Central Lymph Propulsion

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Summary

Dissections reveal that each lymphatic organ characteristic of species is supplied with lymph hearts, smooth muscles, or striated muscles whose contractions (along with transmitted arterial pulsations and changing gravitational forces) coordinately propel lymph centrally during breathing, swallowing, food absorption and joint flexion. In aquatic vertebrates and amphibians lymph hearts, closely related to the gills, propel central lymph into the jugular veins. In aerial vertebrates with well-developed lungs, the striated muscles which enable ventilation, propel central lymph into large veins coursing through the thoracic inlet at rates commensurate with oxygen consumption under normal conditions.

Opportune gravitational forces, transmitted arterial pulsations, many forms of skeletal muscular activity and tonic contractions of the smooth muscles in vessels combine to propel lymph centrally via valved lymphatics and paired sets of central lymph ducts into the blood circulation of vertebrates (1—2). However, in phyla or species lacking discrete lymph hearts (especially birds and mammals), central lymph propulsion becomes complicated because organized lymphatic tissues (such as thymus glands, avian cloacal bursae, tonsils, nodes, intestinal lymphatic tissue) with relatively permeable, valveless lymph sinuses develop to interrupt the peripheral to central flow of lymph (1—2). Along with the connecting lymphatics (2), such lymphatic organs develop *in situ* from periarterial mesenchyme (2—6) to produce lymph (7—8) and filter or process peripheral lymph which emanates from nearby distal or remote ramifying arterovenous capillary circuits supplying parenchymal cells (1—2, 7). Central lymph, then, becomes a mixture of filtered, variably processed peripheral lymph with lymph produced in the lymphatic organs through the release of

small cytoplasm-depleted lymphocytes into colloidal hydrosols resulting from cytoclasmosis (i.e. cytolysis and dissolution of ectoplasm extruded from larger lymphocytes and other relatively large mononuclear cells growing in each lymphatic organ [8]). The purpose of this communication is to analyze how each lymphatic organ characteristic of species is endowed with striated or smooth muscles to enhance central lymph propulsion.

Material and Methods

The lymphoid and lymphatic tissues of cartilagenous fish (3 mosquito-fish), bony fish (3 gold-fish), amphibia (3 Rana pipiens, 3 Xenopus laevis, 1 Hyla regilla — tadpole and adult), reptiles (3 Cyclemis dentata — a fresh water turtle), birds (30 Pekin ducks, 12 mallards, 12 white leghorn chickens, 12 white King pigeons, 2 mourning doves, other accidentally killed birds, including finches, towhees, hummingbirds), mammals (8 rats, many humans recounted elsewhere [7]) of varying, but known ages and nutritional status were dissected — either by stepped serial microscopic sections from head to tail in small animals, or surgical dissection under anesthesia in large ones, followed by serial light and, often, electron microscopic sections. Special attention was directed toward muscles within or surrounding the organized lymphoreticular tissues, as well as the feeding, breathing and locomotor habits of the species dissected.

Observations

1. The organized lymphoreticular tissues (reticular connective tissues supporting dividing lymphocytes) were found distributed as shown in Table 1 (a composite based on personal ex-

Table 1 This table compares hemopoietic activity in the reticular connective tissue of different organs in the same species, and in species representative of different phyla. (– = organ absent or hemopoietic activity microscopically absent within the organ; LR = lymphoreticular stroma with predominant lymphocytopoiesis; LRM = lymphoreticular stroma with predominant myelopoiesis; R-E = stroma primarily reticulo-endothelial; G = functional gill; ? = not dissected or insufficient information)

				Hemopoiesis in adults of different phyla						
	Sponges	Coelenterates	Worms Insects	Cyclostomes	Fish	Bony & Lung Fish	Amphibia	Reptiles	Birds	Mammals
Nodes	–	–	–	–	–	–	(Hemal) LRM	?	(Rudimentary)	LR
Marrow	–	–	–	–	–	–	LRM	LRM	LRM	LRM
Cloacal Bursa	–	–	–	–	–	–	–	– or G	LR	–
Thymus	–	–	–	–	G	LR	LR	LR	LR	LR
Liver	–	–	–	–	← R-E + season & age variable LRM →	LR	LR	LR	R-E	R-E
Kidneys	–	–	–	–	LRM	LRM	(Hibernal/–) LRM	–	–	–
Spleen	–	–	–	LRM	LRM	LRM	LRM	LR	LR	LR
Intestine	LR	LR	LR	LRM	LRM	LR	LR	LR	LR	LR

perience and that of *Jordan* [9] to include the invertebrates).

2. *Thymus glands* were not identified by serial sections from head to tail in mosquito-fish, which respire exclusively by gills. In gold-fish, which facultatively respire above warm or stagnant water by gulping air, discrete paired lymphoepithelial thymus glands were found medial to the gills and surrounded by a thin continuous layer of striated muscle cells. In the amphibia, during metamorphosis, paired lymphoepithelial thymus glands were found just caudal to the eyes variably stranded from the middle gill pouches, and, after metamorphosis, surrounded by crossing bundles of striated muscle cells which move the gullet. In adult turtles discrete, paired lymphoepithelial thymus glands were found beneath the clavicles near the superior caval insertion of the jugular veins and found to contain relatively large numbers of myoid cells surrounding intrathymic sinuses (Fig. 2, inset). In all birds sampled, five discrete paired lymphoepithelial thymus glands were found superficially, lateral to the relatively long trachea, along the entire course of the neck (10). The avian thymus glands seldom contained striated muscle cells, and were not surrounded by muscular tissue. When striated myoid cells were found, their cytoplasmic processes related closely to intrathymic lymph sinuses (Fig. 1). In the mammals dissected, single lymphoepithelial thymus glands normally without contained or immediately surrounding striated muscle cells were found extending below the clavicles and sternum into the anterior mediastinum. Although intrathymic myoid cells have been reported in human thymomas, none were found by light or electron microscopy in more than 100 mammalian glands studied, including six benign thymus glands removed during the surgical treatment of myasthenia gravis in humans (11).

3. *Cloacal bursae* were not identified in the fish, frogs or mammals sampled, but uniformly were found opening into the cloaca just distal to the ureteral orifices in the turtles and young birds. Striated muscles (such as those in the turtle thymus) and smooth muscles (such as those in the gastrointestinal tract) were not found in the turtle or avian bursae; but in all,
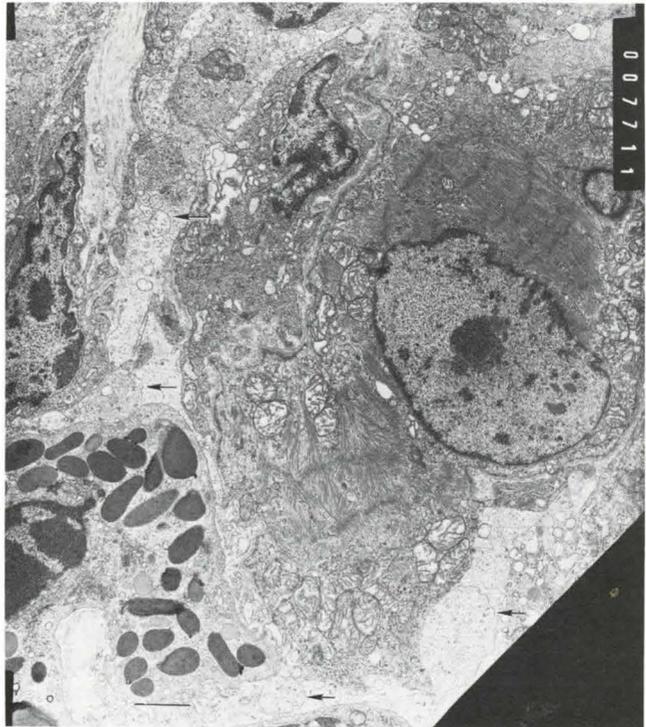
Fig. 1 Thymus from a 3-week old Pekin duckling X5600. A myoid cell with an ovoid nucleus and striated myofibrils in the cytoplasm. Like cardiac muscle cells which propel blood, such myoid cells lack skeletal or ligamentous attachments and apparently develop from mesenchyme to function as lymph hearts propelling lymph from sinuses (2). Note that the sinus to the left and below contains a granulocyte and several cytoplasmic fragments extruded from thymocytes (arrows)

the bursal openings into the cloaca were found invested in striated muscles continuous with those of the levator ani and anal sphincter mechanism (Fig. 3). (It will prove pertinent to the ensuing discussion to note that the internal anatomy of the fresh water turtles and birds dissected is remarkably similar. Age and species variations in the bursae and thymus glands are recounted in detail elsewhere [10, 12]. Aside from the cloacal bursae, common anatomic features include relatively long retractible necks; long redundant tracheae; membranous, instead of muscular diaphragms; and relatively rigid thoraces which cover all of the trunk in turtles and most of the trunk in birds [especially strong fliers].)

4. *Adenoids, palatine tonsils, lingual tonsils* and less organized lymphoreticular tissues which constitute Waldeyer's oropharyngeal ring were always found immediately supported by striated muscles which contract during the act of swallowing in all species. Of course in fish, frogs and turtles, such lymphatic tissues appeared poorly developed, especially in fish and turtles which feed under water. In all birds sampled, the palatine tonsils appeared well-developed three to six weeks after hatching. In rats and humans the tonsils appeared well developed after weaning.

5. *True lymph nodes* were not identified in the fish, frogs or turtles sampled. Rudimentary lymph nodes without penetrating or central lymph sinuses were found occasionally by serial sections of the neck in pigeons (10). In the mammals sampled, lymph nodes appeared increasingly developed until puberty and were found either superficial or deep. The deep nodes were found beside large arteries with generous pulsations in living animals, such as the aorta, carotids, subclavians, axillary, brachial, mesenteric, iliac and popliteal arteries. The superficial nodes were found clustered alongside arteries where joints flex, as in the axillae, elbows, groins, popliteal spaces and under the mandible.
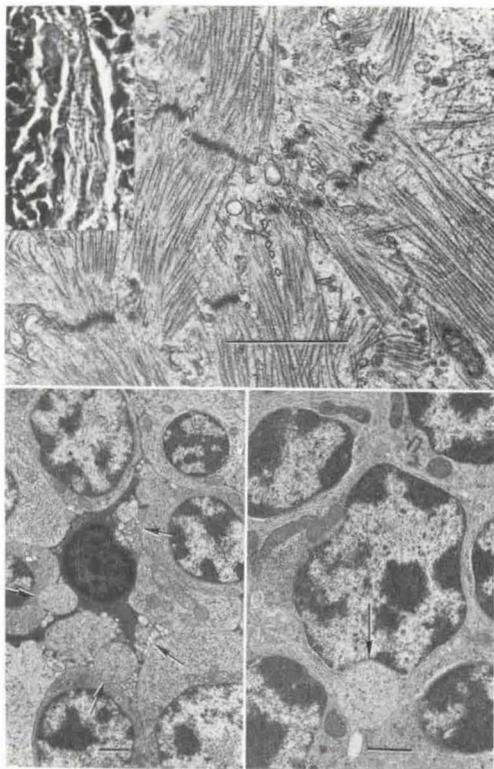
Fig. 2 The inset (above) shows several myoid cells bordering portions of lymph sinuses in a fresh water turtle thymus (under phase microscopy X400). The remainder of the microscopic field (above) shows actin bands in the relatively disorganized, interlacing myofibrils of a myoid cell in a duckling thymus. Like the lymph hearts in general, such cells normally disappear shortly after hatching (2).
Below, a young rat thymus on the left and a duckling thymus on the right, showing potential thymocytic sources of extruded ectoplasmic fragments in thymic lymph sinuses

6. *Intestinal lymphatic tissue* was found to develop incrementally to support the gut epithelium after the onset of oral feeding in all species studied, and appeared diffuse with increasing nodularity in higher phylogenetic orders. In the diffuse intestinal lymphoreticular tissue, lacteals were found parallel to and partially surrounded by bundles of smooth muscle cells in the intestinal villi (Fig. 4); while deeper lymphatics were found parallel to the muscularis mucosa throughout the gut. The nodular and diffuse intestinal lymphoreticular

tissue, both were found completely surrounded by layers of longitudinal and circular smooth muscle cells which form the outer muscularis, and which engender peristalsis during the absorption of food.

7. *Organized lymphoid tissues,* such as the spleen, hemal nodes and periarteriolar lymphoreticular tissue of the marrow – all of which normally lack afferent lymphatics and are relatively devoid of efferent lymphatics – were distributed in various species as shown in Table 1. Such lymphoid tissues were generally found lacking in contained, or immediately surrounding striated or smooth muscle cells (other than those constituting the relatively prominent muscularis of arteries and veins contained). The hemal nodes and spleen appeared well circumscribed by relatively thick fibroelastic capsules; whereas the periarteriolar lymphoreticular tissue of marrow was contained by bones to which striated muscles attach. In all these lymphoid tissues arterovenous sinusoids appeared relatively prominent, and appeared the predominant means of egress of newly formed lymphoid and/or myeloid elements.

Discussion

These observations suggest that the organized lymphatic tissues characteristic of species (or phyla) are each naturally endowed with intrinsic or extrinsic muscles whose intermittent contractions (along with arterial pulsations and changing gravitational forces) may propel lymph centrally during increased functional activity of the tissue with which each is associated.

For instance, the *intestinal lymphoreticular tissue* supports the intestinal epithelial cells throughout the gut, the lacteals in the small intestine, and resides between the muscularis and intestinal epithelium in all thriving species. During the absorption of food, smooth muscle cells in the diffuse lymphoreticular tissue supporting the villi may contract to foreshorten the villi and thus expel lymph toward the muscularis mucosae where smooth muscle cell contractions may propel lymph laterally or longitudinally in relation to the long axis of the gut. Simultaneously, the circular and longitu-

Fig. 3 A longitudinal section of a duckling cloacal bursa close to the cloacal orifice (on the right). The bursa contains no mucosal muscularis and no enveloping smooth muscle tunic. Instead, the posterior aspect of the bursa (below) rests on striated muscles forming portions of the levator ani and anal sphincter

Fig. 4 A cross-section of a rat small intestinal villus X3300. The intestinal epithelium (left) is separated from the lacteal (right) by diffuse lymphoreticular tissue containing a small blood vessel (low left). The lacteal is longitudinally surrounded by separate bundles of smooth muscle cells cut in cross-section. The arrow marks some tiny cytoplasmic fragments in the interstices. (Such cytoplasmic fragments differ from chylomicrons in that they contain ribosomes showing varying degrees of dispersion or disintegration [8])
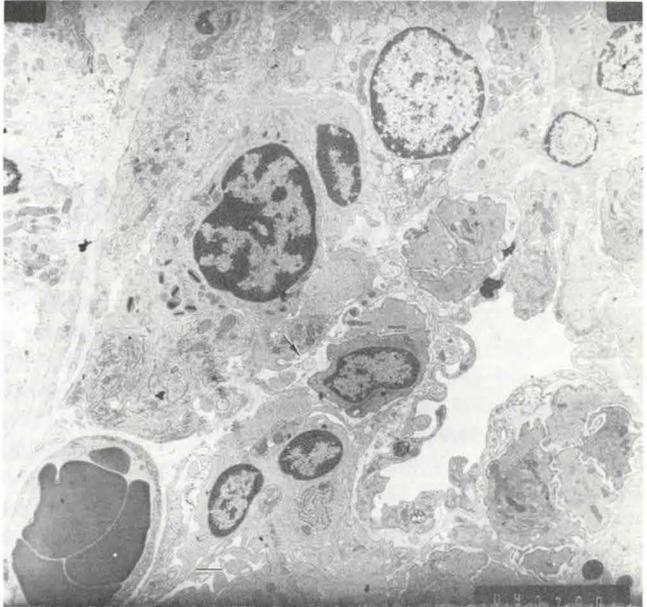
dinal muscles of the outer muscularis may contract to produce peristalsis which not only propels liquified, partially digested food down the gut lumen, but also compresses all gut structures in between. Liquids being incompressible, a result must be the expulsion of intestinal lymph centrally into mesenteric lymphatics via the periarterial lymphatics which penetrate the outer muscularis, along with the entering arterial supply. Increased pulsatile mesenteric arterial blood flow during absorption will correspondingly increase central flow via the mesenteric lymphatics and/or intervening nodes (especially during digested protein absorption [13]).

The *periarterial lymphatics* throughout the body and deep *truncal lymph* nodes of mammals would appear largely dependent upon the pulsations of relatively large adjacent arteries for compression and lymph expression (1).

However, with exercise the *superficial nodes,* in addition, may be compressed intermittently by flexion of striated muscles spanning joints hinging about nodal clusters.

The *ring of organized lymphatic tissues* which develops to invest invaginating epithelial cells derived from the first and second gill pouches (3) is encased with striated muscles which contract from above downward during the act of swallowing food or secretions. Compression of such organized lymphatic tissues during the act must result in the expulsion and central propulsion of lymph.

The *thymus glands* of aerial vertebrates develop through lymphoreticular investment of invaginating third or fourth gill pouch epithelium (3, 12, 14), as the gills become vestigial and the lungs develop during embryogenesis (or metamorphosis). Depending on the breathing habits (and age) of the species selected, the lymphoepithelial thymus glands show remarkable variations in size, location and muscular investment. In bony fish, such as goldfish (which facultatively respire by gulping air above stagnant water, but usually respire by gills [15]), the thymus glands are surrounded by striated muscles next to the gills in the cervical region. In young adult amphibia, such as Hyla regilla (which breathe mainly by pharyngeal respiration involving movements of the gullet [16]), the thymus glands are surrounded by crossing bundles of striated muscles which enable gulletal movements. In fresh water turtles, such as Cyclemis dentata (which breathe mainly via lungs encased in a rigid shell lacking a muscular diaphragm; and facultatively breathe under water via cloacal pouches described elsewhere [10, 12] and below), the thymus glands under the clavicular insertions contain myoid cells surrounding lymph sinuses like lymph hearts (Figs. 1−2). In young mammals, such as rats and humans, the intrathoracic thymus glands (lacking myoid cells and immediately surrounding striated muscle cells) are decompressed during inhalation by the concerted actions of intercostal muscles and diaphragms; and compressed during exhalation between the sternum, pulsating heart and contracting lungs. With the possible exception of the turtle, in each instance the lymphoepithelial thymus glands (containing epithelia vestigially concerned with aquatic respiration) are phasically pumped to expel and propel central lymph by striated muscles (commonly innervated by the third of fourth cervical segments [2]) which enable aerial respiration.

The thymus glands of birds seem exceptional in that they are scattered along the course of a relatively long neck, do not become intrathoracic, and normally lack surrounding or contained striated muscles. Watching birds feeding or flying, it seems likely that their thymus glands and efferent lymphatics are drained by gravity, especially during undulent neck movements which enable swallowing or with countergravitational movements engendered by wing-thrust during flight. (In their adaptation to flight with relatively rigid thoraces without muscular diaphragms, most species of birds are endowed with relatively long, heavily muscled clavicles whose depression [translated to the wings] supply antigravitational thrust; and whose elevation by air buoyancy [between wing-thrusts] creates negative intrathoracic pressure to increase inflation of the lungs [17−18], and secondarily create relatively negative central venous pressure at the thoracic inlet. Pulmonary ventilation and [theoretically] central lymph flow may be increased twenty-fold during flight in this manner [17−18].) Thus, in flying birds it would appear that the same striated muscles which increase respiration, also enhance central lymph propulsion from the thymus glands and other cervical lymphatic organs.

Cloacal bursae are peculiar to most, if not all, species of birds which naturally fly (14, 17), a few species of turtles accustomed to submerging in cold water (19, 20) and some species of monotremes (21). Disregarding the feathers, shells or fur − the internal anatomy is quite similar, especially with respect to a single vent for the genital, urinary and digestive organs; and a relatively long neck. Whereas the birds naturally migrate to escape winter; the turtles submerge. In such turtles, such as Cyclemis dentata and the almost extinct green sea turtles, the paired cloacal bursae are filled with water and emptied through the actions of the

anal sphincters during cloacal respiration (19, 20) which permits the turtles to hibernate submerged in ice-covered or cold water (19). The homologous, single avian cloacal bursae of Fabricius or "cloacal thymus" variably invested with lymphoreticular tissue (10, 14) seems useless for breathing, but is filled with liquid cloacal contents and emptied in synchrony with respiration (22). Lacking intrinsic smooth or striated muscles (Fig. 3), it is not certain whether such respiratory excursions in the bursa reflect the lack of muscular diaphragms in birds and turtles with relatively extensive, rigid thoraces; the independent actions of the anal sphincters (or both). Nevertheless, changes in intrabursal pressure synchronous with respiration may explain how the avian bursal lymphoreticular tissue is compressed and central lymph expressed. (The avian bursa's role in migration seems obscure, but such phasic respiratory linkages in the cloacal bursae and cervical or intrathoracic thymus glands of all aerial vertebrates may have profound physiologic and clinical implications [7, 12] – particularly when one recalls that the invaginated, erstwhile respiratory epithelium develops to produce lymphotrophic hormones, such as thymosin [7, 23] or bursopoietin [24]; and the investing bursal and thymic lymphoreticular tissue undergo parallel involution with age [7, 14, 25] and sudden involution with stress [such as anoxemia, cold exposure, starvation, infection] to release through cytoclasmosis the lytic or extruded ectoplasmic products of lymphocytes [7, 8, 25–27] centrally for definable trophic or bioenergetic purposes [7].)

Cogent to lymphoreticular development and the central disposition of lymph is that all vertebrates develop gills and lymph hearts under the gills to propel lymph into branches of internal jugular veins during early embryogenesis (2). In fish and amphibia relatively large, paired anterior lymph hearts persist under the gill residua; but the lymph hearts disappear as the lungs develop in reptiles, birds and mammals (2). In addition, most species of vertebrates transiently develop posterior lymph hearts under the sacrum to propel lymph into sacral veins (2). Relatively large posterior lymph hearts persist throughout adult life in many species of amphibia, in all species of reptiles and some birds which do not fly (such as ostriches) (2). The posterior lymph hearts disappear in most species of birds which fly, and are absent after birth in mammals (2). More or less where the principal anterior lymph hearts disappear, appear the thymus glands of all aerial vertebrates; and, later, where the principal posterior (sacral) lymph hearts disappear, appear the avian cloacal bursae – as the swimming progeny lose their gills and become adapted with limbs and lungs to emerge (usually) head-first from aquaeous media, such as ponds, eggs or intrauterine liquors. When pulmonary respiration actually commences after metamorphosis, hatching or birth, the striated muscles which create the negative intrathoracic pressure to suck air take the place of anterior lymph hearts by creating relatively negative central venous pressure at the thoracic inlet to suck lymph into the blood circulation via the jugular or subclavian veins during inhalation. Conversely, during exhalation when intra-thoracic pressure rises with muscular relaxation to approach or (with forced expiration) exceed ambient atmospheric pressure, the results will be to expel the liquid contents of the thymus, pulmonary lymphatic system and thoracic ducts centrally via valved lymphatic channels. Thus, any muscular or metabolic activity which increases the respiratory excursion or rate (such as flexing the extremities, swallowing or absorbing food) will not only increase lymph propulsion from the working part, but also enhance the disposition of central lymph into the blood circulation in proportion to the increase of oxygen consumption necessary for the work performed under normal aerobic conditions. (Under relatively anaerobic or anoxemic conditions, the compensatory roles of the thymus glands, avian cloacal bursae and other organized lymphatic tissues are explored elsewhere [7].)

Summary and Conclusions

These data indicate that each kind of organized lymphatic tissue (Table 1) which develops from periarterial mesenchyme (2–10) to interrupt the central flow of lymph (1) and mediate

absorption or resorption (1, 7) from adjacent or distally located parenchymal tissues of a given vertebrate is supplied with a myoid lymph heart (Fig. 1–2), striated muscles (Fig. 3) or smooth muscles (Fig. 4) whose co-ordinated actions aid the central propulsion of lymph filtered (1) or produced locally by cytoclasmosis (7–8) – especially during increased functional activity, such as absorbing food (in intestinal lymphatic tissue), swallowing (in pharyngeal lymphatic tissue), exercising joints (in the case of limbal nodes) and expiring air (in the case of the thymus and avian cloacal bursae whose epithelia are derived from vestigial gill pouches). Whereas lymph hearts, close to the gill pouches, develop in fish .and amphibia to pump this central lymph into jugular veins (2); in aerial vertebrates with elongated necks and well-developed lungs (excepting turtles with relatively rigid thoracic and abdominal walls) the striated muscles which enable ventilation (through changing intra-thoracic and intra-abdominal pressure) reciprocally suck the central lymph into central veins, and propel central lymph cephaled from lymphatic organs located caudally. After central venous pooling, mixing in the superior or right cardiac chambers, and aeration in the gills or lungs (along with the pigmented products of lymphomyeloid organs and de-pigmented products of the liver gaining access to the blood circulation directly through artero-venous sinusoids) the absorbed or resorbed, aerated composite is distributed efficiently by the inferior or left cardiac chambers via arteries for the oxidative, nutritive and immunologic benefit of all tissues characteristic of species. Of course, in mammals (especially upstanding primates with relatively high metabolic rates), the diaphragm serves as a relatively strong, single "lymph heart" whose contractions during inspiration create positive intra-abdominal pressure to pump lymph from visceral and periaortic lymphatic tissues via the cisterna chyli into the thorax – as well as, negative intra-thoracic pressure to simultaneously suck air into the lungs, suck caval venous blood into the heart and suck (or siphon) thoracic duct along with cervical lymph into superior caval tributaries coursing through

the thoracic inlet (28–29). Conversely, diaphragmatic relaxations during expiration enable central lymph from lymphatic organs above and below to be expelled craniad against relatively adverse, but variable gravitational vectors by the pulsatile, muscular and peristaltic forces operatively described with respect to each contributing lymphatic organ. Thus, under normal aerobic conditions the overall rate of central lymph accumulation from many contributing organs into the blood circulating pool remains proportional to the depth and rate of respiration which, in turn, is regulated by the rate at which absorbed and resorbed substances in the re-circulating pool are oxidized to produce rapid-diffusing carbon dioxide to stimulate central nervous system respiratory centers and water to enhance the central flow of the diverse dissolved or suspended substances absorbed or resorbed.

References

1 *Yoffey, J.M., F.C. Courtice:* Lymphatics, Lymph and the Lymphomyeloid Complex. Academic Press, London, 1970
2 *Kampmeier, O.F.:* Evolution and Comparative Morphology of the Lymphatic System Charles C. Thomas, Springfield, 1969
3 *Arey, L.B.:* Developmental Anatomy. W.B. Saunders Philadelphia, 1942
4 *Downey, H., F. Weidenreich:* Über die Bildung der Lymphozyten in Lymphdrüsen und Milz. Arch. Mikr. Anat. 80 (1912) 306–395
5 *Thiel, G., H. Downey:* The development of the mammalian spleen with special reference to its hematopoietic activity. Am. J. Anat. 28 (1921) 279–333
6 *Bloom, W.:* Lymphatic tissue, lymphatic organs. In: Handbook of Hematology. H. Downey Ed., Hoeber, New York (1938) 1839–1962
7 *Shields, J.W.:* The Trophic Function of Lymphoid Elements. Charles C. Thomas, Springfield, 1972
8 *Shields, J.W.:* Cytoclasmosis in central lymph production. Lymphology 12 (1979) 49–58
9 *Jordan, H.E.:* Comparative Hematology. In: Handbook of hematology. H. Downey, Ed., Hoeber, New York (1938) 699–862

10 Shields, J.W., D.R. Dickson, W. Abbott, J. Devlin: Thymic, bursal and lymphoreticular evolution. Dev. and Comp. Immunol. 3 (1979) 5–22

11 Shields, J.W.: Thymic germinal center polarity in myasthenia gravis. Ann. N.Y. Acad. Sci. 274 (1976) 435–438

12 Shields, J.W.: Bursal dissections and gill pouch hormones. Nature 259 (1976) 373–376

13 Shields, J.W.: Intestinal lymphoid tissue activity during absorption. Am. J. Gastroenterol. 50 (1968) 30–36

14 Jolly, J.: La bourse de Fabricius et les organes lymphoepitheliaux. Arch. Anat. Micr. 16 (1915) 363–547

15 Omaney, F.D. et al.: The Fishes. Time-Life, Inc., New York, 1963

16 Hughes, G.M. (Ed.): Respiration of amphibious vertebrates. Academic Press, London, 1976

17 Welty, J.C.: The Life of Birds. W.B. Saunders, Philadelphia, 1975

18 Schmidt-Nielsen, K.: How birds breathe. Sci. Amer. 225 (1971) 72–79

19 Smith, H.M., L.F. James: The taxonomic significance of cloacal bursae in turtles. Trans. Kansas Acad. Sci. 61 (1958) 86–96

20 Porter, K.R.: Herpetology. Saunders, Philadelphia, 1972

21 Grassé, P.O.: Traité de Zoologie. Masson et Cie, Paris, 1955

22 Schaffner, T., M.W. Hess, H. Cottier: A reappraisal of bursal functions. Series Haemat. 7 (4) (1974) 568–592

23 Goldstein, A.L., A. Guha, M.M. Zatz, M.A. Hardy, A. White: Purification and biological activity of thymosin, a hormone of the thymus gland. Proc. Natn. Acad. Sci. USA 69 (1972) 1800–1803

24 Goldstein, G.: Lymphocyte differentiation induced by thymopoietin, bursopoietin and ubiquitin. Symp. Soc. Devel. Biol. 35 (1978) 197–202

25 Marine, D.: The thyroids, parathyroids and thymus. In: Special Cytology. E.V. Cowdry Ed., Hoeber, New York (1932) 797–868

26 White, A., T.F. Dougherty: The role of lymphocytes in normal and immune globulin production and the mode of release of globulin from lymphocytes. Ann. N.Y. Acad. Sci. 46 (1946) 859–882

27 Selye, H.: The Physiology and Pathology of Exposure to Stress. Acta. Montreal, 1950

28 Dumont, A.E., K.M. Rifkind: Evolutionary significance of the thoracic duct. Nature 219 (1968) 1182–1183

29 Browse, N.L., D.R. Rutt, D. Sizeland, A. Taylor: The velocity of lymph flow in the canine thoracic duct. J. Physiol. 237 (1974) 401–403

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