Conklin

SECOND PAPER

CARDIO-VASCULAR CHANGES

DUE TO LITHAEMIA.

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OF NO PART of the body is it more true, than of the heart and arteries, that continued perversion of function leads to structural change. A law, universally applicable to organized matter, is that of adaptation and compensation, which work for conservation, and as abnormal conditions become fixed upon the human body, such metamorphoses of structure follow as are, in a measure, compensatory to the primary departure. It is in this manner structural change follows upon functional perversion.

But compensatory growth has its limit, and unfortunately compensatory tissue tends to early decay. Structural degeneration then marks the spot that, for a time, was saved by hypertrophy. Structural disintegration may be primary when force is so great, or suddenly applied, as to leave no time for compensatory growth, as in dilatation, aneurism, or rupture of the heart or arteries. Degenerative changes, without antecedent hypertrophy, as myocarditis, dilatation and "anæmic necrosis," may follow as trophic changes upon occlusion of a coronary artery.

Cardiac hypertrophy is probably always compensatory, as, in the opinion of Thoma, is also arteriofibrosis, while sclerosis marks the secondary process of degeneration.

Virchow denied the existence of an acute idiopathic endarteritis, but, latter-day opinion reflects a belief in a form which Jno. A. Wyeth in his work on surgery calls, "Traumatic Arteritis, resulting from causes within the vessels." Though classified as idiopathic inflammations, these cases "are none the less due to violence—the impinging force of the blood current," and occur at points in the arterial system where pressure is greatest, as, "the sinus magnus of the aorta, at the aortic bifurcation into the two common iliacs and the arch of the innominate." This is in keeping with the law that, the nearer the heart the greater the blood pressure.

Most latter-day writers concur in assigning to gout, rheumatism and lead poisoning a prominent rôle in the causation of

endarteritis and arteriosclerosis, but err, I think, in explaining their influence by assuming a local action of circulating toxins, else we should expect to find these results more diffused. Gout and rheumatism are recognized localized expressions of uric acid retention, and, as we know now that lead retards the elimination of uric acid, this may explain the causative influence of plumbism in a large group of diseases.

H. Vaquez, of Paris, with the aid of the tonometre, has made a very interesting study of plumbism. He finds blood pressure constantly high, reaching its maximum during the paroxysms of colic and running parallel with the abdominal vascular spasm, which he likewise finds constant, and names as "the forerunner and maintainer of the hypertension." Confined at first to the splanchnic vessels, the result is abdominal spasm and colic, but, as vascular contraction becomes generalized, hypertension spreads to the cerebral vessels, and the encephalopathy—convulsions, etc., follow. The lesson he draws is this: "This long persistence of hypertension is remarkable, as hypertension due to vasoconstriction was always supposed to be more briefly transient."

M. Bach, of Germany, reports an interesting series of cases of "Splanchnic Colic," which give some support to the theory of the angiospastic origin of the colic of plumbism. All his cases had high blood pressure, and certain cases presented cardiac hypertrophy, accentuation of the aortic sound, contracted kidney, and one case had, also, attacks of angina pectoris. Theobromin, diuretin and strophanthus, which dilate the blood vessels, promptly relieved the attacks. "No other form of abdominal colic is thus amenable to these drugs, and this success is pathognomonic of arteriosclerotic colic."

Immediately following the short, sharp second sound of the heart, announcing the closure of the aortic valve, the ascending portion and arch of the aorta is sustaining the highest degree of pressure that comes to any part of the arterial system, and it is this factor, strain, which involves this part more often than arteries more remote from the heart, in the various processes of structural change.

Admitting that the improved arteriometres of the day metre, with an approach to accuracy, blood pressure in arteries to which they may be applied, we are still without means of measuring aortic or cardiac pressure, for it must be true that a measure of systolic pressure is momentarily stored in the elastic coat of the aorta, the recoil of which forces the blood on into the accessible arteries, under more uniform and somewhat lower pressure. In the aorta and larger arterial trunks, elastic tissue largely displaces muscular tissue in the media, and in these parts high blood pressure gradually exhausts the elasticity of the vessels; dilatation ensues, and atheromatous degeneration is the terminal stage. In the smaller arteries, muscular tissue predominates in

the media and strain begets hypertrophy—arteriofibrosis, in keeping with physiological law.

The causes of fibrosis and sclerosis, as recognized for years, may be epitomized by the word strain, increased blood pressure, and this, latter-day writers are largely unanimous in assigning to contraction of the arterioles, resulting from the toxic action of retained products of metabolism. Arteriofibrosis is compensatory hypertrophy; arteriosclerosis is ultimate degeneration. They should not be confounded though the former may end in the latter. The one means a thickened, tortuous but compressible artery, the other an unyielding, straight, but beaded tube —a "pipestem artery." With fibrosis, sclerosis and atheromatous degeneration established, the question of relative weakness determines when, and where, the weakened wall yields to dilatation, aneurism or rupture.

Of the classical signs of arteriosclerosis—"increased arterial tension, palpable thickening of the arteries, hypertrophy of the left ventricle and accentuation of the aortic sound," the first is the causative factor, of which the others are the result, and all follow logically upon contraction of the peripheral circulation, as in lithæmia. The greatest advantage to be gained from an appreciation of this, the most important factor in the causation of vascular degeneration, is not the suggestion of a rational therapy, though this is not to be under-estimated, but, the opportunity it offers to institute a preventive regime.

We prefer to believe with Albutt, of Eng., that high blood pressure does not, at all times, mean an already-developed arteriosclerosis, as von Basch, of Germany, and his followers claim, but that there is a presclerotic stage in high-blood pressure, when its consequences are functional only—a stage when we face the parting of the ways. The straight and narrow way leading to longevity and the rapid transit route to presenility. It is during this presclerotic stage only, that our efforts will avail against those vascular and cardiac changes that lead to premature decay. The sclerotic stage admits of palliation only.

Dr. Henry Wireman Cook, of Richmond, before the Virginia State Medical Society, in 1904, in an interesting paper on "The Early Recognition of Hypertension," spoke in prophetic language the profession will do well to ponder. He divides the causes of death into two groups, "traumatic, including infection," and "the wear and tear of life," and concludes: "It is in this group that a larger and larger proportion of maladies belong, and finally when our methods of sanitation and prophylaxis are perfected, it is the way practically all will die." Longevity will then, indeed, become a cardio-vascular question.

Since no part of the greater circuit escapes the consequences of high blood pressure, there is no organ of the body, save the lungs, that may not be thought alone at fault, while reflecting only a general hypertension, or arteriosclerosis. Renal symptoms, for instance, may easily be mistaken for nephritis. Car-

diac hypertrophy, dilatation, and systolic murmurs may impress the physician that "heart disease" is his patient's primary and sole trouble. Such periodical symptoms as migraine, vertigo, myalgia and claudication are suggestive of malaria, while the bradycardia of hypertension, in keeping with Marey's law, and the tachycardia of an overworked heart may be dismissed, by the thoughtless physician, as matters of individual idiosyncrasy.

The significance of hypertension, as a cause of both cardiac and renal perversion, is shown by their association in the broad condition known as Bright's disease. The cardio-vascular symptoms, showing high blood pressure, may precede the renal symptoms, or, may be secondary to the lesions in the kidney. "The former occurs, I believe, with much greater frequency than has been supposed." *Osler.*

There is little warrant for the contention that the impairment of the circulation, in an organ so small as the human kidney, would have the mechanical effect of appreciably raising the general blood pressure, and hence, of inducing arteriosclerosis. If so, it should be likewise a result of nephrectomy, and in cirrhosis of that much larger organ the liver. Is it not more logical to conclude that, a primary functional impairment of elimination, leading to toxæmia and hypertension, is responsible for the general arteriosclerosis, of which that in the kidney is a part?

The influence of high blood pressure upon the function of the kidney is shown by the fluctuations of the urine, in quantity and sp. gr., a uniform amount of fluid being drunk; albuminuria (physiological) from the increase in blood pressure upon assuming an upright position; and hyaline and granular casts, in the absence of nephritis. This perversion continued over a period of years invites structural change.

A contracted circulation means diminished secretion, in glandular organs, while localized compensatory hyperæmia brings increased secretion, or exudation. Impaired nutrition, affecting both growth and repair, sensory and motor disturbances and trophic degenerations, likewise, follow upon a contraction of the circulation. Pruritus, formication, numbness, sensations of heat and cold are common toxic symptoms in lithæmia. Chorea, epileptiform convulsions, hysteroid spasm and spasmodic asthma illustrate exaggerated motor impulses springing from the same cause. Paralysis of the rectus muscles of the eye and recurring paralytic involvement of muscular groups in the limbs are conditions of recognized toxic origin, to say nothing of hemiplegia following the rupture of a cerebral vessel from hypertension or arteriosclerosis.

To such an extent does this contraction of the circulation in lithæmia affect nutrition, that a form of spurious anæmia has been pointed out, by various writers, as a feature of this diathesis. A blood count, however, shows a normal number of red blood corpuscles and a normal percentage of hemoglobin.

There is ischæmia, but not anæmia, and, as pointed out by the writer three years ago, is now very generally attributed to contraction of the cutaneous vessels. The quantity of blood at the surface, not the quality, is reduced.

In writing of arteriosclerosis, Alfred Stengle speaks of it thus: "The important fact, however, must be recognized, that apparently progressive anæmia, without alteration in the blood count, or the amount of hemoglobin, is significant of arterial disease, though not, of course, pathognomonic." The lithæmic is not so pale as sallow; the complexion lacks the pink hue of health and the marble look of anæmia. Subdermal tissue has shrunken and the dry inelastic skin closes down upon the irregular contour of bone and muscle.

This bloodless condition of the surface of the body, clearly visible, it seems to me, alone, refutes Haig's contention of "obstruction of the capillaries," on which he builds the superstructure of his voluminous work on uric acid. Obstruction means "hyperæmia and stasis on the arterial side," as he argues, for it cannot be denied, but "hyperæmia" presents the picture of fullness of tissue, with heat and redness, and is diametrically opposed to that which really presents.

A study of the circulation in lithæmia furnishes ample confirmation of the terse statement of Prof. James Barr, made a year ago, at the opening of the Liverpool Medical Institute. "Diseases of the heart most frequently arise from causes acting on the periphery, and hence there is here no room for specialism." Among such causes he adds: "The effects of wines and malt liquors in the production of gout are well known, but the excessive indulgence in nitrogenous foods is even more pernicious to the vessels. The retention products in diseases of the kidneys are potent factors in producing arteriosclerosis." "The purin bodies, whether of endogenous or exogenous origin, contract the arterioles and so raise the blood pressure."

When a uniformity of means and methods employed brings harmony to conclusions drawn, we shall probably accept as normal a systolic blood pressure of from 125 to 140 mm. Hg. and 75 to 90 mm. Hg. during diastole. Being influenced by as many factors, it must be as variable as pulse rate.

Regardless of what may be considered normal, the fact that blood pressure increases as we approach the heart explains the relative frequency of aortic and cardiac lesions, arising from hypertension. The aorta sustains the very maximum of arterial tension, and, as is well known, suffers from aneurism more often than any other artery, and for the same reason, the arch and thoracic portions suffer more often than the abdominal by twenty to one. Atheroma, likewise, is most often seen in the arch of the aorta, and particularly along its greater curvature, which receives the direct impact of the blood stream as it leaves the heart.

If it be recalled that the coronary arteries are branches of

the aorta, arising immediately distal to the aortic valve, it will be seen they, too, come within the area of maximum blood pressure, and strain once more explains the frequency with which these arteries are involved in sclerosis, and the maximum pressure they bear explains why they may be nearly obliterated by atheromatous degeneration, with little evidence of vascular change elsewhere, as seen occasionally in fatal angina pectoris. Being thin walled, with a minimum of muscular tissue, the coronaries, like the cerebral vessels, undergo sclerosis rather than fibrosis. In proportion as the middle coat of an artery is made up of muscular instead of elastic tissue, strain will be met with hypertrophy and fibrosis will precede sclerosis.

Again, the coronaries being end arteries, an obliterating arteritis shuts off the nutrition of the distal part, as when 'anæmic necrosis' ("one of the common causes of sudden death"—*Osler*) results from a blocking of a main branch, or a like process in the primary trunk brings fibrous myocarditis, acute dilatation, aneurism, or even rupture, especially with the left ventricle.

Angina pectoris is but relative heart weakness. It is weak in relation to the work to be performed. This may be from intrinsic heart weakness, increased peripheral resistance, or both. The form of toxæmia we are considering not only increases peripheral resistance, but, as pointed out, weakens the heart muscle at the same time. That angina may result from hypertension alone, is shown by the absence of coronary disease, or other structural change, in some fatal cases. Blood pressure transcends heart power, over distension of its cavities explains the agonizing pain, and the heart stops in extreme diastole; its cavities being found post mortem distended with clot.

Brodie in 1846 pointed out the incapacity of sclerosed arteries for supplying the necessary amount of blood to muscles to repair the waste incident to severe or even slight exercise, and Charcot two years later attributed pain in the limbs to the same condition, and when occurring in old age is premonitory of impending gangrene.

It is not the aorta and cardiac walls alone that suffer from hypertension. Fully one-half of all cases of valvular disease are of the mitral valve. Again, relative strain explains relative frequency of involvement. The mitral valve, of all the cardiac valves, feels the maximum strain, since it sustains the pressure of left ventricular systole while the aortic valve yields to it. Seeming trifles often point a lesson. Why the seeming fortuitous distribution of vegetations upon the auricular surface of the mitral valve and upon the ventricular surface of the aortic valve, when involved in endocarditis?

With the mitral valve, pressure is upon its ventricular side. It is made to bulge into the left auricle and strain falls more heavily upon the delicate endothelium of its convex surface. Conversely, the maximum of pressure upon the aortic valve is from the aortic side, during diastole, its segments are made to

bulge into the left ventricle and the endothelium on the convex surface, as with the mitral, feels the greater strain. It is impossible to get away from the factor strain in studying cardio-vascular lesions, or from the conception that they are mere mechanical injuries 'resulting from causes within the vessels.'

The thickened endothelium, with its vegetations, is a form of hypertrophy, a conservative process; and we see the same change going on with the chordæ tendinæ, especially of the mitral valve, and with the columæ carneæ of the left ventricle. As a chain is no stronger than its weakest link, so, the left ventricle can withstand no greater increase in peripheral resistance than can be borne by its weakest point: and as its walls are strengthened by hypertrophy, it would mar the infinite beauty and wisdom of the conservative process did not its valves, too, participate in the fortifying transformation.

Valvular lesions upon the right side of the heart are rare indeed, save as they occur secondarily to left side lesions, or, in fœtal life. This argues that some force is operative upon the left side of the heart and not upon the right. Will the present-day theory of the bacterial origin of valvular endocarditis explain the preponderance of left-side lesions in the adult and right-side lesions in the fœtus? By no means; and furthermore, any pathogenic germ entering the system would be borne upon the lymphatic and venous currents to the right side of the heart first. We know no difference, in vulnerability, between the valves of the two sides, nor, between valvular and mural endothelium, yet the latter is not commonly affected save in syphilis.

We are driven to the conclusion that the frequency of left-side lesions is due to some factor beyond the heart itself, and other than bacteria. It is the factor strain, reflected by the systemic circulation upon the left heart. The same factor explains right-side lesions only, in the fœtal heart, for it is the right side of the heart then that has most to do with propelling the entire circulation. Right-side valvular lesions in the adult, follow upon pneumonia, emphysema, or mitral insufficiency, all of which, by obstructing the pulmonary circulation, put more work upon the right heart, and unusual strain upon the tricuspid and pulmonary valves. Whatever cardiac lesion we take up, we find strain has gone before.

The freedom with which the blood makes the round of the pulmonary vessels, which, as compared with the systemic, are short, not supplied with vasomotor nerves favoring contraction, and are wonderfully distensible; calls for little power in the right heart, hence, we see its walls but one-fourth as thick as the left, and the tricuspid segments much thinner than the mitral. Even under conditions of increased pressure in the pulmonary vessels, their thin elastic walls, surrounded by soft and yielding peri-vascular tissue, become greatly distended before reflecting that strain back upon the heart.

Any one cause of valvular disease is a simile of all the rest

laid down in our text books and their coefficient is strain. This falls most heavily upon the mitral, aortic, tricuspid and semilunar valves, in the order here given, and explains the frequency of their involvement which is in the same order. The mitral valve sustains the maximum pressure of left ventricular systole, and is greater than pressure upon the aortic valve, which represents arterial tension, by just so much as is necessary to force approximately two ounces of blood into the aorta, after the aortic valve has been thrown open. Furthermore, the instant left ventricular pressure equals arterial tension, all strain upon the aortic valve is overcome, and at this supreme moment, fortunately of brief duration, the mitral valve is bearing the strain of ventricular contraction, aortic recoil and peripheral resistance.

Thus we see how the condition lithæmia leads to valvular endocarditis, through "causes within the vessels," and we have only to recount the structural changes that legitimately follow upon inflammation of valvular tissue to understand how contraction and puckering leads to incompetency, and thickening and rigidity, with calcareous degeneration and adhesions, bring about stenosis.

Valvular lesions being established, it becomes only a question of time, when grave changes will follow in the cardiac walls. What these changes will be may be quickly told and readily remembered if the following rule be borne in mind. The first effect to follow upon stenosis, or incompetency, is that the chamber of the heart lying immediately behind that valve, speaking with reference to the direction of the blood current, is habitually over-distended. Over-distension of a cavity means strain upon its walls which, sooner or later, begets hypertrophy, or dilatation, or a measure of each. Once more we find the factor strain leading to mechanical injury.

In a general way, we may predict that dilatation will ensue in all weakened states of the heart muscle, under sudden and severe strain, and with valvular insufficiencies permitting diastolic over-distension; while hypertrophy will as generally occur, the heart being well nourished, with a constant increase in peripheral resistance, and with valvular lesions requiring forcible systolic contractions to drive the blood through stenosed openings. As Osler says: "In consequence of the peripheral resistance and increased work, the left ventricle increases in size, and some of the finest examples of simple hypertrophy occur in this condition. The chamber may be little if at all dilated."

The race, however, is not always to the fleet or victory to the strong. Time levels many inequalities, and a powerful heart that at first triumphs over increased peripheral resistance, eventually bears the scars of the unequal contest and dilatation follows upon hypertrophy. Mechanical force triumphs over compensatory growth, or in the language of Alfred L. Loomis, "The vital powers of hypertrophy gradually merge into the mechanical process of dilatation."

Rzentkowski, of Warsaw, and Jouse induced high blood pressure, experimentally, by injecting rabbits, intravenously, with adrenalin. The morbid changes noted were: (1) hypertrophy of the heart, (2) numerous localized patches of calcification in the aortic walls, and (3) cirrhosis of the liver and hyperæmia of the kidney. Some rabbits died in a few days of acute dilatation of the heart. Adrenalin, as is well known, raises blood pressure by contracting the smaller blood vessels, thus paralleling the action of faulty metabolism, in bringing about what Dr. Cook, of Richmond, calls "autotoxic contraction of the arteries."

The error is still being perpetuated of holding gout and rheumatism responsible for cardio-vascular troubles, as shown by the following quotations: "The two influences, rheumatism and perverted metabolism, acting together, no doubt are accountable for a considerable number of cases of atheroma and chronic arteritis." "Disturbances of metabolism, including gout, are by far the most prolific cause of cardio-vascular disorders and disease after forty, at any rate, amongst the middle and higher classes."

"Whatever be the cause, all writers recognize gout or rheumatism as a possible factor in the production of sclerosis. In this connection may be mentioned the so-called rheumatism of many claimants (for pension) showing well-marked evidence of arterial disease, with but little or none of the joint changes of rheumatism." *R. B. Baker, Washington, D. C., Pension Surgeon.*

No one knows better than the pediatrist that a rheumatic arthritis, per se, has little to do with the occurrence of endocarditis or other heart lesions that may, or may not co-incidently appear. Children are prone to cardiac injury when suffering from faulty metabolism and may suffer from severe valvulvar inflammation without ever having had an arthritis, or other symptoms of rheumatism save 'growing pains,' myalgia, cramps in the legs or an iritis. A relationship between gout and rheumatism and certain cardio-vascular changes cannot be denied, but, it is not that of cause and effect. A gouty or rheumatic arthritis never caused endocarditis, myocarditis or arteriosclerosis. It should be taught, rather, that nitrogenous products of metabolism are the common cause of each. When deposited in the joints they occasion an arthritis, and while circulating in the blood, by raising blood pressure, either coincidently with, or quite independent of the arthritis, may work an injury of the valves of the heart in the manner we have shown. Rheumatism is not a cause of endocarditis, but that which induces the one induces the other.

As Albert E. Roussel, of Phila., has correctly observed: "True gouty subjects (rare in this country), are less apt to show myocardial change than those in whom the joints have never been inflamed, but who suffer from other irregular manifestations of the disease. This American gout, or lithæmia, which is

often difficult of recognition, is doubtless, in many instances, an explanation of those cases in which an apparent etiological factor could not be found."

"The treatment of angina then resolves itself into the treatment of high arterial tension. The resistance in the peripheral circulation which gives rise to this, I place, primarily, in the capillaries, and it is attributable to the presence in the blood of impurities which provoke this resistance. The object before us then, is to prevent the formation and promote the elimination of these toxins." "During the paroxysms the one condition of the circulation which seems to be always present is contraction of the peripheral arterioles." *W. H. Broadbent, Sr., M. D., London.*

Prof. Osler divides the causes of cardiac hypertrophy into "conditions affecting the heart itself" and "conditions acting upon the blood vessels: (1) General arteriosclerosis, with or without renal diseases; (2) all states of increased arterial tension induced by the contraction of the smaller arteries, under the influence of certain toxic substances, which act as Bright suggested, by affecting 'the minute capillary circulation, render greater action necessary to send the blood through the distant sub-division of the vascular system'."

Huchard, of France, tells us: "Strong and repeated emotions can induce cardiac affections by their incessant action on the peripheral circulation." Masso teaches that the emotions cause a contraction of the arterioles with resulting high blood pressure. This is a fact, coming so often under our observation as to hardly attract attention. Shock, grief, fright, and the deeper emotions generally are accompanied by ashen pallor, caused by contraction of the cutaneous arterioles, and it is recorded that fits of intense anger have been followed by sudden death. In short, any sudden and extreme emotion that throws the peripheral vessels into a state of tonic spasm, dams the blood back upon the heart and may stop its action in extreme diastole. If so the victim clutches the praecordial region, utters an agonizing shriek (anginal pain) and expires.

As with other manifestations of lithæmia, urinalysis may, or may not, aid the clinician in reaching a diagnosis of cardio-vascular troubles. If he is looking for a single condition of urine pathognomonic of a single definite cardiac or vascular lesion it will not be found: nor is there a single constant condition of urine showing the presence of lithæmia. The urine of the lithæmic varies from day to day, and over a wide range, in amount, sp. gr., color, percentage of solids and toxicity as well as at times showing albumin and casts. When this is not explainable by diet or variations in amount of fluid taken on different days, it may be taken as an index of fluctuations in blood pressure and the variations in the degree of contraction of the renal arterioles.

Increased blood pressure, theoretically, compensates vascular contraction, but the condition is one not favorable to glandular

activity. With a uniform blood pressure renal elimination will be inversely as vascular contraction: a scanty, highly-colored, highly acid urine of high sp. gr. showing a contraction of the renal vessels, and a free, light-colored urine of low sp. gr. indicating a patulous state of the vessels. Compensatory hypertrophy may bring polyuria without vascular relaxation as seen in the advanced stages of nephritis, blood pressure being very high.

After all, the true criterion by which to measure renal activity is the elimination of the urinary solids. These form the toxic part of urine. Is there daily normal elimination? The amount of urine signifies little. Concentration may compensate for diminished bulk and elimination be adequate, or, an increased bulk may fail to carry off a normal amount of solids. Manifestly the only reliable information to be gained is from measuring the amount of urine for twenty-four hours and testing a sample, of the total excretion, to determine the total daily elimination of solids as measured by urea or total nitrogen content. Not once, but daily, such an examination should be made until a perfect estimate of renal elimination is formed.

A practical rule I have found for estimating renal activity is to multiply the number of ounces of urine passed in twenty-four hours by the last two figures of its specific gravity and add to the product ten per cent. This shows approximately the number of grains of solids in the twenty-four hours' urine. By comparing this with Prof. Ethridge's tables showing the normal amount for men and women of different body weight we may readily determine if elimination is sufficient.

Prof. Roussel, of Phila., places a good deal of stress on the urinary excretion in cardio-vascular troubles. He says, in part: "A point, however, I consider of particular importance in these cardiac degenerations is the diminished amount of urine which is often only one-fourth, or one-half the normal amount. The amount passed should, therefore, be carefully measured in all doubtful cases. According to Bouchard there is diminished toxicity of the urine." "Cardiac degeneration" implies lack of heart power to compensate increased arterial tension. The toxicity of the urine will be diminished directly as the percentage of the solids is reduced.

Beverly Robinson, treating of "Neurotic Heart," calls attention to the fluctuating urine: the free light-colored urine of low specific gravity with diminished urea output, and, "Again, I have often seen urine of high specific gravity, moderate or small in quantity, with large urea output, upon cooling throwing down a large deposit of pink urates or red crystals of uric acid."

What, then, is the great significance of high blood pressure, as seen in lithæmia? It leads directly to those cardio-vascular changes that belong normally to old age and thus invites presenile decay. No other one factor is responsible for so much of human suffering and directly, or indirectly, responsible for so

many early deaths as our "strenuous life," with its impaired metabolism, imperfect elimination, resulting toxæmia and cardio-vascular changes. In common with alcohol and tobacco, its blighting influence upon the race should be taught, by our sanitarians and in our public schools.

"Ill fares the land to hastening ills a prey
Where wealth accumulates and men decay."

No more promising field presents for preventive medicine than the one we are considering. Its possibilities are boundless and determine the measure of human longevity. The full fruition of our best endeavors in this direction, however, will never be realized for the reason that our scheme of redemption carries with it so much of self-sacrifice for the individual and such radical reform in his manner of living.

What is the remedy for this suicidal pace, which the few set, and all must follow who stay in the race; a pace which if slackened invites financial ruin; a race which if won leads only to premature decay? The harvest is of the seed sown, and as the pace is fast the race must be short. As physicians, we may advise a more quiet life and moderation in eating and drinking, but only exceptionally can, or will, such advice be followed, and the field of the physician becomes limited to the softening of blood pressure by drug action and the palliation of its results. Our success will be measured by our ability to correct metabolism and stimulate the kidneys to the prompt elimination of such nitrogenous products as we have seen lead through toxæmia to hypertension.

Regardless of whether it is due to the resulting uric acid or some other product, we do know that an animal diet raises blood pressure, and for that reason our first duty is to curtail the use of meat; and those who believe only in the purin origin of uric acid may arrange the diet on the basis of purin content. Systematic exercise increases oxidation, improves capillary circulation and through this elimination. Tobacco, emphatically, should not be used in any form, in any amount, because its physiological action is to contract the blood vessels and raise blood pressure.

Alcohol has, I am aware, for years been condemned as a causative factor in arteriosclerosis, but I think, too severely. Alcohol dilates the peripheral blood vessels and does not increase blood pressure, and I am sure I have seen good results follow its use in cases of contracted blood vessels with hypertension. I would counsel moderation, however, and fix a limit of two to four ounces of whiskey in twenty-four hours. I would exclude malt liquors and wines because of their acidity. Water should be freely consumed to aid the work of elimination. The bowels may be kept open with soda phos.—the laxative for the lithæmic—adding benzoate of soda, if there is intestinal sepsis and auto-

intoxication, though I believe by far the larger part of the toxic products inducing hypertension, is formed in the tissues throughout the body, wherever the physio-chemical changes of cellular activity occur: an inadequate interchange between oxygen and carbonic dioxide.

Whatever the origin of the product, or products, inducing hypertension, it is true it, or they, prove toxic only while circulating in the blood, and those we are considering, the uric acid group, are intended for elimination through the kidneys. This is why the greatest measure of success following our application of drugs comes from the class—renal depurants. The salts of lithium, potassium and sodium, as is well known, are our best renal eliminants. In cardio-vascular cases the simultaneous use of such other remedies as have a special action upon the heart or arteries, or both, define the limit of our therapeutic possibilities.

The vasodilators, for instance, of which soda nitrite is the type, may be used in emergencies to reduce high-blood pressure and lessen the work of the heart, temporarily, pending the removal of the cause. When a strong heart action threatens dilatation or rupture of the arteries they may be fortified by the action of ergot or atropia. When the heart feels the consequences of high pressure more than the vessels we may, in turn, support it by such drugs as strengthen its contractions without increasing the contraction of the peripheral vessels. Our best agents of this class are caffeine, strophanthus, sparteine.

On the other hand, we have the alternative of lessening the resistance offered by the stronger part to spare the weaker. Instead of giving heart stimulants, we may prescribe vasodilators and take some work off the heart, and when the heart is sending the blood into the arteries with a force that threatens their walls we may spare them by lessening the force of the cardiac contractions with veratrum viride. Actual, instead of relative blood pressure, as measured by the arteriometre, will aid us in determining the end to be sought and the means to be employed. High pressure with weak heart calls for vasodilators, and with weak arteries calls for veratrum viride. Low pressure with weak heart and normal arteries is an indication for caffeine or strychnia and low pressure from relaxed arteries, with normal heart action will be benefited by ergot or adrenalin. A clear conception of the physiological action of the cardio-vascular remedies is imperative in treating the consequences of hypertension, and they should be used only upon reliable indications.

The conditions presenting in lithæmia, with high-blood pressure and cardio-vascular changes, are covered by a prescription combining a renal eliminant and a heart tonic which induces the least rise in blood pressure. As before stated, the alkaline salts are our best eliminants, and the heart tonics that cause the least contraction of the arteries are caffeine, sparteine and strophanthus. A ready-made formula combining the alkalies and caffeine is Alkalithia, and it is one of the best all-round prescriptions for

the cases we are considering I have used. Special cases, of course, will require in addition special remedies.

A contingent in the profession, I am aware, will take exception with me and prefer the salicylates as eliminants, but aside from their unpleasant action upon the stomach, the practitioner who becomes unmindful of the depressing effect of salicylic acid upon the heart may, in the very class of cases we are considering, meet with a very unpleasant reminder in the occurrence of cyanosis and heart failure. On the contrary, the alkalies have long been credited with warding off heart complications in rheumatism. "Potash, soda and ammonia, in small quantity, increase the tonicity of the muscular walls of the heart." *Bartholow.*

Though already long, I feel my paper would be incomplete did I not say a word, in particular, about digitalis and caution against its use. It is a time-honored remedy in diseases of the heart, and it is probably no exaggeration of the truth to say, that with nine-tenths of the profession, high and low alike, a diagnosis of cardiac trouble, functional or structural, is justification for prescribing digitalis. This is all wrong. It is not scientific medicine. It is not even justifiable empiricism, for the therapeutic results do not warrant the loose practice. Digitalis is not a remedy for every condition covered by the generic term "heart disease," and it is high time a halt was called and some regard paid to its physiological action, which is to greatly increase blood pressure by contracting the arterioles.

Increased blood pressure, from any cause, brings more forcible cardiac contractions to maintain a normal circulation in the face of peripheral resistance, and this compensatory action has been attributed to a direct action of digitalis on the heart muscle, thus crediting the remedy with tonic properties to a degree it does not possess. To make the heart beat harder or faster, by putting more work upon it, is not the action of a tonic.

Digitalis finds no place in the treatment of high blood pressure or its consequences up to the terminal stage of broken compensation, and even here, a remedy like caffeine or strophanthus, which has not so undesirable an action upon the arterioles is to be preferred. We have seen how high blood pressure becomes a direct cause of cardiac hypertrophy and the broken compensation that follows, if the cause be not removed. To give digitalis to fortify a heart that has been overcome by high blood pressure is a snare and a delusion, for at best, it can only increase the disparity between cardiac power and work to be performed. A better indication for digitalis would be low blood pressure from feeble heart action or low pressure from vascular relaxation, heart action being normal. Broken compensation calls for a true heart tonic that does not add to the work to be done by the heart.

Lauder Brunton and a co-laborer found on injecting digitalis into the circulation of a dog, that the arterioles were contracted to such an extent that the secretion of urine was either greatly reduced or ceased entirely, notwithstanding a marked rise in

blood pressure. This parallels the action of the uric acid group of toxins in some cases of urinary suppression. "In what is called the 'preventive treatment' of valvular lesions, following acute endocarditis, most commonly resulting from rheumatism. Dr. Fothergill emphasises the great necessity of giving these parts rest," and warns us of the "great danger of giving—what is very often ordered in these cases—digitalis, for it is well known, but unfortunately not a commonly recognized fact, that digitalis contracts the arterioles and thereby increases the blood pressure, the very condition which we should do our utmost to prevent."

A. Abrams, San Francisco. This writer gives us some very interesting tables recording the measurement of blood pressure which seem to show that, when arterial tonus is eliminated by amyl nitrite, digitalis has no effect to raise blood pressure; in other words, the high blood pressure following the use of digitalis is "illusory," and is compensatory to increase peripheral resistance, as stated above, instead of representing drug action. "This action is not uncommon in the administration of digitalis owing to its constrictor influence, and when the latter action implicates the coronary blood vessels the nutrition of the heart must suffer."

"The action on the heart of the digitalis substances is to increase the work of both ventricles, but, in not a few instances, increased work on the part of the left ventricle signifies an increased blood pressure which is very often an undesirable condition, as in nephritis and arteriosclerosis."

Merck gives us a short but "meaty" article in the "*Archives*" *for June, 1905,* on the joint use of digitalis and caffeine, wherein he says, in part: "In arterial disease, in hypertrophy of the heart, in diseases of the aorta and in chronic nephritis digitalis has been dethroned from its place among the cardiac drugs." "Caffeine, sparteine, ammonium carbonate, &c., have been pushed forward as perfect substitutes for digitalis, answering all the requirements of the heart stimulants without producing the unfavorable contraction of the arteries and the poisonous effect upon the heart muscle."

He cites also the facts observed by L. Braun, in his investigation upon mammalian hearts, of the simultaneous use of digitalis and caffeine. "The use of digitalis alone caused a marked constriction of the coronary arteries resulting in a pronounced paling of the organ. This is not the case when a combination of digitalis and caffeine is employed; the quantity of blood traversing the coronary arteries being by far greater than in the former case." "In the case of small doses the capacity of digitalis to narrow the vessel is entirely abolished." "The conclusion is readily drawn that caffeine neutralizes the vasoconstrictor elements of digitalis action." "The explanation of this favorable antagonism is that the blood supply of the heart is improved."

"It would seem as if the standard by which cardiac stimulants are to be judged is this: Do they reduce the blood supply to this organ? If they do they have to be considered toxic." Judged by this standard, certainly caffeine is not toxic, as Haig and his followers tell us: "In spite of the increased aortic blood pressure upon the administration of digitalis and caffeine the coronary arteries remain wide. How caffeine inhibits the vaso-constrictor action of digitalis is unknown."

It must be admitted, I think, that a remedy that can antagonize the constricting influence of digitalis upon the arteries has, itself, a diametrically opposite effect on them. It is inconceivable that caffeine has a different effect upon the arteries of one part than of another, and if it will restore the coronary arteries to a patulous condition in spite of digitalis it cannot have a like action to digitalis, in contracting the arteries throughout the body. A remedy that fortifies the action of the heart by improving its nutrition through a better circulation in the coronary arteries is alone entitled to the name, heart tonic. Such a remedy is caffeine; a remedy of which Bartholow wrote in the last edition of his "*Materia Medica and Therapeutics.*" "Until recently its powers as a substitute for digitalis were not appreciated." "Having the same kind of action on the heart, but not cumulative, and unirritating as digitalis, he has obtained as good results and with far less discomfort to the patient with caffeine." The weight of evidence is clearly against the use of digitalis in lithæmia with high blood pressure. Let me urge instead the use of caffeine or strophanthus, and when combined with the alkalies, as in Alkalithia, we are removing the cause and palliating its results with a single prescription.

It is proper also to caution against the use of ergot and adrenalin in cases of high blood pressure, for the reason, they have the effect of contracting the blood vessels and increasing arterial tension. Another word of warning and I am done. It is well known that whenever and wherever arteriosclerosis or atheroma occur, and with valvular degenerations following upon endocarditis, there is deposited interstitially in the pathological tissue limey matter, in proportion to the amount of available lime salts in the system; the so-called calcareous degeneration—"calcareous plaques." It is a part of the process of calcification of the arteries and to be expected as an inevitable sequence of long-continued high blood pressure. Our duty to the lithæmic is to anticipate this deposit of the lime salts and do nothing to favor the process. The salts of lime as therapeutic agents should not be given in cases of lithæmia showing continuous high blood pressure. This principle is recognized by all who have written on the subject of longevity, and is the basis on which the daily use of dilute phosphoric acid is advised in old age to put off senile changes. Calcium and magnesium are alkaline earths, instead of fixed alkalies, and it is the salts of the latter only that make up the "alkaline treatment" for uric acid troubles.