ARTERIO-SCLEROSIS AMONG THE INSANE.

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THOSE forms of arterial disease and degeneracy embraced in the terms "arterial sclerosis," "chronic endarteritis," "atheroma, etc.," are thought to have their beginning in certain inflammatory changes, regarding the exact nature and etiology of which some confusion as well as diversity of opinion exists. The disease, whatever its nature and origin, while it may in some cases involve all the coats of the blood-vessel, has its usual and characteristic situation in the intima, and for its usual and characteristic effect, sclerosis and loss of resiliency in the arterial wall. The process may be a diffuse one, but it is most commonly distributed irregularly, the inner surface of the vessel exhibiting patches of sclerosis separated by areas of comparatively healthy tissue, or is furrowed or wrinkled with irregularities. In many cases also there occurs a deposition of new material within the affected area of the vessel wall, this newly-formed tissue being in some cases hyaline and nearly structureless ("hyaline degeneration"); in others containing round cells, few or many, embedded in a hyaline or gelatinous matrix. This newly-formed tissue, furthermore, is very prone to early and extensive, slowly progressive, degenerative changes, fatty or, less frequently, calcareous in nature, which render the diseased areas more distinctly visible, giving rise to the familiar "atheromatous plaque." In later stages there is often breaking down and disintegration of the atheromatous patch with formation of shallow depressions, having ragged, irregularly contoured walls, —"atheromatous ulcers." A possible concomitant result of this disintegration is the formation of *emboli*, bits of the eroded wall being carried away by the blood-current to lodge in some smaller artery. Another effect of this degeneration and partial destruction is, necessarily, a localized weakening of the arterial wall favoring rupture with hemorrhage, or in certain cases resulting in the development of aneurism.

In those cases in which the degenerative change is calcareous in character, the formation of irregular chalky masses, or of smooth "calcareous plates," is a common result. In extreme cases these deposits may involve the entire circumference of the vessel for long distances, rendering the arterial wall so brittle that instead of bending it fractures under application of force. The fatty and calcareous degenerative changes are often combined; indeed, in the more serious cases this is the general rule, the

deposition of calcareous matter appearing as a later stage of the fatty degenerative atheroma.

The patches of atheroma are raised, usually encroaching slightly upon the lumen of the artery, although in ordinary cases they interfere only in very minor degree with blood-flow. In some instances, however, the processes which result in formation of new tissue seem especially active, the affected areas bulge greatly, seriously obstruct the flow of blood, or even eventually obliterate the lumen of the vessel. This is the "endarteritis obliterans" of the text-books.

This chronic arterial disease begins usually in the aorta, and in some cases is confined entirely to the aorta and its larger branches, although in most cases in which any symptoms of arterial sclerosis are discoverable during life, the disease is found more widely distributed, in some instances affecting the larger venous walls as well as the smaller arteries throughout the body.

The frequency with which these degenerative arterial diseases are met with among insane people, as well as their correlation with certain more or less characteristic clinical symptoms, mental and physical, has already been commented upon more than once, and will become sufficiently evident to any who study the disease even from its clinical aspect alone; more especially to those who have the opportunity of observing cases during long periods, and of following fatal cases to the autopsy table and confirming or correcting clinical diagnosis by post-mortem examination.

A hospital for the insane offers a peculiarly favorable field for the investigation of such forms of chronic disease as the one under consideration, since a large percentage of the patients remain under treatment for long periods. And where all cases are given a careful physical examination at time of admission, followed subsequently with reasonable care, and post-mortem examinations made in a large proportion of the fatal cases, an amount of material bearing upon the several aspects of the arterio-sclerotic question must necessarily accumulate. It is with a view of briefly recording some of the results of our observation of this disease among the insane at this hospital that this report is made.

While we have the records of several thousand cases of insanity in which one or more physical examinations have been made, including in every case examination of the heart and blood-vessels and analysis of the urine, chemical and microscopical, it is intended here to deal chiefly with those cases in which post-mortem examination has removed all doubt as to diagnosis.

At the two hundred consecutive autopsies here used as the basis of our study we find that the macroscopic examination included the condition of the heart; the aorta and its larger branches; the coronary arteries; the arteries of the base of the brain,—basilar, circle of Willis, and larger branches of the same,—and the large veins. In about one hundred and fifty of the cases subsequent microscopic study of the kidneys was

made, and in a smaller number sections of the brain, of the liver, spleen, and other organs were made and examined with the purpose of discovering the condition of the smaller arterial and venous twigs.

To give even a brief outline of the pathological changes noted in all of these cases, or even a synopsis of the condition of the circulatory system alone, would extend this paper to a quite unreasonable length. The cases will therefore be summarized and studied collectively. An analysis of the two hundred cases results as follows:

Frequency of Arterial Sclerosis and Atheroma.—About thirty-five per cent. of our cases show either no macroscopic evidence of arterial disease or the abnormalities are confined to a very few pale, inconspicuous yellowish patches in the arch of the aorta: only about fifteen per cent. of the two hundred cases are *absolutely free* of the disease in some stage.

Sixty-five per cent. show distinct arterio-sclerosis, something more than one-half of these exhibiting atheromatous patches or sclerosis of the aorta, without extension of the disease to the smaller vessels; the other smaller half, about twenty-eight per cent. of the whole number examined, show the degenerative change in a high degree in the aorta, and the lesion is detected in the smaller arteries. The veins are rarely involved, and in no case to any marked degree.

Our cases, then, fall into three groups nearly equal in numbers: one showing practically no arterial disease; one, slight involvement of the larger arteries; the third exhibiting well-marked and widely diffused degenerative and sclerotic change throughout a considerable portion of the arterial system. Of course, these groups shade almost imperceptibly into one another, the lesions in group three being obviously a later stage of the milder disease shown in group two, and this second or transition group passing by impercepible gradations into those cases included in group one, where the disease is shown in pale, scarcely visible patches in the aorta, or in which examination is entirely negative.

Race.—Of the whole number, one hundred and thirty-one of the cases were white, sixty-nine colored. The percentage of atheromatous disease was found to be somewhat greater among the negro patients than among the white, a difference which is more significant if the fact be taken into consideration that the average age at the time of death was greater among the whites. Attention has previously been directed to the fact that arterial degeneracy is especially common among colored races, and our results seem to corroborate this view.

Sex.—The *females* of both races seem more liable to the disease than do the males, contrary to what is usually taught; the difference, however, is slight, and the number of cases not sufficiently large to establish a general rule. I would mention in this connection, however, that, as previously reported, we have found renal diseases also more common among the *females* of both races.

Age obviously plays an important part in the development of arterial

degeneracy, the average age at time of death of the patients showing no disease being thirty-two; of those exhibiting acute early stages of the affection, forty-one; of those in whom the disease was well advanced and widely diffused, fifty-five. The youngest patient in whom well-marked atheromatous disease of the aorta was found was twenty-one; the youngest showing a high grade of the disease with extensive distribution was forty-three.

Causes of Death.—An analysis of the causes of death in the two hundred cases brings to light some interesting facts. Among the non-atheromatous the deaths were chiefly due to tuberculosis, acute diseases, including acute nephritis and epilepsy, cerebral hemorrhage, heart-disease; chronic renal affections being conspicuously absent. In the second group the causes of death are tuberculosis, acute diseases, nephritic troubles, both acute and chronic, valvular heart lesions, general paresis, and one death from cerebral meningeal hemorrhage, with several other instances of subdural effusion of blood. When we reach group three—the markedly atheromatous—chronic forms of renal disease become conspicuously frequent, and of the fifty-five cases in this group, five died directly from intracranial hemorrhage, and in eleven other cases subdural hemorrhage ("pachymeningitis interna hemorrhagica") was noted. Heart complications were also more common. In short, the non-atheromatous die of acute disease, and suffer rarely from chronic renal disorder, heart complications, and cerebral hemorrhage; the atheromatous die of chronic diseases, renal especially, have frequent heart disorder, and cerebral hemorrhage is common.

Character and Distribution of the Lesions.—As above noted, in about one-third of the whole number of cases examined, the lesions are confined to the aorta, favorite situations of the splotches being the orifices of the intercostal arteries, the bifurcation of the abdominal aorta at the pelvic brim, and the first inch of the aorta, near the bases of the heart-valves, and around the openings of the coronary arteries; but in those cases in which the disease in the aorta is at all well marked, the degeneration can be traced into the smaller arterial branches.

Thus, in fifty-five atheromatous cases in group three, there was sclerosis and atheroma of the coronary arteries in thirty-six, of the larger cerebral arteries in thirty-five, and in the forty-two cases of this group in which sections of the kidneys were made and examined with the microscope, disease of the renal arteries was noted in thirty-six instances. No cases showing disease of the coronary arteries, of the cerebral arteries, or of the smaller renal branches, failed to show the lesion in a higher degree in the aorta. Disintegration of the atheromatous plaques, with the irregular, depressed "ulcers" consequent therefrom, were noted in five cases only; in none of these were emboli discovered. Calcareous plates or irregular, chalky deposits were much more common,—seen in eleven of the fifty-five cases; and in two cases many of the arteries, including the cerebral, could be broken like pipe-stems, the entire wall being infiltrated with calcare-

ous matter, rigid and unyielding. In one case a large aortic aneurism was found.

Some morphological differences exist between the sclerotic degenerative changes noted in the larger arteries and those occurring in some of the smaller vessels. It is especially in the larger vessels that the atheromatous areas, ulcers, calcareous plates, etc., are seen, and here the disease affects the inner arterial coat in particular. In the smaller vessels of the kidney, heart, liver, spleen, etc., the histological changes commonly assume the form of "arterio-capillary fibrosis," described in the oft-quoted work of Gull and Sutton. Here there is a diffuse fibroid or hyaline thickening of the adventitial coat as well as of the intima, and the muscular layers show frequent atrophic changes, these changes in the blood-vessel wall being often associated with thickenings and general increase in connective-tissue framework of the several organs.

The changes of atheroma and "arterio-capillary fibrosis," while differing in histological character, have a probably common etiological origin. The differences seem to depend largely upon the structure and relations of the vessel affected. When the arteries lie comparatively free, having not very intimate relation with surrounding tissues (aorta and large arteries in thoracic and abdominal cavities, meningeal arteries, etc.), the irregularly distributed atheromatous patch is common, and adventitial thickening is not pronounced. When the arteries lie within and intimately connected with the stroma and cells of the glandular organs, kidney, liver, etc., adventitial thickenings and the diffuse hyaline and fibroid degeneration above referred to become more evident.

Whether in these glandular organs the thickening begins in the blood-vessels and extends secondarily to connective-tissue framework, or, occurring primarily in the latter, extends at a later period to the blood-vessels, is not in all cases determinable; probably in many instances the changes are simultaneous, and due to a common cause. In some undoubtedly the primary lesion is in the vessel walls.

Heart.—A frequent situation of early atheromatous disease, as noted above, is the first inch of the aorta, so it is not surprising that, as the disease advances, it invades not only the remainder of the arterial system, but extends to the valves and endothelial lining of the heart as well. A large percentage of the cases in group three show atheromatous degenerative changes in small, oval or irregular, yellowish, raised or thickened patches upon that segment of the mitral valve which is, at its base, continuous with the inner surface of the aorta, and, in a smaller number of cases, the lesion is noted upon the remainder of the mitral valve, upon the cusps of the aortic valve, and upon the endocardium. The bases of the aortic cusps are not rarely involved. Calcareous masses and plaques upon valves and endocardial lining have also been noted, and in some cases where the yellowish atheromatous plaque was not noticeable, a diffuse sclerosis and stiffening of the valves of the left side of the heart have been present. This extension of

the disease to the valves of the heart was noted in twenty-six out of the fifty-five atheromatous cases.

The frequency of atheroma of the coronary arteries has been previously alluded to. The heart muscle, in many cases, probably in consequence of the increased demand made upon it as a result of the diminished elasticity of the arterial system, as well as, in certain cases, by insufficiency of the cardiac valves, becomes hypertrophied, the weight in twenty-five per cent. of the fifty-five cases being more than twelve ounces, the six largest hearts weighing, freed from blood-clots, twenty-six and a quarter, twenty and a quarter, nineteen and three-quarters, eighteen and three-quarters, sixteen, and fifteen ounces. This cardiac hypertrophy, however, is not by any means a universal accompaniment of arterial disease or of valvular heart lesion, even when these two are combined with arterio-sclerotic nephritis, for of our atheromatous cases, quite thirty per cent. showed hearts weighing less than eight ounces; and among these were many instances of valvular heart lesion also. These small atrophic hearts were usually found in subjects in which a general marasmatic state prevailed; many of them, undoubtedly, showed degenerative changes in their muscular tissue. Reckoning all together, the average weight of the heart among the atheromatous is less than among the non-atheromatous.

Among some seven hundred white patients examined by my colleague, Dr. Ruffin A. Wright, in course of an inquiry into the cardiac complications of insanity, evidences of organic heart lesion were discovered in about eleven per cent., and of this eleven per cent. a large proportion also exhibited some indication of arterial degeneracy; the proportion of cardiac valvular disorder among the non-atheromatous being infinitely less than among those showing diseased arteries. Of our fifty-five fatal atheromatous cases, cardiac lesion had been detected before death in *eighteen*. Almost without exception, the cases in which heart lesions had been recognized by examination before death exhibited at post-mortem examination some degree of arterial sclerosis.

Kidneys.—Practically every one of the atheromatous cases exhibited renal disease, the commonly noted condition being the "red granular" arterio-sclerotic contracted kidney, the organs being smaller than normal, firmer, of a dark red, capsule thickened and adherent, bringing away bits of tissue when stripped off, and leaving behind the characteristic "red granular" surface. The cut surface of the kidney is red, cortex irregularly thinned, the markings indistinct, pyramids dark colored. The chief lesions shown under the microscope are: thickening of interstitial tissue, thickening of arterial walls, of capsules of glomeruli, destruction of many tufts through degenerative changes in their component vessels, and degenerative changes in the tubal epithelial cells, the latter lesion varying much in different cases. This description would apply with scarcely a change to about two-thirds of the kidneys in our cases of endarteritis. The remaining third, while almost without exception exhibiting disease of their arteries, depart in some partic-

ulars from the arterio-sclerotic type. Many of these variations are obviously due to intercurrent acute forms of nephritic disease, to which, naturally, the arterio-sclerotic kidney is as liable as is a more nearly normal organ, or even more liable. In seven of these atypic cases, in which there was disease of the renal arteries without the characteristic "red granular" appearance, the causes of death were peritonitis (two cases), pneumonia (two cases), septicæmia (one case), and miliary tuberculosis (two cases), in each of which seven cases there was, in consequence of the acute disease, an acute exacerbation of renal disorder.

In only two cases was there pronounced disease in the aorta and in the smaller arteries of other portions of the body—coronaries, cerebral vessels, etc.—without degenerative or fibroid changes in the renal vessels. In the forms of early and but slightly advanced atheroma included under group two, however, the renal vessels were, as a rule, free from disease. In no instance was a "red granular" kidney found, or a kidney showing any degree of degenerative change in arteries, or any "arterio-capillary fibrosis," without atheroma in other portions of the arterial system.

Among the cases free of arterial disease, or showing this disease in minor degrees, the average weight of the kidneys was greater, and the percentage of nephritic disease somewhat smaller. The renal disease, too, when present, was most often of an acute form, or of a chronic parenchymatous form, without affection of the renal blood-vessels.

The urine was found to contain albumin as well as renal tube-casts in every case showing arterial atheroma in an advanced stage.

Brain.—The condition of the brain in cases of advanced atheroma is commonly one of sclerosis and atrophy. Among the non-atheromatous or slightly atheromatous cases the average weight of one hundred and forty-five brains is forty-four ounces; among these were many general paretics. Among those who show atheroma in marked degree, fifty-five cases, the weight averages forty-two ounces. In many of these brains the atrophy, the shrinking of the convolutions of the vertex, gaping of sulci, general hardening of the tissue, etc., are extreme. The lightest of the atheromatous brains weighed thirty-two, thirty-three and one-half, thirty-four and one-quarter, thirty-five, thirty-seven, and thirty-seven and one-half ounces respectively. Occasionally a brain in which there is disease of the arteries will show no atrophy; occasionally atrophy of a brain will be noted without degenerative disease of the arteries, but usually when there is arterial degeneracy there is cerebral atrophy; when there is cerebral atrophy there is some degenerative arterial disease. The indications of disease in the histological elements noted in microscopic study of sections of the brain from cases of arterio-sclerosis are, briefly, those described in senile and terminal dementia,—destruction of many nerve-cells, degenerative changes in other nerve-cells, thickenings in smaller blood-vessels, changes in neuroglia-tissue elements, etc. The miliary aneurisms, upon the occurrence of which so much stress has been laid by some, have been conspicuous by their absence,

or at least we have failed to detect them. A not uncommon lesion in advanced cases is granular thickening of the ependymal lining of the ventricles.

The pia-arachnoid has usually been found thickened, opalescent, tough, dense, œdematous, being often removable in large sheets without difficulty. A frequent lesion is intrapial or subdural hemorrhage, which, like intracerebral effusions of blood, have been rarely noted except in cases exhibiting disease of the arterial system. Thus, in our two hundred autopsies, nineteen instances of subdural or intrapial hemorrhage were discovered, and in eleven of these there was a high grade of atheroma throughout the arterial system; in seven other cases earlier stages of arterial degeneracy, and in one instance only was no degenerative change in the blood-vessels noted. In addition to these meningeal hemorrhages, there were five cases of intracerebral effusion, three of these occurring in basal ganglia or internal capsule, one in the white substance of a cerebral hemisphere, one in the pons. Each was the direct cause of death, as noted above, and in each there was disease of the arteries.

The very frequent occurrence of arterial disease among general paralytics has been made the subject of remark by Beadles and others. A review of the lesions noted post mortem in our cases of paresis confirms this opinion in so far as the frequent existence of arterial degenerative changes is concerned, almost every case of paresis showing some arterial disease. I would say, however, that in no instance have we found the degenerative changes well marked, not one of our fatal paresis cases falling under our atheromatous "group 3." In two of the cases no arterial degeneracy was noted. The six other cases did exhibit an early stage of disease.

Condition of other Organs.—The *liver* has usually been found smaller and firmer than normal,—*i.e.*, cirrhotic,—and no case of hepatic cirrhosis without general arterial disease, as well as similar disease of kidneys, heart, brain, etc., has been seen.

The spleen also in the majority of cases is firmer, smaller, harder, more fibrous than normal, save in the cases dying of infectious disease. The suprarenal capsules are often dry, firm, shrunken, with brilliant yellow cortex and dark-red medullary substance, the color contrast greater than normal. The ribs, and to a less noticeable extent the other portions of the osseous system, are atrophic, softened, show diminution or even absence of inorganic salts, and break or bend easily.

The most striking general feature of the bodily condition is emaciation, with marasmatic atrophy, and the changes already familiar as accompaniments of senility, and this chronic degenerative disease in the arteries may be regarded as one of the most characteristic pathological features of that chronic, progressive, incurable disease, old age.

It is also worthy of note that the cases of endarteritis showing most typically the marasmatic state above referred to are usually those in which the nephritic complication is most pronounced. Occasionally, when renal

or other complication is not pronounced, the subjects remain in a remarkably well-nourished state to the last.

Clinical Symptoms.—The existence of any considerable degree of arterio-sclerosis is generally recognizable during the life of the patient, although early stages of the malady do not make their presence manifest. In advanced cases there is the well-known sclerosis of the arteries, perceptible in radial, facial, temporal, and other arteries which can be felt. The arteries are also tortuous and the pulse harder and less compressible. The heart-sounds are apt to be roughened, and distinct murmurs are not rare. (Note above that in fifty-five atheromatous cases autopsied, heart murmurs had been recognized during life in eighteen.) The roughness is noted with both first and second sounds, there is accentuation of the aortic tone; the murmurs are chiefly systolic.

The *arcus senilis* is often present, and has not yet been by us observed in a case free from arterial degeneracy. Hemorrhagic or petechial spots upon the skin—most usually the forearms and the back of the hands—are common, and are obviously hemorrhages, and in many cases not obviously due to traumatism. One man, the subject of great arterial disease and dying of cerebral hemorrhage, had a crop of small, irregular hemorrhagic splotches over chest, face, and extremities two days before death; another had a similar abundant crop upon face, neck, and body, appearing without discoverable exciting cause, and slowly disappearing by absorption. A female patient having an extensive and well-marked arterial disease with nephritic, hepatic, and cardiac complications, had, three weeks before death, an extensive hemorrhagic effusion into the skin of the abdominal wall, the splotch being something near one square foot in extent; it was gradually absorbed, passing through the stages of discoloration shown during absorption of blood effused after a bruise. These hemorrhages, when not due to trauma, we may regard as of angio-neurotic origin, but arterial degeneracy seems in either case necessary to their occurrence. We have noted *no case* in which there was no disease of the arteries.

Other symptoms shown in these cases are vertigo, buzzing in the ears, easy exhaustion, palpitation of heart, irregularity of same, attacks of syncope, etc., these occurring particularly where there is cardiac disease. The cirrhotic liver and the diseased kidneys also contribute their quota of symptoms, chronic uræmic manifestations being especially common.

The urine is in advanced cases invariably albuminous and invariably contains tube-casts.

Delafield and Prudden make reference to the occasional development, in serious arterio-sclerosis, of symptoms almost identical with those shown in cerebral hemorrhage. One such instance has fallen under notice here. A patient suffering from advanced arterial disease developed a progressive hemiplegia (becoming in its later stages bilateral), and the symptoms of extravasation were so well marked as to lead to diagnosis of hemorrhage into brain. The autopsy discovered no hemorrhage whatever, but a high

grade of arterial disease in all arteries, with calcareous deposits and partial obliteration of many of the cerebral twigs.

Among the causes of arterio-sclerosis, poisons in the blood exerting a direct irritant action upon the vessel wall have long been accorded a prominent place. These poisons may be such as are introduced into the system from without, as alcohol, opium, and other habitually-used stimulants or narcotics, lead, etc., or may result from diathetic or acute or chronic infectious diseases, as syphilis, rheumatism, gout, or may be developed in the body, as in intestinal auto-infection or "uræmia" from defective excretion of waste products.

These last-mentioned states of auto-poisoning probably play a greater part in the causation of the arterial degenerative changes under consideration than has heretofore been recognized.

We are coming slowly to an adequate appreciation of the frequency of these states of auto-infection among the insane, and to recognize their important influence upon the functional activities of the brain and other organs. Attention has been several times directed to the common occurrence among insane people of nephritic disorders with their accompanying uræmic symptoms. If, as seems abundantly justifiable, we may assume that toxic-blood states favor the development of arterial sclerosis and degeneracy, we have in the frequently noted auto-infections among the insane a sufficient reason for the frequent occurrence of arterio-sclerosis among the same class.

The probable origin of these arterial degenerative diseases in chronic infection offers also reasonable explanation of the otherwise scarcely explicable although long-observed relationship between Bright's disease, heart-disease, and hepatic cirrhosis, and between these three and arterial degeneration.

The presence in the blood of substances which exert an irritant or injurious influence upon the vessel walls must produce a somewhat similar effect upon the cells of the brain, kidneys, liver, and other organs, and must result sooner or later in pathological changes readily recognizable upon examination, such as atheromatous and fibroid degenerations in the walls of the blood-vessels; degenerations or parenchymatous metamorphoses in the cells of the kidney, liver, etc., together with changes in connective-tissue elements (thickening and increase in); degenerative changes in the nerve-cells, with cerebral atrophy, as noted in terminal and senile dementia.

A given degree of toxæmia will act by no means uniformly throughout the animal organism, the points of greatest pathological activity depending probably upon inherent power of resistance of the different organs and tissues, which resistive power necessarily varies with the individual. In one having an unstable cerebral organization the cortical cell will suffer prominently, resulting in perversions of cerebral function, mental disorders, or in insanity, or permanent dementia if the toxic state be severe or long con-

tinued. In another the renal cells may be most affected, leading to sundry forms of nephritic disease; or the hepatic tissue may show greatest changes, as in the cases in which cirrhosis of the liver is prominent; or the blood-vessels themselves may be chiefly diseased. Usually the result in any case is a combination of the pathological effects above referred to. Whatever the initial toxæmia may be due to, in later stages there is added the poison of defective excretion whenever the kidneys become diseased, together with the ill effects of disordered heart action, of diminished arterial elasticity, of derangement of the nervous mechanism, etc. We find, in short, that those forms of Bright's disease in which there is endarteritis or arterio-capillary fibrosis of the renal vessels occur only in patients suffering from general arterial sclerosis; that atheromatous, chronic, sclerotic, and degenerative disease of the cardiac valves and endocardium is usually accompanied by similar changes, in a higher degree and more advanced stage, in the arteries; that in all cases of chronic Bright's disease which in their later stages become complicated by cardiac hypertrophy of valvular disease, widely distributed atheromatous or sclerotic arterial degeneracy is present.

It would seem, then, that the more constant and characteristic pathological condition in these cases is the arterial disease, a point which has been insisted upon by many who have studied the subject and apparently confirmed by our results here.

Bright's disease, then, does not cause disease of the heart, but the two, together with the cirrhotic changes in other internal organs and the degenerative changes in the arterial system, represent concurrent results of a common cause,—toxæmia.

What relation exists between sclerotic degenerative disease of the arteries and mental disorder? Probably an intimate one. No brain whose arteries are atheromatous is as well nourished, active, and fit for work as is the brain supplied by more normal vessels, a fact equally true of the sane and the insane. With sclerosis and atheroma we have the inevitable loss of elasticity in the cerebral arterial twigs, cardiac weakness or insufficiency, with general circulatory disorder; disease of the kidneys with its resultant auto-poisoning, as well as cirrhotic changes in the liver and other organs, and behind and above all the initial toxic state to which the complex of pathological changes is presumptively due. Under such unfavorable circumstances the cortical cell must necessarily suffer. That demonstrable changes in the nerve-cells of the brain do occur is shown by examination of the cortical tissue after staining by the Nissl method, and in preparations made by the Golgi silver process, and by Berkley's modification of the same. These cellular degenerative changes, as previously mentioned, are those already becoming familiar as the pathologico-anatomical basis of terminal dementia and of the senile insanities, and will not be entered upon in detail here, but may form a part of a subsequent report. In this connection some of Berkley's recently published work is interesting ("Lesions of Cortical Tissues caused by Acute Experimental Alcoholic Poisoning," *Journal*

of Nervous and Mental Diseases, April, 1896) as showing "the large dependence of the lesions of the nerve elements upon the vascular," "all the alterations of importance being in the neighborhood of damaged vessels." What is true of acute alcoholic poisoning is probably true in at least a measurable degree of chronic poisoning from alcohol and other toxic agents. Regarded as a result of continued toxæmia, and a phase of the pathological anatomy of chronic poisoning not improbably occurring at an earlier date than the degenerations of the nerve-cells of the cortex, the subject of arterio-sclerosis assumes a renewed interest, and should be accorded an important place in the pathological anatomy of insanity.

Reviewing our two hundred cases, it is noticeable that the non-atheromatous insane suffer from acute forms of mental disorders; the atheromatous from chronic and incurable forms; when in the atheromatous, as sometimes occurs, there is an acute outbreak of mania or melancholia, the underlying mental dulling is generally noticeable. In short, the characteristic and ever present mental expression of arterio-sclerosis is *dementia* of some kind and degree.

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