Thus *recognizable* pressor effects have been eliminated as a complicating factor. We have not, however, up to the present, eliminated the possibility of other pressor or depressor substances having a speed of action and disappearance comparable to that of calcium ions. On the other hand, we have encountered no instances suggesting the presence of such substances.

Using the method as described the calcium ion concentration in certain biological fluids has been estimated. (Table 1).

TABLE I.
Estimations of Ca^{++} Concentration in Biological Fluids.

Fluid	Source	Diagnosis	Total Ca mM/L	Ca^{++} mM/L
C.S.F.	Human	Epilepsy	1.37	1.15
Serum	"	Normal	—	1.0
C.S.F.	"	No diagnosis	1.24	1.0
C.S.F.	Dog	Tetany	1.04	0.95
Serum	"	Normal	2.36	0.9
Chest	Human	Heart failure	2.11	0.8
Ascitic*	"	Pick's disease	3.00	1.05

*High protein content.

The concentration of calcium ions in the fluids studied was approximately 1.0 millimol per liter. From this, the non-ionized, diffusible calcium is estimated at not more than 0.25 millimol per liter in cerebrospinal fluid and, after allowance is made for the calcium bound by protein, not more than 0.5 millimol per liter in serum.

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Electrical and Mechanical Changes in Isolated Heart Following Changes in Calcium Content of Perfusing Fluid.

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The experiments here reported were performed on the isolated heart of the rabbit perfused at 38°C. by the method described by Locke, but without recirculation of fluids. Changes in amplitude of contraction were recorded on a drum, and electrical changes were recorded with a string galvanometer from one circuit only, the connections being made through non-polarizable electrodes to the aorta and to the apex.

Because of the known unphysiological nature of Locke's solution the solutions used for perfusion were based upon those described by van Dyke and Hastings, with the addition, in many instances, of sodium citrate and a higher total calcium concentration. In these solutions the calcium ion concentration has been calculated from the dissociation constant of calcium citrate as simultaneously reported. The solution used as the standard of reference usually contained 0.7 millimol of calcium ions per liter, and 0.8 millimol per liter of non-ionized calcium in the form of calcium citrate.

In solutions without citrate the amplitude of contraction of the heart varied directly with the amount of calcium in solution up to concentrations which produced irreversible changes. Omission of calcium from the perfusing fluid was followed by almost total cessation of contraction. Electrical impulses continued, as has been reported by others, although considerably modified, and recovery from these solutions was rapid. When, however, a small amount of citrate was added to the solutions containing no calcium all mechanical and electrical activity ceased and the heart did not recover in physiological solutions. Our interpretation in this case is that calcium ions are necessary for the continuation of electrical as well as mechanical activity, and that unless citrate is added to the perfusing fluid, sufficient calcium remains in the heart for electrical activity to continue.

With other conditions constant, a moderate reduction of Ca^{++} was followed by a prolongation of electrical systole, and usually by a reduction in the height of the T-wave. On the other hand, increase in Ca^{++} was followed by shortening of electrical systole, with no consistent change in the T-wave. A striking feature of all our observations, except under extreme conditions, was the disproportion between mechanical and electrical changes, the former being more marked. This is in contrast to the effects of potassium, which produces electrical changes disproportionately greater than mechanical changes.