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SOME PRINCIPLES OF DRUG TREATMENT IN CARDIOVASCULAR CONDITIONS.

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Therapy as a science has not kept pace with pathology and diagnosis, largely due to a lack of method that will enable us to place it on the same sure footing as the above-named branches. Its scientific basis rests chiefly on experiments on normal animals. The dosage and frequency of repetition has been left largely to clinical experience, which too frequently consists of personal impressions rather than conclusions from recorded facts, and certainly lacks the accuracy of a true science.

The pharmacologic action of a drug on a normal animal may have reached the certainty of a chemical test and yet give very misleading information as to its action or indications for its use on the diseased human. It now rests with clinicians, in conjunction with pharmacologists and physiologists, to take up this subject, and by experimental work on animals in which the disease has been artificially produced, and by bringing pharmacologic and physiologic methods to the bedside, to clear up this subject as far as the means at hand will permit.

With our modern clinical appliances for accurate determination of both systolic and diastolic blood pressure, the field of cardiovascular therapeutics is gradually being placed on a firm basis. In fact, there is no other therapy, except that of the specifics, that at the present time rests on such a scientific foundation.

The most important cardiac remedies may be divided into two groups: those which act chiefly on the heart—*digitalis* and *strophanthus*; and those whose chief action is on the vessels—the vasoconstrictors, *adrenalin*, *caffeine*, *camphor* and *strychnin*, and the vasodilators, *alcohol*, *nitroglycerin* and the *nitrites*. In making such a subdivision we must bear in mind that they are all cardiovascular drugs affecting both heart and vessels, however, in varying degrees. It is not my intention to detail the indications for the use of cardiac remedies. In general, however, they are indicated when there is imperfect distribution of blood, due either to cardiac insufficiency or to a lack of the proper vascular tone.

THE DIGITALIS GROUP.

The digitalis group is, therefore, to be used in cases in which this improper distribution is dependent on heart insufficiency, the result either of valvular or of muscular changes. The idea that the digitalis group is contraindicated in myocarditis is not well grounded, although we must remember that greater care should be observed in regard to dosage and that the final results of the treatment must, from the nature of the trouble, be less satisfactory than in valvular lesions with good

heart muscle. This group is, furthermore, not necessarily contraindicated in cardiac trouble with marked arteriosclerosis, or high blood pressure, as it is rare that in the physiologic doses these drugs increase blood pressure sufficiently to endanger the vessel wall. Sahli¹ has shown that cardiac insufficiency may be associated with high blood pressure which has its basis in stimulation of the vasomotor centers by the poorly oxygenated blood; improve the pulmonary circulation and the blood pressure falls. Heart insufficiency associated with slow pulse is often relieved by digitalis, due to a more complete emptying of the heart in each systole, better circulation in the coronary vessels, with consequently improved nutrition of the heart muscle. There is still considerable difference of opinion as to the value of digitalis in aortic regurgitation on account of its prolonging diastole. It is generally conceded that the prognosis in uncompensated aortic regurgitation is bad, probably, as Sahli has suggested, due to the presence of essential passive congestion; that is to say, the leakage is so marked, before evidence of incompensation occurs, that even with complete systole and normal diastole it is impossible to maintain the proper amount of blood in the arterial system, while in mitral lesions, on account of the early passive congestion in the lungs, the individual is conscious of the disturbed compensation before the stage of essential passive congestion is reached.

It is well to remember that digitalis increases the systolic output, which compensates in a measure for the greater amount that returns during diastole and, even prolonging the diastole, has its advantage, as it allows the auricle to empty itself more completely. Finally, the recent painstaking work of Stewart² has shown that, after all, the amount of regurgitating blood is slight and prolonging the diastole is not a serious matter.

The action of the various members of the digitalis group of drugs is practically identical; the main difference is one of degree and some slight differences in the amount of vasoconstrictor action. The less well-known members of this group—*convallaria*, *apocynum* and *cactus*—do not possess any advantage over digitalis, are much less constant in action and will not be discussed.

Digitalis.—Since Traube's time it has been a disputed question whether digitalis acts principally on the heart or on the blood vessels, and whether the increase in blood pressure is chiefly of cardiac or of vascular origin. The recent work of Gottlieb and Magnus,³ now generally accepted, shows that the chief action is on the heart, the rise in pressure being due to more complete systole with a consequently greater flow of blood into the aorta. Its vascular action is chiefly constriction of the splanchnic arteries with dilatation of the peripheral vessels, includ-

1. Verhandl. d. Cong. f. inn. Med., 1901, xlx, 53.

2. Arch. Int. Med., 1908, i, 102.

3. Arch. f. exper. Path. u. Pharmacol., 1902, xlviii, 262.

ing those in the brain, due partly to increased pressure exerted on the interior of the vessel, but mainly ascribed to a reflex stimulation of the vasodilator center arising from constriction of the splanchnics. The various active principles have a somewhat different effect from the crude drug. The digitoxin especially has a decidedly greater vasoconstrictor action, and dilatation of the peripheral vessels does not always follow. It is generally conceded that strophanthus has less vasoconstrictor action than entire digitalis, thus resembling digitalin.

In addition, all this group of drugs stimulate the vagus, causing slowing of the heart. As a result of the more complete systole the output of blood with each ventricular contraction is much increased, and Gottlieb has shown that the systolic output in a cat may be increased threefold by digitalis. This would lead to a very marked rise in blood pressure, were it not associated with lessened engorgement of the right heart, and better emptying of the veins, thus lessening the peripheral resistance to the arterial blood. For this reason marked increased systolic output after digitalis does not necessarily mean increased blood pressure.

It is unfortunate that a drug which possesses such a desirable physiologic action should also have its objectionable features. The chief of these is its variable strength, irritating action on the gastrointestinal tract, and, finally, its cumulative effects. The physiologic activity of the leaf depends on the soil in which it is grown, the time of year it is gathered, the method of drying, and especially the length of time it has been kept in the dried state. Not merely does it vary in strength, but the proportion of the various active principles is not constant. Focke⁴ has shown that leaves gathered in July or August have deteriorated 25 per cent. by October, and the following summer are only one-quarter as powerful as the fresh leaf. Buhner⁵ found that the fluid extract purchased from various druggists in Germany showed variations in strength up to 400 per cent. Edmunds⁶ in this country found that the tincture obtained from indifferent sources varied 350 per cent. in strength.

It is almost incredible that a scientific profession could be content to use a preparation of such inconstant activity, especially when it may be largely remedied. Gottlieb is certainly in the right when he maintains that digitalis preparations should be physiologically standardized, just as are the curative serums. As the tincture deteriorates very little on keeping, there is no reason why a standardized preparation of this sort should not be made. The dried leaves can not be satisfactorily standardized on account of rapid deterioration. In this country we have tinctures shown to be physiologically active and German chemists have prepared carefully titrated tinctures of uniform strength.

All digitalis preparations are decidedly irritating to the gastrointestinal tract. Attempts to overcome this property have been unsuccessful, as the irritative qualities are present in the isolated active principles and especially marked in the most powerful of these, the digitoxin. For this reason it is only fair to assume that a digitalis preparation which is free from irritating qualities is physiologically inert. There can be extracted from digitalis leaves a small amount of a heavy oil which acts as a gastrointestinal irritant. The quantity

contained in a dose of digitalis, however, is too minute to be considered as acting in this manner. The same statement holds true in regard to cumulative effect. There are on the market various digitalis preparations which are recommended on account of their non-cumulative action. The only conclusion we can draw is that the statements are false or that the preparation is physiologically inert, as it is well known that the isolated active principles have a cumulative action, this being especially true of the digitoxin. Recently Fraenkel⁷ has shown that, contrary to Cloetta's statement, the much-lauded digalen⁸ has a cumulative action. The best means at hand to avoid the cumulative effect is to use a preparation of known strength, like the titrated tincture, and then carefully to observe the urinary output and the character and frequency of the pulse. To avoid its irritating action recourse has been made to subcutaneous and more recently to intravenous medication. All preparations, including the digalen, are more or less irritating when given subcutaneously.

In what form shall we administer the digitalis? What shall be the dosage and how long should we continue its use? It is the generally accepted view that better results are obtained from the combined active principles than from any single one. The results from digitoxin, the most powerful of the active principles, is not especially satisfactory, due to its greater vasoconstriction action and the close approximation of the physiologic to the toxic dose (Fraenkel⁷). In Germany, where the plant thrives and where stringent regulations are in force in regard to renewal of the leaves, the powdered leaves and infusions are almost exclusively used. According to Cushney, the infusion contains all the active principles in about the same proportion as the dried leaves; the insoluble digitoxin in the presence of digitonin passes into the watery solution in suspension. When made from the active powdered leaves it is an excellent preparation, somewhat less powerful than the same amount of dried leaves; and for this reason the dose is about twice the amount. Many druggists prepare an infusion by diluting a fluid extract; such a preparation is useless, as the active ingredients are largely precipitated. In this country, on account of the uncertainty in the activity of the leaves, the tincture is the favorite preparation.

In the case of every patient who is given digitalis, the daily secretion of urine and character and frequency of the pulse should be noted. The first evidence of the physiologic action of the drug is an increased secretion of urine, which begins, on an average, forty-eight hours after the treatment is instituted. When this point is reached the dosage of digitalis should be lessened, as this is evidence of the breaking up of the vicious circle; and when once the normal distribution of blood is restored, it will often be maintained with very slight cardiac stimulation, provided the necessary precautions in regard to rest are observed. This smaller dosage may be continued for a considerable period of time without much danger of cumulative effect, even for months or years, as recommended by Fraentzel, Kussmaul and others. This long-continued digitalis therapy is indicated only in exceptional cases. When digitalis is ad-

7. Arch. f. exper. Path. u. Pharmacol., 1907, lvii, 79.

8. We have recently tested four bottles of digalen, and were unable to obtain any digitalis effect on dogs from doses of 2 c.c. administered intravenously. Two of the samples were tried on frogs' hearts and also failed to show any digitalis action. A decided digitalis effect was obtained on the same dogs with 0.1 c.c. of a tincture of strophanthus.

4. Ztschr. f. klin. Med., 1902, xlvi, 377.

5. Cited by Gottlieb: Verhandl. d. Cong. f. inn. Med., 1901, xix, 90.

6. THE JOURNAL A. M. A., 1907, xlviii, 1744.

ministered in the above manner there is little danger of cumulative action. In patients who do not yield to this method of treatment, increased secretion of urine does not occur, and in these cases the drug may be continued for ten days, carefully observing the pulse. The appearance of marked slowing or arrhythmia is evidence of intoxication, and the dosage must be reduced or the drug entirely discontinued.

It is well to bear in mind that very marked intoxication causes increased pulse-frequency; clinically, however, the earlier stage of bradycardia is rarely absent. Too much stress can not be laid on the presence of arrhythmia as an evidence of intoxication. A patient who is taking full doses of digitalis must be seen daily, if we wish to avoid cumulative effects. With a preparation of known strength and with the patient carefully watched, intoxication should never occur. A very moderate slowing of the pulse is desirable, as it means more complete systole and better suction action by prolonging the diastole. Very decided slowing is harmful, as the increased volume of blood expelled at each systole is overshadowed by the infrequency of contraction, so that the amount of blood leaving the heart in a unit of time is reduced. When one preparation of digitalis fails to increase the flow of urine, we may resort to another form. It can not be too strongly emphasized, however, that the results depend on the amount of active digitalis and not on any particular pharmacopeial preparation.

In case of failure with an active preparation administered by mouth, we may resort to intravenous medication, as there is always a possibility of incomplete absorption, especially in patients with a high degree of circulatory disturbance. Kottmann⁹ was the first to use digitalis intravenously, employing digalen, a soluble digitoxin. Beginning with 1 c.c., he later used 10 to 15 c.c. at a dose and recommends the larger dosage. The technic is simple, the injection being made into a superficial vein of the arm. The advantages of this method are: Certainty of absorption, promptness of action and absence of gastric irritation. A rise in blood pressure occurs in five minutes, reaches its maximum of from 5 to 30 mm. of mercury in one-half to one hour, the effect continuing about twenty-four hours, then the dose may be repeated. Diuresis begins in a few hours. Occasionally evidence of intoxication, especially of bradycardia, may be observed after a single intravenous dose, but this disappears after a few hours.

Recently others have confirmed Kottmann's results. Mendel¹⁰ did some experimental work with intravenous injections. After using various preparations, he found the digitalone the most satisfactory. In man he used daily injections of 2 c.c. Fraenkel still more recently has used strophanthin intravenously. This is a glucosid obtained from strophanthus. The preparation is now on the market in sealed tubes containing 1 c.c., which represents 1 mg. of the strophanthin. The usual dosage is 0.5 to 1 mg., repeated, if necessary, in twenty-four hours. The action is similar to that of digalen, but Fraenkel thinks that it continues longer. Certain untoward results, as chill, nausea or bradycardia, are occasionally observed after an injection. In addition, we must consider the danger of acute dilatation of the heart from the rather suddenly increased work thrown on it and the possibility of grave toxic symptoms in certain individuals, especially when preparations con-

taining large amounts of digitoxin are used, and, finally, the dangers of arterial degeneration from intravenous medication, such as Fischer¹¹ has produced in rabbits with digalen. At the present time intravenous medication had better be reserved for those cases in which prompt action is required, where gastric conditions render administration by the mouth impossible or where digitalis by mouth has failed to give results.

Strophanthus.—The only other member of the digitalis group which I shall consider is strophanthus. Its action is practically identical with that of digitalis, but much less powerful. It is a gastrointestinal irritant. The tendency to cumulative effect is much less marked than with digitalis, but still occurs (Fraenkel¹²). Edmunds has found its toxicity about fifty times that of digitalis, and he considers the good effect obtained at times when digitalis has failed as due to the relatively greater dosage. It is chiefly valuable in cases in which a moderate cardiac stimulation is desired, and in ambulatory patients when we fear to use digitalis on account of its greater tendency to cumulative effect. It varies in strength like digitalis, but a titrated tincture may now be obtained.

THE VASOCONSTRICTORS AND VASODILATORS.

The next group to be considered consists of the vasomotor drugs. First, the vasoconstrictors, of which the most important are adrenalin, caffeine, camphor and strychnin. These remedies are indicated in cases in which there is vasomotor paresis. The arteries in the great splanchnic reservoirs, with their wonderful capacity to dilate, are engorged with blood, and, while the peripheral vessels suffer from the same paresis, they are usually poorly filled and the patient appears pale, in striking contrast to the cyanosis of cardiac stasis. The contraction of the heart may be normal, but on account of insufficient filling of the ventricle, a very small volume of blood is expelled at each systole. A classical picture of vasomotor paresis is seen in chloral poisoning, shock, and chloroform and ether narcosis. The important experimental work of Romberg and Passler¹³ has shown that the heart failure of acute infections, as pneumonia and diphtheria, is in reality a vasomotor paresis. Here, then, is a large field for the vasoconstrictor remedies.

Adrenalin.—The most active member of this group is adrenalin. It is the remedy *par excellence* in shock or heart failure during anesthesia, as it causes a very prompt and marked rise in blood pressure by its action on the nerve endings in the vessel wall. The increase in pressure is so marked that the heart is called on to do an enormously increased work, which may be safely borne by the good heart muscle of the patient in shock, but may lead to acute dilatation and serious consequences if the muscle is diseased, as is often the case in the acute infectious diseases. Again, as the action is exceedingly transitory, five to ten minutes, it is of little value in cases in which prolonged effect is demanded, as in the acute infectious diseases. Adrenalin must be given subcutaneously or intravenously, as its vasomotor action is absent when given by mouth. The dosage is 10 to 15 minims of the 1 to 1,000 solution.

Caffein.—As a vasoconstrictor in the acute infections, caffeine holds the first place. Passler demonstrated in animals, when heart failure had been induced by acute

9. Ztschr. f. klin. Med., 1905, lvi, 128.

10. Therap. d. Gegenw., 1905, xlv, 398.

11. Deutsch. Med. Wchnschr., 1905, xxxi, 105.

12. Verhandl. d. Cong. f. inn. Med., 1906, xxiii, 257.

13. Deutsch. Arch. f. klin. Med., 1899, lxi, 652.

infection, that caffeine caused a more pronounced and prolonged rise in pressure than digitalis. The rise in pressure was maintained about one and one-half hours. Caffeine is best given subcutaneously in two to three grain doses, repeated every three to four hours.

Camphor.—Camphor, with practically the same action, is less constant in its effects, probably due to its lessened solubility. Its dosage is the same as of caffeine.

Strychnin.—Strychnin has been very extensively used in America as a heart tonic. Its effect on the heart, however, consists entirely of a stimulation of the inhibitory center, leading to slight slowing of the pulse; and even this action is inconstant. The rise in blood pressure observed after its administration is due to stimulation of the vasomotor center, and in animals is only apparent when given in quantities approaching very closely that required to produce general spasm. Crile¹⁴ has shown that the same is true in man, the effect on pressure being very inconstant and apparent only when given in doses sufficient to cause increased nerve excitability as shown by increased reflexes and muscular tone. Cook and Briggs¹⁵ have demonstrated that subcutaneous injections of one-tenth of a grain is necessary to increase pressure. In the doses ordinarily recommended strychnin can not be considered a vasomotor drug. It is only when the dose approximates the toxic one that blood pressure is increased, and, for this reason, it is less valuable than caffeine.

The vasodilator remedies occupy a rather uncertain position in cardiovascular therapy, although they are extensively used. With our present knowledge, nitrites and nitroglycerin in physiologic doses are absolutely contraindicated in the heart failure of acute infections. We are dealing here with a vasomotor paresis and a vasodilator would only augment the difficulty.

Alcohol.—The value of alcohol as a cardiac stimulant has long been much disputed. We have been told by the pharmacologist that it has a depressing action on the cardiovascular system, dilatation occurring with fall of pressure. Many clinicians, on the other hand, have maintained that it is a valuable remedy in shock and in the heart failure of acute infections; this divergence of views may be explained if we accept Dixon's¹⁶ recent work on the effect of alcohol. He found that in moderate doses, well diluted, it has little effect on the rate of the normal heart. In animals showing circulatory disturbances, the heart is accelerated, the output increased and the blood pressure raised. Moderate amounts given by mouth produce a dilatation of the peripheral vessels, with constriction of the splanchnics. These experimental results are in accord with clinical experience, and, if confirmed, would secure for alcohol a place in the treatment of shock and those conditions in which we have engorgement of the splanchnics with insufficient filling of the peripheral vessels.

THE VASODILATORS IN HYPERTENSION.

Most frequently the vasodilators are employed to reduce high arterial tension. Two phases of the subject must be considered: first, whether it is advisable to reduce high arterial pressure; second, whether the vasodilators can be relied on to bring this about.

We are, perhaps, too prone to consider hypertension a pathologic condition that must be relieved. There is abundant evidence that general arteriosclerosis does not,

as a rule, lead to hypertension, unless, as Hasenfeld¹⁷ and Hirsch¹⁸ have shown, there is involvement of the thoracic aorta or splanchnic vessels. Nephritis is the most frequent cause of very high blood pressure. Many are inclined to believe that in these cases the high pressure is a protective measure, an effort to increase kidney elimination, and the important question to decide in this group of cases is whether lowering pressure modifies elimination through the kidney. Up to the present time investigations on this point have given conflicting results.

Rosbach¹⁹ experimented on patients with interstitial nephritis, administering one-sixtieth grain of nitroglycerin every three hours, and found increased secretion of urine. Kinnicutt²⁰ and Bourginski²¹ have also reported increased urine in nephritis after nitroglycerin. Leech²² says that neither in animals nor man can it be shown that the nitrites influence the urinary secretion, except in large doses, when the urine is always lessened. He confined his experiments to patients without kidney trouble. Twelve such were given three grains of sodium nitrite three times a day for a period of one week. Seven passed slightly more urine, five less. He also determined the amount of urea and found it unchanged. The most recent and, I think we may say, the most careful work on this subject has been reported by Loeb²³ in Krehl's clinic. Three nephritics were given sufficient nitroglycerin to reduce the pressure 35 to 55 mm. The amount of urine and its freezing point and sodium chlorid content was determined. Loeb found in each case lessened secretion of urine and solids. Straus has also found reduced elimination in nephritis after nitroglycerin.

We are unable to form any definite conclusions from such conflicting results. More careful work on the subject is needed, the patients to be kept under rigid observation as regards diet, liquids ingested and elimination of fluids through skin and bowel. Only by this means can be determined the important question of whether reduction of hypertension modifies renal elimination. Meanwhile, we may safely employ vasodilators in cases of extreme hypertension (over 200 mm. of mercury), as here the danger to both heart and blood vessel must be apparent; also in patients with hypertension who have headaches which are relieved by lowering pressure. Small doses should always be tried, first one one-hundredth grain of nitroglycerin or two grains of sodium nitrite, as Leech has shown almost as marked and prolonged effect is obtained from small amounts. Both remedies act very promptly after administration, the duration of effect from one-half to three hours; the effect of the nitrite being somewhat more prolonged than the nitroglycerin.

When we consider the second phase of this subject, viz., whether hypertension can actually be lessened by the nitrite group, we meet with more conflicting results. These are to be explained in part by the varying activity of the preparation on the market and in part by idiosyncrasies of the individual. S. A. Matthews and I have found that preparations of the alcoholic solution of nitroglycerin and freshly prepared solutions of sodium nitrite, purchased from reliable pharmacists, may be

17. Deutsch. Arch. f. klin. Med., 1897, lix, 193.

18. Deutsch. Arch. f. klin. Med. 1900, lxxix, 503.

19. Berlin. klin. Wehnschr., 1885, xxii, 83.

20. New York Med. Jour., 1886, xliii, 219.

21. Lancet, London, 1885, ii, 733.

22. Brit. Med. Jour., 1893, ii, 6.

23. Deutsch. Arch. f. klin. Med., 1905, lxxv, 577.

14. Blood Pressure in Surgery, p. 265.

15. Johns Hopkins Hosp. Rep., 1903, xl, 419.

16. Jour. Physiol., London, 1906-07, xxxv, 346.

totally inert, even when injected intravenously into animals.

It is well known that nitroglycerin in tablet form is very unreliable. Brinz was unable to detect any nitroglycerin in many of these. Not all individuals react in the same way to an active preparation. Hewlett²⁴ has shown that a rise in pressure, after administering nitroglycerin to man, is almost as frequent as a fall. These same varying results can be demonstrated in animals, as the tracings (Figs. 1 and 2) show.

It is not improbable that many of the failures to lessen pressure with nitroglycerin and the nitrites have been due to the use of inactive preparations. Furthermore, there are some individuals who are able to take very large doses of nitroglycerin with very little effect. Hewlett reports fifteen to thirty drops of the 1 per cent. alcoholic solution with very little, if any, effect. Stewart²⁵ refers to an instance in which he gave a patient fifty minims of a 10 per cent. solution—equivalent to five grains of pure nitroglycerin—without any great change in pressure. On the other hand, Loeb reports severe collapse after one one-hundred-and-twentieth of a grain. We are unable to explain this diversity of action.

Fig. 1.—Tracing showing usual effect of nitroglycerin on a dog; 3 mg. given intravenously.

Fig. 2.—Tracing showing how nitroglycerin may at times cause a rise in pressure. Dog received 3 mg. on the tongue. The second X shows where alcohol was placed on the tongue in order to prove that the rise was not due to the alcohol in the solution of nitroglycerin.

Mac Nider²⁶ has shown that a rise in pressure occurs chiefly in old dogs, and that the fall is much more marked in young animals. This probably also holds true in man, as the arteriosclerotic vessel does not respond to stimuli as does the normal. Romberg²⁷ has demonstrated this disturbance of vasomotor action in patients with vascular changes. He found that the vessels in the arm failed to react to heat, cold, or to the increased demand of the extremity for more blood during muscular activity.

TREATMENT OF ANGINA PECTORIS.

Before leaving the subject of vasodilators, it may be advisable to consider the treatment of angina pectoris. Authorities are agreed that anginal attacks are usually due to disturbance in the blood supply of the heart muscle. Autopsy findings in patients who have suffered from angina show arteriosclerosis of the coronary vessels and numerous areas of focal necrosis in the heart

muscle. A very few cases have been reported with normal coronaries, and here the attacks have been ascribed to vasomotor spasm of the coronary vessels.

Since Brunton's recommendation of amyl nitrite and nitroglycerin for the treatment of an attack, those remedies have been generally used. Brunton's observations were based on a single case in which sphygmographic tracings showed a marked *pulsus tardus* during the attack, the pain disappearing and the character of the pulse changing after amyl nitrite. A review of the cases in which pulse observations have been made during an attack shows that Brunton's patient in this respect was exceptional.²⁸ In the majority of patients little change has been observed in the tension of the pulse during an attack, and this conforms to what occurs in animals after ligation of a coronary artery. Clinical experience has shown that a rather small percentage of cases receive prompt relief with amyl nitrite or nitroglycerin—probably only those cases in which vascular spasm plays a rôle. In the group of cases in which the attack is due to obstruction by embolus or thrombus, two therapeutic problems arise: Shall we try to raise blood pressure and thus force blood through the anastomosing²⁹ vessels to the anemic area, lessening the

amount of infraction, and by doing this throwing increased work on a weakened ventricle, or shall we attempt to lower pressure, relieving the heart work, meanwhile increasing possibly the area in which necrosis may occur?

This problem has received our attention during the past year. When the coronary arteries of a dog are ligated just sufficiently to cause slightly disturbed heart action, the use of adrenalin, while causing a momentary rise in pressure, is followed by dilatation of the left ventricle and death. If we use digitalis instead of adrenalin, the contraction of the ventricle becomes more complete and a return to normal occurs, and then additional branches may be ligated without material disturbance. If nitroglycerin be used in place of the adrenalin or digitalis, there is no improvement in the heart's action, death occurring as in the untreated animals. In other words, a heart under the influence of digitalis allows of much more extensive ligation of the coronary vessels

24. Jour. Med. Research, Boston, 1906, xv, 383.

25. THE JOURNAL A. M. A., 1905, xlv, 1676.

26. Am. Jour. Med. Sc., 1908, cxxv, 99.

27. Verhandl. d. Cong. f. inn. Med., 1904, xxi, 60.

28. Fraenkel: Verhandl. d. Cong. f. inn. Med., 1891, x, 274.

29. Spalteholz and Hirsch: Deutsch. Med. Wehnschr., 1907, xxxiii, 730.

without serious consequences than a heart under the influence of vasodilators. A more complete report on this work is to be published later.

These results are suggestive at least of the fact that the digitalis group may be indicated in attacks of angina pectoris. In order to obtain the promptness of action required in these cases, the drug must be given intravenously or subcutaneously.

TREATMENT OF ARTERIOSCLEROSIS.

In the medicinal treatment of arteriosclerosis, only one drug has any claims to efficiency. Clinicians quite uniformly believe that alleviation of symptoms, due to arteriosclerosis, follow prolonged use of the iodids. Various symptoms, as angina pectoris, dyspnea and vertigo become less marked after the continued use of 5 to 10 grains of sodium iodid three times a day. Huchard believed that its good effects were due to its vasodilator action. It has been shown, however, by Boehm and Berg³⁰ and Stockman and Chartens³¹ that iodid does not lower blood pressure. There is no evidence that it has a specific effect on the arterial changes, except possibly those of syphilitic origin. The beneficial effects have been ascribed to its power of lessening the viscosity of the blood. Ottfried Müller³² has shown when a patient had received a total of about two hundred grains in daily doses of twenty grains, decidedly lessened viscosity of the blood could be observed. As long as the iodids were continued this lessened viscosity was evident. As a result of this increased fluidity of the blood, less work is required by the heart in forcing it through the narrowed vessels. Determann,³³ an experienced worker in this field, has been unable to confirm Müller's findings, thus leaving the question still unsettled.

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THE DEVELOPMENT OF THE INFANTILE STOMACH.*

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In caring for an infant we should ever keep in mind the desired ultimate result, viz., the development of a perfect adult with a normal adult stomach. The kind of a stomach possessed by an adult of 25 years depends considerably on how he was fed during the first two years of his life. The stomach at birth is little more than a straight tube continuous with the esophagus above and the duodenum below, and hangs nearly vertical in the abdomen. It is elastic and easily distended, and is in contact with, and more or less pressed on by, the other abdominal viscera and the diaphragm. There is a slight fulness on one side, showing where the greater curvature and the fundus will be, and if it is distended it assumes a shape approaching that of the adult stomach. We do not know accurately its capacity. The means that have been used to measure the infantile stomach are faulty.

The plan of weighing the infant before and after nursing has these objections, viz., (1) we are never sure the stomach is entirely empty when the infant starts to

nurse; (2) we do not know how full it is when he stops; (3) at the first weighing there may be gas, lighter than air, in the stomach or intestine which is expelled during the nursing; (4) gas lighter than air may be formed in the stomach before the second weighing; (5) some of the breast-milk may escape on the infant's clothing, or into the intestine, and (6) we are never sure that it is a normal stomach. The plan of removing the stomach and filling it with liquid is probably still more inexact. The stomach is in an unnatural position; it is not under the natural pressure of the surrounding organs and the abdominal wall, in a closed cavity; it is easily distended, and we do not know how much to distend it; it may be altered by the disease that killed the baby.

I wish to suggest the following plan as overcoming some of these objections—a plan that I have not had an opportunity to put into practice. Let the subject be a baby that has died very suddenly, from accident or otherwise; make as small an incision in the abdominal wall as will do; ascertain that the stomach is empty; ligate both ends of the stomach with as little disturbance of the organ as possible; then through a small slit fill the stomach with modified milk, at a temperature of 100 F., using a spoon to avoid hydrostatic pressure. This should be done as soon after death as possible.

It is not necessary, however, to know the exact capacity of the infantile stomach as a guide to proper feeding. The fact that we do know that capacity approximately has led to what I believe to be grave errors in infant feeding, especially where the infant is given artificial food. This knowledge, together with the approximate knowledge of how long it takes the infant stomach to digest food, has led to the giving of a certain fixed quantity of food at certain regular intervals, which I believe to be wrong.

The problem is, how to develop this simple tube into the complex organ that it should be in later life. The adult stomach is essentially a muscle lined with a secreting membrane, and covered with a serous membrane. It is, or should be, highly elastic, and have strong powers of contraction. These functions are far more apt to be impaired than its secreting functions. One of our main objects, therefore, in feeding an infant should be to develop a stomach with good contracting powers and a strong muscle. We all know that the best way to make a muscle grow strong is to use it. If a muscle never does any work it soon loses the power to work.

What happens under the plan of so-called "scientific" feeding, i.e., the giving of a certain fixed quantity of food at certain regular intervals? In the first place, the stomach is never distended with food, and in consequence the muscle is never adequately stretched: i.e., properly exercised. Second, when the regular feeding time comes again there may be, and often is, some of the last feeding still in the stomach. This residual food is often in a state of mild fermentation. When the new food is added to it the fermentation is increased, giving rise to symptoms of indigestion, sometimes to diarrhea. Third, the regular feeding time often comes at a moment when the infant should not be disturbed; he may be asleep, or enjoying a quiet hour in the open air, and is better left alone. Fourth, frequent feeding, with continuous stimulation, or a "teasing" of the stomach, results in an atonic condition, and dilatation of the stomach. A nerve or a muscle, when asked too frequently to functionate, loses the power to respond to a

30. Arch. f. exper. Path. u. Pharmacol., v.

31. Brit. Med. Jour., 1901, 1520.

32. Müller and Inada: Deutsch. med. Wehnschr., 1904, xxx, 1751.

33. Deutsch. med. Wehnschr., 1908, xxxiv, 871.

* Read in the Section on Diseases of Children of the American Medical Association, at the Fifty-ninth Annual Session, held at Chicago, June, 1908