.5	58.3
Ciliary muscle	33.3	70.0	84.9	82.4	50.0	72.2
Fibrosis						
Corona ciliaris						
Basal lamina	75.0	100.0	100.0	100.0	100.0	97.2
Ciliary process	41.7	80.0	100.0	94.1	100.0	90.7
Ciliary muscle	25.0	80.0	69.8	82.4	100.0	72.2
Atrophy of ciliary muscle	25.0	70.0	64.2	82.4	100.0	68.5
Epithelial hyperplasia	50.0	90.0	84.9	94.1	100.0	85.2
Hyalinized ciliary process	0.0	10.0	15.1	17.6	50.0	18.5
Pars plana cysts	0.0	1.0	24.5	23.5	50.0	23.1
[a]Lipid deposition N =	8	8	8	8	8	40

Table 11. Per cent of incidence of various histological and histochemical changes in the choroid in 86 dogs ranging from 0.1 (1 day) to 13.1 years of age

Histological and histochemical changes	Age Groups I (0.1-4.0 mo) N = 13[a]	II (5.4-9.9 mo) N = 17[a]	III (11.0-12.9 mo) N = 16[a]	IV (1.5-4.4 yr) N = 11[a]	V (6.0-9.9 yr) N = 14[a]	VI (10.0-13.1 yr) N = 15[a]	Total (0.1 mo-13.1 yr) N = 86[a]
Lipid deposition							
Segment A[b]	0.0	0.0	0.0	36.4	25.0	50.0	21.9
Segment B	0.0	0.0	0.0	36.4	25.0	42.9	20.3
Segment C	0.0	0.0	0.0	27.3	33.3	21.4	15.6
Mineralization							
Segment A	7.7	11.8	43.8	63.6	78.6	86.7	47.7
Segment B	7.7	29.4	56.3	72.7	85.7	80.0	54.7
Segment C	23.1	41.2	62.5	81.8	85.7	80.0	61.6
Fibrosis							
Segment A	0.0	29.4	6.3	36.4	100.0	86.7	43.0
Segment B	7.7	29.4	37.5	72.7	92.9	100.0	55.8
Segment C	30.8	58.8	75.0	90.9	100.0	100.0	75.6
Vascular changes							
Intimal sclerosis	7.7	17.6	75.0	63.6	57.1	20.0	39.5
Medial sclerosis	0.0	23.5	37.5	81.8	100.0	93.3	54.7
[a]Lipid deposition N =	10	10	10	11	12	14	64

[b]Note Figure 2 for delineation of the choroidal segments.

Table 12. Per cent incidence of various histological and histochemical changes in the choroid of 108 hogs ranging from 0.1 month (3 days) to 8.0 years of age

Histological and histochemical changes	Age Groups I (0.1-6.0 mo) N = 12[a]	II (6.2-11.9 mo) N = 10[a]	III (1.2-2.9 yr) N = 53[a]	IV (3.1-5.9 yr) N = 17[a]	V (6.0-8.0 yr) N = 16[a]	Total (0.1 mo-8.0 yr) N = 108[a]
Lipid deposition						
Segment A[b]	0.0	0.0	2.5	0.0	2.5	5.0
Segment B	0.0	0.0	2.5	0.0	2.5	5.0
Segment C	0.0	0.0	2.5	0.0	0.0	2.5
Mineralization						
Segment A	50.0	80.0	79.2	70.6	93.8	76.9
Segment B	58.3	90.0	84.9	70.6	93.8	81.5
Segment C	25.0	90.0	90.6	64.7	93.8	79.6
Fibrosis						
Segment A	8.3	60.0	64.2	70.6	100.0	63.9
Segment B	0.0	0.0	75.5	100.0	100.0	71.3
Segment C	0.0	0.0	79.2	100.0	100.0	76.9
Vascular changes						
Intimal sclerosis	0.0	0.0	0.0	0.0	0.0	0.0
Medial sclerosis	0.0	50.0	50.9	76.5	93.8	55.6
[a]Lipid deposition N =	8	8	8	8	8	40

[b]Note Figure 2 for delineation of the choroidal segments.

Table 13. Per cent incidence of various histological and histochemical changes in the lens of 81 dogs ranging from 0.1 (1 day) to 13.1 years of age

Histological and histochemical changes	Age Groups I (0.1-4.0 mo) N = 11	II (5.4-9.9 mo) N = 17	III (11.0-12.9 mo) N = 14	IV (1.5-4.4 yr) N = 11	V (6.0-9.9 yr) N = 14	VI (10.0-13.1 yr) N = 14	Total (0.1 mo-13.1 yr) N = 81
Mineralization							
Nucleus							
All forms	45.5	100.0	100.0	100.0	100.0	100.0	92.6
Multiple focal aggregates	36.4	52.9	28.6	18.2	28.6	7.1	29.6
Cortex	18.2	94.1	92.9	100.0	100.0	100.0	86.4
Anterior capsule	18.2	35.3	28.6	27.3	92.9	100.0	51.9

Table 14. Per cent incidence of various histological and histochemical changes in the lens of 106 hogs ranging from 0.1 (3 days) to 8.0 years of age

Histological and histochemical changes	Age Groups I (0.1-6.0 mo) N = 12	II (6.2-11.9 mo) N = 10	III (1.2-2.9 yr) N = 51	IV (3.1-5.9 yr) N = 17	V (6.0-8.0 yr) N = 16	Total (0.1 mo-8.0 yr) N = 106
Mineralization						
Nucleus						
All forms	66.7	100.0	100.0	100.0	100.0	94.9
Multiple focal aggregates	0.0	30.0	15.1	11.8	25.0	15.7
Cortex	50.0	90.0	73.6	64.7	68.8	70.4
Anterior capsule	41.7	70.0	79.2	60.0	93.8	75.0

Table 15. Per cent incidence of various histological and histochemical changes in the retina of 86 dogs ranging from 0.1 month (1 day) to 13.1 years of age

Histological and histochemical changes	Age Groups I (0.1-4.0 mo) N = 13	II (5.4-9.9 mo) N = 17	III (11.0-12.9 mo) N = 16	IV (1.5-4.4 yr) N - 11	V (6.0-9.9 yr) N = 14	VI (10.0-13.1 yr) N = 15	Total (0.1 mo-13.1 yr) N = 86
Peripheral cystic degeneration	0.0	35.3	56.3	81.8	100.0	100.0	61.6
Chorioretinal degeneration	0.0	0.0	31.3	45.5	35.7	60.0	27.9
Peripheral	0.0	0.0	25.0	27.3	28.6	53.3	22.1
Central	0.0	0.0	18.6	27.3	28.6	26.7	16.3
Pigment epithelial cell hypertrophy	15.4	35.3	56.3	72.7	78.6	93.3	58.1
Mineralized excrescences	0.0	29.4	62.5	45.5	50.0	53.3	40.7
Peripheral retinal pigmentation	0.0	0.0	0.0	63.6	92.9	86.7	38.4

Table 16. Per cent incidence of various histological and histochemical changes in the retina of 108 hogs ranging from 0.1 (3 days) to 8.0 years of age

Histological and histochemical changes	Age Groups I (0.1-6.0 mo) N = 12	II (6.2-11.9 mo) N = 10	III 1.2-2.9 yr) N = 53	IV 3.1-5.9 yr) N = 17	V 6.0-8.0 yr) N = 16	Total (0.1 mo-8.0 yr) N = 108
Peripheral cystic degeneration	66.6	100.0	100.0	100.0	100.0	96.3
Chorioretinal degeneration	83.3	100.0	100.0	100.0	100.0	98.1
Peripheral	83.3	100.0	100.0	100.0	100.0	98.1
Central	0.0	0.0	0.0	0.0	6.3	0.9
Pigment epithelial cell hypertrophy	41.7	70.0	84.9	94.1	93.8	81.5
Mineralized excrescences	25.0	20.0	62.3	35.3	43.8	47.2
Peripheral retinal pigmentation	0.0	10.0	3.8	29.4	37.5	13.0

Table 17. Mean nuclear thickness of the inner and outer nuclear layers of the retina of 86 dogs ranging from 0.1 (1 day) month to 13.1 years of age

Nuclear layer and segment of the retina	Age Groups I (0.1-4.0 mo) N = 13	II (5.4-9.9 mo) N = 17	III (11.0-12.9 mo) N = 16	IV (1.5-4.4 yr) N = 11	V (6.0-9.9 mo) N = 14	VI (10.0-13.1 yr) N = 15	Percentage nuclear loss, Age Group I-VI
Retinal segment A[a]							
Outer nuclear layer	8.2	4.9	4.4	3.8	3.1	2.4	70.7
Inner nuclear layer	4.9	2.9	2.4	1.8	1.4	1.3	73.5
Retinal segment B[a]							
Outer nuclear layer	11.4	8.7	8.2	7.3	5.6	5.0	56.1
Inner nuclear layer	5.1	3.2	2.6	2.3	2.1	2.1	58.8
Retinal segment C[a]							
Outer nuclear layer	13.1	12.8	10.8	9.9	8.4	7.7	41.2
Inner nuclear layer	6.4	4.2	3.6	4.0	3.6	2.9	54.7

[a]Note Figure 2 for delineation of the retinal segments.

Table 18. Mean nuclear thickness of the inner and outer nuclear layers of the retina of 108 hogs ranging from 0.1 (3 days) months to 8.0 years of age

Nuclear layer and segment of the retina	Age Groups I (0.1-6.0 mo) N = 12	II (6.2-11.9 mo) N = 10	III (1.2-2.9 yr) N = 53	IV (3.1-5.9 yr) N = 17	V (6.0-8.0 yr) N = 16	Percentage nuclear loss, age group I-V
Retinal segment A[a]						
Outer nuclear layer	3.2	2.9	2.4	2.1	2.4	25.0
Inner nuclear layer	2.3	2.2	1.9	1.5	1.5	34.8
Retinal segment B[a]						
Outer nuclear layer	5.5	4.9	4.6	4.8	3.9	29.1
Inner nuclear layer	3.8	3.7	2.8	2.8	2.7	28.9
Retinal segment C[a]						
Outer nuclear layer	8.4	6.5	5.6	5.4	4.9	41.7
Inner nuclear layer	6.8	5.6	4.1	4.1	4.1	39.7

[a]Note Figure 2 for delineation of the retinal segments.

APPENDIX C

SCHEMATIC ILLUSTRATIONS AND PHOTOMICROGRAPHS

Figure 1. External dimensional parameters of the globe

Bulbus Oculi

AB	Anteroposterior diameter (Geometric Axis)
CD	Vertical diameter
IJ	Transverse diameter
A	Anterior pole
B	Posterior pole (optic nerve enters bulbus oculi lateral and ventral to posterior pole)

Cornea

EF	Transverse diameter
GH	Vertical diameter
EAF	Transverse curvature
GAH	Vertical curvature

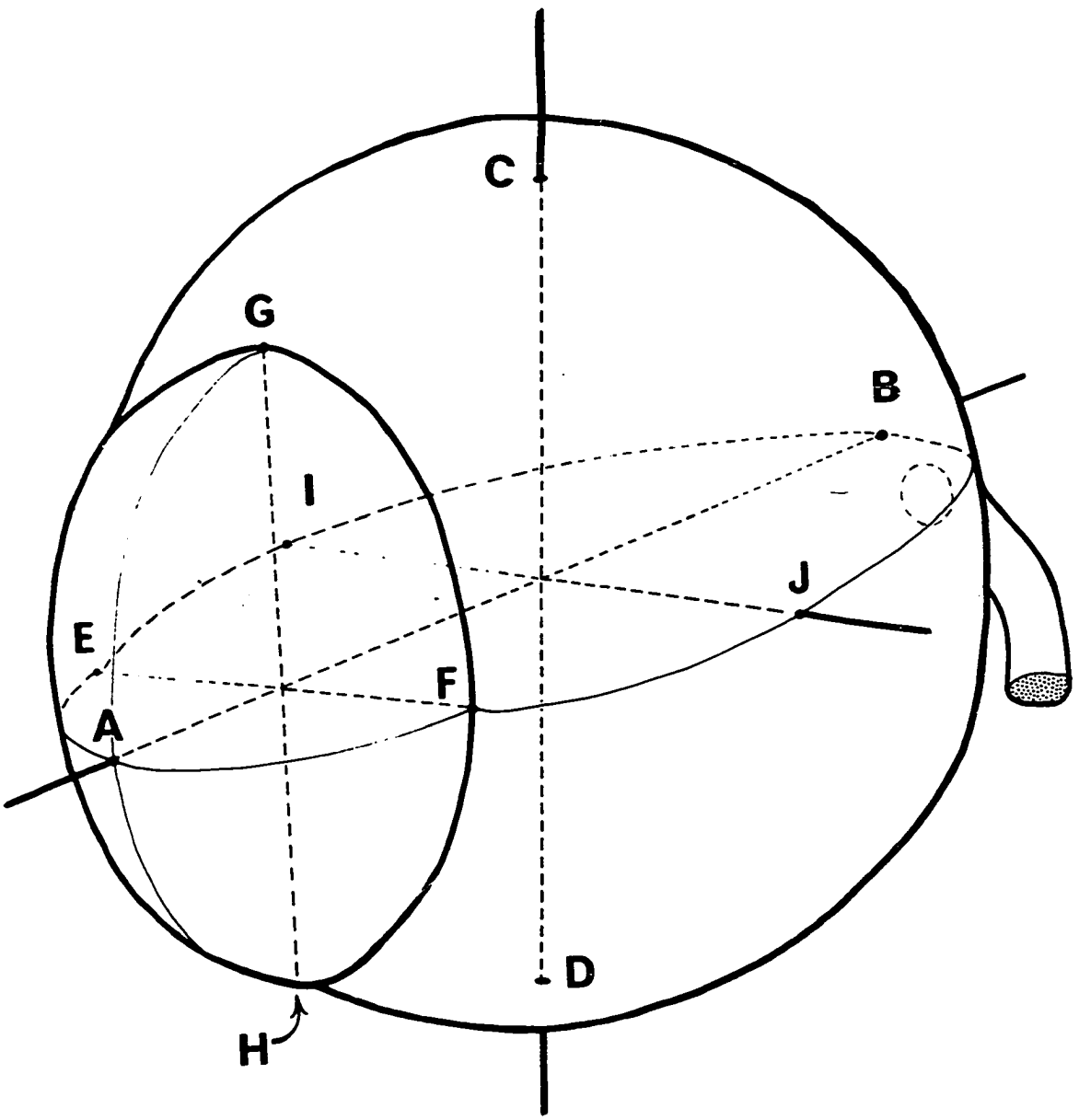

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Figure 2. Schematic representation of the internal structures various dimensional parameters and the blood supply of the eye of the dog and hog (Modified from Leber)

A,B,C	Arbitrary segments of the choroid and retina
DR	Geometric axis of the bulbus oculi
E	Cornea
F	Iris
G	Anterior lens capsule
H	Zonular ligaments
I	Ciliary body
J	Sclera (ciliary segment)
K	Medial rectus muscle
L	Retina
M	Choroid
N	Sclera (posterior segment)
O	Optic nerve
P	Polar diameter of lens
Q	Equatorial diameter of lens
1	Scleral venous plexus
2	Anterior conjunctival artery and vein
3	Posterior conjunctival artery and vein
4	Anterior ciliary artery and vein
5	Vortex vein
6	Choroidal vein
7	Episcleral artery and vein
8	Long posterior ciliary artery
9	Choroidal artery
10	Short posterior ciliary artery
11	Retinal artery and vein
12	Long posterior ciliary artery and vein

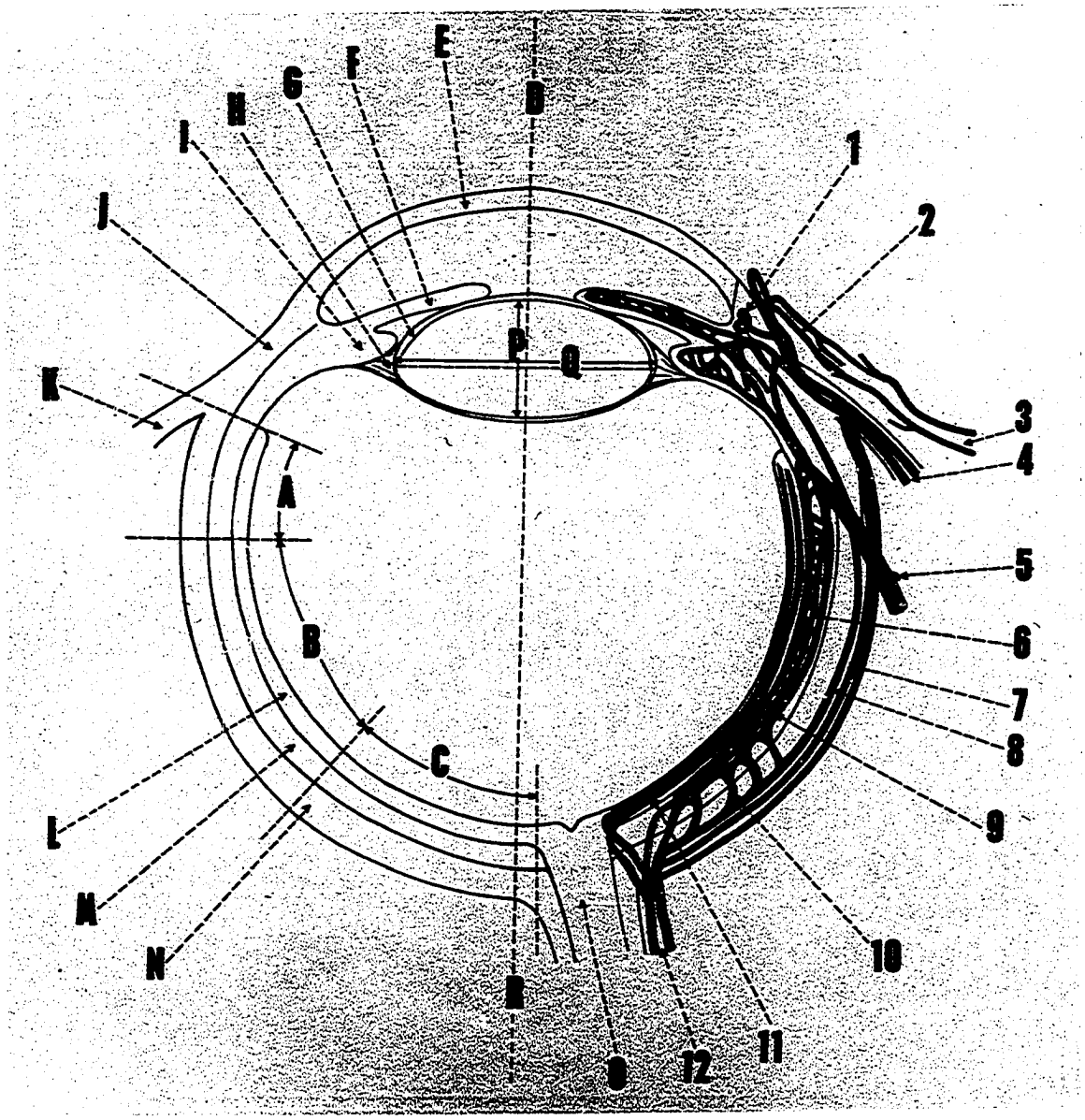
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Figure 3.
Dog No. A52. 0.1 month. Male.
Cornea, iris.
Iris partially adherent to the posterior surface of the cornea. Extensive cellularity of the corneal stroma. Corneal epithelium only 2-3 cells in thickness.
Hematoxylin and eosin stain.
X 100.

Figure 4.
Dog No. A 52. 0.1 month. Male.
Cornea, iris, and lens.
Peripheral accumulation of acid mucopolysaccharides in the cornea.
Cellular debris in anterior chamber.
Colloidal iron stain.
X 40.

Figure 5.
Dog No. 061. 0.2 month. Male.
Cornea, iris, ciliary process, and lens.
Iris adherent to posterior surface of the cornea. Lens in close proximity to the iris and cornea. Extremely small anterior chamber.
Hematoxylin and eosin stain.
X 44.

Figure 6.
Dog No. 061. 0.2 month. Male.
Same as Figure 5.
Weigert's resorcin-fuchsin stain.
X 44.

Figure 7.
Dog No. B51. 4.1 years. Female.
Cornea.
Stromal deposition adjacent to Descemet's membrane.
Oil red O stain. Gelatin embedment.
X 250.

Figure 8.
Dog No. B73. 11.9 years.
Female.
Cornea.
Lipid deposition in Descemet's membrane and corneal stroma.
Oil red O stain. Gelatin embedment.
X 250.

Figure 9.
Dog No. M48. 10.5 years. Male.
Cornea.
Lipid deposition in the peripheral cornea along corneoscleral junction.
Oil red O stain. Gelatin embedment.
X 100.

Figure 10.
Dog No. B73. 11.9 years.
Female.
Cornea.
Subepithelial accumulation and slight stromal deposition of lipid.
Oil red O stain. Gelatin embedment.
X 40.

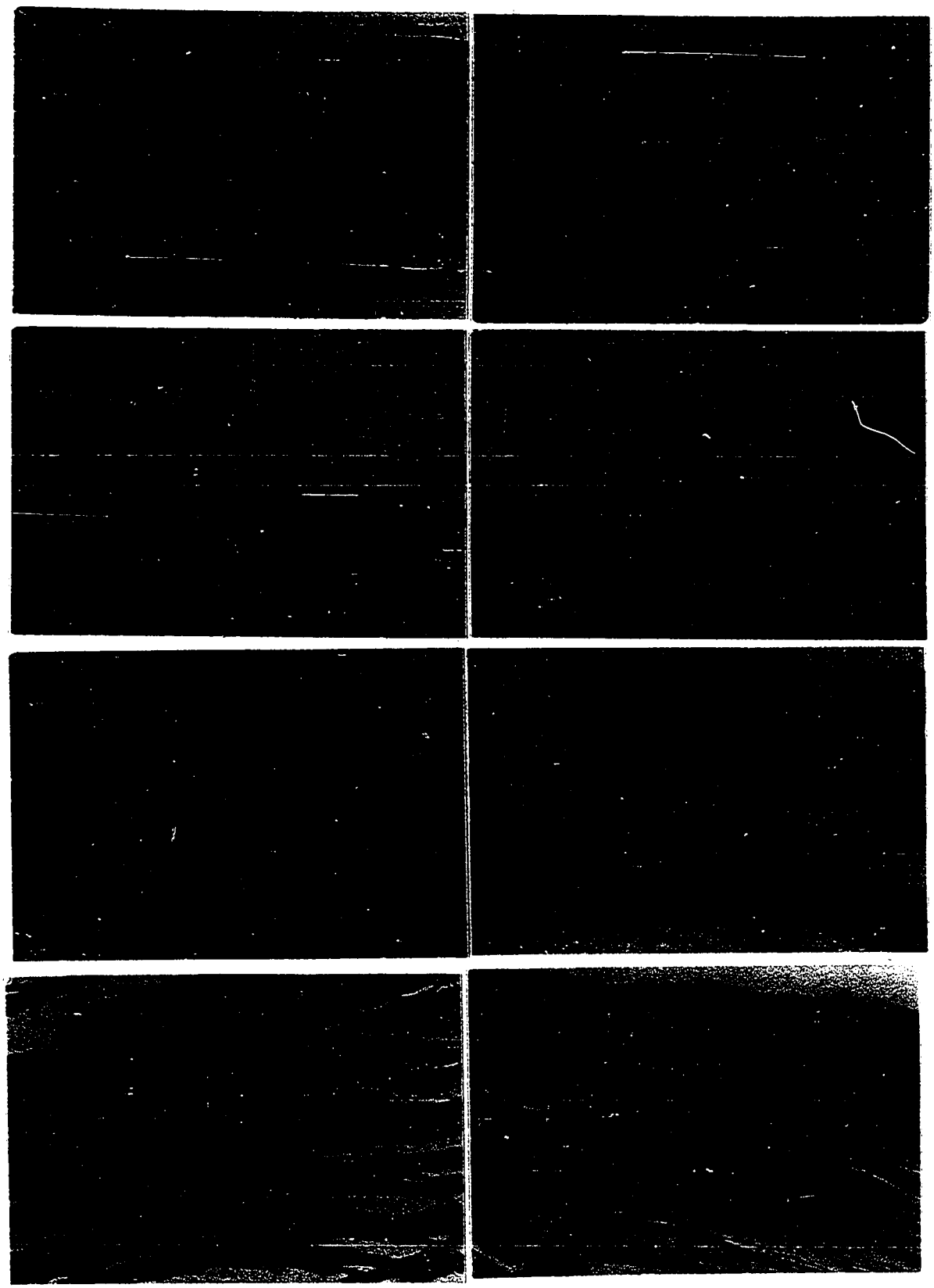

Figure 11.
Dog No. B88. 3.1 years. Male.
Cornea, sclera.
Deep corneal pigmentation.
Pigmentary invasion adjacent to Descemet's membrane.
Hematoxylin and eosin stain.
X 40.

Figure 12.
Dog No. M46. 9.9 years. Female.
Cornea, sclera.
Deep corneal pigmentation.
Hematoxylin and eosin stain.
X 100.

Figure 13.
Dog No. M38. 10.4 years. Female.
Cornea.
Peripheral enlargement of Descemet's membrane with marked attenuation of corneal endothelium. (Typical Hassal-Henle body).
Hematoxylin and eosin stain.
X 400.

Figure 14.
Dog No. M38. 10.4 years. Female.
Cornea, sclera.
Pigment invasion of Hassal-Henle body.
Hematoxylin and eosin stain.
X 100.

Figure 15.
Dog No. B71. 8.1 months. Male.
Cornea.
Fibro-pigmented nodule on posterior surface of cornea.
Disruption of Descemet's membrane.
Hematoxylin and eosin stain.
X 400.

Figure 16.
Hog No. 119-259. 7.0 years.
Female.
Cornea, sclera, iris.
Pigment invasion of the central portion of the cornea.
Hematoxylin and eosin stain.
X 25.

Figure 17.
Dog No. 068. 2.5 months. Male.
Cornea.
Intracellular mineralization of stromal and epithelial cells.
Mineralized excrescences on posterior surface of cornea.
Von Kossa's stain.
X 100.

Figure 18.
Dog No. B47. 1.9 months. Male.
Cornea.
Focal and diffuse extracellular mineralization of the substantia propria.
Von Kossa's stain.
X 250.

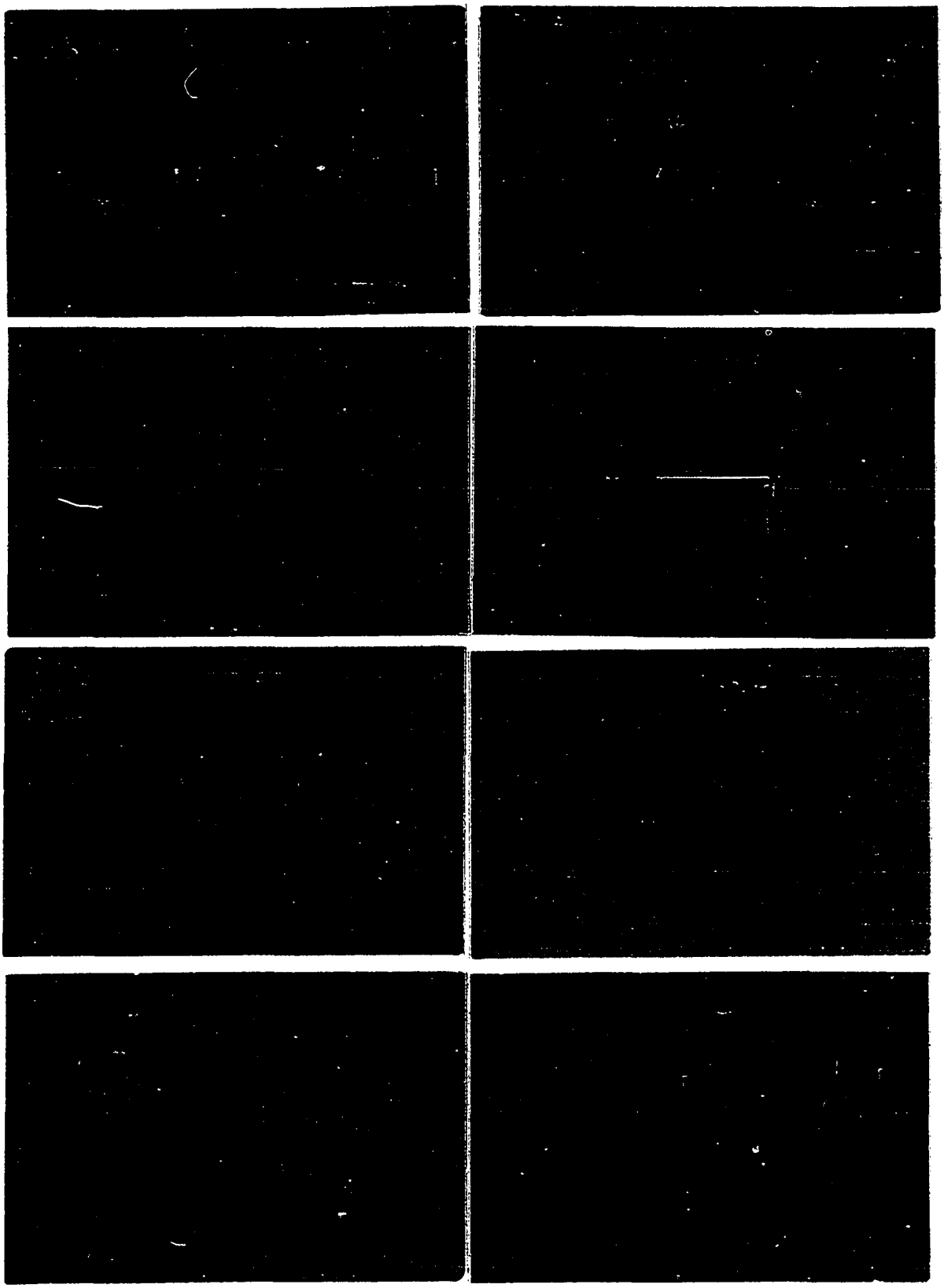

Figure 19.
Dog No. M52. 7.5 years. Male.
Cornea.
Intracellular mineralization of corneal endothelial cell.
Alizarin red S stain.
X 400.

Figure 20.
Dog No. 5FD. 12.1 months. Male.
Cornea.
Diffuse extracellular mineralization of substantia propria.
Von Kossa's stain.
X 250.

Figure 21.
Dog No. 068. 2.5 months. Male.
Cornea.
Mineralized excrescences along posterior corneal surface.
Detached corneal endothelium and mineral debris in anterior chember attributed to sectioning process.
Alizarin red S stain.
X 40.

Figure 22.
Dog No. 068. 2.5 months. Male.
Cornea.
Prominent accumulation of acid mucopolysaccharides at sites of the mineralized excrescences.
Colloidal iron stain.
X 40.

Figure 23.
Dog No. M39. 13.1 years. Male.
Cornea.
Mineralized excrescences on posterior surface of the cornea.
Mineral debris in anterior chamber attributed to sectioning process.
Hematoxylin and eosin stain.
X 250.

Figure 24.
Hog No. 5093. 9.1 months. Female.
Cornea.
Mineralized excrescences on posterior surface of cornea. Diffuse extracellular mineralization of substantia propria.
Von Kossa's stain.
X 250.

Figure 25.
Hog No. 1362. 2.9 years. Female.
Cornea.
Mineralized excrescences on posterior surface of cornea.
Intracellular mineralization of endothelial and stromal cells.
Alizarin red S stain.
X 100.

Figure 26.
Hog No. 2941. 2.3 years. Female.
Cornea.
Focal mineralization of substantia propria.
Von Kossa's stain.
X 100.

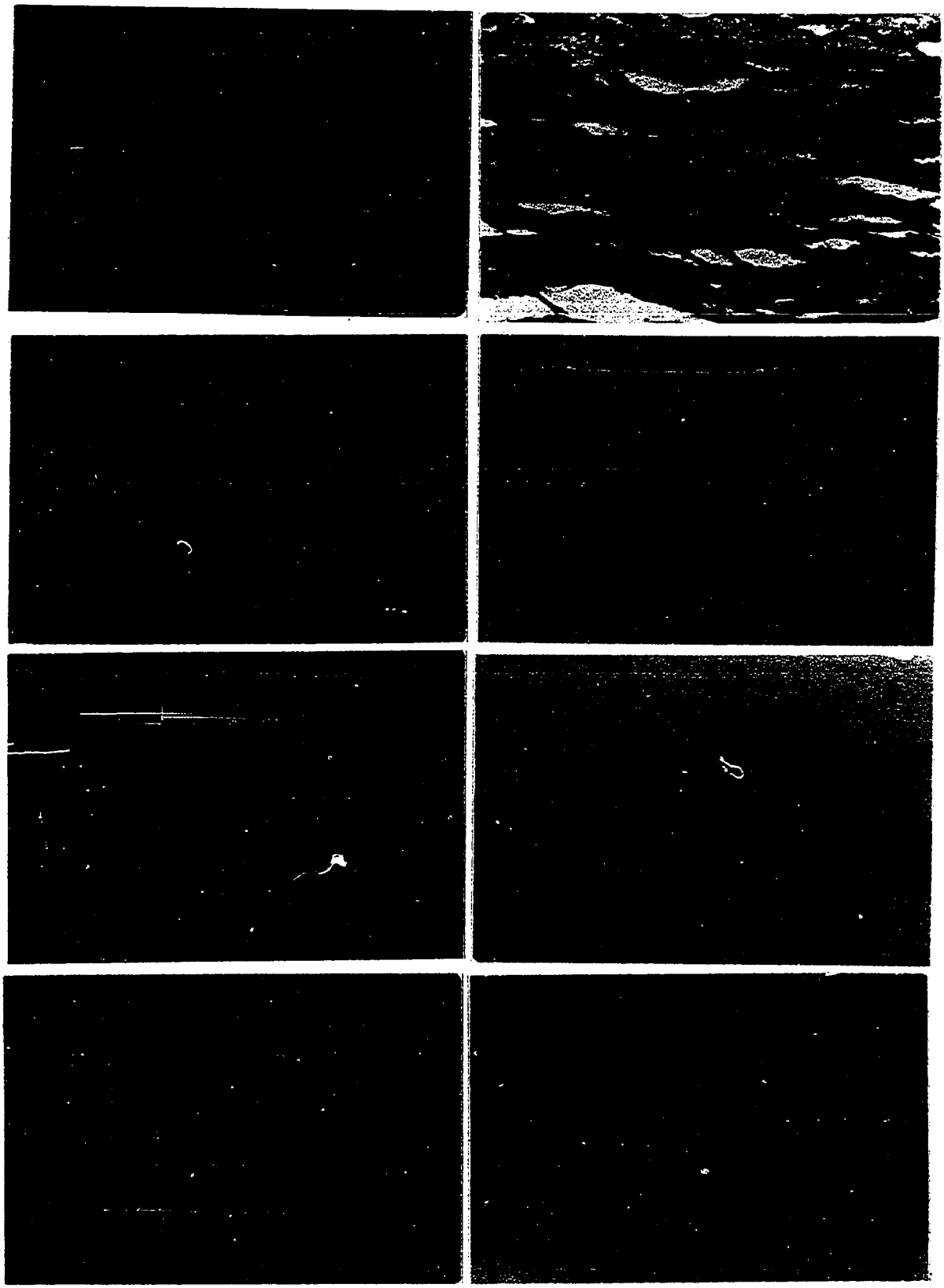

Figure 27.
Hog No. 9713. 4.2 months. Female.
Cornea.
Focal mineralization of epithelium and adjacent portion of the substantia propria.
Von Kossa's stain.
X 250.

Figure 28.
Dog No. B47. 1.9 months. Male.
Cornea.
Accumulation of acid mucopolysaccharides at site of mineralized excrescence and beneath the epithelium.
Colloidal iron stain.
X 100.

Figure 29.
Dog No. B44. 7.8 years. Female.
Cornea.
Corneal swelling as denoted by distension of acid mucopolysaccharides between stromal lamellae.
Colloidal iron stain..
X 250.

Figure 30.
Hog No. 4460. 1.5 years. Female.
Cornea, sclera.
Dense concentration of acid mucopolysaccharides in the peripheral portion of the cornea.
Colloidal iron.
X 25.

Figure 31.
Dog No. 059. 2.8 months. Female.
Sclera.
Intracellular mineralization of endothelial cells of vessel in the scleral venous plexus and the stromal cells of the sclera.
Alizarin red S stain.
X 250.

Figure 32.
Dog No. A46. 9.0 months. Female.
Sclera.
Mineral plaque in vessel of the scleral venous plexus.
Alizarin red S stain.
X 100.

Figure 33.
Dog No. 5FD. 12.1 months. Male.
Sclera.
Nodular intimal plaquation of an intrascleral branch of the long posterior ciliary artery.
Weigert's resorcin-fuchsin stain.
X 400.

Figure 34.
Dog No. 5FD. 12.1 months. Male.
Sclera.
Same vessel as in Figure 33.
Accumulation of acid mucopolysaccharides in intimal plaques.
Colloidal iron stain.
X 400.

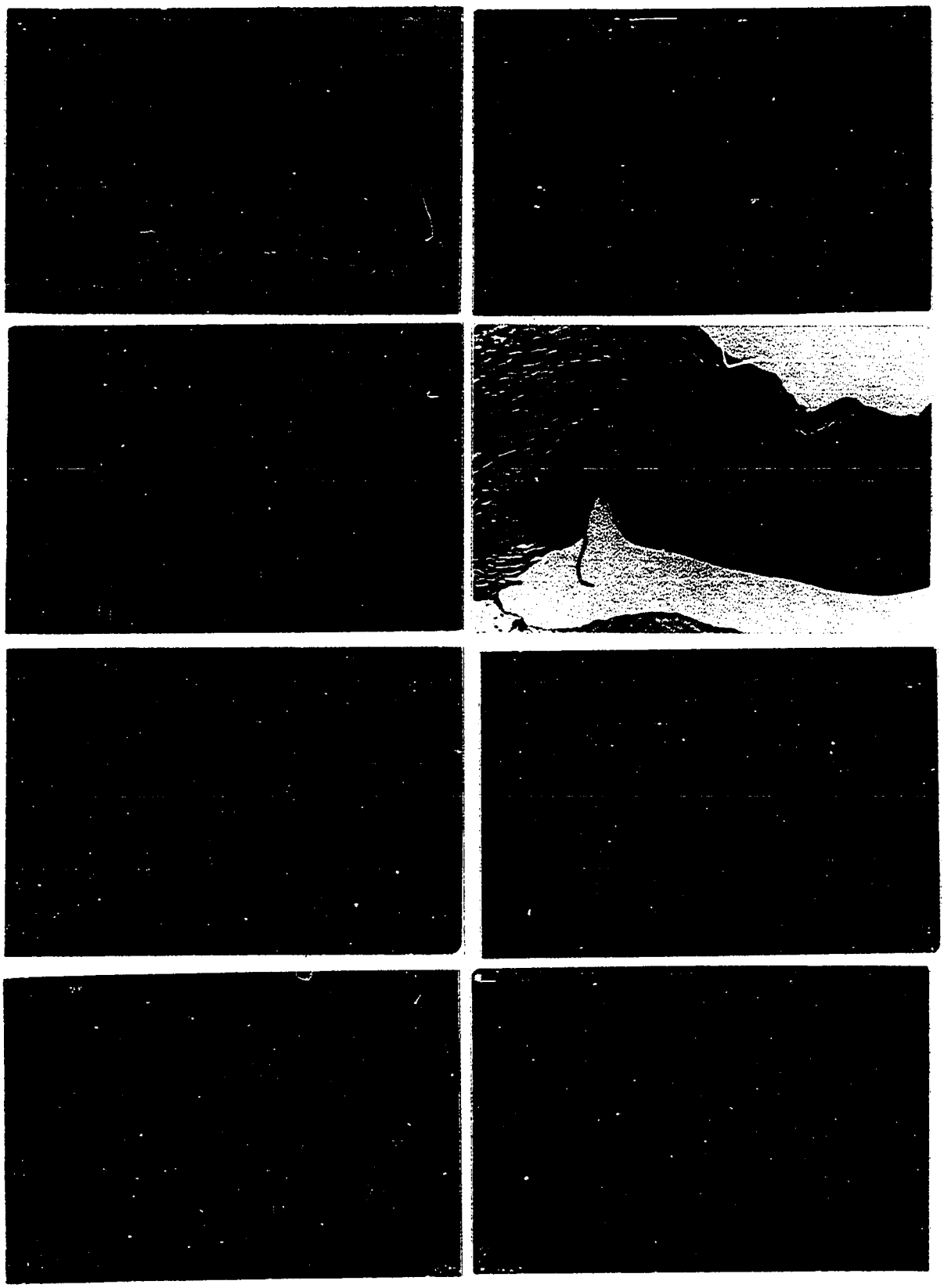

Figure 35.
Dog No. B44. 7.8 years. Female.
Sclera.
Extensive nodular intimal plaquation of an intrascleral branch of the long posterior ciliary artery.
Hematoxylin and eosin stain.
X 400.

Figure 36.
Dog No. B44. 7.8 years. Female.
Sclera.
Same vessel as in Figure 35.
Disruption of internal elastic lamina. Increased fibro-collagenous tissue in plaque and in tunica media.
Weigert's resorcin-fuchsin stain.
X 400.

Figure 37.
Dog No. B44. 7.8 years. Female.
Sclera.
Same vessel as in Figure 35.
Acid mucopolysaccharides dispersed uniformly in intimal plaques and in tunica media.
Colloidal iron stain.
X 400.

Figure 38.
Dog No. B44, 7.8 years. Female.
Sclera.
Same vessel as in Figure 35.
Mineralization absent in plaques and in tunica media.
Alizarin red S stain.
X 400.

Figure 39.
Dog No. M37. 13.1 years. Female.
Sclera.
Intimal and medial sclerosis of an intrascleral branch of the long posterior ciliary artery.
Hematoxylin and eosin stain.
X 250.

Figure 40.
Dog No. M37. 13.1 years. Female.
Sclera.
Same vessel as in Figure 39.
Disruption and fragmentation of the internal elastic lamina.
Marked increase of fibro-collagenous tissue in the tunica media with formation of collagenous nests containing degenerate smooth muscle cells.
Weigert's resorcin-fuchsin stain.
X 250.

Figure 41.
Dog No. M37. 13.1 years. Female.
Sclera.
Same vessel as in Figure 39.
Multiple focal deposition of mineral in the intimal plaque and in the tunica media.
Alizarin red S stain.
X 250.

Figure 42.
Dog No. M37. 13.1 years. Female.
Sclera.
Same vessel as in Figure 39.
Acid mucopolysaccharides predominantly in intimal plaque.
Colloidal iron stain.
X 250.

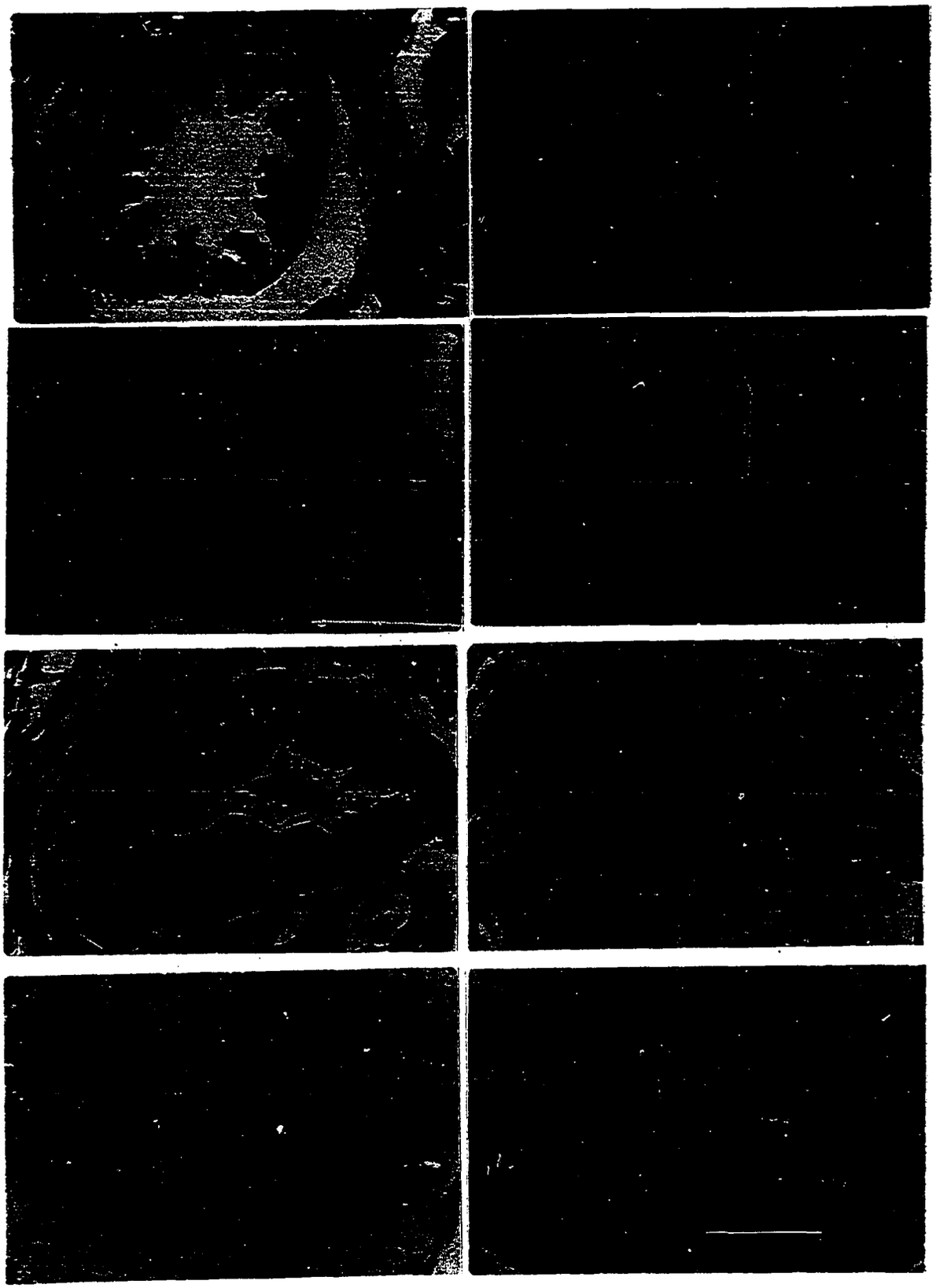

Figure 43.
Dog No. M37. 13.1 years. Female. Sclera.
Intimal deposition of lipid in intrascleral portion of the long posterior ciliary artery.
Oil red O stain. Gelatin embedment.
X 400.

Figure 44.
Hog No. 4460. 1.5 years. Female. Sclera.
Early intimal plaque in intrascleral portion of the long posterior ciliary artery. Disruption of internal elastic lamina. At the site of disruption and in the plaque smooth muscle cells are oriented perpendicular to vessel lumen.
Weigert's resorcin-fuchsin stain.
X 100.

Figure 45.
Hog No. 22-160. 5.9 years. Male. Sclera.
Medial and intimal sclerosis of intrascleral portion of long posterior ciliary artery. Disruption of internal elastic lamina. Increased fibro-collagenous tissue in tunica intima and media.
Weigert's resorcin-fuchsin stain.
X 250.

Figure 46.
Hog No. 312. 6.8 years. Female. Sclera.
Large fibrous intimal plaque in intrascleral portion of the long posterior ciliary artery.
Weigert's resorcin-fuchsin stain.
X 100.

Figure 47.
Hog No. 312. 6.8 years. Female. Sclera.
Acid mucopolysaccharide accumulation in plaque of same vessel in Figure 46.
Colloidal iron stain.
X 400.

Figure 48.
Dog No. B51. 4.1 years. Female. Choroid, sclera.
Diffuse lipid deposition in choroidal vessels and in the scleral fibers.
Oil red O stain. Gelatin embedment.
X 250.

Figure 49.
Dog No. M48. 10.5 years. Male. Sclera.
Dense lipid deposition in scleral fibers. Intracellular lipid deposition in endothelial cell of vortex vein.
Oil red O stain. Gelatin embedment.
X 250.

Figure 50.
Dog No. M48. 10.5 years. Male. Sclera, choroid.
Dense lipid deposition in scleral fibers. Flight intramural lipid accumulation in choroidal vessel.
Oil red O stain. Gelatin embedment.
X 250.

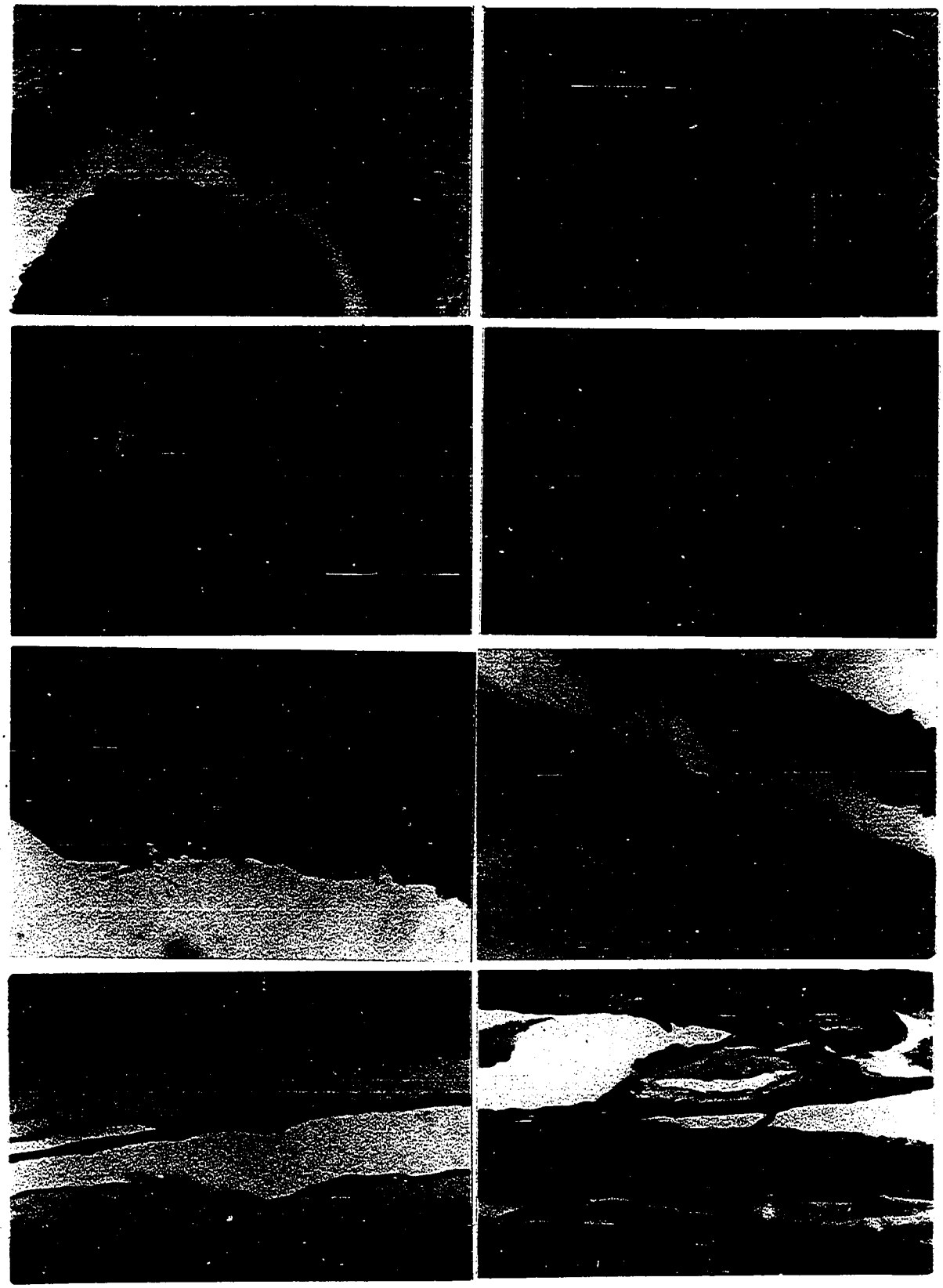

Figure 51.
Dog No. M40. 9.7 years. Female.
Sclera.
Diffuse and focal mineralization of the sclera.
Von Kossa's stain.
X 400.

Figure 52.
Dog No. B57. 12.0 months. Male.
Sclera, choroid, retina, orbiculus ciliaris.
Focal mineralization in sclera, choroid and orbiculus ciliaris.
Alizarin red S stain.
X 40.

Figure 53.
Dog No. B53. 9.9 months. Male.
Iris, ciliary body, sclera, cornea.
Slight fibrosis and pigmentation in iridal stroma. No changes in dilator muscle.
Weigert's resorcin-fuchsin stain.
X 40.

Figure 54.
Dog No. M51. 9.3 years. Female.
Iris.
Extensive stromal fibrosis and pigmentation. Atrophy of dilator muscle. Alternate atrophy and hypertrophy of sphincter muscle. Proliferative and cystic changes in the pigmented epithelia on the posterior surface of the iris.
Weigert's resorcin-fuchsin stain.
X 25.

Figure 55.
Dog No. M49. 10.3 years. Male.
Iris.
Lipid deposition and extensive pigmentation in the iridal stroma.
Oil red O stain. Gelatin embedment.
X 100

Figure 56.
Hog No. 221. 6.4 years. Female.
Iris, ciliary body, sclera.
Extensive fibrosis in the iridal stroma and in the basal lamina and ciliary processes of the ciliary crown.
Weigert's resorcin-fuchsin stain.
X 40.

Figure 57.
Hog No. 13-258. 8.0 years. Female.
Ciliary processes.
Lipid deposition in the connective tissue core of the ciliary processes.
Oil red O stain. Gelatin embedment.
X 250.

Figure 58.
Dog No. M49. 10.3 years. Male.
Ciliary crown.
Lipid deposition in the basal lamina and ciliary processes.
Oil red O stain. Gelatin embedment.
X 100.

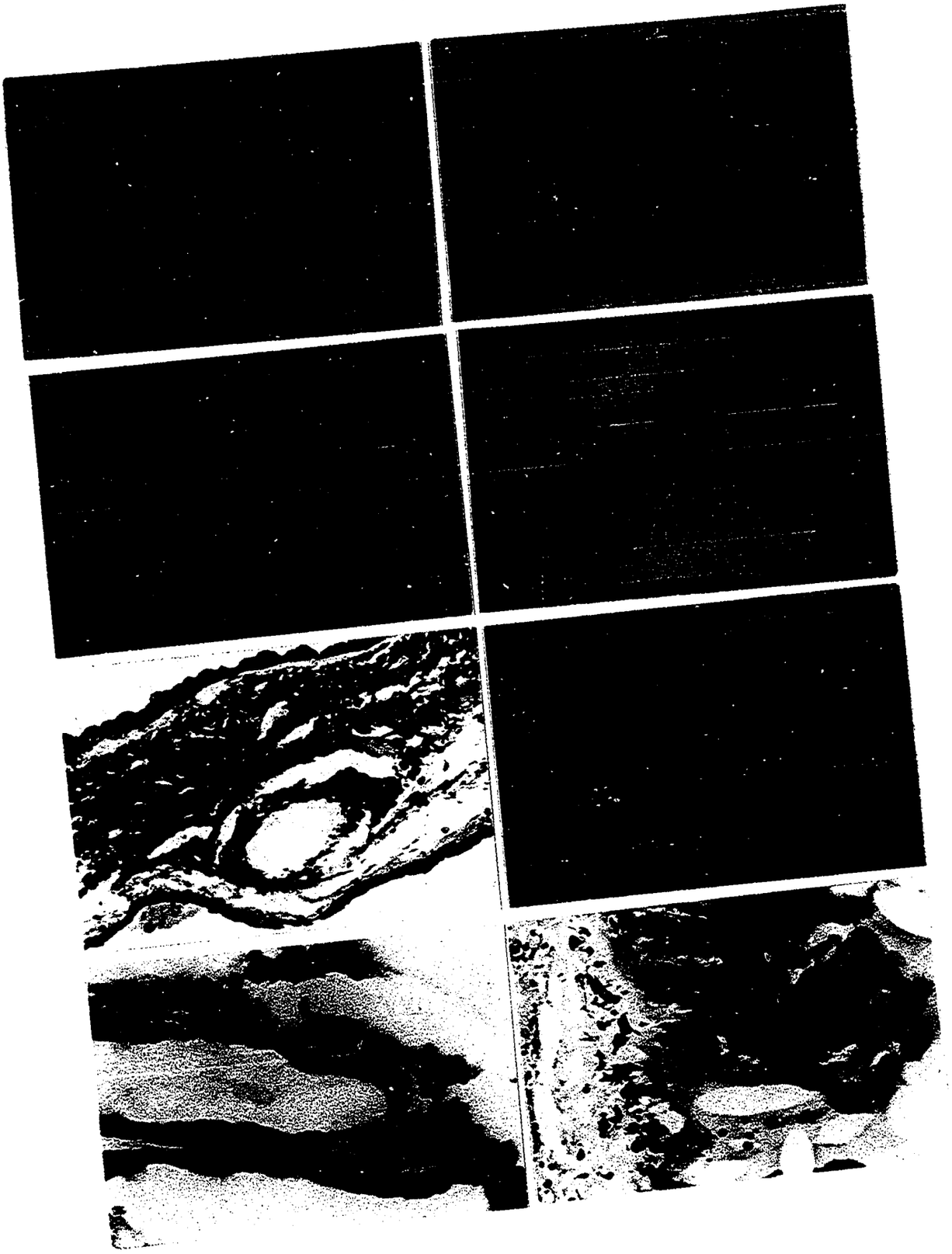

Figure 59.
Dog No. M34. 13.1 years. Female.
Ciliary body.
Lipid deposition surrounding capillary in the basal lamina of the ciliary crown.
Oil red O stain. Gelatin embedment.
X 250.

Figure 60.
Dog No. 7BAB. 12.2 months. Female.
Ciliary crown, sclera, iris.
Focal mineral deposit at the anterior chamber angle.
Alizarin red S stain.
X 40.

Figure 61.
Dog No. M39. 13.1 years. Male.
Ciliary crown, iris.
Mineralization in the basal lamina of the ciliary crown and the iridal stroma.
Alizarin red S stain.
X 100.

Figure 62.
Dog No. M52. 7.5 years. Male.
Ciliary crown.
Fibrosis of the basal lamina of the ciliary crown and hyalinization of the ciliary processes.
Weigert's resorcin-fuchsin stain.
X 100.

Figure 63.
Dog No. M39. 13.1 years. Male.
Ciliary crown.
Accumulation of fibro-collagenous tissue in the basal lamina of the ciliary crown.
Hematoxylin and eosin stain.
X 312.5.

Figure 64.
Dog No. M37. 13.1 years. Female.
Ciliary body, sclera.
Atrophy of ciliary muscle as a result of pigment accumulation between the muscle fibers.
Fibrosis of the basal lamina of the ciliary crown.
Hematoxylin and eosin stain.
X 44.

Figure 65.
Dog No. M38. 10.4 years. Female.
Ciliary process.
Senile epithelial hyperplasia.
Hematoxylin and eosin stain.
X 250.

Figure 66.
Dog No. M44. 12.0 years. Female.
Orbiculus ciliaris.
Cystic dilatation of the orbiculus ciliaris. Acid mucopolysaccharide accumulation within the cystic cavity.
Colloidal iron stain.
X 250.

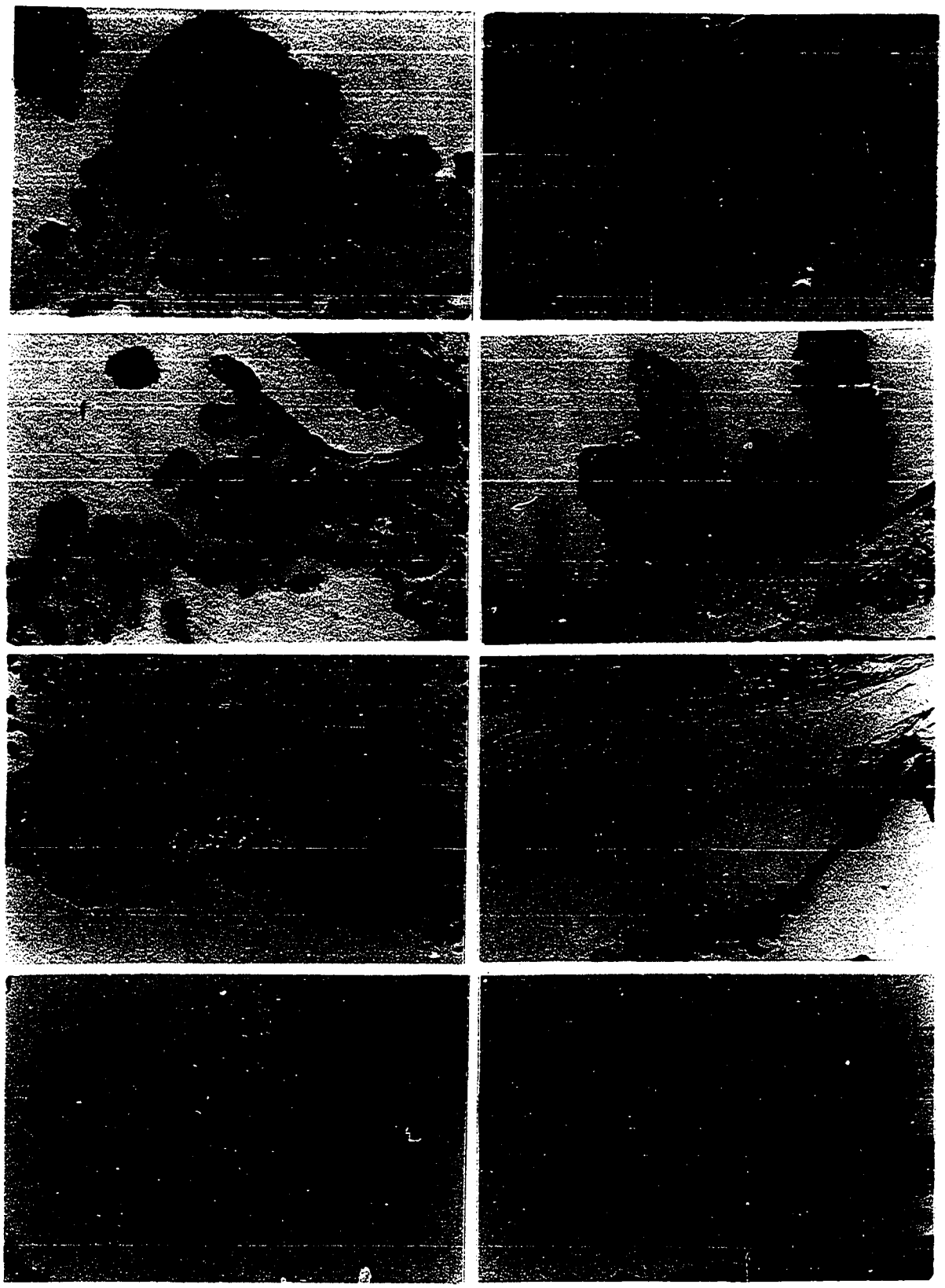

Figure 67.
Dog No. B65. 3.6 years. Female.
Choroid.
Diffuse intramural deposition of lipids in the peripheral choroidal vasculature.
Oil red O stain. Gelatin embedment.
X 400.

Figure 68.
Dog No. M34. 13.1 years. Female.
Choroid, sclera.
Intense lipid deposition in the scleral fibers and in the adjacent choroidal vasculature.
Oil red O stain. Gelatin embedment.
X 100.

Figure 69.
Dog No. B65. 3.6 years. Female.
Choroid.
Fatty intimal plaque in choroidal artery.
Oil red O stain.
X 400.

Figure 70.
Dog No. M48. 10.5 years. Male.
Sclera, choroid, retina.
Intense mineralization in the choroidal stroma. Mild intracellular mineralization of the ganglion cell of the retina.
Alizarin red S stain.
X 156.

Figure 71.
Dog No. B48. 7.9 months. Female.
Choroid.
Extrusion of mineral from the choroid through break in chorioretinal barrier forming "cauliflower-like" excrescence.
Alizarin red S stain.
X 250.

Figure 72.
Dog No. M48. 10.5 years. Male.
Choroid, retina.
Chorioretinal mineralized excrescence.
Alizarin red S stain.
X 250.

Figure 73.
Dog No. 5FD. 12.1 months. Male.
Sclera, choroid, retina.
Chorioretinal mineralized excrescences. Scleral and choroidal mineralization. Intracellular mineralization and hypertrophy of the pigment.epithelial cell of the retina.
Alizarin red S stain.
X 100.

Figure 74.
Dog No. 9. 8.7 years. Male.
Sclera, choroid, retina.
Fibrosis of the choroidal stroma; Nodular intimal plaquation of choroidal arteries. Chorioretinal degeneration.
Weigert's resorcin-fuchsin stain.
X 100.

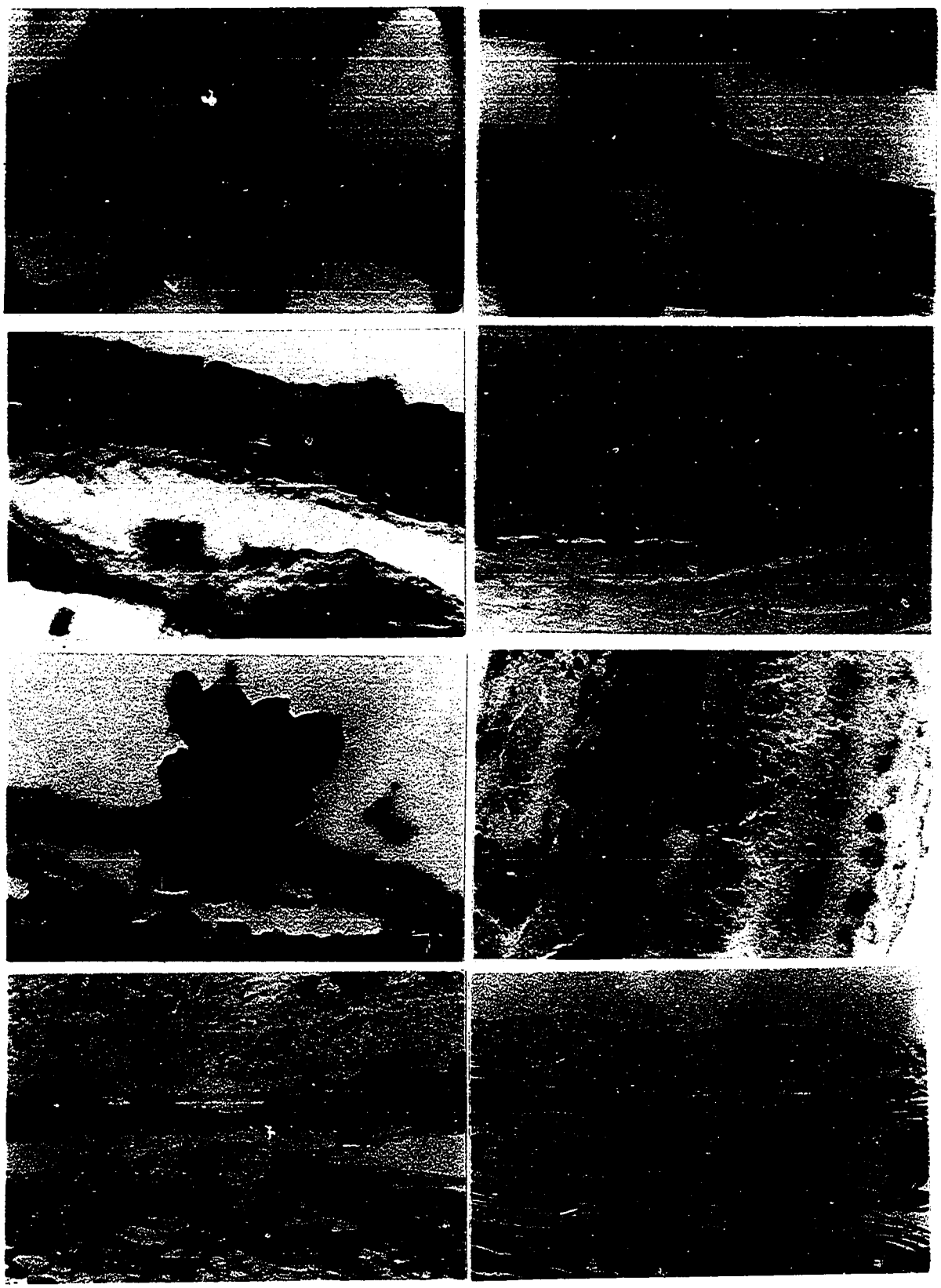

Figure 75.
Dog No. 053. 2.8 years. Female.
Choroid.
Nodular intimal plaquation of choroidal artery.
Weigert's resorcin-fuchsin stain.
X 250.

Figure 76.
Hog No. 24. 5.2 years. Male.
Choroid.
Hyalinization of the choroidal artery. Fibrosis of the choroidal stroma.
Hematoxylin and eosin stain.
X 250.

Figure 77.
Hog No. 24. 5.2 years. Male.
Choroid.
Same artery as in Figure 76.
Weigert's resorcin-fuchsin stain.
X 250.

Figure 78.
Hog No. 24. 5.2 years. Male.
Choroid.
Same artery as in Figure 76.
Intramural accumulation of acid mucopolysaccharides.
Colloidal iron stain.
X 250.

Figure 79.
Dog No. 061. 0.2 month. Male.
Retina (peripheral).
Combined inner and outer nuclear layers. Lange's fold at ora serrata.
Hematoxylin and eosin stain.
X 312.5.

Figure 80.
Dog No. 061. 0.2 month. Male.
Retina (central).
Beginning cleavage of inner and outer nuclear layers.
Hematoxylin and eosin stain.
X 312.5.

Figure 81.
Dog No. 1F. 6.6 years. Female.
Retina.
Spontaneous retinal atrophy.
Loss of nuclei in inner and outer nuclear layers.
Hematoxylin and eosin stain.
X 500.

Figure 82.
Dog No. M37. 13.1 years. Female.
Retina.
Peripheral retinal atrophy.
Absence of inner nuclear layer and rods and cones; Loss of nuclei in outer nuclear layer.
Thickening of arteriolar wall.
Neurogliosis and cystic degeneration.
Hematoxylin and eosin stain.
X 400.

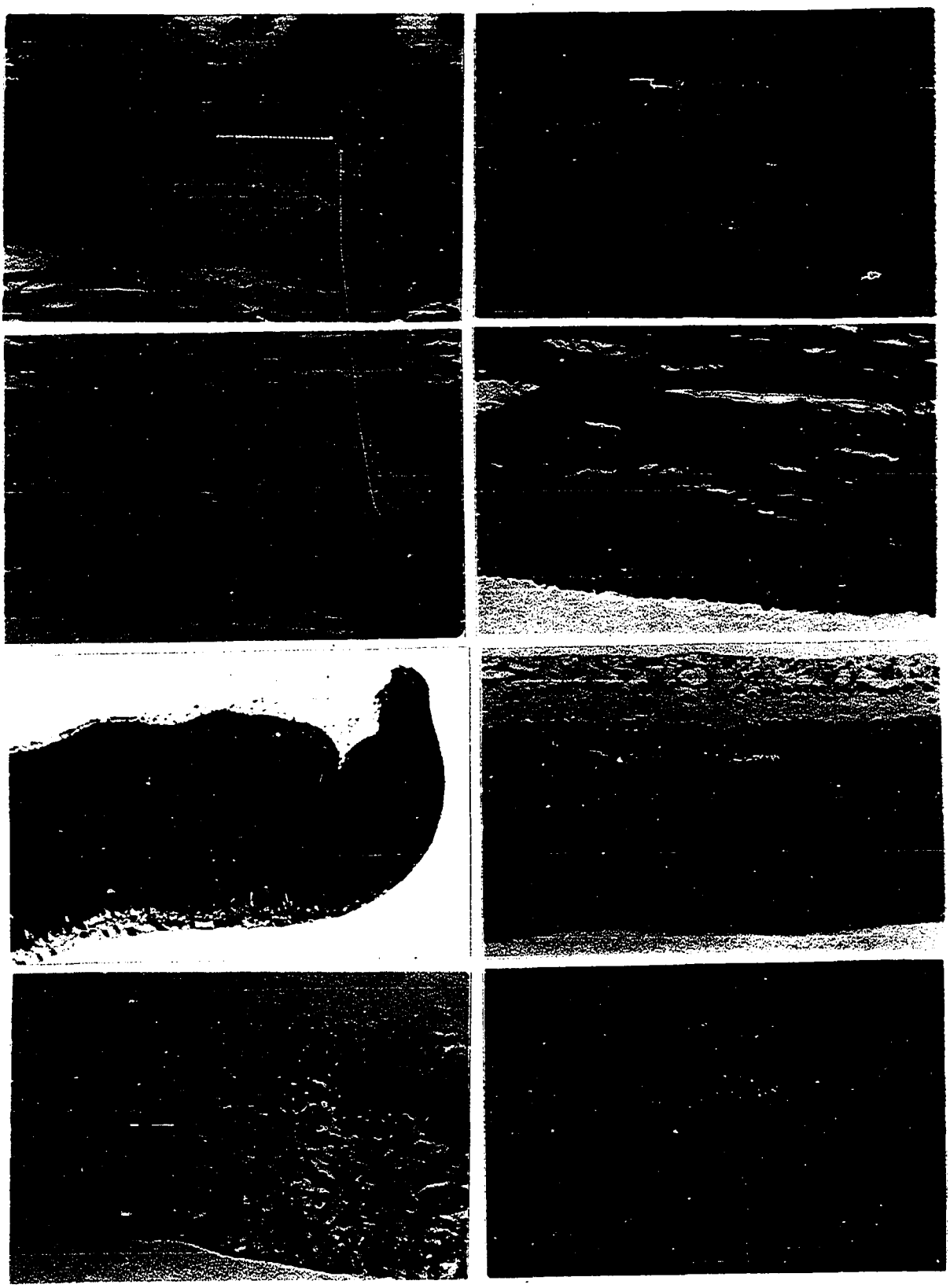

Figure 83.
Dog No. B44. 7.8 years. Female.
Retina.
Spontaneous retinal atrophy.
Loss of nuclei in inner nuclear layer. Vacuolation and degeneration of ganglion cell. Cystic degeneration.
Hematoxylin and eosin stain.
X 500.

Figure 84.
Dog No. B44. 7.8 years. Female.
Retina.
Spontaneous retinal atrophy.
Thickening of Mullers fibers.
Hematoxylin and eosin stain.
X 500.

Figure 85.
Dog No. M37. 13.1 years. Female.
Retina.
Peripheral cystic degeneration.
Hematoxylin and eosin stain.
X 40

Figure 86.
Dog No. M39. 13.1 years. Male.
Retina, orbiculus ciliaris.
Cystic degeneration of peripheral retina and orbiculus ciliaris.
Hematoxylin and eosin stain.
X 40.

Figure 87.
Dog No. M39. 13.1 years. Male.
Retina, orbiculus ciliaris.
Accumulation of mucoid debris in cysts depicted in Figure 86.
Colloidal iron stain.
X 40.

Figure 88.
Dog No. 9. 8.7 years. Male.
Retina (ora serrata).
Peripheral pigmentation of retina.
Hematoxylin and eosin stain.
X 500.

Figure 89.
Hog No. 7710. 4.5 years. Female.
Retina (peripheral).
Cystic degeneration and peripheral atrophy. Thickening of arteriolar wall and Mullers fibers.
Hematoxylin and eosin stain.
X 312.5.

Figure 90.
Dog No. B64. 10.1 years. Female.
Retina.
Marked retinal atrophy.
Hematoxylin and eosin stain.
X 500.

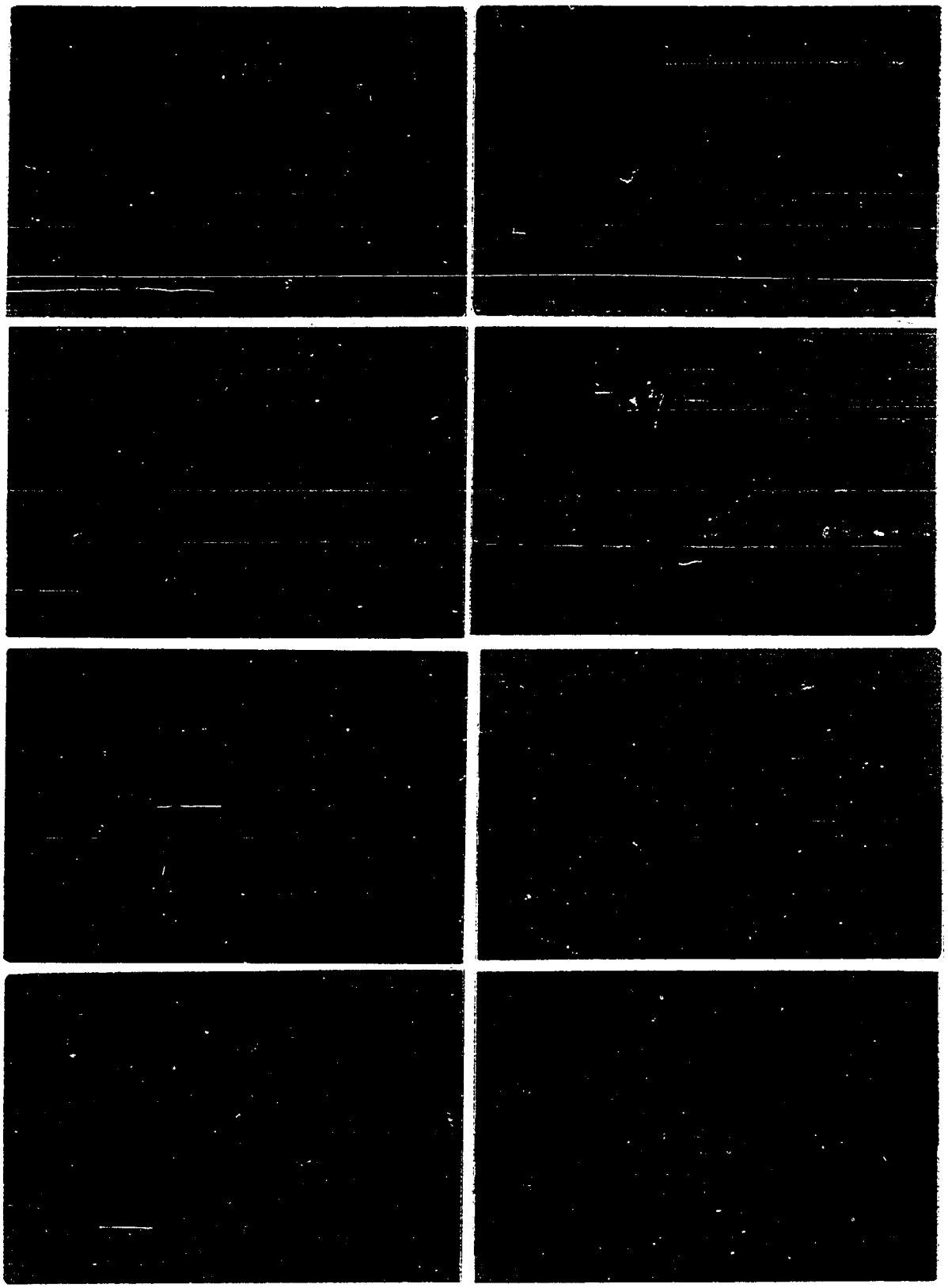

Figure 91.
Dog No. 7BA. 6.4 years. Female.
Retina, choroid.
Central chorioretinal degeneration. Arteriosclerotic lesions in retina and choroid.
Hematoxylin and eosin stain.
X 500.

Figure 92.
Dog No. 7BA. 6.4 years. Female.
Retina, choroid.
Hyperplasia of pigment epithelial cells of retina with focal mineralization. Chorioretinal atrophy. Absence of rods and cones.
Hematoxylin and eosin stain.
X 250.

Figure 93.
Dog No. B73. 11.9 years. Female.
Pigment epithelial cell of retina, choroid.
Hypertrophy of pigment epithelia. Binucleate cells.
Hematoxylin and eosin stain.
X 400.

Figure 94.
Dog No. B63. 9.2 years. Male.
Pigment epithelial cell of retina, choroid.
Intracellular mineralization and hypertrophy of the pigment epithelia.
Alizarin red S stain.
X 250.

Figure 95.
Dog No. B43. 7.8 years. Female.
Pigment epithelial cell of retina.
Dense accumulation of acid mucopolysaccharides in hypertrophic pigment epithelial cell.
Thickened lamina basalis.
Colloidal iron stain.
X 1250.

Figure 96.
Dog No. B43. 7.8 years. Female.
Pigment epithelial cell of retina, choroid.
Hypertrophy and depigmentation of pigment epithelial cell.
Colloidal iron stain.
X 1250.

Figure 97.
Dog No. B43. 7.8 years. Female.
Pigment epithelial cell of retina, choroid (tapetum).
Lipid deposition in hypertrophic pigment epithelial cell.
Oil red O stain. Gelatin embedment.
X 400.

Figure 98.
Dog No. A46. 9.0 months. Female.
Retina, choroid.
Dome-shaped mineralized excrescences attached to pigment epithelial cell.
Alizarin red S stain.
X 250.

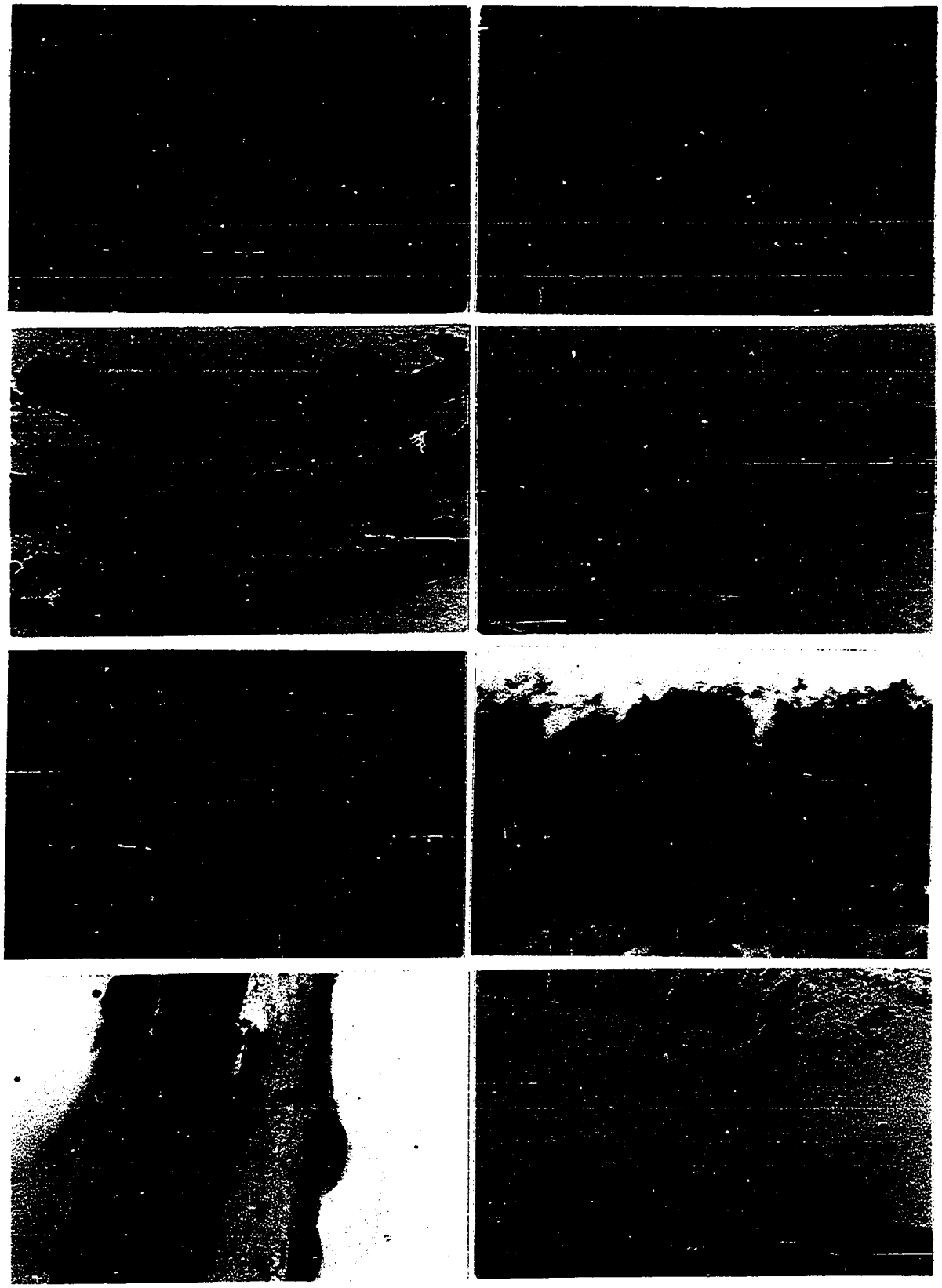

Figure 99.
Dog No. 5FD. 12.1 months. Male.
Retina, choroid (tapetum), sclera.
Mineralized excrescences attached to pigment epithelial cell of retina.
Hematoxylin and eosin stain.
X 100.

Figure 100.
Dog No. 5FD. 12.1 months. Male.
Retina, choroid (tapetum).
Mineralized excrescences attached to pigment epithelial cell of the retina.
Von Kossa's stain.
X 156.

Figure 101.
Dog No. 5FD. 12.1 months. Male.
Retina, choroid (tapetum).
Mineralized excrescences attached to pigment epithelial cell of the retina. Accumulation of acid mucopolysaccharides in the excrescences.
Colloidal iron stain.
X 156.

Figure 102.
Hog No. 3093-259. 7.0 years. Female.
Retina, choroid (peripheral).
Peripheral chorioretinal degeneration. Intense pigmentation in peripheral choroid.
Hematoxylin and eosin stain.
X 156.

Figure 103.
Hog No. 2943. 2.2 years. Female.
Pigment epithelial cell of retina, choroid.
Intracellular mineralization, depigmentation, and hypertrophy of pigment epithelial cell.
Alizarin red S stain.
X 500.

Figure 104.
Hog No. 3093-259. 7.0 years. Female.
Retina, choroid.
Chorioretinal mineralized excrescences.
Alizarin red S stain.
X 500.

Figure 105.
Dog No. B73. 11.9 years. Female.
Retina.
Thickening and splitting of PAS-positive basement membrane in retinal artery.
Periodic acid-Schiff stain.
X 500.

Figure 106.
Dog No. B44. 7.8 years. Female.
Retina.
Cellular and fibrous proliferation in the wall of retinal artery.
Weigert's resorcin-fuchsin stain.
X 500.

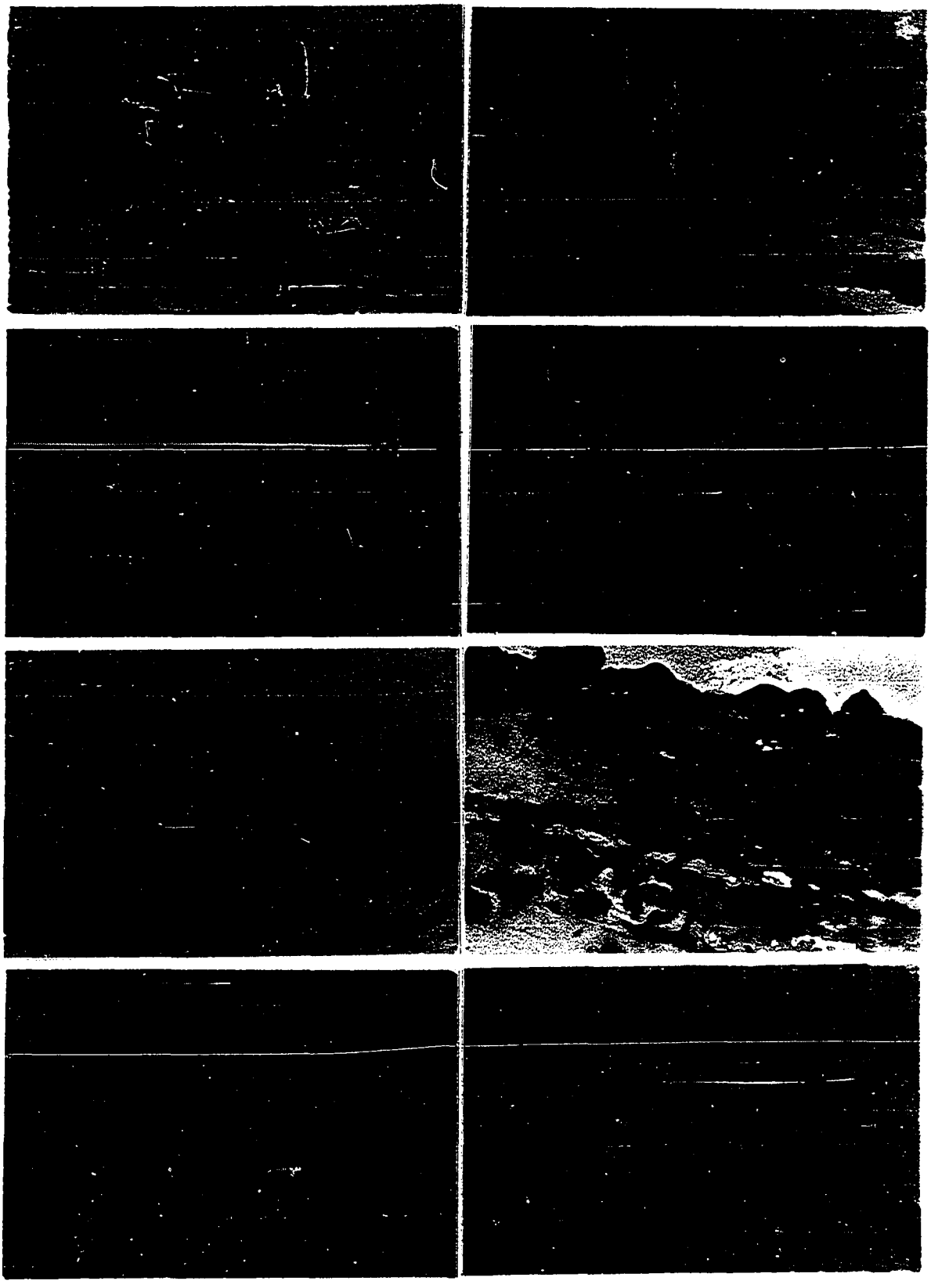

Figure 107.
Dog No. 059. 2.8 months. Female.
Lens.
Early nuclear sclerosis.
Hematoxylin and eosin.
X 40.

Figure 108.
Dog No. 059. 2.8 months. Female.
Lens.
Early proteinogenous changes in the lens nucleus. Compare with Figures 111 and 114.
Weigert's resorcin-fuchsin stain.
X 40.

Figure 109.
Dog No. 059. 2.8 months. Female.
Lens.
Acid mucopolysaccharide accumulation in the lens nucleus.
Colloidal iron stain.
X 40.

Figure 110.
Dog No. B68. 2.7 years. Female.
Lens.
Nuclear sclerosis. Sharp demarcation between lens nucleus and cortex.
Hematoxylin and eosin stain.
X 40.

Figure 111.
Dog No. B68. 2.7 years. Female.
Lens.
Proteinogenous changes in the lens nucleus. Compare with Figure 108.
Weigert's resorcin-fuchsin stain.
X 40.

Figure 112.
Dog No. B68. 2.7 years. Female.
Lens.
Marked accumulation of acid mucopolysaccharides in lens nucleus.
Colloidal iron stain.
X 40.

Figure 113.
Dog No. B68. 2.7 years. Female.
Lens.
Mineralization of the lens nucleus.
Alizarin red S stain.
X 40.

Figure 114.
Dog No. M48. 10.5 years. Male.
Lens.
Marked proteinogenous alteration in the lens nucleus. Compare with Figures 108 and 111.
Weigert's resorcin-fuchsin stain.
X 25.

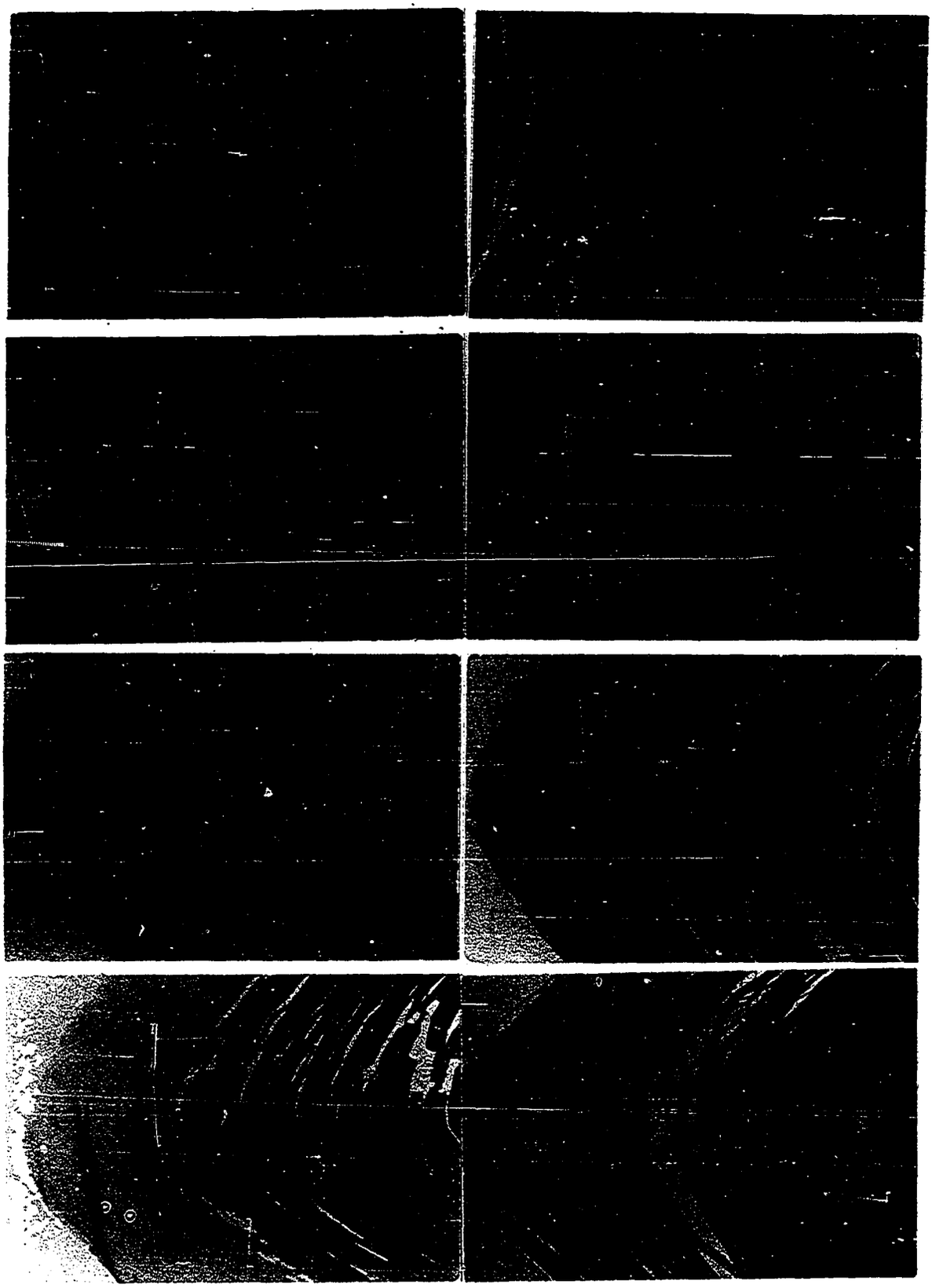

Figure 115.
Dog No. 5FD. 12.1 months. Male.
Lens.
Mineralization along serrated borders of the fibers of the lens nucleus.
Alizarin red S stain.
X 400.

Figure 116.
Dog No. B43. 7.8 years. Female.
Lens.
Multiple focal mineralization of the anterior capsule and cortex.
Alizarin red S stain.
X 312.5.

Figure 117.
Dog No. 049. 5.4 months. Female.
Lens.
Multiple focal mineralization of the lens nucleus.
Alizarin red S stain.
X 312.5.

Figure 118.
Hog No. 6333. 1.6 years. Female.
Lens.
Mineralized excrescences attached to anterior capsule of the lens.
Pigment debris within excrescence.
Alizarin red S stain.
X 500.