Abnormalities of the Digital Vasculature as Related to Ulceration and Gangrene

By MARGARET C. CONRAD, PH.D.

SUMMARY
Plastic casts were made of digital vessels of 13 extremities amputated for severe atherosclerosis obliterans. Prior to amputation, blood flow averaged 0.02 cc/min/5 cc of digit (normal, 0.5), and digital systolic pressure average 16 mm Hg. There were more occlusions of terminal arteries (<30 μm in diameter) in the first and fifth toes than in the third toes and on the plantar and proximal dorsal surfaces than in the nail bed; this observation suggests relationship to local trauma and shoe pressures. Occlusion was most severe in 30 to 50 μm arteries, decreased with increasing vessel size, and was greater in uninvolved areas of ulcerated toes than in nonulcerated toes. Occluded arteries smaller than the digital artery terminated abruptly; this observation suggests stasis thrombosis; occlusions did not occur preferentially at sites of branchings. In occluded digital arteries, areas of partial occlusion lay adjacent to complete block, reflecting plaque formation. At the rim of an ulcer crater all vessels terminated abruptly which suggests destruction of vasculature secondary to necrosis. The findings suggest the following sequence of events: (1) marked reduction in pressure and flow due to proximal disease, (2) resultant stasis thrombosis accentuated by shoe pressures and local trauma, and (3) death of tissue in ischemic digits leading to further loss of vasculature in the necrotic area.

Additional Indexing Words:
Peripheral vascular disease  Atherosclerosis obliterans  Digital circulation
Vascular anatomy

The digits of the lower extremity are the primary site of ulceration and gangrene in atherosclerotic arterial occlusive disease. In view of this, it seemed desirable to study the anatomy of the digital circulation in severe atherosclerosis obliterans to try to discern whether the determinant abnormality is in the vessels of the digit itself or whether severe ischemia leading to necrosis is the consequence of more proximal disease.

Severe ischemia and necrosis could be produced primarily in the digits by at least four possible mechanisms: (1) The proximal occlusion and subsequent increase in vascular resistance could be so severe that sufficient oxygenated blood does not reach the terminal end of the vascular bed of the extremity. (2) There could be a primary lesion of a major digital vessel or (3) a combination of proximal occlusion plus occlusion of a major digital vessel, resulting in severe local ischemia. (4) Changes in the digital microcirculation secondary to the proximal disease and local trauma or to micro-emboli could be causing further interference with blood flow beyond that induced by the occlusions in the proximal arteries.

Methods
Experimental Material
Casts were made of the entire vascular lumen of the digits of lower extremities amputated for severe ischemia and gangrene. The digits of one lower extremity were studied from each of 13 patients. Eight of the patients were
diabetes; the length of time since diagnosis of diabetes ranged from 20 years to the present hospital admission with an average duration of 4.9 years. The diabetics were 47 to 71 years of age (average, 59 years) and the nondiabetics were 37 to 82 years (average, 61). Seventy-five percent of the diabetics had frank ulceration or gangrene of one or more digits compared to 46% of the nondiabetics. All patients exhibited one or more trophic changes such as thinning of the skin, loss of hair, discoloration, abnormal nail appearance, and edema. Thirty-three percent of patients were female.

Vascular Studies

In 50% of the patients, blood flow, systolic arterial pressure, and skin temperature were measured in the digits prior to amputation. Digital skin temperatures were monitored on the first, third, and fifth toes in a laboratory maintained at 20°C (±0.4°C) with the patient in the supine position. The torso was comfortably warmed with blankets and heating pads while the digits were exposed to the environment. Temperatures were recorded on a Honeywell strip recorder which sampled each point every 3 minutes with copper-constantin thermocouples. The values reported represent the average temperature of the three digits after equilibration with the environment and following maximal response to a dilating agent (two doses of 60 cc each of 86 proof ethyl alcohol taken orally).

Blood flow and digital artery systolic pressure were measured with the venous occlusion volume plethysmograph using air-filled digital cups in the control state and following alcohol dilation.1

Preparation of Casts of the Vascular Tree

The amputated extremities were photographed

Figure 1

Organization of the digital microcirculation. (a) Surface capillary loops; (b) superficial venous plexus and terminal arteries (<30 μm in diameter); (c) sub-superficial venous plexus and fifth branchings of the primary arterial arcade (30 to 50 μm in diameter); (d) deeper venous plexus and fourth branchings of the primary arterial arcade (50 to 100 μm in diameter).

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to record pathological changes in the skin after which the anterior tibial artery was cannulated and the vessels of the foot were flushed with saline. Green acrylic plastic* was injected into the cannulated anterior tibial artery, and this was followed by injection of red plastic.² The injection was stopped when the color of the skin began to turn from green to red, at which point the red plastic should have reached the capillaries, the green being pushed ahead into the veins. The toes were removed, and after the plastic had hardened, the flesh was macerated from the digits using 40% potassium hydroxide. The cast was washed in warm soapy water to remove residual fat. Extremities were prepared in order of amputation, whenever a diagnosis of severe atherosclerotic disease had been made.

Since the digital vascular anatomy had not been studied previously in this manner, the first part of the experiment involved an orientative study of the digital vasculature. The surface capillaries of the cast were examined microscopically, after which the superficial vessels were removed layer by layer and deeper vessels were observed.

**Orientation Study**

**Superficial Capillaries**

On the plantar surface of the digit, the capillary loops were arranged in essentially parallel rows which lay within the ridges of the skin that comprise the “toe print” (figs. 1a and 2a). The capillaries were about 15 μ in diameter at the top of the loop and were on the order of 200 μ in length. A single row of loops contained, on the average, one capillary every 40 μ, and there were at times more than one row of capillaries in a single “ridge.” The arterial limb of the capillary lumen was smaller than the venous segment

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*A Batson’s corrosion solution.

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**Figure 2**

Capillaries on the plantar (A) and dorsal (B) surfaces of the digit and in the proximal (C) and distal (D) portions of the nail bed.
and broadened prior to the surface bend of the loop.

On the dorsum of the finger, where the prominent ridges of the skin are absent, the parallel alignment of the capillaries was lost—the loops maintaining regular distances from their neighbors without grouping in any manner (fig. 2B). The density and size of the dorsal capillaries were similar to those on the plantar surface.

The nail bed presented an interesting arrangement of surface vessels. In the cuticle, the vessels were gnarled with dilations on twisted capillary loops (fig. 2C). In the more distal portion of the nail bed the capillaries lay in parallel rows which ran in a proximal to distal axis (fig. 2D). These vessels were often as long as 500 μ and, as elsewhere on the surface, rose perpendicular to the surface.

The Subcapillary Superficial Plexus

Immediately beneath the surface capillary loops lay a superficial arterial and venous network of horizontally arranged vessels (fig. 1b). The arteries comprising the inflow plexus were extremely fine (10 to 15 μ in diameter). These fine horizontal arteries gave rise, at regular intervals, to the perpendicular twigs forming the arterial limb of the capillary loops.

The venous vessels at this level were on the order of 20 to 40 μ in diameter, and like the arteries, were joined periodically by the perpendicular branches that formed the venous limb of the capillary loops. On the plantar surface of the digit, the arterial and venous plexuses maintained a roughly parallel orientation and ran with the skin ridges as did the rows of capillary loops (fig. 3A). On the dorsum of the digit, the plexus formation...
had no axial orientation. In the cuticle area of the nail bed, the superficial plexus formation was scanty, which may account for the pale color of this area in the intact digit.

**Deeper Plexuses**

Below the subcapillary superficial plexus lay another venous plexus (figs. 1c and 3B), which we will call the "sub-superficial plexus." At this level, the axial orientation of the plantar vessels was lost. The veins at this level were about 50 μ in diameter and lay in a horizontal plane, joined by branches which connected to the superficial plexus. The arteries did not maintain this same extreme horizontal orientation (fig. 1c). In general, the arteries branched just below the sub-superficial plexus, and arterial branches with a diameter of about 30 μ or less passed in a slanting path through the network of veins before rebranching to form the superficial arterial plexus. These arteries later will be designated "terminal arteries," that is, the branches just proximal to the superficial plexus of arterioles.

Removal of the sub-superficial plexus revealed a third horizontal network of venules, the "deeper plexus" (fig. 3C). The veins at this level had a diameter of about 70 μ before branching, and the perpendicular branches connecting the sub-superficial plexus were about 50 to 60 μ wide. The arterial branching seen at this level produced the vessels which passed through the sub-superficial venous plexus and rose to form the superficial plexus (fig. 1d). Before branching, the arteries were about 50 to 60 μ and the branches, 30 to 40 μ in diameter. Again, the arteries did not form a horizontal network before rebranching.

Figure 3

Plantar superficial plexus (A), sub-superficial (B), and deeper (C) venous plexuses. Plantar view of major arterial tree of the digit (D).
giving off perpendicular branches as did the veins, but rather formed a simple, slowly angled branching pattern on their way from the depths to the surface of the digit.

**Major Arteries and Veins**

In general, the major branches of the digital arteries started deep in the pad of the digit near the bone and rose quickly to the surface. The veins tended to occupy a relatively superficial position and displayed a very shallow branching pattern with extensive interconnections.

On the plantar side of the digit, the arteries entered the toe at a lumen diameter of about 800 to 900 μ and formed an arcade or loop (fig. 3D a), with a diameter of about 700 μ, giving off branches of about 500 μ in diameter which passed proximally and distally with a slant toward the surface. On the dorsum, a similar arrangement was found with the loop occurring in a more proximal position (proximal to the nail bed) (fig. 3D b). There were anastomoses of the branches, usually at a vessel size of about 200 μ, connecting the major branching systems and through the branches, the plantar and dorsal arcades (fig. 3D c).

In the deep areas of the toe were masses of very close-packed fine vessels which usually had an axial orientation, rather than forming a mesh or network. These are probably vessels which supply nutrients and storage materials to the fat and other tissues deep in the digit.

**Findings in Atherosclerosis**

**Vascular Studies**

Digital blood flow was markedly reduced in the extremities prior to amputation and did not change significantly following the oral ingestion of alcohol (table 1). Digital artery systolic pressure also was quite low, indicating a marked increase in resistance to flow in the larger arteries proximal to the digital artery. Skin temperature was in the
normal range, in spite of the very low flow, but did not increase with alcohol. The relationship between flow and skin temperature differed from normal in that the skin temperature was high per unit of blood flow to the digit (table 1).

**Digital Vascular Anatomy**

The capillary bed was observed microscopically in each of the digits of the 13 extremities studied. The capillaries were then removed and the terminal arteries (less than 30 μ diameter) were graded as to percentage of the vessels occluded. The observations were made on the plantar and dorsal surfaces of the digit and in the nail bed. The superficial and sub-superficial plexuses were examined and any abnormality noted.

The veins of each first toe only were removed by microdissection to reveal the total arterial tree. Only the first toe of each extremity was studied in this manner due to the very tedious work involved in the extensive dissection.

**Capillaries**

Unexpectedly, the capillary loops on the surface of the digit were frequently of normal density in spite of marked trophic changes in the toe. The capillaries rose at intervals, ranging from one every 57 μ to one every 29 μ as compared to the normal interval of 40 μ. In a few cases the capillaries were dilated, but usually the diameter was decreased; this gave the general impression of sparsity of vessels in spite of the normal number per unit area. Occasionally the number of capillaries was significantly decreased (fig. 4A). Patchy occlusion could occasionally be seen in the ascending limbs of the capillary loops, though the occlusions were generally found below the superficial plexus.

When there was severe ulceration or gangrene, the capillaries were absent in the ulcerated area but often appeared in normal density right up to the edge of the ulcer (fig. 4B).

**Venous Plexuses**

The venous plexuses were typically normal. The veins were of normal size and density and did not seem to be affected by the disease state in any appreciable manner.

**Terminal Arteries (Less Than 30 μ in Diameter)**

Terminal artery occlusions, at about the level of the sub-superficial plexus, were present, at least to a small degree, in all digits and usually appeared in patches in which a high proportion of occluded vessels were separated by areas with a lower proportion of occluded vessels (fig. 4C). The severity

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Table 1

<table>
<thead>
<tr>
<th>Vascular Studies</th>
<th>Patients Av</th>
<th>St</th>
<th>Normals Av</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digital blood flow (cc/min/5 cc digit)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>0.020</td>
<td>(0.003)</td>
<td>0.54</td>
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<tr>
<td>Alcohol</td>
<td>0.025</td>
<td>(0.0063)</td>
<td>1.06</td>
</tr>
<tr>
<td>Digital artery systolic pressure (mm Hg)</td>
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<td></td>
<td></td>
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<tr>
<td>Control</td>
<td>15.71</td>
<td>(6.01)</td>
<td>equal to</td>
</tr>
<tr>
<td>Alcohol</td>
<td>17.51</td>
<td>(5.73)</td>
<td>brachial</td>
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<tr>
<td>Digital skin temperature (°C above environment)</td>
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<td></td>
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<tr>
<td>Control</td>
<td>5.38</td>
<td>(0.440)</td>
<td>6.56</td>
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<tr>
<td>Alcohol</td>
<td>4.60</td>
<td>(0.622)</td>
<td>12.14</td>
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<tr>
<td>Skin temperature/blood flow (°C/cc/min)</td>
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<td></td>
</tr>
<tr>
<td>Control</td>
<td>318</td>
<td>(64.7)</td>
<td>12.2</td>
</tr>
<tr>
<td>Alcohol</td>
<td>237</td>
<td>(75.7)</td>
<td>11.4</td>
</tr>
</tbody>
</table>


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*CONRAD*
Capillaries decreased in number (A) and at rim of an ulcer crater (B). Occlusions of terminal arteries (< 30 µ in diameter) (C) and of 30 to 50 µ vessels (D).
of occlusion at this level was significantly higher on the plantar and proximal dorsal surfaces of the digit than in the nail bed (fig. 5a). The first and fifth digits of the foot tended to have a greater degree of terminal artery occlusion than the second, third, and fourth toes (fig. 5b), the differences between the third toe and the first and fifth toes being statistically significant.

There was no difference in the severity of terminal artery occlusion between diabetics and nondiabetics (table 2A). There was no increase in terminal artery occlusion in the uninvolved areas of ulcerated digits (table 2B) although the terminal arteries were typically absent in the ulcer crater itself.

**Fifth Branchings of the Digital Artery Arcade**

(Diameter 30 to 50 μ)

Arterial occlusions at the level of 30 to 50 μ diameter arteries (fig. 1c) were usually quite extensive, and it was not unusual to find 90% of these vessels occluded. The occlusion always took the form of a sudden, blunt termination of the vessel lumen, and the imprint of the occluding mass could be seen in the end of the cast of the lumen (fig. 4D). There was, again, no difference in severity of occlusion between diabetics and nondiabetics (table 2A); however, in the uninvolved areas of ulcerated toes there was a significant increase in the percentage of arteries occluded at the 30 to 50 μ diameter level in both diabetics and nondiabetics (table 2B).

**Fourth Branchings of the Digital Artery Arcade**

(50 to 100 μ)

At this slightly deeper level (fig. 1d), the percentage of arteries that were occluded was significantly reduced (table 2). Again, the occlusions took the form of sudden, blunt terminations (fig. 6A). Nondiabetics tended to have fewer occlusions than diabetics, but this difference was not significant (table 2A).

### Table 2

**Percentage of Arteries Occluded**

<table>
<thead>
<tr>
<th>Vessel size</th>
<th>Ulcerated Diabetic</th>
<th>A nonulcerated Diabetic</th>
<th>Diabetic Ulcerated digits</th>
<th>B nondiabetic Nonulcerated digits</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 30 μ (terminal arteries)</td>
<td>Av 17</td>
<td>20</td>
<td>17</td>
<td>19</td>
</tr>
<tr>
<td>30-50 μ (5th branching)</td>
<td>S₃ (2.21)</td>
<td>(0.89)</td>
<td>(1.83)</td>
<td>(0.93)</td>
</tr>
<tr>
<td>50-100 μ (4th branching)</td>
<td>S₃ (14.2)</td>
<td>(9.1)</td>
<td>(4.8)</td>
<td>(12.06)</td>
</tr>
<tr>
<td>100-200 μ (3rd branching)</td>
<td>S₃ (13.0)</td>
<td>(11.0)</td>
<td>(15.2)</td>
<td>(10.71)</td>
</tr>
</tbody>
</table>

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Figure 6

Oclusions of the 50 to 100 μ vessels (A), at the end of an ulcer (B), and in tertiary branches of the primary arcade (C). Partial digital artery occlusion (D).
However, there was a significant increase in the number of occlusions of vessels of 50 to 100 μ in diameter in toes with ulceration, even in the nonaffected portions (table 2B). At the edge of an ulcer crater, all vessels terminated abruptly, an imprint of the occluding mass being left in the blunt end of the cast (fig. 6B). The endings of the vessels, rather than having partial occlusion prior to abrupt termination, often terminated with knobby swellings of the lumen which suggested wall damage due to the necrotic process.

*Larger Arteries*

Only a small proportion of the tertiary branches of the primary arcade were occluded, but when occlusions were present, these again took the form of blunt terminations (fig. 6C). On the average, only 12% of tertiary branches (100 to 200 μ in diameter) were occluded, and there was no significant difference between diabetics and nondiabetics (table 2A). In the uninvolved areas of ulcerated toes, the severity of occlusion was five times that of nonulcerated digits (table 2B).

No occlusions of secondary branches of the arcade were noted in the digits studied.

In only one case were primary branches occluded. These branches stemmed from an occluded digital artery and the flow path was interrupted below their point of branching.

Only two digital arteries were found to be completely occluded in the digits dissected. Both of these were from nondiabetics. In one of the digits with a complete occlusion, there was a partial occlusion of the opposite digital artery (fig. 6D). These occlusions were of a completely different nature from those of the smaller vessels described above. Narrowing of the artery could be seen prior to the complete occlusion and there was a clear print of the plaque in the cast of the lumen of the partially occluded artery (fig. 6D).

**Discussion**

The vascular studies made prior to amputation showed the expected marked reduction in blood flow and digital artery pressure; however, the skin temperature still was in the normal range, indicating a very effective transfer of the heat brought to the surface. This finding is similar to that formerly seen in patients with significant arterial occlusion, but not requiring amputation. The findings in the anatomic studies are compatible with an efficient heat transfer mechanism. By far, the major volume of blood held near the surface of the digit for ready transfer of heat to the skin is in the venous plexuses, the arteries being very fine in the superficial plexus and passing through the sub-superficial plexus in a relatively perpendicular manner, without forming a network. Therefore, in spite of very extensive occlusion in the tiny arteries, an essentially normal volume of blood is still held under the surface of the skin. With a large volume and surface area for heat exchange, a great proportion of the heat contained in the very slow-flowing blood would be lost to the surrounding tissue, leaving very little heat to be carried back to the core; that is, the venous blood temperature would become more nearly equilibrated with the skin temperature.

The capillary bed was also essentially intact, in spite of occlusion of 70% of the 30 to 50 μ vessels. It seems impossible to maintain patency of capillaries distal to such extensive occlusion until one considers the connections in the superficial plexus. Due to this network of tiny vessels, the capillary bed can maintain a minute flow, although only a small proportion of the supplying vessels remain patent.

The lack of significant differences between the severity and pattern of occlusion in diabetics and nondiabetics is compatible with previous studies on the small vessels of the leg muscle and the skin of the foot, which showed essentially equal severity of occlusions in diabetics and nondiabetics.

Although digital artery occlusions are often indicated in pedal arteriograms in diabetics, no digital artery occlusions were seen in the diabetics of this series, in spite of ulceration and gangrene of the toe. A possible explanation for this discrepancy is found in the
the anatomic pattern of vessels at the distal end of the foot. There are large anastomotic channels connecting adjacent digital arteries at their point of takeoff and connecting plantar and dorsal arteries. With very high resistance to flow through the digit itself, as occurs with the type of multiple microscopic vessel occlusions described above, the blood could be reasonably expected to flow preferentially through the relatively low resistance anastomosis, with the contrast medium appearing to stop abruptly at the point of entrance of the digital artery into the toe, where flow is very slow.

The differences in severity of occlusions of the terminal arteries (less than 30 μ in diameter) as related to sites examined suggest that mild trauma of shoe pressures may be related to the development of occlusion. The number of occlusions were significantly increased in the plantar and proximal dorsal areas over those in the nail bed, where the nail may offer some protection against trauma. Also, the occlusions were more severe in the first and fifth toes than in the third toe, the third toe being protected against pressures from shoes by virtue of its position.

The anatomic characteristics of the branch artery occlusions points to their development in response to stasis rather than to active plaque formation or microemboli. That the occlusions occurred very extensively in the arteries with diameters of 30 to 50 μ, less severely in those with diameters of 50 to 100 μ, and still less extensively in those with diameters of 100 to 200 μ, suggests that the preferential buildup of occlusion is from 30 μ arteries to larger. The sudden abrupt ending of the occluded vessel lumen, with the imprint of the occluding mass seen in the end of the cast only, suggests a thrombotic or embolic occlusion without plaque formation. If plaques were being formed in the wall of the vessel, one would expect to see an area of partial occlusion prior to, and at times instead of, the sudden termination of the vascular lumen. The occlusions did not appear to occur preferentially at the site of branchings, suggesting that the occlusion was due to locally developed thrombi rather than to microemboli cast from proximal occlusions.

The few primary digital artery occlusions observed were due most certainly to plaque formation, as evidenced by areas of narrowing with the imprint of the plaque clearly visible in the cast. The absence of evidence of plaque formation in vessels smaller than the digital arteries supports the view that the smaller arteries are immune to atherosclerosis, perhaps, as Dible\(^5\) suggested, due to their independence from the vasa vasorum for nutrition.

In the digits with ulcers, even in the uninvolved areas, there was a marked increase in the severity of very small artery occlusions. This increase in small vessel occlusion probably accounts for the further ischemia of these particular digits which led to tissue death. The findings point to this general increase of small vessel occlusion, without significant change in pattern, as the factor initiating ulceration rather than any sudden thrombotic accident in a major digital or branch artery. Actually, it would seem unlikely that occlusion of a single major branch would result in severe local ischemia since there are large arterial anastomoses connecting the major branching systems in the digit.

On the other hand, the abrupt, complete occlusion of all vessels, both arteries and veins, at the edge of the ulcer crater and the "knobby" appearance of these terminations suggests that this severe vascular abnormality occurs secondary to the death of tissue rather than initiating it.

The findings would then suggest the following sequence of events in ischemic ulceration: (1) Atherosclerotic occlusion of vessels proximal to the digits, resulting in a marked decrease in digital artery pressure and blood flow. (2) Secondary occlusions of very small arteries due to stasis and accentuated by local pressures and trauma, as from shoes. (3) Death of tissues occurring first in more severely ischemic digits and leading to the secondary loss of vasculature in the necrotic area.
Acknowledgment

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References


Mystery of Being (Perspective of Half-Century Ago)

It behoves us always to remember that in physics it has taken great men to discover simple things. They are very great names indeed that we couple with the explanation of the path of a stone, the droop of a chain, the tints of a bubble, the shadows in a cup. It is but the slightest adumbration of a dynamical morphology that we can hope to have, until the physicist and the mathematician shall have made these problems of ours their own.

How far, even then, mathematics will suffice to describe, and physics to explain, the fabric of the body no man can foresee. It may be that all the laws of energy, and all the properties of matter, and all the chemistry of all the colloids are as powerless to explain the body as they are impotent to comprehend the soul. For my part, I think it is not so. Of how it is that the soul informs the body, physical science teaches me nothing: consciousness is not explained to my comprehension by all the nerve-paths and "neurones" of the physiologist; nor do I ask of physics how goodness shines in one man's face, and evil betrays itself in another. But of the construction and growth and working of the body, as of all that is of the earth earthy, physical science is, in my humble opinion, our only teacher and guide.—D'Arcy Wentworth Thompson: On Growth and Form. Cambridge, University Press, 1917, p. 8.
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