Circulatory Pathophysiology: I The Role of Capillary Compression in the Etiology of Essential (Idiopathic) Hypertension

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SUMMARY:
Evidence is presented and discussed showing that essential hypertension may result from compartmental capillary compression. The increased resistance to blood flow presented by capillaries flattened to varying degrees by increased tissue pressure requires augmentation of blood pressure to accomplish adequate perfusion.

Three common causes of increased tissue pressure are (1) increased tone of voluntary muscle, (2) obesity and (3) fluid retention. In turn, these are most commonly caused in our society by stress, intake of food beyond the metabolic requirements of the body and excessive intake of sodium chloride.

"There is a real difference between recognizing the 'cause' of a particular hypertension and describing its mechanism."

Robert C. Tarazi and Ray W. Gifford, Jr.

It has been known since William Harvey's discourse in 1628 that blood circulates. It wasn't until 1660 that Marcello Malpighi was able to visualize the capillaries of the frog's lung and actually see the microcirculation in action for the first time. It seems strange that it took another 200 years and more before much attention was paid to the capillaries and stranger still that relatively little is said about them in many of the very latest texts and journals. One's perspective about this sort of thing is sharpened when it is realized that it was 194 years after the discovery that citrus fruits prevent scurvy before this knowledge was applied in a regular way by the British Navy. In the total scheme of things scientific, we have written only the prologue; there is much to be discovered and, as we well know, it is one thing to make a discovery and another to understand it fully.

Lack of time and space deny me the privilege -- and you the burden -- of a discourse on the history of our knowledge of the hard pulse and the many painstaking researches which led eventually to the development of an acceptable, accurate and convenient instrument for measuring blood pressure. Instead of the laborious and scholarly approach which would be more satisfying, I shall limit myself to the proposal of a theory regarding the development of essential (idiopathic) hypertension and perhaps mention a few of the ramifications and consequences of this thinking, leaving their fuller discussion to future communications. No attempt is made to be exhaustive in the documentation nor will I attempt to establish priorities. The work is truly a collective effort and I, as much as anyone, realize that we "stand on the shoulders of giants," those who have gone before us over the centuries and recorded the observations which are harvested here.

Remember, as you read, Tarazi's words: "we need to develop a tolerance for non-homogeneity and for the complexity of hypertension but also a keen eye to recognize the simplistic explanations that sometimes lie behind apparently complex diagrams."

Compartmental Capillary Compression
For blood to pass from the arterial to the venous side of the peripheral circulation, it must normally pass through the systemic capillaries; in the thorax, it passes from the venous to the arterial side through the pulmonary capillary bed. Assuming a fixed caliber of the larger vessels, if the vessels of a
capillary bed offer no significantly increased or decreased resistance to passage at atmospheric pressure, the blood pressure required to maintain the circulation may be considered to be "normal"; if the resistance is lower than normal, the blood pressure required may be lower than "normal". If the resistance of a substantial portion of the capillary bed is greater than normal without compensatory decreases elsewhere, systemic blood pressure will rise automatically. Regardless of what is happening in the distant parts of the body, markedly increased resistance in any capillary bed will require elevation of blood pressure if the same degree of perfusion is to continue as it was before the onset of the higher impedance to flow.

A simple illustration to make the point: there is a house fire. The fire truck comes, the firemen hook a hose to a hydrant, the water is fed into the pumper and a hose is carried off to spray water on the fire. All is going well until an auto drives up and parks with a wheel on the hose, obstructing flow. The "compartment" is bounded by a membrane of some kind, varying from the thinnest, flimsiest of connective tissues through tough tissue capsules and thick fascial sheets. The whole body is encased in a membrane -- the skin -- and the various tissues are encapsulated, ensheathed or compartmentalized by connective tissues or membranes of various kinds with varying degrees of flexibility or ability to stretch under pressure. There are also varying degrees of permeability.

If a tissue compartment were to be flooded with more fluid than it can dispose of by reabsorption, lymphatic drainage or discharge in a timely way, the increase in the fluid content will enlarge the compartment if its membrane yields readily. Otherwise, the additional fluid will quickly raise the hydraulic pressure within the compartment. Such pressure is exerted equally in all directions, against the limiting membranes but also to the same extent upon every cell in the compartment, including the walls of the capillaries which traverse it. The increased pressure on the outside of the capillary is opposed only by the pressure within it, the capillary pressure. As capillary pressure is exceeded, the capillary will be compressed and it will collapse totally if the tissue pressure is sufficiently high, just as the vessels collapse in the arm when the sphygmomanometer cuff pressure sufficiently exceeds the vascular pressure. This happens because the vessels are "open-ended" and the blood escapes into the venules and veins. If there were no escape route, the equal pressure on all sides of the vessels would prevent their collapse.

The Situation in Skeletal Muscle

Skeletal muscle accounts for a large percentage of the body weight of the average adult. This tissue is extremely well vascularized to enable the muscle to transport the body rapidly in emergency situations, to perform other useful work and, at rest, simply to maintain posture, etc. This is well illustrated in the accompanying figure showing the...
richly anastomosing capillary network among the individual muscle fibers of the rectus abdominis muscle. It takes little imagination to see what will happen to the capillaries when the muscle contracts: they will be flattened according to the extent of muscular intrusion.

This is both good and bad. It is good when muscular contraction is intermittent as it is with walking, running, chewing, bending and so forth; it is bad when the muscle contraction is sustained. One action makes the muscle serve as an auxiliary heart, pumping the blood forward with the assistance of the venous valves; the other action is that of a tourniquet which obstructs the forward propulsion of blood.

It is perhaps needless at this point to say that it will require higher blood pressure, all other things being equal, to force blood through a contracted muscle than through a relaxed one. Unfortunately, from the blood pressure standpoint, there is such a thing as muscle tonus. Some people are so relaxed, they don't seem to have any; others are so tense that if they are touched, they vibrate. Most of us are in between.

If, in doing a physical examination, we find it difficult to elicit the patellar reflex, it is a common practice to use "reinforcement". The patient is asked, for example, to clasp his hands in a relaxed manner and to stay relaxed until commanded to "Pull!". The reflex hammer is applied simultaneously and, in a normal situation, the sought after reflex is produced. Why? Simply because the patellar tendon and associated muscles are now in a state of increased tonus because of the muscular contraction elsewhere. It is very difficult, if not impossible, without training to contract one skeletal muscle without simultaneously tensing others in totally different parts of the body; they will not be contracted maximally but the tone will be increased. And so will be the pressure on the capillaries everywhere in the skeletal musculature. Unless there is a simultaneous capillary dilatation in the splanchic circulation — and this is precisely the opposite of that which normally occurs -- the blood pressure will rise, as it must, to overcome the muscular compression.

The work of Azuma and Oka, cited by Palmer, "predicts that closure of a microvessel may result from increased muscle tone (muscle contraction) or from increased extravascular pressure but cannot result from reduced intravascular pressure alone", providing additional support for the thesis presented.

A chiropractor claims that he successfully lowered blood pressure in his patient by successfully treating a painful lumbar muscle spasm; he probably did, on both counts. Muscular relaxation, whether induced by sleep, anesthesia, hypnosis, heat, massage, meditation or through training will successfully lower blood pressure during the period of relaxation, provided that the elevation was due to increased muscle tone. There are other causes.

Obesity

One of these is obesity -- the accumulation of excess fat which occurs almost exclusively because of the intake of more calories than are required for the maintenance of a state of equilibrium at a "normal" weight. Some people think of fat as existing pretty much like depots of lard and, to be sure, it may appear that way. But Wertheimer and Shapiro, experts on the subject, tell us that "Adipose tissue is a tissue with a special structure and a special type of cell. It is supplied by a comparatively dense capillary net and innervated by sympathetic fibers."

Wasserman remarks that Toldt, in 1879, had shown that developing fat lobules in the embryo had their own vascular system and were clearly separated from the surrounding connective tissue. Wasserman himself reemphasized the rich vascularization of fat in 1926 and, in the reference cited here, repeatedly comments on the rich capillary network present in adipose tissue. His Figure 5 illustrating the circulation of a primitive fat organ.
looks startlingly like a glomerular tuft of capillaries.

Quoting Wassermann directly, “In microscopic sections of mature adipose tissue, the capillaries seem to be scarce because they are separated by the large fat cells. In the past certain observers have stated that this tissue had a poor blood supply. However, Gersh and Still (1945) calculated the ratio of the surface of the vascular bed of adipose tissue to that of the volume of protoplasm in the cells and found that the capillary bed is actually far richer than that of muscle. Recently, Hausberger and Widelitz (1963) determined the vascularity of muscle and adipose tissue by measuring the activity per gram of tissue after injecting Cr\(^{51}\)--labeled erythrocytes. Their conclusion was that ‘the vascular bed of adipose tissue is of the same order of magnitude as that of muscle.’ It is therefore certain that the rich vascularity of the primitive organs remains a characteristic feature of the fat organs.”

It appears that the usual method of fat accumulation is simply by enlargement of existing individual fat cells wherein the cell diameter may increase up to 7-10 times its original size. New fat cells may appear, most likely from the same reticular stock which originally gave rise to the existing capillaries and fat cells.

Of interest is Hausberger’s observation that “excessive fat deposition, regardless of origin, is accompanied by growth of new fat cells as shown by cell count and DNA determination. These newly formed cells show a remarkable tendency to persist during prolonged periods of weight reduction. They apparently do not easily revert into less differentiated cells.”

Sheldon was equally emphatic in his remark that “the large number of blood vessels in fatty tissue has recently been reemphasized and one can liken the relationship of fat cells to the capillaries in replete fat tissue to the relationship of the alveolar cell of the lung to the pulmonary capillaries.”

Sheldon’s Figure 1 shows an electron micrograph illustrating the close relationship of the adipose cells to the capillaries: “An erythrocyte (rbc) lies within a capillary cell in the middle of the plate, and portions of five adipose cells can be seen surrounding the capillary” (emphasis my own).

Other supportive information is supplied by Tedeschi who noted that “the pericellular reticulum of argentaffin fibers is more prominent when the fat cells become smaller, and under this condition the density of blood capillaries increases also.” Since the density of blood capillaries is unlikely to change in a magical fashion, this observation supports my view that the capillaries were already there but not visible because of compression. As the fat cells decrease in size by lipid depletion, tissue pressure is reduced and full capillary expansion occurs more readily.

Tedeschi is further supportive in the following passage: “Gersh and Still (1945) have determined that the mean diameter of the capillaries is 6\(\mu\) in fat-rich and 7\(\mu\) in fat-poor adipose tissue. They have also indicated that the mean surface area of capillaries per unit volume of fat (S/V) is 23.5 in well-developed fat and 64.1 in lean fat tissue, and that the ratio of the surface of the capillary bed to the volume of tissue supplied by the vessels is 51.9 in fat-rich tissue and 222.2 in fat-poor tissue. Thus, for purposes of metabolism, the capillary bed of the adipose tissue is even richer than that of the striated muscle.”

FIG. 3 Capillaries coursing between fat cells; peri-lobular fat, guinea pig thymus. (Original magnification x500). Photo by the author.

Describing a pathological disorder of fat apparently due to a Vitamin E deficiency, and referring to the work of Davis and Gorham (1954) and Granados, et al., (1947), Tedeschi noted: “The pressure exercised by the accumulation of pigment causes collapse of blood capillaries, resulting in impaired circulation and tissue edema, as well as necrosis of fat cells.”

In sum, the evidence presented supports the view that a compartment containing many fat cells and capillaries but little fat accumulation may well have its capillaries fully opened; the same compartment now filled with fat may greatly compress its...
capillaries, thus requiring a greater blood pressure for perfusion. My thesis is that people who carry excess fat are apt to be hypertensive; loss of weight, even a few pounds, could have the salutary effect of reducing tissue pressure and dropping blood pressure to a greater degree than one might suppose without an understanding of the mechanism. It seems logical to assume that tissue membranes are very important structures to consider here for, if they yield readily -- and many have been previously stretched -- tissue pressure will not build up as rapidly nor as surely.

**Fluid Retention**

When more sodium is taken into the body than the kidneys can remove in a timely way, the blood and tissue concentrations of sodium can be held at a physiologic level only by dilution. Increased fluid intake provides an increase in blood volume which is accompanied by an increase in blood pressure which then results in higher filtration pressure at the capillary level. This is reflected by greater filtration by the glomeruli and a loss of fluid into the extracellular space of the tissues. Some fluid is normally reabsorbed at the venule end of the tissue capillaries and some is carried off in the lymphatic drainage. When filtration exceeds removal, the tissue compartment will fill with fluid and, if its membranes are flexible and not significantly opposed, the compartment may enlarge without much initial change in tissue pressure. However, if the membranes are unyielding or stretched under tension, the pressure in the compartment must increase, as previously noted. The pressure required to keep the capillaries open will necessarily be greater than when the tissue pressure was “normal”. This increase in capillary blood pressure can be provided normally in only one way: the systemic blood pressure must be raised. To reverse the procedure, remove the excess sodium from the tissues by decreasing the amount in the blood; tissue pressure will fall as salt and fluid leave it to maintain the equilibrium as sodium levels decrease in the circulating blood.

Tobian’s remarks are supportive: “A high NaCl intake may produce hypertension if it increases extracellular fluid volume. The same high NaCl intake produces no hypertension if extracellular fluid expansion is prevented.”

One should keep it in mind that the capillary pressure will vary with the level of the vessels relative to the heart. The weight of the fluid will add to the hydrostatic pressure in the capillaries so that there is a higher head of filtration pressure in the dependent parts of the body, resulting in greater influx of fluid into the tissues. This is modified when the body is immersed in water due to the changed external pressures upon the body.

**Discussion**

I don’t think it is necessary to go into any protracted discussion about the facts which are already well-established concerning hypertension and excess salt consumption, hypertension and obesity and hypertension and stress. Removal of these factors has been the mainstay of treatment for the past 75 years, with ups-and-downs from time to time. There is no doubt that these things work; what I have tried to do is figure out why. The answer I have come up with is so simple that it seems to be incredible but I have been unable to come up with anything to destroy it in spite of six months of searching actively after six years of just thinking about it and discussing it with friends, some of whom have assured me that they have always understood my answer to be the mechanism. Why they never told me is unforgivable! On the other hand, it is so simple that small children seem to have no trouble grasping the concept. Using my body as the heart, my right arm as the artery, touching the tips of my fingers together to build a capillary network which runs into my left arm as the venous return, I ask what would happen to the circulation if all the “capillaries” were squeezed shut? “It would stop if you didn’t use more force -- if you didn’t raise the pressure!” Higher pressure is “essential”.

Which brings us around to a consideration of what we are doing when we lower the pressure in essential hypertension by means other than those outlined here. Certainly we are protecting the heart and the integrity of the vessels and, in time, if the problem is salt retention, it can be corrected by dietary modification and drugs to increase salt excretion. But this doesn’t do much for those who are fat or tense -- or both. With lowered pressures, tissues may not be nourished adequately and some “side effects” of drug therapy may be referable to tissue ischemia and malnourishment in the presence of “normal” pressure.

Obviously, the best way to treat hypertension is to prevent it and avoid the delayed physical changes in the heart and arterial vessels which may be irreversible.

A major advantage of having plausible explanations of mechanisms is that a more convincing story can be told as part of our preventive medicine package. Another advantage is that it provides a new direction for research activities regarding the treatment of essential hypertension and other circulatory phenomena. Perhaps not least, it provides a rational basis for other therapeutic approaches.

This theory makes it reasonable to expect an elevation of blood pressure from static exercise of various kinds and from acute and chronic pressure increases on or in body tissues. A rise in intracranial pressure is accompanied by an increase in blood pressure sufficient to exceed the tissue
pressure; we have known this for over 75 years and assumed it was due to an effect on the medulla; perhaps it is not. It was demonstrated 70 years ago that pressure exerted on the external surface of the kidneys by oncometers producing external pressure exceeding the systolic level will raise blood pressure. And whereas the whole body may be placed in a pressure chamber and subjected to moderately increased pressure without striking blood pressure changes, increasing the pressure on the body with the airway in full communication with the atmosphere will raise the pressure since the pulmonary capillary bed is placed at a pressure level lower than that of the rest of the body. This suggests that the reverse procedure might be useful in the treatment of congestive heart failure, i.e., if the body were placed in a chamber below atmospheric pressure, a lower blood pressure would be required for systemic capillary perfusion. Without the necessity for hyperbaric oxygen, the gas supplied at normal pressure may suffice to assist in the recovery of the heart’s vigor and appropriate nourishment of peripheral vessels and tissues. Following a sufficient degree of recovery, gradually increased chamber pressure or increased pressure on the torso and lower extremities by water immersion or other means could produce a good diuresis. Perhaps it has already been done.

Orbiting astronauts experience weightlessness with its associated loss of hydrostatic pressure and a shift of about 2 liters of blood and interstitial fluid from the lower body to the head and thorax. A similar shift occurs when water immersion occurs with the head out, greater changes being noted with the body in the erect position. The early work of Crile and more recent studies have indicated that positive pressure breathing may control this shift, presumably due to the effect on capillary blood pressure in the pulmonary circulation. Since all body capillaries may be considered to be at heart level in immersion or at zero gravity, positive pressure in the pulmonary bed or induced negative pressure on the lower body should counter the vascular changes typical of the weightless state.

With particular regard to hypertension, an observation cited by Epstein is of special interest. He reported that Lange et al. found that one of ten subjects undergoing head-out immersion failed to redistribute his blood volume significantly and showed only a small change in cardiac blood volume; this subject had marked hypertension. This suggests to me that the compartmental capillary compression theory may be applicable to explain this phenomenon.

It could well be that the accumulation of fat and tissue fluids commonly seen in middle-aged females accounts in part for their greater incidence of hypertension. The thought also occurs that the elasticity of tissue membranes, known in some cases to be inheritable, might be an important genetically determined factor affecting blood pressure in some individuals.

May I suggest that before rushing to the laboratory to test the thoughts presented here, one might profitably review the references listed, certainly not neglecting the observations reported in 1903 by Crile. In this and other outstanding researches, one will find supporting evidence in abundance. For those who prefer to wait, the second article in this series will be devoted largely to detailing, organizing and interpreting the work which has already been done but which could not be discussed at this time.

I cannot end this paper without paying tribute to Dr. Simon Rodbard and his associates. His work was unknown to me until a few months ago when I ran across it in the course of my investigation; I tried to call to tell him of the arrival of another with similar thinking but learned that he had died in 1975. His work is outstanding -- including circulatory models -- and is totally supportive of the concepts presented here. Others over the years, not the least of them Richard Bright, have come very close to this discussion. Bright’s remark in 1836 occurs in his discourse on the cause of the increased work that led to cardiac hypertrophy in the absence of valvular disease: "...This naturally leads us to look for some less local cause, for the unusual efforts to which the heart has been impelled: and the two most ready solutions appear to be, either that the altered quality of the blood affords irregular and unwonted stimulus to the organ immediately; or, that it so affects the minute and capillary circulation", as to render greater action necessary to force the blood through the distant sub-divisions of the vascular system." To Dr. Bright, my compliments; to all others unsung, including the library staff who have labored in this vineyard, my thanks!

"Emphasis my own

REFERENCES CITED


15. Bright, Dr.: *Cases and observations, illustrative of renal disease, accompanied with the secretion of albuminous urine*. Guy's Hospital Reports, 1:338-400, 1836. London.

**OTHER BACKGROUND SOURCES**


