

REFLEXOGENIC AREAS OF THE CARDIOVASCULAR SYSTEM

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With 89 Illustrations



LONDON

J. & A. CHURCHILL LTD

104 GLOUCESTER PLACE, W.1

1958

This book is dedicated
to the memory of
JEAN-FRANÇOIS HEYMANS
and
SAMSON WRIGHT
Beloved teachers and great physiologists

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PREFACE

SHORTLY after the discovery by H. E. Hering in 1924 of the baroreceptor reflex function of the carotid sinus there appeared several monographs on the reflex control of the circulation. Notable were those of Hering (1927), Heymans (1929) and Koch (1931). By 1931 the concept of the baroreceptor reflex control of the circulation by the sino-aortic areas was reasonably well documented.

In 1927 and in 1930-31 Heymans and his colleagues discovered the chemoreceptor function of the aortic and carotid bodies and provided convincing proof of the important reflex effects of these zones on respiration and circulation. Shortly afterwards the monograph of Heymans, Bouckaert & Regniers (1933) summarized the rôle of the baroreceptor and chemoreceptor reflexogenic zones in the control of breathing and circulation. Since the appearance of their monograph, no book has been written which provided a full discussion of the problems which they considered.

The present monograph is not merely an expanded version of that written in 1933, but is an entirely new book. In addition to a full discussion of the work done in the last twenty-five years on the functional rôle of the baroreceptor and chemoreceptor sino-aortic reflexes much more new material is presented. This includes a review of the vascular receptors in the thoracic aorta, mesenteric vessels and peripheral vasculature and their function. Recent developments in the study of the reflexes from the heart itself and from the lung vessels have resulted in an improved understanding of these important reflexogenic zones. The last section of the book deals with a study of the cardio-pulmonary reflexes ; methods ranging from those of classical perfusion to those of electrophysiology are described and the results obtained therefrom discussed. Evidence from pharmacological studies and from the effects of multiple capillary embolization reveals that the lung vessels are important reflexogenic sites. The behaviour of the atrial and ventricular receptors suggests that they subserve functions such as were adumbrated ninety years ago for the depressor nerve endings by Cyon & Ludwig, who mistakenly believed that the depressor nerve arose from the heart itself.

Although the main bulk of the book is devoted to an account of the physiology of the cardiovascular reflexes considerable attention has been paid to pharmacological effects exerted on these mechanisms and to the rôle of the reflexes in patho-physiological states. It is therefore hoped that this book will be of interest not only to physiologists, but to pharmacologists and clinicians.

We wish to thank our colleagues for permission to publish figures abstracted from their published or unpublished work. We are grateful to the following journals for permission to reproduce figures : *Acta Anatomica*, *Acta Physiologica Scandinavica*, *American Journal of Anatomy*, *American Journal of Physiology*, *Anæsthesiology*, *Archives internationales de Pharmacodynamie*, *Archivio di Italiana di Anatomia e di embriologia*, *Circulation Research*, *Compte rendu hebdomadaire des séances et mémoires de la Société de biologie*, *Journal of Anatomy*, *Journal of Physiology*, *Proceedings of the Society of Experimental Biology and Medicine*, *Quarterly Journal of Experimental Physiology and*

Trabajos del Laboratorio de investigaciones biológicas de la Universidad de Madrid. The following publishers have kindly allowed us to use figures from monographs published by them : G. Doin, of Paris (*Le sinus carotidien*, 1933, by Heymans, Bouckaert & Regniers), and T. Steinkopff, of Dresden (*Die Karotissinusreflexe*, 1927, by Hering, and *Die Reflektorische Selbststeuerung des Kreislaufes*, 1931, by Koch).

Our secretaries deserve a heartfelt word of praise for their efforts in transmuting difficult manuscripts into respectable typescript.

Lastly we wish to thank the publishers, and particularly Mr. J. Rivers and Mr. J. A. Rivers for every courtesy and help and to congratulate the printers on the excellence of their work.

C. HEYMANS

E. NEIL

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Section 1 The Arterial Baroreceptors

CHAPTER 1

ANATOMY AND HISTOLOGY OF THE ARTERIAL BARORECEPTOR AREAS IN THE MAMMAL

The Carotid Sinus of the Mammalia

THE CAROTID SINUS is a dilation of the internal carotid artery situated at the origin of the vessel (Fig. 1).

FIG. 1. The right carotid sinus and carotid bifurcation of the dog. The tip of the aneurysm needle is introduced under the right internal carotid artery and immediately to the left in the picture the sinus itself is clearly seen. The external carotid artery is shown as the larger branch of the bifurcation. Between the internal and external carotid arteries can be seen a mass of tissue which includes the carotid body and the sinus nerve. The white nerve trunk seen on the right of the picture is the vago-sympathetic nerve.—(C. Heymans.)



The presence of a dilatation in this site had been known to the anatomists for a long time, but it seems that the older workers (e.g., Henle, Arnold, Luschka & Schwalbe) had not distinguished it in any particular way from the enlargement which is commonly found in vessels at the point of branching or division.

L. Meyer (1876) seems to have been the first to recognise that the dilatation was associated with a marked thinning of the arterial wall but the very title of his paper—

“Über aneurysmatische Veränderungen der Carotis interna bei Geisteskranker”—did not suggest that the sinus was a normal structure or for that matter that it occurred in normal people. Schäfer (1877) however showed that the dilatation was present in normal adult cadavers and Binswanger (1879) confirmed this. He distinguished three different sites of the dilatation: (a) situated exclusively on the internal carotid, (b) at the bifurcation of the common carotid extending into both branches, and (c) involving both the bifurcation and the internal carotid artery. In 182 cases which he examined, 81 belonged to the first, 59 to the third and 42 to the second type. Binswanger confirmed the thinning of the arterial wall which he described as beginning sharply at the origin of the internal carotid artery and stated that the thinning was due to the sparsity of muscular tissue in the media. He could not find any evidence of the “sinus dilatation” in infants. De Castro (1926, 1928) and Hering (1927) have since shown that the structure is present in infants, although De Castro found that it could not be recognised in the foetus.

With the exception of the ruminants, the carotid sinus is present in all other mammalia. In the ruminant the origin of the occipital artery is the site of a dense baroreceptor innervation which corresponds to that of the sinus in the other mammals (De Castro, 1928).

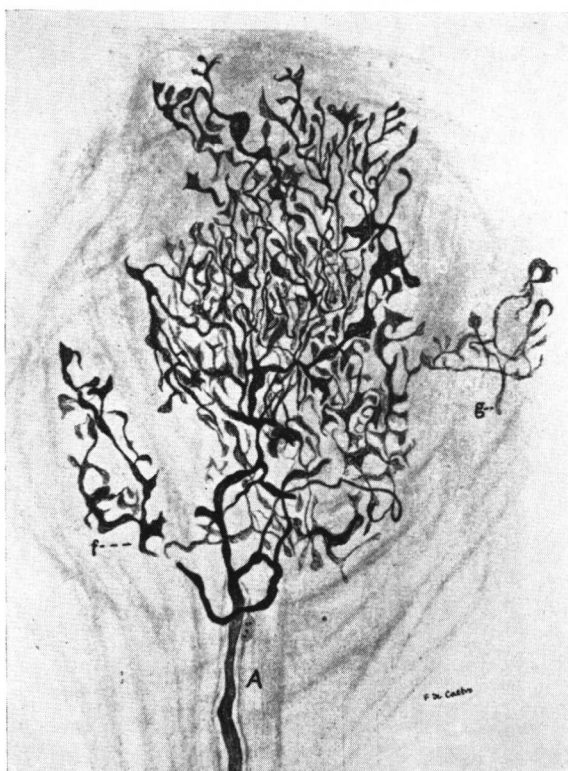
Knoll (1885) first described as “Sinusnerv” the branch of the glossopharyngeal nerve which runs to the region of the carotid bifurcation. In general, however, the anatomists of the last century regarded this glossopharyngeal branch as only one of the many nerve twigs which contributed to the intercarotid plexus described by Arnold. The vagus and sympathetic contributions to this plexus were so numerous as to overshadow that of the deeper-lying sinus nerve. Indeed it was only the proof by Hering that the stimulation of the central end of the sinus nerve caused reflex bradycardia and systemic hypotension that focused interest on the details of the innervation of the carotid sinus itself. Hering also showed that the vascular reflexes aroused by mechanical stimulation of the sinus wall were entirely abolished by section of the sinus nerve. Although Braeucker (1922) and Danielopolu and his co-workers (1927) insisted that the vagus, sympathetic and glossopharyngeal nerves contributed to the innervation of the sinus, this experimental proof of the overwhelming importance of the glossopharyngeal sensory innervation has been widely confirmed.

Shortly before the demonstration that the carotid sinus was a reflexogenic area, Gerard and Billingsley (1923) had described the innervation of the carotid bifurcation and the adjacent carotid body in cats, dogs and men. They found in the nerve a great preponderance of small myelinated fibres ($2-4\mu$) and only a few fibres in the $9-12\mu$ range.

De Castro (1926, 1928) was the first to demonstrate the extraordinary richness of the sensory innervation of the carotid sinus. Using silver impregnation methods or the methylene blue technique, he shewed that the wall of the sinus was the site of two types of sensory nerve ending. Type I were diffuse arborizations, and Type II were circumscribed glomerular-like structures (Fig. 2). Generally speaking, the receptors lay between the collagen fibres of the adventitia, particularly in its deeper layers, parallel to the longitudinal axis of the vessel. Sunder-Plassmann (1930) also recognized two sets of afferent receptors but called the arborizations of coarse structure Type I and referred to those which showed more diffuse arborization with slender branches which ended in fine terminal nets as Type II. There seems no very good reason for differentiating the receptors

in this way, particularly as the nomenclature adopted by Sunder-Plassmann differs from that already suggested by De Castro. The work of Abraham (1941, 1949, 1953 and 1955) on the histology of this area and its homologue, the aortic arch, suggests that the terminal fibres of the sinus nerve (or the aortic nerve) are transformed into very variable forms of ending. They may be ivy-shaped neurofibrillary plates, coils, or dense latticeworks. The important point would seem to be that the sensory innervation is rich. De Castro, Sunder-Plassmann and Abraham all aver that the sensory endings occur only in the

FIG. 2. Type II receptor, from the sinus wall of an adult man. Tangential section; magnification $\times 1050$. A = large myelinated nerve fibre. g, f = terminal nerve endings.—(F. De Castro, 1928. *Trab. Lab. Invest. biol. Univ. Madr.*, 25, 331).



adventitia. Others (Estable, personal communication, Rijnders, 1933, Ochoterena, 1936, Palme, 1934, and Meijling, 1938) have claimed that some nerve endings may be found in the media.

De Castro pointed out that the thinning of the media which so characterizes the wall of the carotid sinus, was particularly obvious on the ventromedial surface of the sinus at the point of entrance of the sinus nerve—i.e. at the very origin of the internal carotid artery (Fig. 3). The adventitia in this region is fairly dense. The media on the other hand is almost free from muscle fibres but contains a high proportion of elastic fibres. Sunder-Plassmann (1930) referred to an annular thinning of the media in the wall of the sinus, especially just below its equator (see also Addison, 1944, 1945). Adams (1955) noted that the ventromedial part of the sinus wall near the site of the carotid body is particularly



FIG. 3. Sagittal section (slightly oblique) through the carotid bifurcation region of cat embryo (42 mm.). Cajal technique.

c.e. = external carotid; *c.i.*; *ci.* = internal carotid; *c.p.* = common carotid; *n.d.* = aortic nerve; *l.s.* = superior laryngeal nerve; *a.oc.g.* = vessel supplying carotid body from the occipital artery; *gl. cat.* = carotid body; *r.a.gl.* = anastomotic branch (third branch) of glossopharyngeal; *ni.* = sinus nerve; *r.simp.* = sympathetic branch from superior cervical ganglion; *r.gl. 2* = second branch of glossopharyngeal; *gl.* = glossopharyngeal nerve; *r.f.v.* = pharyngeal branches of nodose ganglion; *r.d.hip.* = ramus hypoglossi.

Note the rich innervation of the carotid bifurcation derived from the sinus nerve.—(F. De Castro (1940), *Trab. Lab. Invest. biol. Univ. Madr.*, 32, 297).

thin in the case of the opossum, *Trichosurus vulpecula*, and figure 17 of his paper shows beautifully the striking loss of muscularity in the media at this point.

Wolhynski (1937) claimed that the sinus wall undergoes a compensatory thickening at the point where it receives the greatest impact of the altered direction of blood flow, and suggested that opposite to this the sinus wall became thinner. This improbable explanation of the thinness of the ventromedial wall is treated with justifiable scepticism by Adams (1955) who points out that no part of the sinus wall is thicker than that of the internal carotid artery distal to the sinus. Adams suggests that the circumscribed thinning of the sinus wall on its ventromedial aspect may be simply developmental in origin, being due to the great mesodermal proliferation associated with the formation of the carotid body

opposite this site. This may well be so; on the other hand, Boss & Green (1956) have reported thinning of the media at the site of innervation of various baroreceptor areas scattered along the common carotid artery. Here the thinning would simply be referred to the entrance of the nerve fibres as was suggested in the case of the sinus by De Castro.

In view of the findings of all other authors it is strange that De Boissezon considers the innervation of the carotid sinus to be hardly superior to that of other vessels (De Boissezon, 1942). This author believes however that the baroreceptor function of the carotid bifurcation is subserved by the vessels of the carotid body. There is of course no doubt that the vessels supplying the carotid body possess a baroreceptor innervation. De Castro himself (1940, 1951) has shown this by histological methods, and in addition has demonstrated that the electrical stimulation of the nerve endings in the wall of the root of the occipital artery causes reflex cardiovascular effects hardly distinguishable from those evocable by sinus stimulation. However, Heymans and his co-workers, Bouckaert & Pannier (1942) have shown that the baroreceptor reflexes arise in the main from the sinus itself whereas the chemoreceptor reflexes take origin from the carotid body. If a ligature is tied on the external carotid artery between the occipital artery and the bifurcation, then the baroreceptor reflexes can be produced by perfusing the carotid sinus segment whereas little baroreceptor reflex responsiveness exists in the arterial segment rostral to the ligature (Gollwitzer-Meier, 1934). This disposes of the arguments advanced by De Boissezon, which are similar to those previously expressed by Jacobovici, Nitzescu and Pop (1928) and Drüner (1925).

Lastly, it may be conceded that the sympathetic nerves and the pharyngeal vagal branches contribute to the innervation of the carotid sinus and carotid bifurcation. Their contribution is of little importance however, for section of the sinus nerve invariably abolishes the reflex responses which can normally be evoked by stimulation of the sinus area. Hovelacque, Maes, Binet & Gayet (1930), and Code, Dingle & Moorhouse (1936), give details of the innervation of the sinus area in dogs, and the first-named authors also refer to the anatomy in man (see also Delmas & Laux, 1933).

The Common Carotid Baroreceptor Areas

Green (1953, 1954) has described a baroreceptor area in the common carotid artery at the level of the superior thyroid artery. This area is supplied by a vagal branch which Green named the "common carotid nerve". This nerve usually emerges from the baroreceptor area close to the origin of the dorsal muscular branch, opposite to that of the superior thyroid artery, and courses separately from the vagal trunk until it joins the nodose ganglion. Occasionally the common carotid nerve joins the aortic nerve or the superior laryngeal nerve. The accompanying figure (Fig. 4) shows the course of this nerve. In addition Green (1954, 1956) has described several other sites of baroreceptor endings in the wall of the common carotid artery between the level of the superior thyroid artery and the subclavian bifurcation (Fig. 4). These areas are supplied by nerve fibres which join to form the aortic nerve on the right side. Similar areas exist on both sides of the neck in the cat. Green found these areas by testing all nerve twigs emerging from the wall of the common carotid artery for signs of impulse activity. This electroneurographic

method should prove of great use in future investigations of this nature. By perfusion of this segment of the carotid, Green was able to show that the baroreceptor areas exerted reflex effects on the circulation and respiration similar to those evocable from the carotid sinus and aortic arch.

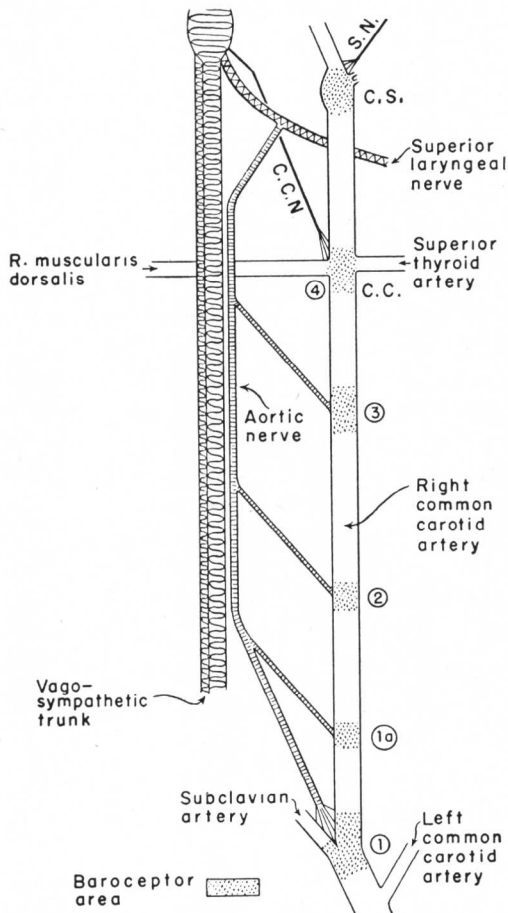


FIG. 4. Diagram shows relative positions of baroreceptor areas associated with the cat's right common carotid artery. Area 4 (C.C.) is the common carotid baroreceptor area with its baroreceptor nerve (C.C.N.), and is also present on the left side. The nerves from areas 1, 1a, 2 and 3 form the right aortic (depressor) nerve; the left aortic (depressor) arises from the aortic arch. C.S. = carotid sinus baroreceptor area. S.N. = sinus.—(J. Boss and J. H. Green (1956) *Circ. Research*, 4, 12).

Boss & Green (1956) reported on the histological features of the arterial wall in these baroreceptor areas. The great advantage of these sites is that with the exception of the so-called "common carotid area" the arterial wall structure is not complicated by the presence of branches. The nerve fibres tended to enter the arterial wall on one side and then ramified in the inner adventitia, the innermost nervous structures being situated immediately next to the outermost part of the media. The mass of nervous structures was thus applied to the outer aspect of the media on the side corresponding to the entry of the nervous trunk, and such a mass extended around the artery for about one-third of its circumference. The following characteristics distinguished the arterial walls in these areas: (1) there was less muscle in the media, (2) the elastic tissue of the media was less corrugated in section, (3) there were sometimes fewer elastic laminae in the media.

Baroreceptors of the Aortic Arch

Cyon & Ludwig (1866) believed the depressor nerve described in the rabbit by Theile (1825) arose from cardiac receptors. Roever (1869), Wooldridge (1883), Kazem Beck (1888) and Smirnow (1895) claimed that some endings at least occurred in the aortic arch, whereas Köster & Tschermak (1902, 1903) localised the receptors in the aortic arch and its immediate thoracic branches and stated that cardiac endings of this nerve were not found (von Schumacher agreed, 1902). Tello (1924) showed in mouse embryos that the left aortic (Wooldridge, 1883) or depressor nerve endings were confined to the region of the aortic arch. The right aortic nerve, on the other hand, arose from the subclavian-carotid angle and the neighbouring part of the brachiocephalic artery. In embryos of

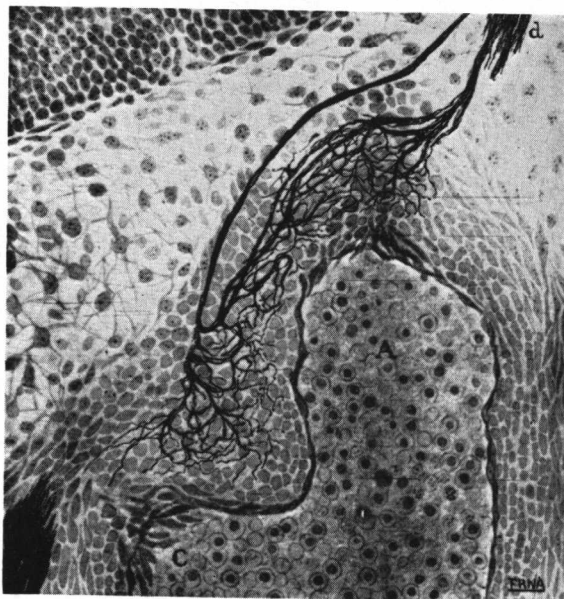


FIG. 5. Endings of the aortic nerve in the embryo (12 mm.) of a white mouse. d = Aortic nerve. A = Aorta.—(J. F. Tello (1924), *Trab. Lab. Invest. biol. Univ. Madr.*, **22**, 295).

4 mm. the fourth branchial arch lay close to the nodose ganglion, being almost surrounded by the superior laryngeal nerve. At the 12 mm. stage the migration of the arch system towards the thorax was accompanied by the appearance of the adult aortic nerve formed from a branch of the superior laryngeal nerve (Stelling, 1867; Finkelstein, 1880; Sarkar, 1922; Perman, 1924). The nerve endings were shown to be distributed throughout the circumference of the newly formed aortic arch (Fig. 5). For details of the histology of the endings of the depressor see Abraham, 1945, 1949b, 1953, 1955.

In the adult dog, cat or rabbit the aortic nerve is most easily located by defining its junction with the superior laryngeal nerve at the angle between the latter and the vagal trunk. In the rabbit the aortic nerve is separate in the neck. In the cat this is commonly the case although the separate nerve is bound together with the underlying vagus "in eine gemeinsame Scheide" (Bernhard, 1868). Green (1954) has recently shown that baroreceptor areas in the common carotid artery are supplied by thin branches from the aortic

nerve. The general anatomy of the aortic nerve in the monkey is similar to that in the cat. In the dog and in man the aortic nerve, identified by its junction with the superior laryngeal nerve, is rarely separate in the neck from the remainder of the vagal fibres.

In amphibia the nerve is never separate from the vagal trunk except presumably at its ending in the arterial wall (Nikoforowsky, 1912-13; Kuno & Brücke, 1914; Neil, Ström & Zotterman, 1950). In reptiles the nerve passes as a long thin filament throughout the length of the vagus from the region of the heart (Gaskell and Gadow, 1883; Mills, 1885; Mills & Kronecker, 1885).

Tigerstedt (1923) and Koch (1931) should be consulted for literature on the comparative anatomy of the aortic nerves. Anufriew (1928) and Schurawlew (1928) give full accounts of the literature in studies on cats and dogs respectively. The left depressor nerve commonly leaves the vicinity of the vagus trunk above the annulus of Vieussens and passes behind or just lateral to the left common carotid lying in the lower third of its course anterior to the trachea. It reaches the anterior surface of the aortic arch between the origin of the brachiocephalic and left subclavian arteries.

For further details of the anatomy of the aortic nerves in mammals see Marmorstein (1929, 1933), Marmorstein *et al.* (1934), Hirohata & Hashimoto (1936). Velluda has given very full descriptions of the origin and course of the nerves in the rabbit (1927*a*), the dog (1927*b*) and in man (1928-9).

About 450 fibres of which two-thirds are myelinated are found in the aortic nerve of the cat (Agostoni *et al.*, 1957). The myelinated fibres have a bimodal distribution with peaks in the 2-4 μ and 8-10 μ diameter groups. Langley (1892) and Sarkar (1922) found myelinated fibres (4-8 μ) in the aortic nerve of the rabbit as well as non-myelinated fibres. The presence of myelinated afferents (A fibres) and non-myelinated afferents (C fibres) was inferred by Douglas, Ritchie & Schaumann (1956) from action potential studies of the aortic nerve in the rabbit.

CHAPTER 2

COMPARATIVE EMBRYOLOGY AND COMPARATIVE ANATOMY

The Morphology of the Baroreceptor Areas

EBERHARD KOCH (1931) brilliantly interpreted the significance of the anatomical sites of the baroreceptor areas in the mammal. He suggested that these sites were those which survived of the embryonic visceral arch vessels and argued that these arch vessels were all provided with corresponding visceral nerves in the embryo. Thus the carotid sinus being formed from the IIIrd arch should be innervated by the nerve supplying that arch, i.e. the glossopharyngeal, and the aortic arch being formed from the IVth visceral arch vessel should be innervated by a branch of the superior laryngeal nerve. He also drew attention to the vagal sensory innervation of the ductus arteriosus—a VIth arch structure.

There is now a great deal of positive evidence for Koch's hypothesis derived from studies of comparative anatomy, embryology and comparative physiology. Before this can be properly appreciated, however, it is necessary to consider the evolution of the visceral arches in the vertebrates.

The primitive chordate animals from which the vertebrates developed were "filter" feeders. Cilia, in their buccal cavity and pharynx, by their movement created a current of water which, entering the mouth, passed via the pharynx laterally through gill slits in the sides of the pharynx and the body wall. During this passage of water, filtering mechanisms in the gill slits strained off plankton and gaseous exchanges occurred in the gill capillaries.

With the development of the vertebrates from these simple chordate forms two major changes took place: (1) Important modifications occurred in the mouth region; as a result the animal was equipped for macro-feeding; (2) the increase of size resulting from macro-feeding was associated with further development of the respiratory function of the gills.

In contrast to amphioxus which possesses some 200 visceral clefts the higher vertebrates possess only 4–7. Each cleft develops as a pouch laterally from the pharynx to become continuous with the skin of the body wall. Necessarily these clefts divide the mesoderm of the body wall into a series of "visceral" arches of tissue lying between them. The generic terms "visceral arch" or "visceral cleft" are strictly accurate. Only if the sidewalls of the visceral clefts form respiratory gill filaments, however, is it correct to speak of them alternatively as "gill arches" or "branchial arches" (*branchiae* = gills). In the Agnatha, where no elaborate jaws are found, the visceral clefts and arches are seven in number, relatively unmodified in structure from that of the more primitive forms. However, with the evolution of the Gnathostomata, the first visceral cleft fuses with the mouth and the skeletal tissue of the first visceral (mandibular) arch is modified to form the jaw skeleton. The second visceral arch (hyoid) also becomes modified to give support to the jaw and loses its respiratory functions, except in the cartilaginous fishes in which it survives as a small circular opening (the spiracle) with an associated gill-like structure,

the pseudobranch. In bony fish the spiracle may be closed. In the Amphibia and Amniota the cleft and skeleton of the hyoid arch contribute to the formation of the middle ear. In fish and in Amphibian larvæ the last five visceral clefts develop gills, are respiratory in function and are therefore called branchial clefts. In the adult Amphibia and the Amniota the fate of the last five visceral clefts is complicated. From them arise the thymus, parathyroids and the ultimo-branchial bodies.

Blood Supply of the Visceral Arches

In primitive forms it seems probable that a blood vessel (aortic arch) ran in each visceral arch (caudal to the corresponding visceral cleft) from a median ventral aorta to the lateral dorsal aorta. Deoxygenated blood in the ventral aorta could thus be oxygenated in the gill capillaries stemming from the "afferent" arch vessel and then passed from these capillaries via an "efferent arch" artery to the dorsal aorta. In the Agnatha, where there is no complicated jaw apparatus and the visceral clefts are relatively unmodified, the arterial arches correspond to the above primitive arrangement. But in the dogfish (a *Gnathostome*) only six arterial arches develop. Of these the first arterial arch is modified on account of the specialisation of the related mandibular arch and the consequent loss of the spiracular (hyoid) cleft. Though the proximal part of the mandibular arterial arch disappears in all other Gnathostomata, in the dogfish the distal portion of the arch persists as the hyoidean artery. The remaining five arterial arches serve as branchial arteries and each comprises afferent and efferent vessels to and from the gills respectively.

In the larval frog (tadpole) again the first or mandibular visceral arch is incorporated in the jaw. The second or hyoid cleft develops into the middle ear and loses its corresponding aortic arch. The other four visceral clefts (3-6 inclusive) which develop gills possess arterial arches which supply blood to these gills. With the development of the adult frog the third arterial arch persists; its distal part runs into the dorsal aorta and becomes the internal carotid artery. The fourth arch persists as the systemic arch which joins the corresponding vessel on the opposite side to form the dorsal aorta. The fifth arch disappears. The sixth arch loses its connection with the dorsal aorta and supplies the lung and skin as the pulmo-cutaneous arch (see Marshall, 1893; Goodrich, 1930).

The Mammalia

In the early stage of development of the mammalian embryo there are two primitive aortæ which are continuations of the two endocardial tubes. Each of these vessels consists of a short ventral aorta, an aortic or visceral arch vessel and a descending aorta. Later the fusion of the cardiac tubes is accompanied by the formation of a single truncus arteriosus or "aortic sac" from the two ventral aortæ. In the mammalian embryo six pairs of aortic arches appear during development but are never present simultaneously (Fig. 6). The first two aortic arches are present together, stemming from the aortic sac, and join the dorsal aortæ; with the successive appearance of the third and fourth aortic arches the first and second aortic arches disappear. The segment of the dorsal aorta cephalic to the point of junction of the third aortic arch persists as the cranial end of the internal carotid artery. The third arch vessel itself forms the common carotid artery from its ventral part and buds off the external carotid artery. Distal to the external carotid bud, the dorsal part of the third aortic arch forms the origin of the internal carotid artery.

Meanwhile the fifth and sixth aortic arch vessels stem out from the aortic sac to join the dorsal aortæ. The fifth, like "a walking shadow, a poor player which struts and frets his hour upon the stage and then is heard no more" rapidly disappears. The sixth arch vessels each give off a descending branch to the developing lung bud. Development of the spiral bulbar septum into the aortic sac causes diversion of blood from the right ventricle into the sixth arch vessels, whereas blood from the left ventricle is pumped into the third and fourth arches.

The dorsal aorta between the junction of the third and fourth aortic arches degenerates in most Amniota (Sphenodon and many Lacertilia provide exceptions to this statement). This segment of the dorsal aorta is known as the ductus caroticus; its disappearance may

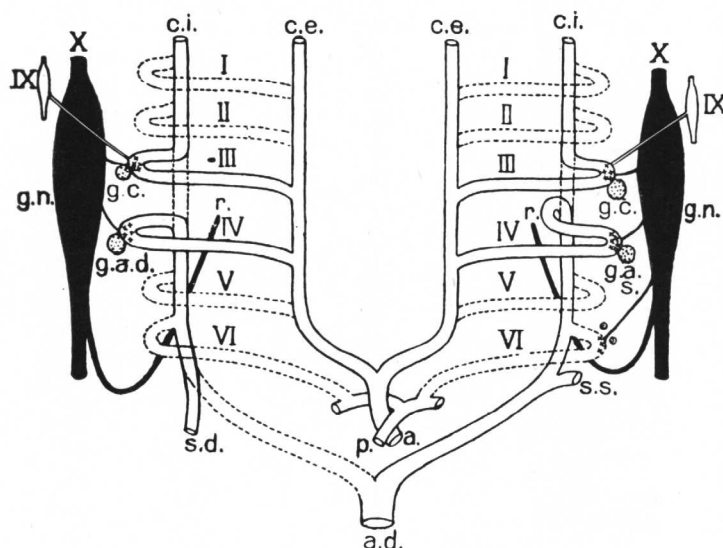


FIG. 6. Scheme of the innervation of the aortic arches in the mammal.

X = vagus nerve; IX = glossopharyngeal nerve; c.i. = internal carotid; c.e. = external carotid; g.c. = carotid glomus; g.a.d. = right aortic body; g.a.s. = left aortic body; r. = recurrent laryngeal nerve; s.s. = left subclavian; s.d. = right subclavian; a.d. = dorsal aorta. I, II, III, IV, V, VI = embryonic aortic arches; a = aortic arch; p = pulmonary artery; g.n. = nodose ganglion of vagus.—(G. Muratori (1937), *Arch. Ital. Anat.*, **38**, 387).

be related to the increasing encephalisation of higher forms and to the caudal migration of the heart which also accompanies the appearance of the embryonic neck (see Hamilton *et al.*, 1952; Arey, 1942).

The right dorsal aorta undergoes important changes in mammalia. The segment between its junction with the fourth right aortic arch and its junction with the left dorsal aorta, disappears. The right sixth aortic arch henceforth supplies only the developing lung bud and becomes the right pulmonary artery. The left dorsal aorta still makes connection with the sixth left aortic arch; that part of the sixth left arch between the left pulmonary artery and the left dorsal aorta persists until birth as the ductus arteriosus of Botallo (Fig. 7).

The left horn of the aortic sac and the left fourth aortic arch form the aortic arch