

The Vertebrate Dermis and the Integumental Skeleton

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SYNOPSIS. The comparative histology of the dermis is reviewed. Some recent data on the connective tissue components of this vertebrate organ are summarized with emphasis on collagen and ground substance. The biomechanical role of the dermis is stressed within the concept of the integumental skeleton. The series of homologous developmental events involved in the formation of these "skeletal" structures are described, with some emphasis on the hypothesis of epidermal co-participation. Finally, a classification of the spectrum of integumental skeletal structures is given.

INTRODUCTION

The dermis shares a common characteristic with many other organs; it is capable of encompassing a substantial number of scientific disciplines. Accordingly, it is not surprising that dermatologists, anatomists, surgeons, immunologists, endocrinologists, neurologists, and chemists of many varieties, to enumerate but a few of the more obvious, have seemingly disparate, but hopefully interrelated, common interests in an integumentary layer common to all vertebrates. Further, there is little reason to hope that any truly comprehensive review of this organ has yet appeared. Each approach inevitably is flavored by the particular interests of individual students. The diversity of this symposium is an accurate reflection of this condition. Nor is this paper an exception, placing its major emphasis upon the structural, or skeletal, role of dermis. It is specifically stated that this paper is intended as a review for the non-specialist. However, if the period of conceptual synthesis is not yet arrived for the integument, it is still possible to review, yet once again, the general properties of the dermis.

The dermis is defined here as the connective tissue layer of vertebrates immediately subjacent to the epidermis, together

with which it forms the skin. Considered as an organ, the dermis variably contains a number of epidermal derivatives, glands of several types, scales, bone, feathers, and hair. Further, its adipose, pigment cell, vascular, and neural components are related importantly to the several functions the dermis subserves. Finally, the dermis generally is competent to interact with the overlying epidermis in a number of important developmental and structurally maintaining processes. Accordingly, while it may be appropriate to study the dermis in isolation with respect to some of its properties or components (to study collagen fibrillogenesis, for example), it is frequently difficult to isolate it from the functions of the skin as a whole.

COMPARATIVE HISTOLOGY

A basic source of information on the vertebrate dermis is found in Bolk et al., (1931). Similar encyclopedic treatment of mammalian dermis is given by Horstmann (1957) and by Pinkus (1927). Andrew (1959) has reviewed the comparative histology of this layer. Dermis proper is a uniquely vertebrate structure. Its structure is related both to the mode of life as well as to the phylogenetic position of the animal. In *Amphioxus*, a thin (2.4μ) densely fibrous layer is found subjacent to the epidermis, beneath which there is a much thicker gelatinous layer containing single

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collagen fibers. The cyclostome *Petromyzon* has coarse bundles of collagen fibers, often crossing at right angles to each other. Fine, "pre-elastic" fibers form an additional fine meshwork. Fat tissue is also observed in these agnatha. It is in elasmobranchs that true elastic fibers are found for the first time in conjunction with the division of the dermis into a superficial layer of looser construction and a deeper, more compact, layer of collagen fibers. An alternating pattern of collagen bundles is seen, with diagonal intersections forming a regular pattern. In the higher fishes, the bilaminar dermis is seen also. Importantly, chromatophores may now be found, usually subjacent to the epidermis. As a general rule, but with significant exceptions, the dermis is thinner in fishes with scales than it is in those without them. In the fins of all fishes only a basement membrane is present; otherwise the dermis is absent in these sites.

Amphibia mark the acquisition by the dermis of the secretory function formerly held by the epidermis. Multicellular glands are found now in the dermis. Excluding the thin basement membrane, the dermis may be said to be bilaminar. The loose, more superficial layer is highly cellular in amphibia, and it may contain many large glands as well as a large amount of "ground substance." This layer is especially well marked in amphibia. Elastic fibers tend to form "arches" here, and smooth muscle is found for the first time, either as single fibers or as small bundles. Additional specializations of amphibian dermis include large lymph spaces, related to their smooth muscles, which play a role in water uptake. The same layer may contain many capillaries, playing a significant role in respiration, especially in those forms with essentially functionless lungs. Chromatophores may be plentiful. Dermal glands are missing in both reptiles and birds. In the former the typical vertebrate bilaminar structure is seen, while in birds the dermis frequently contains both solitary lymph follicles and masses of diffuse lymphoid tissue. Further, birds usually

have a very loose skin, with a relatively thin dermis which contains an irregularly woven meshwork of fibers and is especially rich in sensory end-organs.

The mammalian dermis may also be said to be bilaminar. It is customary to differentiate between the more superficial papillary layer, containing blood vessels, nerves, lymphatics, glands, and fat, and the deeper reticular layer, some of whose dense collagen fiber bundles pass down to the subcutaneous fascia, while others pass upwards towards the epidermis (*see also* Ballard, 1964; Waterman et al., 1970).

INDUCTIVE INTERACTIONS

This topic is reviewed elsewhere in this symposium (Kollar, 1972) as it has been recently by us (Moss, 1969a). (*See also* Fleischmajer and Billingham, 1968.) It is sufficient to state here that many dermal structures and functions originate from such processes operative between the epidermis and dermis.

Dermal-epidermal interactions continue throughout life. The maintenance of adult epidermal characteristics seemingly requires a constant dermal contribution. Interestingly, it is not necessary for this dermis to be histologically intact, nor is this effect dermal site specific. Further, other non-dermal connective tissues are equally capable of supporting continued epidermal structures. In this aspect, it is the type of tissue comprising the dermis, rather than any specifically structured "dermal" attribute which is operative (Briggaman and Wheeler, 1971).

DERMAL CONTENTS

The dermis recently has been the subject of an excellent review (Montagna et al., 1970; *see also* Montagna, 1962).

The dermis, as a connective tissue may be said to consist of a fibrillar framework, enmeshed in, and partially united with, an "amorphous" ground substance. The fibers are predominantly collagenous with lesser, yet functionally significant, elastic components. The ground substance is rich

in a variety of mucopolysaccharides (glycosaminoglycans). Fibroblasts (and fibrocytes, according to the terminology of some workers) are the predominant cell type, while most cells, histiocytes, and melanocytes are found variable. Considered as an organ, the dermis variably contains holocrine, merocrine, and apocrine glands, smooth muscle, nerves, and sensory end organs, epidermal derivatives (feathers, hair, scale, teeth) and circulatory vessels. An excellent review of the biochemical parameters of the dermal connective tissues is found in Schubert and Hamerman (1968).

FIBERS

Collagen which forms approximately 30 percent by weight of normal dermis is the subject of much work, and many aspects of its formation, composition, structure, and physical parameters are known (*see* Ramachandran and Gould, 1968, for a systematic treatise). Dermal collagen forms a three-dimensional, highly oriented, and covalently linked fibrous network whose precise topography is not yet completely clear, although it seemingly is related to the mechanical needs of specific dermal regions (Jackson, 1970; Szirmai, 1971). It is reasonably clear that at higher levels of structural organization collagen is bound to at least one quantitatively significant glycosaminoglycan component of the ground substance, dermatan sulfate (chondroitin sulfate B). Hence the older dichotomy between fibrous and amorphous dermal components may not be strictly true *in vivo*.

Collagen is aggregated into increasingly larger structural elements by several processes. The fibrils themselves are stabilized by covalent cross-linkages. Larger fibrils are then bound to mucoproteins, while in large fibers mucopolysaccharides such as dermatan sulfate play a significant role in their further structural stabilization. It need only be added here that yet further cross-linkages and further "stabilization" can account for the gradual alteration in elastic properties of the dermis with age

(Elden, 1970). It remains only to note here that there are many specific variations in the composition of collagen at most levels of taxonomic organization whose further biological significance is not yet known (*see* Mathews, 1967).

Elastic fibers are relatively sparse in the dermis. Elastin polymerizes extracellularly to form a cross-linked, three-dimensional gel, which exists in a two-phase hydrophilic and hydrophobic system. This excellent elastomer also undergoes significant alteration of physical properties with age, perhaps related to the fact that mature cross-linked elastin has an unusual metabolic inertia (Partridge, 1970).

GROUND SUBSTANCE

This ill-defined dermal component has been called the "extravascular, extracellular, extrafibrillar phase of dermis" (Pearce and Grimmer, 1970). As noted above there is good reason to suggest that many glycosaminoglycans do not exist freely in the ground substance, but rather are bound to fibrous components. Plasma protein and hyaluronate are the two principal macromolecular components of the ground substance. The role these materials play in regulating dermal characteristics and properties remains unknown. For data covering the composition of the ground substance, *see* Pearce and Grimmer (1970) and their included references.

It is reasonable to believe that ground substance significantly enables connective tissues to bind cations, and so act as another reservoir for mineral homeostasis. It is interesting to speculate that the role of osseous tissues in this process may simply be a specific example of a more general connective tissue phenomena (Bentley, 1970). This same author describes other possible roles of the ground substance. Of particular interest is the concept that the dermis may play a role in glucose homeostasis (Fusaro and Johnson, 1970).

OTHER DERMAL FUNCTIONS

As an organ, the dermis contains many

structures and carries out associated functions. The scope of this paper precludes their encyclopedic consideration. The neural, vascular, and secretory structures and functions have been ably reviewed in many places (see particularly the several volumes of the *Advances in Biology of the Skin*, Montagna, 1960-1965). In passing, it is noteworthy that the view is gaining that the structures of dermal sensory end organs are not as specifically related to function as was held previously (Sinclair, 1967; Grossman and Hattis, 1967).

Having reviewed some salient features of dermal structure and function, we will consider now one specific function in detail, that of mechanical protection and support. The combination of dermal structures carrying out this function is the integumental skeleton.

THE INTEGUMENTAL SKELETON

The vertebrate skin participates in a number of functions: sensations, secretions, water balance, thermal regulation, and many others. The degree to which any particular function is taxonomically significant obviously is variable, and as we have indicated above, is reflected in the specific histologic attributes of the dermis, as well as of the epidermis. There is one function, however, which appears to be universally carried out, that of providing protection and/or support for the enclosed body mass. It is possible to consider that all vertebrates possess an integumental skeleton, which while participating variably in several other functions, also plays this bio-mechanically important role.

Both fossil and recent materials easily demonstrate that a number of distinctive and characteristic structural (and biochemical) modifications have occurred to both the dermal and epidermal layers of the skin which presumably have been of selective advantage to specific vertebrates. The earliest known vertebrates from the early and middle Ordovician present us with a picture of a highly organized and structurally complex dermis containing os-

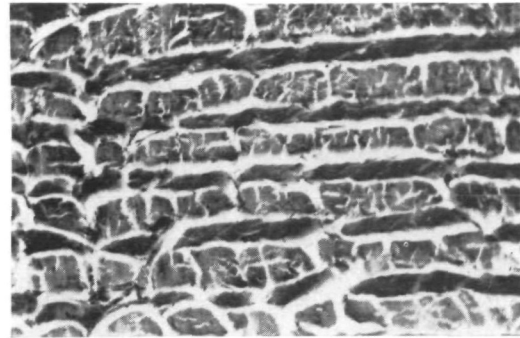


FIG. 1. The regular, alternating structural array of the dense dermal collagen fiber bundles of *Acipenser oxyrinchus* (the Atlantic sturgeon) is seen. This uncalcified tissue serves well as an integumental skeleton. This figure serves as a prototype of the fiber pattern array of many other mineralized dermal skeletal structures.

seous and dental tissues arranged in several ways (see Orvig, 1967; Moss, 1964, 1968a). We do not know, and we may never, what the integumental skeleton of still earlier vertebrate ancestral forms was like; it seems unlikely that they were as fully armored as those of the earliest remains. It is at least reasonable, if not provable, that such earlier forms did possess a dermis within which the organized collagen fiber tracts were so arranged as to give the requisite protection and support. It might be argued, for example, that the fiber patterns of the dermal bone of the earliest known agnathic fishes may have pre-existed in ancestral forms which did not yet possess the ability to form ossified tissues (Figs. 1-5). It is important to note

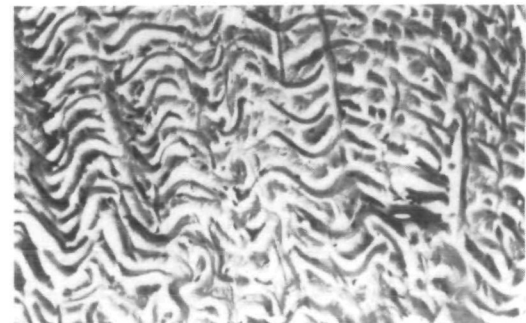


FIG. 2. The uncalcified dermal collagen fibers of *Heloderma horridum* (Gila) show an array essentially similar to that in Figure (1).

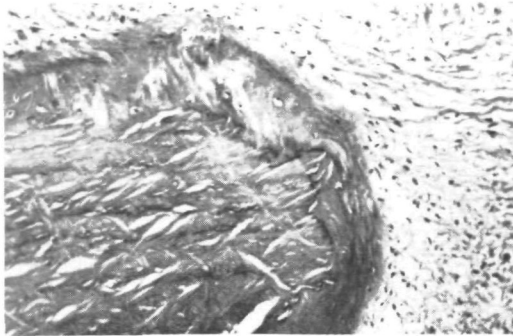


FIG. 3. This view of a mineralized osteoderm of *Heloderma horridum* well illustrates that the dense regular array of collagen bundles is maintained. The outermost tissue is bone, while the main mass of this osteoderm is a tissue of indeterminate nature.

that the presence of dental tissues surmounted and joined to underlying dermal bone also indicates that the epidermis probably played some co-participatory role. Arguing by homology, the presence of dentin in these Ordovician agnatha suggests that the series of mutually reciprocal inductive interactions characteristic of recent dental tissue odontogenesis was implicated here, too. The problem of fossil agnathic fish enamel as a structured epidermal tissue in the integumental skeleton is still controversial (Moss, 1970).

The integumental skeleton can be studied in many ways. One of the more fruitful recent fields is that of bioengineering research into the physical properties of



FIG. 4. The dermis of *Egernia kingi* (Sauria, Scincidae) shows an extremely well ordered array of collagen to which is superimposed (above) a diffuse calcification.

dermis (see Millington et al., 1971; Elden, 1970). It is tempting, if possibly hazardous factually, to consider the potential relationships between the factors responsible for the "split-line" pattern of dermal collagen bundles (Langer's Lines) and the at least analogous, if not homologous, study of split-line patterns in partially decalcified bone. While the immediate causes may well be different (Moss, 1954), ultimately they may be held to show that dermal bones really retain much of the essen-

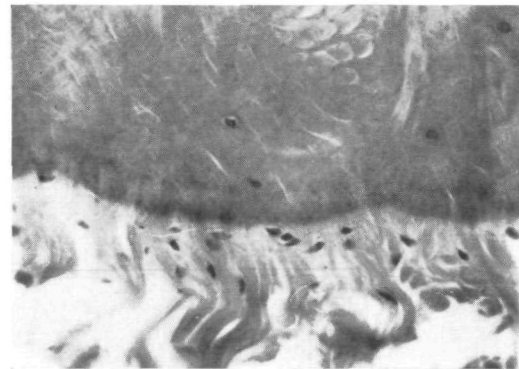


FIG. 5. Dermal sclerifications in the armadillo (*Dasypus novemcinctus*) show an alternating array of collagen fiber bundles basically not dissimilar to those pictured above.

tial patterning of the organized fiber bundles of their possibly uncalcified ancestors. It is true also that as a general rule the osseous components of the vertebrate integumental skeleton show evolutionary trends leading, in general terms, to both a diminution in the number of such osseous structures as well as to their elimination.

We may now describe the integumental skeleton as a protective organ — one in which the epidermis and dermis co-participate developmentally in a number of ways. In the dermis it is possible to find a number of "hard" tissues in addition to collagen fiber bundles. The histological composition of these "hard" tissues tends to be very variable, forming a true spectrum of types with many "intermediate" forms. Accordingly, we prefer to term them sclerified tissues. All vertebrate classes, save *Aves*, contain some representative forms whose dermis contains some sort of

sclerified tissue. While these tissues undoubtedly add in some significant way to the better fulfillment of a mechanically protective role, these same sclerifications possibly perform some additional role in mineral homeostasis, with the probable exception of the acellular bone found in both fossil and recent fishes (the dermal armor of agnathic Heterostraci and the acellular bone of the dermal denticles of recent elasmobranchs, for example) (*see Moss, 1970*).

The integumental skeleton is represented by a number of structural modifications of both epidermis and dermis which variably combine to form a structural and functional whole. I believe it is reasonable to suppose that despite the apparent and oft-times great differences in structural expressivity demonstrated in the vertebrate integumental skeleton, a series of basically homologous developmental processes underlies them all. Previously, I have discussed these concepts as the epidermal co-participation hypothesis (*Moss, 1968b*). It is suggested that (1) inductive interactions occur between the epidermis and dermis (and in some cases at least involves ectomesenchymal cells); (2) either or both the epidermis and dermis form structural derivatives; (3) the epidermis always contributes something, even if it is an unstructured but important component of a dermal structural derivative; and (4) delamination plays an important role in topographically organizing the dermal portion of the integumental skeleton. References are given below as I outline the specifics of this hypothesis. Three types of integumental skeletons are found.

A. Epidermal Derivatives: In passing we mention here some types of integumental skeletal forms which are produced solely by structural epidermal derivatives. There are no organized dermal contributions to these forms, although the dermis does play a necessarily initial role in the induction interactions between ectoderm and mesenchyme (*see Spearman, 1964, 1966*). A partial list would include hair, feathers, rhinoceros horn, whale baleen, reptile scales,

turtle scutes, mammalian bones, beaks, claws, and nails. Interestingly, the formation of some sort of epidermal-dermal *papilla* is associated in one way or another with all of these structures.

B. Epidermal-Dermal Derivatives: This group of structures contains structural elements from both sources. In this sense, the two skin layers co-participate in the formation of their skeletal structures. There are three subdivisions in this grouping, in which the evidence of epidermal participation to the formation of visible skeletal derivatives ranges from the most obvious to the least (*see Moss, 1968b*, for a more complete discussion). A partial listing includes:

1. a) vertebrate teeth
b) dermal denticles
2. c) cosmoid scales
d) ganoid scales (paleoniscoid and lepidosteoid)
3. e) fin-ray elastoidin (ceratotrichia)
f) lepto- and actinotrichia (of fins)
g) teleost scales (cycloid and ctenoid)
h) scutes of armored cat fishes, sticklebacks, sea horses, pipe fishes, etc.

C. Structured Mesodermal Derivatives (Sclerifications): In this group there is no visible evidence of a structured epidermal contribution to the integumental skeletal structure. The hypothesis that the epidermis does indeed play a role in the formation of these tissues has been previously discussed (*Moss, 1968b*) and derives importantly from the conjunction of the work of Hay (1964) and of Jarvik (1959). The partial listing includes dermal fibers, calcified tendon, calcified "plates" (*Bufo*), "intermediate" skeletal tissues (branchial arch of fish), antlers, dermal bones in fishes, amphibia, reptiles, and mammalia.

Finally, I wish to consider the dermal sclerifications found in Reptilia. A completely uncalcified yet somewhat structured array of dermal collagenous fibers repre-

sents, in a sense, a primordial type of dermal sclerification. Above I stated that there is some reason to believe that dense dermal fiber bundles did precede dermal bone phylogenetically; the more significant point is that such a three-dimensional structural fibrous network seems to have anticipated the structure of fibrillar phase of dermal bone tissues, at least in some forms, particularly reptiles (Moss, 1969b).

Reptilian bone tissue histology has recently been reviewed by Enlow (1969) without a detailed study of dermal bone (see Moss, 1969a). Reptilian dermal sclerifications exhibit quite a variety of histological types, and they may be compound in nature. When bone tissue is formed, it may be produced in at least three ways: periosteal osteogenesis, tendonous ossification, and metaplasia of secondary cartilage. These dermal skeletal structures are poorly vascularized and remodeled but little. We would observe no strong association between the structure or type of dermal sclerification and the taxonomic position of the species. Further, no evolutionary trends in their structure are apparent. Yet, taken as a whole, the comparative study of histological composition of reptilian dermis permits us to view virtually the entire range of expressivity of the vertebrate dermal skeleton. It only remains to note that the vertebrate dermis apparently retains the ability to produce, not only sclerifications, but specifically, ossifications in normal ontogenetics as well as pathological circumstances by seeming parallel developmental processes. For students of calcified tissues, no less than for workers in many cognate fields, the dermis will continue to provide an exciting and rewarding locale for further investigation.

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