Rete Mirabile of Dolphin:
Its Pressure-Damping Effect on Cerebral Circulation

Abstract. *In the bottlenose dolphin* Tursiops truncatus, *a massive retial complex is interposed between the systemic and cerebral circulations at the cervicothoracic level. Pressure measurements in the retial efferent arteries supplying the brain revealed relatively nonpulsatile pressure profiles. These measurements in the anesthetized dolphin demonstrate the pressure-damping effect of the retia mirabile.*

Our interest in the great whales, dolphins, and porpoises centers primarily on the many adaptations and specializations which permit these air-breathing mammals to live in an exclusively aquatic environment (*1*). Physiological studies of the dolphin *Tursiops truncatus* have been facilitated by the development of a method of anesthesia (*2*) and of surgical techniques for investigating cardiovascular function (*3*). Using these methods, we have performed guided angiographic studies in the cervicothoracic vasculature (*4*) and coronary vessels (*5*); we have used cardiac catheterization to measure cardiac output, intracardiac pressures, and oxygen saturation in the heart and great vessels (*6*). The angiographic studies (*4*) demonstrated the afferent blood supply to the spinal retial complex and established that this system is the sole pathway for supplying blood to the brain. The spinal retial system is continuous with the thoracic retial system through the intervertebral foramina, and the thoracic rete fills from the posterior thoracic and intercostal arteries. We confirmed these findings by dissections and vascular casting techniques (*6*), establishing the anatomical basis of the hemodynamic findings presented here.

Since Tyson (*7*) first described the thoracic vascular complex, which has since been termed the rete mirabile, many authors have commented upon its gross and microscopic anatomy and have speculated on its function (*8–10*). Slijper (*11*) has pointed out that the rete mirabile is massive in most Cetacea and shows greatest development in the dolphin. As defined by the retial nomenclature advanced by Ask-Upmark (*12*), the cervico-thoracic rete in the dolphin is of the ambicentric type, possessing both afferent and efferent limbs. The predominant afferent vessels of the thoracic rete are the posterior thoracic and intercostal arteries. The efferent retial vessels consist of longitudinal arteries, the spinal meningeal vessels (*13*), which are formed by the confluence of the spinal retial vessels coursing in the epidural space. In the simplified vascular diagram (Fig. 1) certain aspects of this retial circulation can be seen. Instead of the usual arterial supply to a capillary bed and consequent venous drainage, the retial circulation represents an arterial supply diverging into innumerable smaller arterioles which again become confluent, forming the efferent arteries. This vascular system constitutes the sole blood supply to the brain; as judged angiographically, the internal carotid artery is not functional in this regard (*4*). The difficulty of carrying out physiological experimentations in the retia mirabile of the dolphin is due to the deep location of these structures, especially to their efferent arteries (Fig. 2) and to the surgical difficulties involved in exposing and cannulating particular vessels in this complex.

We anesthetized (*2*) two dolphins and cannulated the aorta through the external carotid artery (*3*). The efferent retial arteries were exposed through a dorsal laminectomy (*14*) and cannulated with a No. 14-gauge polyethylene catheter under direct vision. The catheters were connected to strain-gauge pressure transducers (*15*) for continuous recording of intravascular pressures (*16*), injection of radiopaque dye, and blood sampling. Measurements of oxygen tension, carbon dioxide tension, and *p*H of blood from the spinal meningeal vessels were identical with those of samples taken simultaneously from the aorta, confirming the arterial nature of these vessels. The tracing of pressure in the aorta (Fig. 3) has a configuration and magnitude similar to those found for other mammals. The pressure tracing obtained from the spinal meningeal artery, however, shows a marked damping and appreciable time delay presumably caused by the relatively long and tortuous course taken by the blood through the coiled retial arteries. In effect, the pulsatile pressure pattern obtained on the systemic arterial side (afferent) of the rete mirabile is transformed into a relatively nonpulsatile pressure pattern in the spinal meningeal (efferent) arterial limb.

Ask-Upmark (*12*) noted the extreme reticularization and arborization of the vessels in the retia of various animals and reasoned that there must be massive resistance offered to the blood stream by such a vascular structure. Our data shows marked damping and a relatively long time constant, indicating an increased capacitance or resistance offered by the thoraco-spinal retia. However, the small difference in estimated mean arterial pressures between the aorta and spinal meningeal artery would indicate an increased capacitance, not resistance. Ask-Upmark went on to list four hydro-

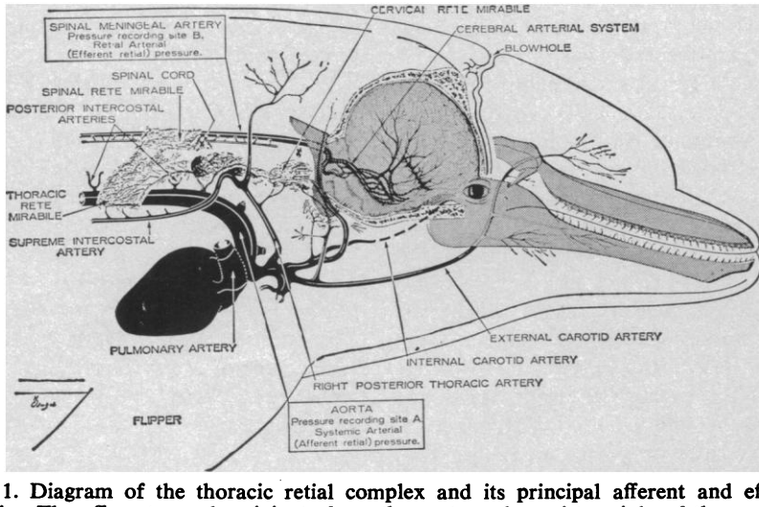

Fig. 1. Diagram of the thoracic retial complex and its principal afferent and efferent arteries. The afferent vessels originate from the aorta and consist mainly of the posterior thoracic and intercostal arteries and their branches. The efferent vessels are the spinal meningeal arteries which continue into the cranial cavity and supply the brain. Catheter *A* was placed in the aorta via the external carotid artery; it measures systemic (afferent) retial pressures. Catheter *B* was placed in the spinal meningeal artery after dorsal laminectomy; it measures efferent retial pressures. See Galliano *et al.* (*3*) for a more complete description of the thoracic vasculature.

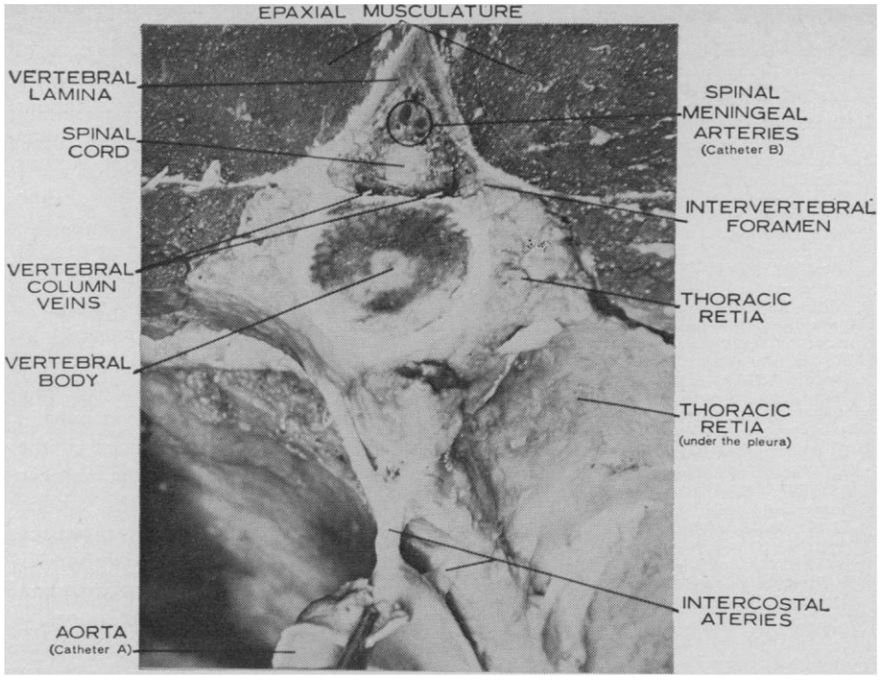

Fig. 2. Photograph of a frontal section of the dorsal body wall of the dolphin at the upper thoracic level, showing the location of the spinal meningeal arteries in the epidural space dorsal to the spinal cord. Note that the thoracic rete is supplied by the intercostal arteries (afferent vessels). The continuity of the thoracic retia with the spinal retia through the intervertebral foramen is shown.

dynamic factors that might be influenced by the interposition of a rete, including rapidity of flow, pressure of flow, storage of blood, and leveling of the pulse amplitude. Thus he correctly described the action of the retia mirabile in markedly modifying the contour of the pulse. One wonders whether his conclusion might not also be correct—namely, that the hydrodynamic effect of the retia mirabile would be to maintain arterial blood pressure to the brain at a convenient and fairly constant level. It is premature to accept this function as the sole purpose of this complex vascular organ; rather one should emphasize the three main possibilities considered by Ask-Upmark in regard to the function of the retia: (i) that the composition of the blood is changed during passage through a rete; (ii) that the rete influences cerebral circulation by means of vasomotor reflexes; (iii) that the rete is of mechanical importance for hydrodynamic management of the blood flow. Nakajima (*9*) conjectured, on the basis of anatomical observations, that the function of the retia mirabile is one of pressure adaptation during diving. Ivanova (*10*) feels that the retia mirabile in various aquatic mammals function in submergence and notes that the need for rapid redistribution of blood and temporary shunting out of a definite region from the general circulation is best carried out by a rete mirabile system. Such redistribution of blood may be accomplished by nervous control of this system; in our dissections we noted what appears to be an elaborate innervation to these retial vessels.

The finding of a relatively nonpulsatile arterial supply in the dolphin may have its correlate in certain extracorporeal perfusion circuits presently used in the performance of open heart surgery in man. Many of the pumps commonly used in such surgery offer a relatively nonpulsatile output, and the presence, absence, or contour of such pulsations may have a definite effect on renal physiology (*17*). Wilkens *et al.* (*18*) recently reviewed the importance of pulsatile blood flow and felt that available data indicated that "nonpulsatile" flow may produce physiologic disturbances such as metabolic acidosis, decreased oxygen consumption, and loss of vasomotor control. It is evident that they did not consider aquatic mammals in their discussion of the phylogenetic significance of pulsatile blood flow. Our finding of a markedly damped (nonpulsatile) cerebral arterial supply in the anesthetized dolphin challenges their general hypothesis and offers a physiological model to workers in the field of extracorporeal circulation techniques.

In the dolphin the cerebral circulation has been "isolated" from the remainder of the arterial system by interposition of a massively developed rete mirabile. One effect of this vascular organ is to markedly alter the arterial pressure profile in the thin-walled longitudinal vessels which supply the brain with blood. We feel that the function of this system with its very high capacitance and its special pulse amplitude-leveling characteristics warrants additional investigations.

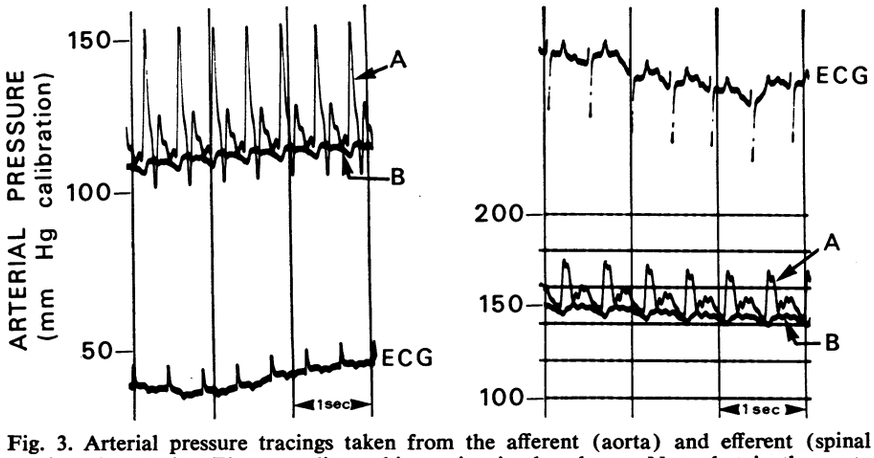

Fig. 3. Arterial pressure tracings taken from the afferent (aorta) and efferent (spinal meningeal) arteries. Electrocardiographic tracing is also shown. Note that in the aorta (*A*) a high pulse pressure is seen [approximately 50 mm-Hg in animal 1 (left) and 30 mm-Hg in animal 2 (right)] whereas in the spinal meningeal artery (*B*) the pulse pressure is only 5 mm-Hg in animal 1 and 6 mm in animal 2. In both animals all pressure measurements were made with slightly under-damped catheter-transducer systems so as to maximize pressure pulsations.

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Puromycin: Action on Neuronal Mitochondria

Abstract. *Puromycin, in dosages that inhibit cerebral protein synthesis and expression of memory in mice, produces swelling of neuronal mitochondria. Acetoxycycloheximide, which inhibits cerebral protein synthesis to the same extent as puromycin, fails to produce swelling of neuronal mitochondria. Puromycin and heximide mixtures produce severe inhibition of protein synthesis, but result in a minimal swelling of neuronal mitochondria and in a decrease of peptidyl-puromycin complexes to a level of 30 percent of that following the injection of puromycin alone. It is concluded that swelling of neuronal mitochondria in the presence of puromycin is not due to inhibition of cerebral protein synthesis per se, but is related to a specific action of puromycin on ribosomal protein synthesis. The findings are consistent with the hypothesis that peptidyl-puromycin complexes are responsible for mitochondrial swelling.*

A previous ultrastructural study showed that intracerebral injections of puromycin, in dosages that suppress expression of the memory of maze-learning in mice, produce extensive swelling of mitochondria in neuronal perikarya and dendrites (*1*). Although no experiments were performed to investigate the mechanism of the action of puromycin on these mitochondria, it was suggested that peptidyl-puromycin complexes, by-products of the action of puromycin on ribosomal protein synthesis, could be responsible for the observed changes. Furthermore, it was pointed out that understanding of the mode of action of this antibiotic on mitochondrial membranes might contribute to an understanding of its assumed effect (*2*) on other cytomembranes, yielding further insight into its effect on memory.

The present ultrastructural and biochemical study was undertaken to investigate the mechanism of the mitochondrial swelling in the presence of puromycin. The following three possibilities have been tested: (i) The swelling is caused by some unknown cytotoxic action of puromycin unrelated to the inhibitory effect of this drug on protein synthesis; (ii) it is secondary to inhibition of protein synthesis per se; or (iii) it is specifically related to the particular mode of action of puromycin on ribosomal protein synthesis.

For ultrastructural study, three mice were injected bitemporally with a mixture containing 90 μg each of puromycin and acetoxycycloheximide; three others were injected with 90 μg of heximide alone, and four control animals were injected with saline. The heximide was used because, when administered alone, it inhibits cerebral protein synthesis at least as extensively as puromycin does (*3*), but by a different mechanism (*4–6*), while in combination with puromycin it inhibits the formation of peptidyl-puromycin complexes (*7*). Some of the mice from each group (those treated with puromycin, a puromycin-heximide mixture, and controls) were killed 7 to 10 hours after injection; the others were killed 18 to 19 hours after injection. Details of the various procedures have been reported previously (*1*, *8*).

Swelling of mitochondria was not observed in the mice treated with heximide. Swollen mitochondria were present after injection of the puromycin-heximide mixture (Fig.1A), but the incidence of swelling was definitely lower than it was after puromycin alone. There was disappearance of the matrix and diminution of the number and length of the cristae of the swollen mitochondria; these changes produced by the mixture were qualitatively similar to those observed after administration of puromycin alone. As with puromycin alone, the abnormal mitochondria were seen mainly in neuronal perikarya or, more rarely, in dendrites. Swollen mitochondria were not seen in axons, presynaptic endings, or glial cells; they were more numerous 18 to 19 hours after injection of the puromycin-heximide mixture than 7 hours after. No more than three abnormal mitochondria per section of neuronal perikaryon were ever observed, while 19 hours after administration of puromycin alone the great majority of the mitochondria of the perikarya and dendrites were swollen (Fig. 1, A and B). Furthermore, the number of neurons with abnormal mitochondria was very small compared with the number found after puromycin alone.

The ribosomes of neuronal perikarya measured about 250 Å in diameter and corresponded in size and number to those of the control animals. Unlike the results observed after the administration of puromycin alone (*1*), disaggregation or abnormal aggregation of polysomes was not observed in either group of mice treated with heximide or with the puromycin-heximide mixture. This finding agrees with the results of biochemical studies in vivo (*7*) and in vitro (*4*), showing that cycloheximide [which has a common mode of action with heximide (*5*)] does not disaggregate the polysomal complexes and partially protects them from the disaggregation caused by puromycin (*7*, *9*).

The amounts of peptidyl-puromycin were investigated in one series of 11 mice that received bitemporal injections of 90 μg of puromycin and in a second series of 5 mice injected bitemporally with a mixture of 120 μg each of puro-