Calcium Therapy in Diseases of the Cardiovascular System

by Edward Podolsky, M.D.

(Reprinted from the Illinois Medical Journal, August 1939)

About fifty years ago Ringer demonstrated experimentally in a striking way that sodium, calcium and potassium were essential for the contraction of the heart muscle. He found that when the concentration of potassium was increased in the solution in which the heart was immersed the contractions decreased, and if the concentration was further increased the contractions became weaker and weaker, the heart finally stopping in diastole and failing to respond to any further electrical stimulation. On the other hand if calcium was added to the solution, the response to stimulation reappeared and spontaneous contractions became stronger, the intervals between them lengthened and the heart finally stopped in a state of tonic contraction, a systolic standstill termed calcium rigor.

According to Barath, the first response to an intravenous injection of calcium is a well marked vagus stimulation with considerable slackening of the heart beat (the drop is from twelve to twenty-five, but sometimes as high as forty beats per minute) followed by a secondary weaker sympathetic stimulation. To the initial vagus stimulation must be attributed the results obtained by Wolffe and Bellet in paroxysmal tachycardia. In this condition, which is not only disagreeable to the patient, but may lead to very serious consequences, calcium by the intravenous route has proved a valuable remedy. Bellet reported a series of five cases in which results were very satisfactory. The tachycardia was controlled with dramatic effectiveness, both to the patient's delight and the doctor's surprise. Petsektakis several years previously had found that calcium in arrhythmia revealed the anxiety, the dyspnea and palpitation while it regularized the rhythm. He also found that the strength of systole was increased, the arterial blood pressure raised, and the rate slowed at the same time.

Heubner found that calcium increased the excitability of the heart, the action being on the ganglia in the ventricles. Stoppage in systole was the ultimate end when doses were increased. Pick expressed the belief that calcium and potassium salts acted equally on all parts of the heart. Billigheimer found that calcium exerted on the heart a vagus stimulation which apparently did not exist when a tropine had been given.

Mancke showed that high calcium concentrations produced vasodilation and increased the coronary circulation. This was confirmed by Hochrein. He also found that the calcium produced promoted heart circulation without causing additional strain on the heart by increased aortic pressure as occasioned by adrenalin, barium choride and lobelin. Turan confirmed the experiences of others with calcium as an agent which reduced the pulse in tachycardia (by 25 to 50 pulsations a minute).

The digitalis-like action of calcium has been noted by many investigators. Cheinisse was among the first to call attention to this fact. Lieberrman in his experimental work with calcium gluconate on dogs noted that arrhythmia, coupling of beats and symptoms of heart block and other digitalis-like effects quite often took place. These were after experimental doses, comparatively much higher than the doses that would be used in man to, and, with the use of the latter, the clinical effect is a synergistic action without toxic effects.

Singer obtained favorable results from a combined calcium and digitalis therapy in severe cases of decompensation and chronic cardiovascular diseases. Billigheimer confirmed these results. He also studied the effect of the lengthening of the pulse curve after the administration of digitalis and squill. He linked the action of digitalis with the calcium content of the tissues. In tetany where there is a hypocalcemia, tolerance to

digitalis is low. In encephalitis where there is a hypercalcemia, it is high. This is explained by the action of calcium on cell permeability which allows the tissues and the heart muscle to take only small amounts of digitalis. Fisher who studied the mechanism of the digitalis-like action of calcium further found there was a difference between the action of digitalis and calcium. There is a unilateral synergism in that when digitalis is first given the heart is sensitized to calcium, while when calcium is first given, even in large doses, the heart is not made more sensitive to digitalis. Singer is a very strong advocate of the conjoint use of digitalis and calcium in orthopnea with the threatening symptom of stasis, cardiac dropsy, myocardial weakness and the cardiorenal syndrome. In chronic myocarditis he advises the use of digitalis and calcium in weekly alternance. Calcium, according to his experience, increases and quickens the effect of digitalis on the heart, but continued over a long period of time it lessens the effects of digitalis on the parasympathetic nervous system. Singer considers calcium the "whip and bridle of digitalis."

The relationship between calcium and strophanthus has also been noted. Loew found increase in systolic strength when calcium and strophanthus were given together. In the presence of calcium the contraction strengthening influence of strophanthus is very pronounced. Loew thinks that strophanthus sensitizes the heart to calcium, and the basis of this observation states that the lack of influence of strophanthus is some cases of decompensation is conditioned weakened reaction ability of the myocardium to the physiological content of the blood. This weakened reaction ability is also the cause of decompensation. There is evidently a synergistic union between the calcium and the strophanthus which brings about the desired results.

Zondek found that calcium had an interesting effect in counteracting the paralyzing influence of chloral hydrate on the heart. He found that chloral hydrate not only influenced the cardiac muscle but also the cardiac ganglia and was let by this fact to study the action of calcium on these ganglia. Later he found that the action of calcium was similar to that of strophanthus but much quicker.

Vermel contributed some very interesting observations on the therapeutic effects of calcium salts in chronic cardiac affections, especially in those presenting more or less myocardial weakness. He used a method of intracutaneous injection which he believes preferable to all other modes of administration. His patients were suffering from myocarditis and subacute or chronic endocarditis with myocardial insufficiency, rapid pulse, dyspnea, cardiac dilation, enlargement of the liver, etc. After ten to 15 treatments with calcium all the symptoms of decompensation usually disappeared as well as dyspnea and unpleasant sensations in the region of the heart. The pulse became fuller and stronger. The heart sounds become more pronounced and the size of the liver decreased.

Calcium exerts a remarkable influence on the patients with congestive heart failure according to Steward. In a series of six cases he observed an increase in the output of urine following oral administration of calcium. The heart rhythm and contractions were also improved. Engelin found that calcium proved of benefit in all forms of circulatory weakness, manifesting itself by general fatigue and high excitability of the heart, all of which is more or less connected with vasomotor hyperirritability.

Klotz ascertained that in circulatory asthenia there was a disturbing of the potassium-calcium ratio, with acidosis, which was speedily corrected under calcium medication in conjunction with ultra-violet rays and increased vitamin intake. Korbusch saw a marked stimulation by calcium of the depressed heart in grippe and pneumonia. Kaffler and Kasper noted the same phenomenon in diphtheria where they used calcium to ward off impending circulatory weakness. Rosenow used high doses of calcium gluconate by mouth in pericarditis with good results.

Among the first to record his observations on the effect of calcium on hypertension was Addison who published results obtained in a series of 13 cases of arterial hypertension before and after the administration of large doses of calcium chloride. In the case of seven of these patients the blood pressure had been under observation for several months before the calcium chloride was given. In the other six patients it was ascertained a short time before the treatment began. In five cases albumin was previously present, and in four cases it disappeared after the calcium chloride. In three cases there was low specific gravity of the urine and comparative calcium decrease. As the kidney function

improved the calcium decreases also increased. The daily doses of calcium chloride amounted to 180 grains in three cases and to 57 grains in one case and to 75 grains in another. In all cases the administration of calcium chloride was followed by a diminution of the blood pressure, systolic and diastolic, and usually the diminution was appreciable.

One year later, Addison and Clair reported a series of 45 patients whom they had been treating with calcium salts, the daily dose ranging from 90 to 180 grains, with blood pressure readings being taken weekly. Of the 45 patients thus treated 26 reacted well, with diminution in blood pressure and improvement in symptoms. A peculiar thing which they observed and which they did attempt to explain was that better results were obtained with calcium therapy in treatments of hypertension during the summer than winter months.

In 1927, Althow and O'Hare treated a series of eleven cases of hypertension with calcium chloride one gram and atropine 0.00025 gram four times a day for from three to four weeks. In six of the cases it had no effect on blood pressure. In the other it did exert an effect. Parathyroid extract was used in three cases with no apparent effect. Althow and O'Hare were not much impressed with calcium as a hypotensive.

Among the latest to study the role of calcium therapy in hypertension was Davis whose series consisted of 55 patients. He found that hypertension like fever may be intermittent, remittent, continuous or pernicious. Davis treated his patients with calcium lactate, eight grains in water, half an hour before meals, in addition to a low salt diet, low maintenance diet, with most the protein from milk, moderate in total amount but adequate in all respects. This regime caused considerable improvement in his patients with hypertension.

The first attempts at an experimental investigation of the way calcium acts on blood pressure were undertaken in 1920 by Krause. He found that there was a variable response of blood pressure to intravenous injections of calcium in warm-blooded animals such as rabbits and guinea pigs. The fall was more or less rapid depending on the rate or amount of the inflow and was strongest and fastest when the heart developed a tendency to stop in systole. Occasionally a slight increase in blood pressure was obtained when the calcium was injected into the blood stream; but the pressor action of calcium is of short duration. It generally begins immediately after the injection and lasts from ten to 20 minutes.

Among the latest and most interesting theories of high blood pressure is that offered by Stephens. He defines blood pressure as that pressure which is exerted on the blood by the tissues, especially on the contractile arteries. The great the pressure of the blood and it corpuscles, the handicapped are the movements of the corpuscles.

When a change is effected on the surface tension of the corpuscles, there is a modification of their internal metabolism as a whole. It is now accepted that sixty per cent of the body weight, excluding water, is composed of calcium. For that reason sixty per cent of the body is therefore metabolism of, and connected with, the calcium salts and their assortment in organic compounds and suitable ions. Increased blood basic pressure then is closely associated with calcium metabolism.

Kylin found that there was a shifting of the potassium-calcium quotient in favor of potassium in essential hypertension and was able, by calcium injections, to make good the calcium depletion and thereby lower the hypertension.

Other investigators also are of the opinion that calcium is most logically indicated in essential hypertension. They base their arguments on one or both of two premises: 1. Calcium is antagonistic towards guanidine. Guanidine is believed to be a very important factor in the pathogenesis of increased arterial tension, and the neutralization of this toxic substance by calcium paves the way for a removal of the tension. 2. Calcium has been know for quite a while to have a depressing effect upon sympathetic tonus and is believed by many clinicians to be heightened in essential hypertension. Therefore, the administration of calcium which decreases the abnormal sympathetic tonus also depresses the hypertension.