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THE RELATION OF CARDIAC HYPERTROPHY TO NEPHRITIS.

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The significant frequency of the co-existence of nephritis and cardiac hypertrophy is recognized as establishing some causal connection between the two, either as dependent one on the other, or as independent effects of a common cause. It is also to be taken as the decided opinion of the medical world that the nephritis does not result from the cardiac hypertrophy or dilatation. Moreover between the other two relations, the dependence of the hypertrophy on the nephritis on the one side and on the other that of both on a common cause, the strong balance of opinion and, as it seems to me, of evidence is in favor of the former. But even if nephritis directly tends to produce overgrowth of the heart muscle, no one can absolutely deny that the list of cases in which nephritis co-exists with the hypertrophy may be increased from other sources; a general arteriosclerosis for example may favor the development of nephritis; nor can we gauge at present the strength of this influence. On the other hand the inefficient working of a heart hypertrophied and dilated from over-exertion may tend to the development of the renal disease. Because, however, we cannot but admit that additions to this class of cases may be made in ways such as these, and although we are not in a position to estimate the value of such contributions or to completely enumerate their possible sources, we are not thereby obliged to give up thinking that the direct influence of the nephritis is not only a real cause but the predominant or even essential cause of the co-existence of these two features of these cases.

But, while up to this point medical opinion, although far from unanimous, is on the whole decided, beyond and with reference to the ways in which the nephritis produces the hypertrophy, there prevails the utmost variety of opinion. The critical examination of these various views is not within the scope of this paper, which is to present a single case of nephritis, examined with reference to this question, that it may contribute with whatever weight it may seem to have, both to the confirmation of the belief that nephritis produces hypertrophy and to more definite and confident conceptions of the way in which the kidney disease works to produce the cardiac peculiarity.

The subject requires the confrontation of established physiological results with clinical observation, and no simpler or more fruitful method suggests itself than to develop and enumerate the various ways in which overgrowth of the heart muscle is physiologically possible, and then, after reviewing the case, eliminate those ways which the special features of the case show to be inapplicable to it, and thus restrict the possible lines of causation to as small a number as possible.

The hypertrophy of the heart can be produced only when its work is increased and it is furnished with an adequate supply of suitable blood. If nephritis produces overgrowth of the heart muscle it must increase its work, and we have to consider the ways in which the work of the heart may be increased. This work is measured by the amount of blood thrown into the aorta in a given time, multiplied by the aortic blood-tension. The amount thrown in, as long as the cavity is unchanged, depends on the pulse rate and the completeness with which the cavity is filled and emptied. The pulse-rate in ordinary conditions, and so at the beginning of hypertrophies, probably measures with a fair approximation the amount of blood thrown into the aorta.

The blood tension in the aorta depends on the relation between the peripheral resistance and the aortic inflow. Thus if the peripheral resistance remain the same and the pulse rate be increased the aortic tension will be raised, and the heart will do more work, both because it is forcing more blood into the aorta, and because it is working against a greater pressure. But if through reduction of vasomotor tone the aortic tension be again reduced to normal, the heart still does more work than normal, because it injects more blood against the same tension.

If on the other hand the peripheral resistance be increased while the aortic inflow remains the same, the work is increased because the same injection is performed against a greater pressure.

In either of these ways then the work of the heart may be increased and the necessary physiological condition of hypertrophy be furnished; the difference is that between light and heavy gymnastics. But they may not be equally favorable to hypertrophy. The comparatively short diastole of a rapidly acting heart does not favor its recuperation and growth, and possibly interferes with the due supply of blood to its deeper layers, which are compressed during the systole. On the other hand the increased aortic tension of the other condition would aid the coronary circulation. It would thus appear probable that with equal amounts of work the case in which there was the same amount of aortic influx against an increased aortic tension would be more favorable to hypertrophy than that in which there was a greater aortic influx with the same aortic tension.

But to suit the necessities of the organism the various factors of the circulation are regulated with respect to one another, so that interference by accident or design at one point may be met by compensatory changes at another, and it is necessary to consider the behavior of this mechanism that we may not include cases among the ways of increasing the heart's work, where changes which would tend to increase it are balanced by others which would tend to diminish it.

The due permeation and nutrition of the tissues can only be achieved by the maintenance of a certain head of aortic tension which must vary with the ever varying needs of the organism. For any given state of activity there is a certain aortic tension which is sufficient. A tension less than this renders the nutrition less perfect; a tension greater than this throws useless work upon the heart. When we interfere in a normal animal to raise or lower the blood tension, our efforts are often counterbalanced by the reaction of the organism. If we cut off a leg, or clamp its artery, and thus increase the peripheral resistance by rendering some paths from the arterial to the venous side of the circulation impermeable, we produce no permanent increase of blood pressure. Neither can we produce it by injecting blood into the arterial channels. If we compress the ascending aorta with a view to lessening the blood pressure in the arteries, we find that the press-

ure in the carotid and the femoral remain unchanged, although the systolic endocardiac pressure and the tension of the aorta on the cardiac side of the constriction may be enormously increased. This regulation of the circulation with direct reference to the nutrition of the tissues is a function of a portion of the nervous system. We recognize the cardiac-inhibitory and other cardiac fibres of the vagus, its vaso-motor depressor fibers, the accelerator nerves, and the vaso-motor nerves together with certain cerebro-spinal centers as portions of this mechanism; but we are far from being fully acquainted with it.

We are warranted, I think, in holding, however, as the result of direct experiment that no modification of single factors of the circulation, unless extreme, will affect the blood pressure except in those cases where such modification directly impedes the supply of pure blood to living tissues, and, except, where the nervous mechanism is directly affected in a definite way.

We may now enumerate the ways in which cardiac hypertrophy is physiologically possible when the heart valves are intact.

A. Where there is increased pulse rate and aortic influx without rise of blood pressure, as apparently in some cases of Graves's disease.

B. Where there is increased blood pressure due to

a. Very much increased pulse-rate not entirely counterbalanced by vaso-motor depression, as apparently in other cases of Graves's disease.

c. Disease of the arterial walls diminishing their elasticity and the lumen of the vessels, thus obstructing the passage of the blood to the tissues as in arteriosclerosis.

d. Increased friction of the blood due to its changed character, as was supposed by Ewald to be the case in Bright's disease.

e. Vaso-motor spasm produced by direct effect of substances in the blood on the peripheral vaso-motor mechanism.

f. Derangement of the central nervous mechanism by which it is, as it were, set for a higher tension.

g. Direct stimulation by substances in the blood or by processes in the kidney of the afferent nerves of this mechanism which produce increased tension.

I have spoken with reference to the left ventricle alone. The right demands some attention. When the work of the heart is increased by increased aortic influx due either to quickened pulse

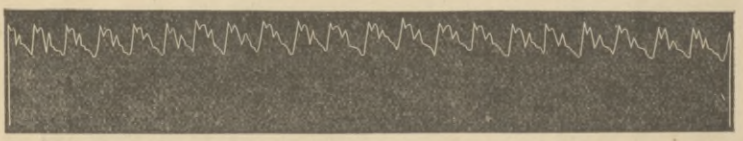
rate or to more complete filling and emptying, the right ventricle must be affected equally with the left. But when the increased work of the left heart is due simply to raised aortic tension, it is not clear how increased work of the right heart may be brought about. Since the aortic influx is supposed unchanged, pulmonary influx must also remain the same. So that increased work of the right heart, if it occurs in such a case, must depend on raised pulmonary tension.

In the following case of scarlatinal nephritis in a boy of seven, the blood tension and some related points were carefully observed during two periods, one during the height of the nephritic state, and one some weeks later when almost all nephritic signs had disappeared. On the contrast between these two periods depends the interpretation of the pathological process.

The first set of records extends from April 17th to April 24th. The scarlatinal attack began before the middle of March and was not severe. The nephritis showed itself first three or four days before April 17th, being marked at the time by very scanty urine loaded with casts and containing albumen. There was slight œdema about the face, none elsewhere. There was troublesome vomiting but no headache or other uræmic symptoms. Blood also appeared in the urine. During the period named the quantity of urine varied from 805 to 1190 c. c.; the sp. gr. from 1012 to 1019, the albumen from 17 to 33 per cent. of boiled settlings. Blood was constantly present, and casts were frequent. The tension in the two radial and the two temporal arteries as given below was taken with Basch's sphygmomanometer. The figures indicate millimeters of mercury. Care was taken in the observations of both periods to make them at the same time of day and with the body in the same supine position and after at least a short period of perfect quiet.

	R. Rad.	L. Rad.	R. Temp.	L. Temp.
April 17	165	165	140	140
18	160	155	130	130
19	150	150	125	125
21	155	155	120	120
23	135	135	120	120
24	150	150	125	125
Average	152	152	127	127

The tensions with Basch's manometer measure the maximum amount of pressure, but the pulse was to the finger a firm hard one, the opposite of collapsing, so that the mean tension must have come nearer to the maximum tension than is usual. The pulse rate at these times during this period was about 96. The sphygmographic tracing with Dudgeon's instrument is introduced here. The pressure was 160 grams.



The radial and temporal arteries could be felt to be quite contracted, small as well as hard. The heart sounds, especially the aortic, were markedly increased in intensity. The left border of the heart could be distinctly felt a quarter or a third of an inch to the left of the nipple. The skin of the arms presented a faint cyanotic mottling.

The second period is from the 11th to the 18th of May. No blood was found after the 28th of April; no casts after the 30th. The albumen, which had become reduced to 1.5 per cent. of boiled settlings on May 5th, has since that shown only the faintest trace. The slight œdema was not perceptible after the first period. The daily quantity of urine during this second period varied from 750 to 1000 c. c., and thus was somewhat less than during the first. The specific gravity varied from 1014 to 1018.

During this period the child was in excellent appetite and spirits, active, laying on flesh and daily improving in appearance.

The tensions were as follows:

	R. Rad.	L. Rad.	R. Temp.	L. Temp.
May 11	89	90	80	80
12	98	94	85	80
13	81	78	76	70
14	83	85	78	76
16	77	76	75	74
17	66	84	61	78
18	86	84	74	71
Averages	83	84	76	76

These do not differ much from average normal tensions for that age.

The heart sounds, and this is true of both the aortic and pulmonary sounds, were distinctly less intense than in the first period and perhaps not louder than normal for so thin-walled a chest. The pulse rate was again about 96.

The following sphymogram was taken with a pressure of 160 grams.

The arteries to the finger were comparatively soft and large, and the pulse collapsed more quickly than previously. The apex beat, and the left border of the heart, could not be felt to the left of a line just to the right of the nipple.

Now the comparison of the two periods shows that in the first we have a blood tension raised very much, about 75 per cent., above the later approximately normal tension; that so far as we can trust a comparison of the pulmonary valve sounds, there was some increase in the tension of the pulmonary artery; that the systemic arteries were very much contracted; that, however, the pulse rate remained the same though the heart seemed to fill itself somewhat more completely in the nephritic period. The inference with regard to the pulmonary blood pressure is in accord with the observations of Friedländer on autopsies in scarlatinal nephritis where he found that the whole heart was hypertrophied to 40 per cent. on the average, and that this affected both sides of the heart, though most the left ventricle. (*Arch. für Physiol.*, 1881, p. 168.)

Now we will compare this case with the list of ways in which it is possible that the work of the heart be increased.

A is not applicable because the pulse rate is unchanged. The same is true of B *a*.

B *c* is not admissible in this case of a young child with an acute attack, with no signs of organic arterial disease.

B *d* may be thrown out because direct observation proved that the increased peripheral resistance was due to increased contraction of the arteries.

The case is confined with fair certainty to the remaining three

possibilities, vaso-motor spasm from direct stimulation of peripheral mechanisms, derangement of the central nervous mechanism, or direct and unusual stimulation of the afferent nerves of this mechanism. In the present state of knowledge nothing definite and decided can be adduced to determine a choice between these. The hypothesis that waste products circulating in the blood or inefficiency of renal action stimulate afferent nerves raising the blood pressure and thus tending to secure the elimination of these substances, that this adaptation has been acquired like other adaptations, and that the high pressure in such cases as this one is produced in the same way under an unusual and prolonged stimulus, is contrary to no known facts. This by no means involves the necessity of the conclusion however, that because this working is beneficial for low grades of stimulus it is also for high. It may be that the high blood tension in a given case of nephritis is advantageous, or on the other hand that it is overdone and prejudicial. This paper looks toward that question; it does not answer it. That must be decided in the individual case by therapeutic experiment. Thus only can we come to know whether it is *usually* apt to be one thing or the other.