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# DIURETICS—HIRSCHFELDER

With reference to the question of determining that a person is homosexual:

A patient came to me who was said to have nothing the matter with his sexual life, but who had convulsions. I had seen him not more than three times when I said to him. "You are homosexual," and I explained what I meant. He told me that while at college he never indulged in sexual acts, and that for this reason he used to wrestle, during which he would have ejaculation, and he selected his partners. Unquestionably from the beginning of his existence he was homosexual, although he was able to have sexual intercourse with his wife, but he was compelled to marry when quite young; he was "prodded into it," as he said. He came to me to be treated for neurosis, but the neurosis was simply the result of homosexual lack of gratification.

We should be particularly careful not to suggest anything. I never tell a patient at once that he is homosexual. Be reasonably sure that he is homosexual and you need not then hesitate to tell him so.

Answering Dr. Sterne's question as to how I can determine that the patient is cured:

A patient who comes to me and tells me, for example, that he will commit suicide if he cannot be relieved of his terrible condition. When that patient suddenly changes and falls in love with a woman and marries her, I can see no reason to doubt that he is cured when he never had any such feeling before. Moreover, the man does not come to me at my solicitation. He comes to me with something definite; I follow the case for months or perhaps more than a year; I know him better than any one else in the world, and he has no reason to lie.

Those men are, as a rule, no different from a crowd of heterosexuals, and, further, they belong to some of the finest types. Those are the only cases that I have analyzed, and I believe that only persons of a high type should be analyzed, for those are the ones we should reclaim. We cannot accomplish anything satisfactory in the case of ignorant persons.

### DIURETICS IN CARDIAC DISEASE

## A GENERAL REVIEW \* ARTHUR D. HIRSCHFELDER, M.D. BALTIMORE

In considering the subject of diurctics in cardiac discase it is essential that we frame in our minds some tentative idea of the forms of cardiac disease in which it is desirable to resort to diurctics at all; secondly, that we form a clear idea of the manner in which the lesion of the heart affects the action of the kidney; and thirdly, that we consider the mode of action by virtue of which the particular diurctic drugs under consideration may be expected to remedy these disturbed conditions.

With full realization that I am making rough and arbitrary divisions, I may say that one might consider the advisability of resorting to diurctic measures in five forms of disease of the circulation: (1) infective endocarditis; (2) arteriosclerosis with periodic attacks of the various disturbances associated with localized arteriosclerosis, vertigo, headaches, transitory cardiac asthma or pulmonary edema, angina pectoris and vasomotor crises; (3) chronic or paroxysmal hypertension without edema; (4) acute cardiac overstrain, and (5) broken systemic compensation with chronic passive congestion, and edema with or without general anasarca, ascites, hydrothorax or hydropericardium, arising from myocardial weakness, valvular insufficiency or adherent pericardium.

In acute and chronic infective endocarditis one encounters, it is true, a scanty urine with albumin and red blood-cells just as in passive congestion; but as Bachr<sup>1</sup> has shown, this is due to the presence of a true infective glomerulonephritis with emboli of Streptococcus viridans in the loops of capillaries in the glomeruli, and it should accordingly be treated as a primary nephritis rather than as a primary heart disease. T shall therefore leave this question to be discussed by Dr. Christian.

In the groups of arteriosclerosis and of chronic hypertension one might well be tempted to resort to diuretics to remove products of auto-intoxication or to relieve a possible plethora, but in either case it would be questionable whether or not such an effect could be secured or would be desirable. It is useless to try to lower the blood-pressure by removing water from the blood by diuresis, because that water is immediately replaced from the tissues, and in some cases diuretics may even drive an excess of water from the tissues into the blood (Weber<sup>2</sup>). In both of these conditions, as von Noorden<sup>a</sup> has shown, it is better to spare the arteries and kidneys from overwork by light diet and restriction of salt and water than to remove these substances from the system with diuretics.

In acute cardiac overstrain, on the other hand, such as we meet in athletes after a boat race, a football game or a tug of war, or in the less romantic walks of life in persons who have performed feats of strength or exertion involving hard lifting, pushing or pulling, one is often confronted by a scanty urine containing albumin, casts and even red blood-cells (A. R. B. Myers,<sup>4</sup> da Costa,<sup>5</sup> Meylan<sup>6</sup>). This is due entirely to the congestion of the kidney resulting from venous stasis during the overstrain, and is therefore of primary cardiac origin; but, as these writers have shown, it is of entirely transitory duration and clears up when the strain is over and the heart once more under normal conditions. From a very complete study of the history of many decades of Harvard oarsmen, moreover, Meylan has shown that neither the heart nor the kidney shows signs of damage in after years, and the condition therefore can be left to take care of itself without the intervention of diuretic measures.

The chief condition in which active intervention to induce diuresis is advisable is in broken systemic compensation with edema from stasis in the systemic veins either from failure of the right ventricle, tricuspid stenosis or adherent pericardium (especially Pick's pericarditic pseudocirrhosis). In all cases of passive congestion the changes in the circulation closely simulate those observed in asphyxia, and Cohnheim and Roy7 have shown that in the kidney the first effect of asphyxia is a constriction of the renal vessels and diminution or cessation of flow of urine. This constriction has its origin in the vasomotor center and is absent if the nerves to the kidney are cut or become paralyzed, under

<sup>\*</sup> Read in the Section on Pharmacology and Therapeutics of the American Medical Association, at the Sixty-Fourth Annual Session, held at Minneapolis, June, 1913

<sup>1.</sup> Bachr, G.: Glomerular Lesions of Subacute Bacterial Endo-

Carditta, Am. Jour. Med. Sc., 1912, cxliv, 327.
 Weber, S.: Ueber die Beeinflussung der Resorption durch Diurettea, Verhandl. d. Kong. f. inn. Med., 1906, xxiii, 518.
 3. Von Noorden: Clinical Treatise on Disease of Metabolism, 1903.

<sup>1903.
4.</sup> Myers, A. R. B.: Etiology and Prevalence of Diseases of the Heart Among Soldiers, London, 1870.
5. da Costa, J. M.: On the Irritable Heart: a Clinical Study of a Form of Functional Cardiac Diseases and its Consequences, Am. Jour. Med. Sc., 1871. lx1, 17.
6. Meylan, G. L.: Harvard University Oarsmen, Harvard Grad. Mag., 1904, xil, 362, 543.
7. Colmheim, J., and Roy, C. S.: Untersuchungen fiber die Circulation in der Niere, Virchows Arch. f. path. Anat., 1883, xcil, 424. xcii, 424.

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which condition the volume of the kidney and the amount of blood flowing through it follow and are determined by the general blood-pressure. Prolonged stasis gives rise here as elsewhere to cloudy swelling of the kidney-cells of both the tubules and glomerular capsule, and to swelling of the tissues, which tend still further to choke the circulation through the renal vessels (Fischer<sup>s</sup>), leading in vicious circle to still more degeneration of the renal epithelium and glomeruli and finally to the proliferation of connective tissue which results in the formation of the typical hard red kidney of chronic passive congestion (Slauungsniere, Senator, Aschoff<sup>10</sup>) whether it be of the large or small and contracted type.

The functional power of the kidney in passive congestion has recently been subjected to a very careful clinical, and experimental study by Rowntree, Fitz and Geraghty," testing the function of the glomeruli by Schlayer's<sup>12</sup> lactose test (duration of exerction of 2 gm of lactose in 20 c.c. of water introduced intravenously) and the activity of the tubules by the excretion of salt, potassium iodid and phenolsulphonephthalein (method of Rowntree and Geraghty). They found that in cardiac decompensation the amount of urine may vary and is no absolute index of the funetional power of the kidney, although it is diminished in grades of stasis, but that the ability to excrete salt may be diminished in stasis of moderate grade even before a diminished excretion of phenolsulphonephthalein gives evidence of wide-spread damage to the tubules. Lactose, the index of glomerular function, is always delayed. Nonnenbruch13 in a less complete study also finds that in chronic passive congestion there is evidence of both vascular and tubular injury.

As regards the general edema which accompanies passive congestion Widal and Javal,<sup>14</sup> Strauss<sup>15</sup> and Magnus-Levy16 have shown that it is associated with retention of sodium chlorid by the tissues, and Loeb17 and Fischer<sup>8</sup> have demonstrated that the edema itself is

8. Fischer, M. H.: Edema, N. Y., 1910; Contribution to a Col-loid Chemical Analysis of Absorption and Sceretion, Lancet-Clinic, 1912, evil; Nephritis, N. Y., 1912; The Treatment of Nephritis and Allied Conditions, The Joursan A. M. A., May 31, 1913, p. 1682; 9. Senator, H.: Die Erkrankungen der Nieren, H. Nothnagel's Handb. d. spez. Path. u. Therap., 1902, xix, 1. 10. Aschoff, L.: Lehrbuch der Pathologischen Anatomic, Jena, 1900, H

Aschoff, L.: Lehrbuch der Pathologischen Anatomie, Jenä, 1909, fl.
 Rowntree, L. G., and Geraghty, J. T.: The Phthalein Test, Arch. Int. Med., March, 1912, p. 284. Rowntree, L. G., Fitz, R., and Geraghty, J. T.: The Effects of Experimental Chronic Passive Congestion on Renal Function, Arch. Int. Med., February, 1913, p. 121. Rowntree, L. G., and Fitz, R.: Studles of Renal Func-tion in Renal, Cardiorenal and Cardiac Disease, Arch. Int. Med., March. 1913, p. 258.
 Schlayer and Hedinger: Experimentalle Studien über toxische Nephritis, Deutsch. Arch. f. klin. Med., 1906, xc, 1.
 Schlayer, Hedinger and Takayusu: Ueber nephritisches Oedem, ibid., 1907, xcl, 59. Schlayer and Takayusu: Untersuchungen über die Funktion kranker Nieren, Ibid., 1910, xevili, 17; also 1910, el., 333. Schlayer: Untersuchungen über die Funktion kranker Nieren. B. Chronische vaskuläte Nephritiden, ibid., 1911, eii, 311. Schnid and Schlayer: Untersuchungen über die Funktion kranker menschlicher Nieren, Verhandl. d. Kong, f. inn. Med., 1910, xxvii, 744; Ueber die Ermüdbarkeit der Nierenfunktion, ibid., 1912, xix, 501.
 Nonnenbruch: Zur Kenntniss der Funktion der Stauungs-niere Duutsch Arch f. klin. Med. 1912

xxvi, 744; tener die Ermudoarkeit der Merenfunktion, 10fd., 1912, xxlx, 501.
13. Nomenbruch: Zur Kenntniss der Funktion der Stauungsniere, Deutsch, Arch. f. klin. Med., 1913, cx, 102.
14. Widal, F., and Javal, A.: La cure de dechloruration son action sur Poedeme sur Phydratation et sur l'albuminurie à certaines périodes de l'albuminurie épithéliale, Bull, et mém. Soc. méd. d. hôp. de Parls, 1903, ser. 3, xx, 733. Widal, F.: Die Kochsalzentzichungskur in der Bright'schen Krankhelt, Verhandl. d. Kong. f. inn. Med., 1909, xxvi, 43.
15. Strauss, 11.: Zur Frage der Kochsalz und Flüssigkeitszufuhr bei Herz und Nierenkrankhelten, Therap. d. Gegenw., 1903, N. F., v, 433. Symposium on Therapeutics, Med. News, 1903, lxxxiii, 673. Die Chlorentzichung bei Nieren und Herzwassersucht, Verhandl. d. Kong. f. inn. Med., 1909, xxvi, 91.
16. Magnus-Levy, A.: Dehydration by Dietetic Measures, THE JOURNAL A. M. A., Dec. 17, 1910, p. 2139.
17. Loeb, J.: Physiologische Untersuchungen über Ionenwirkungen, Arch. f. d. ges. Physiol., 1808, lxxi, 468.

determined more by the local formation of acid products which cause the tissue to take water by imbibition than by the changes in the walls of the vessels.

Fischer believes that the same laws of colloid imbibition govern both retention and excretion of water by the kidney, and hence believes that administration of alkalies, by antagonizing the effects of local acid products, gives a therapy applicable to both the edema and the renal conditions.

We owe our knowledge of the most important of cardiac diurctic drugs, the foxglove or digitalis, to an old woman in Shropshire who as Withering<sup>18</sup> (1785) tells us "had sometimes made cures after the more regular practitioners failed"; and since William Withering, according to his own words, was "open to information regardless of the source from whence it springs," he investigated this drug and "soon found the foxglove to be a powerful diuretic" so that he came "to use it in ascites, anasarca and hydrops pectoris, and as far as the removal of the water will contribute to cure the patient, so far may be expected of the medicine." Indeed, the excellent results which that old physician obtained in over a hundred cases justified his optimism. Digitalis is the diuretic of choice in all cardiae conditions with failure of the circulation because it combines in a most fortunate way all the modes of action that are desirable in counteracting the condition. As Traube<sup>19</sup> and Lauder Brunton<sup>20</sup> have shown, it increases the force of the heart-beat, the blood-pressure and as a rule the velocity of blood-flow, and also causes a constriction of the blood-vessels of the skin and intestines. But the experiments of Brunton and Power and of Gottlieb and Magnus<sup>21</sup> demonstrate that the renal vessels do not take part in this constriction due to digitalis, but that on the contrary more blood flows through the kidney than before. All the experimenters from Withering to the present have found that digitalis acts as a diuretic in normal kidneys even when it causes no change in blood-pressure; but in these cases it acts both by dilating the renal vessels and by some specific action on the renal epithelium. Cushny<sup>22</sup> has called attention to the fact that all purgatives have also some diurctic action by giving rise to what he terms "diarrhea of the tubules," and since even before Withering digitalis was known as a purgative drug, it is natural that it also should have some specific action on the renal epithelium, though this is not nearly as marked as with drugs of the purin group.

On the other hand, most of the effect of digitalis depends on its action on the circulation, the velocity of blood-flow and the pulse-pressure. Since Rowntree and Fitz have shown that in chronic passive congestion the power of the kidney to excrete lactose is diminished, and since Schlayer has shown that the lactose excretion

18. Withering, W.: An Account of the Foxglove and Some of Its Medical Uses, Birmingham, 1785.
19. Traube, L.: Gesammelte Reiträge, Berlin, 1871-1878.
20. Brunton, T. Lauder: Digitalis, with Some Observations on the Urine, London, 1868. Brunton and Meyer: Action of Digitalis on the Blood-Vessels, Jour. Anat. and Physiol., 1873, vii, 135. Brunton and Power: The Diurcite Action of Digitalis, Proc. Roy. Soc., 1874, xxii, 240. Brunton and Pye: Physiologic Action of Erythrophleum Guinense, Proc. Roy. Soc., 1876, xxv, 175. The Physiologic Action of Casca Bark, St. Barthol. Hosp. Rep., 1876, xii, 125, and Phil. Trans. Roy. Soc., London, 1876, elxvii, Pt. II, 172, collected in Collected Papers on Circulation and Respiration, London, 1907.
21. Gottileb, R., and Magnus, R.: Ueber Diurese IV, Arch. Diurese III, Bidd, 1001, xlv, 210. Meyer, H. II., and Gottileb, R.: Die Experimentelle Pharmakologie als Grundlage der Arznei-behandlung, ed. 2, Berlin, 1911.
22. Cushny, A. R.: Diuresis of Renal Cells, Jour. Physiol., 1001-1902, xxvii, 420.

may be taken as an index of the ability of the kidney vessels to react, it is evident that in passive congestion the activity of the kidney must depend more on the condition of the general circulation than does the normal kidney. Now Erlanger and Hooker<sup>23</sup> have shown that, other things being equal, there is a close parallelism between the amount of urine excreted and the pulsepressure or the amount of change of blood-pressure with each heart-beat (that is, the difference between maximal and minimal blood-pressure), and on the other hand that in orthostatic albuminuria the albumin is excreted only when the pulse-pressure is low or falling. Gesell<sup>24</sup> has shown that this divisit depends directly on the pulse-pressure because he has been able to produce it in excised kidneys by increasing the pulse-pressure without permitting any change in the amount of blood flowing through the kidney. The pulsation of the blood-stream is communicated as far as the glomeruli, for Nussbaum<sup>25</sup> has been able to watch these structures pulsate in the frog, and it is therefore likely that the pulsation bears a definite relation to filtration in the glomeruli where, on account of the size of the arteries leading to the tuft, pulsation must be much more marked than along the tubules. Now, as stated before, one of the well-marked effects of digitalis is to increase both the systolic output of the heart and the pulse-pressure, and therefore to increase filtration through the glomeruli and bring on diuresis. This is by far the most marked in cases of cardiac irregularity and especially in patients with auricular fibrillation. In these cases before the administration of digitalis the pulse-rate is fast, the beats are small and the pulse-pressure is very small, so that oliguria is the rule. Digitalis blocks off many of the impulses from reaching the ventricles, and slows the latter so that large slow beats with large pulse-pressure result bringing with them the optimum conditions for renal secretion, and within twenty-four hours the urine may be increased fivefold or tenfold.

In using digitalis it is important, as Pratt<sup>20</sup> and Hale<sup>27</sup> have insisted, to obtain a preparation which has been standardized physiologically, so that one can be certain that he is giving an adequate amount of the drug; but whether one use the galenical tincture or the fluidextract or the powder of a good digitalis leaf or resort to one of the special preparations of digitalis bodies, either the digitalin, digalen, digitaline-Nativelle (which is digitoxin), or the digitonin-free digitalis (digipuratum) does not seem to make any essential difference. There is a wide-spread clinical teaching that the infusion of digitalis is preferable, as a diuretic, to the tincture; but most of the evidence is based on studies made before digitalis preparations were standardized. The infusion probably contains more digitonin than the other preparations, but I have thus far found no evidence which is conclusive to me that a good infusion is more efficacious than an equally good tineture or one of the active digitalis bodies, whereas on the other hand infusions are much more subject to variation and to spoiling.

Among the other bodies of the digitalis group I can bear witness to the excellent effects first noted by Fraenkel for the administration of from 0.5 to 1 mg. strophantin into either the veins or muscles. Its diuretic effect seems to run parallel to the effect on the circulation

When we come to the other members of the digitalis group, squill, convallaria, adonis vernalis, hellebore and erythrophlocum, however, a question arises, not of their absolute efficacy, but of whether or not any of them are as efficacious as digitalis or strophanthin as diurctics from quickening of the entire blood-flow through the body; or, on the other hand, as efficacious as are the diurctics of the purin group in their action. The experience of decades has shown that squill is an excellent diuretic, especially when given with digitalis, but the careful critical tests of Mackenzie28 show that when periods of squill administration alternate with periods of digitalis administration in the same patient there is no preponderance of evidence in favor of the superiority of squill.

On the other hand, when we desire a more powerful diuresis than is afforded by digitalis we make use of the diurctics of the purin or caffein group-caffein, theobromin, theophyllin or theocin-which as Loewi<sup>29</sup> has shown act both by dilating the renal vessels and by direct action on the renal epithelium.

According to the studies of Loewi<sup>20</sup> and his collaborators the drugs of this series act largely through bringing on dilatation of the renal vessels, although he has demonstrated that they may also act directly on the renal epithelium when dilatation of the vessels is prevented. Observations by Meyer in diabetes insipidus corroborate this view. The caffein series is particularly efficacious in those cases of cardiac dropsy in which the kidney cells have not yet become greatly damaged, and one will often encounter cases in which these drugs will bring on a diuresis not obtainable by the digitalis series. Of the caffein group theobromin is a more potent diu-. retic than caffein (caffein citrate) itself; and theophyllin, an isomer of theobromin, is still more potent than theobromin. The most convenient form of all is the water-soluble acet-theorin sodium in doses of about 3 grains (0.2 gm.) three times a day; it not only gives greater diuresis but may also cause diuresis in cases in which theobromin sodium salicylate evoked no response whatever. Erich Meyer<sup>30</sup> calls attention to the fact that in cases of primary cardiac disease one obtains an intense diuresis with great benefit to the patient from drugs of the caffein series, in contrast to the cases of primary nephritis, in which he has never seen any recognizable benefit from their use. Indeed, the recent studies of Schlayer, Mosenthal, Christian and Janeway indicates that when there is sufficient damage to the kidney these diurctics soon fatigue the latter, cease to produce a response, and then actually diminish rather

<sup>23.</sup> Erlanger, J., and Hooker, D. R.: An Experimental Study of Blood-Pressure and Pulse-Pressure in Man, Johns Hopkins Hosp. Rep., 1904, xil, 145. Hooker, D. R.: A Study of the Isolated Kidney: the Influence of Pulse-Pressure on Renal Function, Am. Jour. Physiol., 1910, xxvil, 24; Postural or Orthostatic Albuminuria, Arch. Int. Med., May, 1910, p. 491. Hooker, D. R., Hegeman, R. F., and Zartman, L. V.: The Relation of Pulse-Pressure to the Appearance of Albumin in a Case of Orthostatic Albuminuria, Am. Jour. Physiol., 1008-1900, xxili, p. 11.
24. Gesell, R.: The Relation of Pulse-Pressure to Renal Secretion, Am. Jour. Physiol., 1013, xxxii, 70.
25. Nussbaum, M.; Untersuchtungen über die Secretion der Niere, Arch. f. d. ges. Physiol., 1878, xvil, 142; 1878, xvil, 580. Also discussed by Brodie, T. G.: Renal Activity, Harvey Leet., New York, 1909-1910, p. 81
26. Pratt, J. H.: The Potency of Digitalis Preparations, Boston Med. and Surg. Jour., 1910, clxili, 279.
27. Hale, W.: Digitalis Standardization and the Variability of Crude and Medicinal Preparations, Bull. 47, Hyg. Lab., U. S. P. H. S., Washington, 1911.

<sup>28.</sup> Mackenzie, J.: Digitalis, Heart, 1010-1011, ii, 273. Cushny, A. R.: On the Action of the Digitalis Series on the Circulation in Mammals, Jour. Exper. Med., 1897, il, 233. 29. Fletcher, W. M., Henderson, V. E., and Loewi, O.: Mitt-hellungen über den Mechanismus der Diurese, Arch. f. exper. Path. u. Pharmakol., 1905, lili, 15. Alcock, N. H., and Loewi, O.: Ueber den Mechanismus der Salzdiurese, ibid., 1905, lili, 33. Hender-son, V. E., and Loewi, O.: Ueber den Mechanismus des Harnstoff-diurese, ibid., 1005, lili, 49; also Ueber die Wirkung der Vaso-dilatatorenrelzung, ibid., 1905, lili, 56. 30. Meyer, E.: Beitrag zur Wirkungsweise einiger gebrauch-licher Diuretika, Therap. Monatsh., 1011, xxv, 11.

than increase renal secretion. On the other hand, one does encounter cases of long-standing heart-failure in which the administration of these diuretics does not produce a diuresis, or in which, quite comparable to Schlayer's experience in primary nephritis, the first doses are followed by increased output of urine but subsequent doses are not. This is not surprising since Schlayer, Rowntree and Fitz, and Nonnenbruch have shown that in these cases there is a secondary diminution in renal function of both tubules and glomeruli and definite injury of the tissue. Fortunately, Rowntree has provided us in the phenolsulphonephthalein test with a simple, quick and easy method of determining in any given case the exact extent to which the renal epithelium is injured. If we make a phthalein test as soon as we see the patient, we can tell in two hours whether his renal epithelium is working well or is out of function.81

If the phthalein excretion is low-30 per cent. or less in two hours-we can know at once that we are somewhere near the point at which theocin might injure the renal epithelium; and it will be better to rely on the digitalis and try to improve the circulation before trying to stimulate the kidney. If the general circulation improves, as Rowntree and Geraghty and also Erich Meyer have shown, the function of the renal epithelium will return very rapidly to nearly normal and then one need not be afraid of acting on it with these powerful Therefore, we should aim first to improve diuretics. the circulation with digitalis and leave the removal of the edema for the administration of caffein diurctics a few days later.

The same precautions apply to the saline diurctics, potassium acetate, citrate and tartrate, although they are probably less irritant to the kidney than are the caffein series, and their effect also is limited by the same conditions. Unfortunately, this is true also of Martin Fischer's method of administering salt and sodium carbonate intravenously or by rectum, for Fischer states specifically that "when a heart drops below the lowest level of efficiency and has no recuperative powers left in it, alkali and salt cannot supply them." On the other hand, when the circulation is improving, the acetates, citrates and tartrates which are transformed into carbonate in the body and are excreted as such are much easier and more pleasant to the patient than the carbonate.

One of the oldest drugs that has been used in failure of the circulation is calomel, and with many excellent physicians it is a routine to prescribe purgation with calomel as soon as they see a patient with heart-failure. Frequently, however, one finds a copious secretion of urine occurring even before the bowels have moved and at least soon afterward. Flechseder<sup>32</sup> has shown, however, that most of the excess of water that is thus excreted through the kidneys is first exuded into the upper bowel and is then reabsorbed as pure water by the lower bowel and excreted as such through the kidneys, and he finds that the divisitions from calomel is greatly increased if the outflow from the lower bowel is hindered by administration of morphin. The good effects of calomel in cardiac disease is testified to by its long empirical use, particularly in the form of the pill of Addison and Niemeyer (digitalis 1 grain, squill 1 grain

and calomel 1/8 grain). Calomel acts particularly on the tubules, and tends to increase the excretion of sodium chlorid more than the total volume of urine, so that as Meyer has shown, the amount of salt excreted may be raised to six or seven times the former level. It is of course beneficial to deplete the tissues not only of water but also of this excess of sodium; but it must never be forgotten that calomel acts on the kidney by being converted into mercuric chlorid and that any excess may give rise to a bichlorid nephritis which affects chiefly the tubules (Richter, Schlayer). It is particularly dangerous, therefore, in cases in which the renal epithelium is already badly damaged, and the precaution of a phthalein test is therefore doubly advisable. On the other hand, it is probable that the pendulum has swung a little too far toward the side of fear and that in the great majority of cases of decompensation the kidney is not injured enough to be sensitive to a single dose of calomel, especially if no morphin has been given to prevent the normal purgation.

It must also be borne in mind that a number of purely physical procedures may influence the excretory power of the kidney. The pressure within the abdomen from ascites may be so great as to compress the renal vein and cause a congestion oliguria which may subside as soon as the ascitic fluid is removed by paracentesis; the emptying of distended bowels may allow the heart to lie in a better position and enable it to exert more efficient contractions so that the circulation becomes improved, spasm of the kidney vessels passes off, swelling of the renal tissue may subside and restitution of renal function thus set in. So also after the tapping of a hydrothorax or the performance of a venesection; and, indeed, after venesection we have an added acceleration of the blood-stream through the kidneys on account of a decrease in blood viscosity. Hot packs or poultices over the kidneys and abdomen and irrigation of the bowel with liquid at a temperature of from 102 to 105 F. may also cause further dilatation of the kidney vessels from heat alone and thus bring on diuresis.

Since Schlayer has shown us that the kidney fatigues just like the heart it is important in the more severe stages of combined heart and kidney failure to apply to both the principle of rest. This is best exemplified in the Karell<sup>33</sup> dict-giving the patient nothing but from 600 to 800 c.c. (from 20 to 25 ounces) of milk daily until he has begun to improve. During the stage of edema it is also important to limit the ingestion of salt unless one is definitely following the method of Fischer; for, as Rowntree and Fitz have shown, the power to excrete salt may be diminished very early in the stage of congestion. The failing kidneys may also be spared further work if the excess of fluid from the body be removed by a not too vigorous purgation or by mechanical means, either by incisions in the skin or better by puncturing the latter with Southey or Curschmann tubes and allowing the power of a siphon tube down to the level of the floor to add itself to the elastic exudation from the tissues.

In general we should aim first to know the exact state of the kidneys; second, to improve the circulation with digitalis or to spare it with the Karell diet; and, thirdly, to resort to theorem or the saline diurctics to relieve cdema if the renal epithelium is not severely injured.<sup>34</sup>

2245 Linden Avenue.

<sup>31.</sup> I should like to call the attention of those who may consider a phthalcin test a difficult or expensive procedure to the fact that a simple home-made colorimeter can readily be constructed which is accurate to less than 3 per cent. and is very easy to use. A description of this colorimeter will be published soon. 32. Flechseder; Quoted from Meyer and Gottlieb.

<sup>33.</sup> Karell, T.: Arch, gén. de méd., quoted from von Wittich: Ueber den Werth der Karelikur zur Behandlung von Kreislauf-störungen, Deutsch. Arch. f. klin. Med., 1913, cx, 128. 34. In addition to the references given in the text, the follow-ing will be found of interest:

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#### ABSTRACT OF DISCUSSION

Dr. PHILIP S. Roy, Washington, D. C.: Bleeding is one of the most important therapeutic agents in cardiovascular dropsies, in cases in which we want to increase the action of the kidneys. About six months ago I had a man who was eliminating one pint of urine in twenty-four hours. After bleeding a pint the kidneys eliminated two gallons in fortyeight hours. He was taking no drug at that time. Digitalis, of course, acts best in pulsus irregularis perpetuus or fibrillation of the auricle. Mr. Sawyer always gives digitalis when the veins are too full and the arteries not full enough; in other words when the right side of the heart is overtaxed. I have followed Mr. Sawyer's advice in the last few years with good results. I know Dr. Hirschfelder intended to mention rest along with diet in the treatment of diseases of the heart. Rest, digitalis and diet are the three cardinal therapeutic agents in treating diseases of the cardiovascular system, but as I have mentioned, blood-letting will often produce divresis when other agents have failed.

DR. B. FANTUS, Chicago: 1 wonder whether Dr. Hirschfelder purposely omitted reference to the production of hyperemia of the back by means of heat, as by poultices, or of chemical irritants, as by mustard applications, or of suction, as by means of dry cups. It is true that the experimental basis of these procedures is still insufficient. Whether hyperemia of the back produces anemia or hyperemia of the kidney is still one of the mooted questions so far as I know. But that it is well-founded clinically 1 believe some of the practitioners present will agree.

DR. FRANK BILLINGS, Chicago: I should have liked to hear Dr. Hirschfelder say more about the management of this condition without drugs. My own experience is that, in decompensation of the heart with anasarca, with that condition of the kidney of a cyanotic type in which the circulation through the kidney is very small in a given time, to begin with the use of digitalis practically results in failure. Preliminary to the use of the drug must come absolute rest and reduction of fluid intake for any given time to relieve the patient of much of his dropsy. Reduction of the fluid intake may be secured by giving milk alone not to exceed a liter in twenty-four hours or even less, or absolute starvation with water alone. This treatment should be accompanied by excretion through the bowel by free purgation. It is a matter of choice as to what one will use as the cathartic. The objection made by some that the use of salines in these cases may cause the accumulation of more salines in the body that are harmful I think a point well taken, but in that case even one has at hand plenty of other vegetable cathartics. The too early use of heart tonics of the digitalis group with the heart doing all it can may be harmful to the heart fighting against an obstruction it cannot overcome.

DR. ROBERT A. HATCHER, New York: It has long been held that the tineture of digitalis and the infusion have different actions, but no one seems to have tested the matter experimentally. The mare left after making the tincture is inert, hence the tincture must be supposed to contain all of the active principles of the leaf. Different substances have

been called "digitonin" by different observers, leading to a good deal of confusion with regard to that substance. Dig italis leaf contains only traces of the saponin, digitonin, a matter to which I wish to call attention because of the false claims which have been made with reference to preparations of digitalis alleged to be free from digitonin.

DR. A. D. HIRSCHFELDER, Baltimore: For renal hyperemia I mentioned merely hot applications both to the back and to the abdominal wall, which certainly brings about by the heat minor and reflex vasodilatation to the kidney, which I believe is most important. I think that it is quite probable that the very hot rectal infusions that Dr. Martin Fischer recommends in his rectal infusion method of carbonate and chlorid may, by their proximity at least to the left kidney, give rise to a reflex dilutation in those kidneys in which an element of force may be spasm, which was demonstrated by Roy, Cohnheim, Thacher and others as playing a rôle. My general ideas about the management of a case of cardiac failing compensation with edema which demand cardiac measures closely coincide to those of Dr. Billings, but one must avoid too free purgation, for instance, fifteen bowel movements daily, as was in vogue some years ago, especially in those cases of aortic insufficiency which are affected by temporary, sudden rises in blood pressure. Dr. Dandy has demonstrated that in the act of defecation the blood may jump 50 mm. of mercury. In failing aortic insufficiency this may account for some of the sudden deaths at stool. In aiming at drug effects we fire our therapeutics in a volley; we ought in a dangerous case to do as rapidly as possible all that we can at once. In dealing with a dilated heart each measure which tends to relieve the dilatation will tend to place that heart under the mechanical conditions in which it contracts most efficiently and we want to get the overstretched fibers down to the length at which they contract under the conditions of greatest degree of mechanical efficiency by rest, venesection, purgation and digitalis or more probably an intravenous or an intramuscular injection of strophanthin. I cannot say that in my own experience the prompt administration of strophanthin, followed in the next twenty-four hours by digitalis has been, as Dr. Billings suggests, a detrimental procedure. I can well understand that if it were the only procedure used this might be true, but I am not quite clear in my mind as to just what dangers Dr. Billings fears from doing venesection first and then following the temporary, but definite relief of dilatation with immediate injection intravenously of strophanthin. It has seemed to me, both from clinical and experimental work, that it is important to improve the tonus of the heart muscle as well as its power of contraction as quickly as possible. The dilatation depends on a lowered tonicity and increased venous pressure. Digitalis and strophanthin increase tonus and antagonize a high blood-pressure and venescetion lowers blood-pressure; then why are not two measures taken together better than one alone?

DR. FRANK<sup>®</sup> BILLINGS, Chicago: I probably did not make myself clear. You answered my question yourself when you said that you would relieve the venous stasis first. In my own experience I would feel that I could give the digitalis with the best results after the venous engorgement was partially or wholly relieved.

DR. HIRSCHFELDER, Baltimore: The action of digitalis on a heart in that condition may perhaps be different from the action on a perfectly healthy heart and I do not know that any experiments in pathologic pharmacology have been made which would throw light on that important question. I think we shall have to take Dr. Billings' experience in this matter into consideration in contrast to experiments done on healthy heart-muscles.

DR. RAY L. WILBUR, San Francisco: My idea in asking for the papers of this clinical symposium was to get something of an authoritative summary in regard to the treatment of such conditions. When I thought of the barrels of ergot injected into tuberculous patients with hemorrhage and of the hogsheads of sweet spirits of nitre given patients with cardiac lesions I thought it would be well to have some authoritative statements so that we could get a fresh start.