Physiology. — *"Emanation and Calcium"*. By H. ZWAARDEMAKER, T. P. FEENSTRA and M. E. J. M. STEYNS.

(Communicated at the meeting of March 29, 1924).

The well-known relationship which must exist in physiological systems between potassium and calcium induced the authors to examine whether such a relationship could also be discovered between emanation, the most ideal potassium-substitute [1]), and calcium. A few preparatory examinations had already shown that the ordinary formula K/Ca could certainly not be applied here without alteration.[2])

When one of us (S) had invented a contrivance by means of which it was possible to keep an emanation solution shut off from the air, and yet to use it as a perfusing fluid with only a scarcely noticeable change in hydrostatic pressure, the last obstacle was removed to a more systematic research. This contrivance consists of a small Mariotte bottle filled to the brim, the tube for the airsupply being covered with a limp rubber bag (condome). When the fluid escapes from the lower opening the bottle can fill itself with air from above; which however remains entirely separated from the fluid.

The experiments were done with spontaneously pulsating hearts of frogs and lampreys (Petromyzon fluviatilis). In the first a Kronecker cannula was introduced into the ventricle, in the second a simple glass tube was placed in the inferior vena cava, via the hepatic vein. In the first case therefore only the ventricle was perfused, in the second the whole heart. Registration was effected by suspending the ventricle, respectively ventricle and atrium.

The general course adopted was the following: First the organ pulsated during a quarter of an hour with a suitable potassium-Ringer solution. If the circumstances made it desirable, the Ca-ion also was partially or wholly removed from the fluid which was intended to produce a standstill. And lastly when it stood still, the organ was perfused with the fluid we wished to examine.

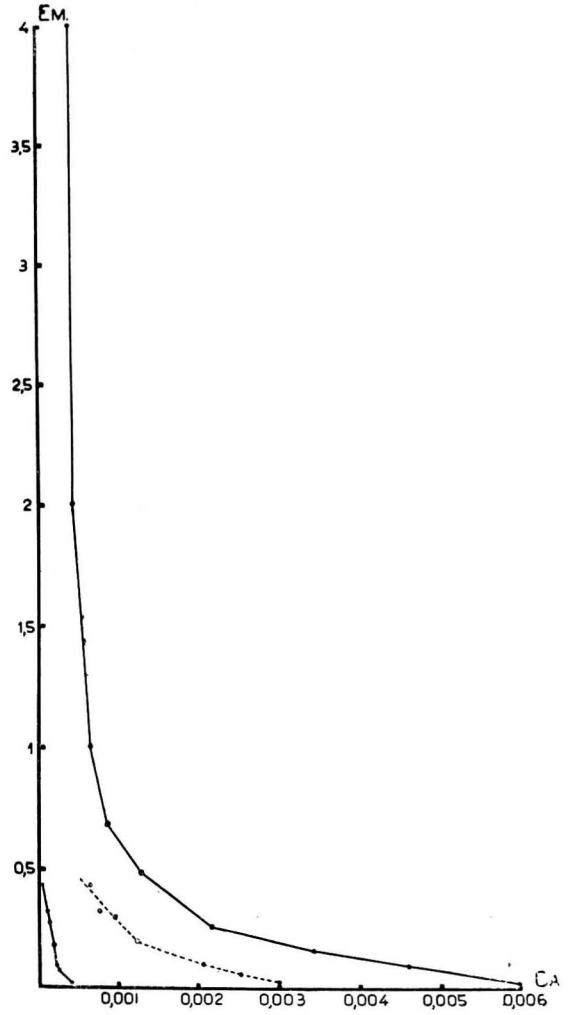
The first series of experiments determined the smallest quantity

[1]) H. ZWAARDEMAKER, Verslag Kon. Akad. v. Wetensch. Amsterdam, Deel XXVI (1917), p. 776; these Proc. Vol. XX, p. 773.

[2]) H. ZWAARDEMAKER et T. P. FEENSTRA, C. R. Soc. de Biol. T. 84, p. 377, 1921.

of calcium ion and the smallest quantity of emanation, which, buffered with bicarbonate of sodium, (100 mgr. p. L.) and mixed with a solution of sodium chloride (6.5 gr. p. L.) just admitted of a regular pulsation.

A second series of experiments determined the largest quantity of calcium ions and the greatest quantity of emanation, which,



buffered with bicarbonate of sodium (200 mgr. p. L.) and added to a sodium chloride solution (6.5 gr. p. L.) just admits of or prevents a regular pulsation.

As a starting point for the addition of calcium chloride we used a concentrated aqueous solution with a specific weight of 1.2294 and containing 25 % dry $CaCl_2$ (according to the tables of LANDOLT and BÖRNSTEIN 4th edit. p. 470).

As a starting-point for the addition of emanation we used 1 microcurie, which we acquired by leaving a solution of radium (1 to a million) in bottles of 100 cm³. to itself during a month, after which the emanation was distilled off into a vacuum. The emanation gas obtained in this manner was then added to the physiological sodium chloride solution to be used in the various experiments.

In the foregoing graph we have summarized the results obtained. On the axis of the abscissae the different quantities of calcium in gram molecules per L. have been noted, on the axis of the ordinates the quantities of emanation in microcuries p. L. Perhaps the last-named figures are slightly too high, as a certain loss of emanation ensues from a small dead space in the outlet tube of the emanation bottle.

The highest line is the line of maximum quantities. Above this line the heart stands still, and below it it pulsates. The lowest line is the line of minimum quantities. Below the line the heart stands still and above it it pulsates. In cases responding to points above the maximum line no electrocardiogram was visible; below the minimum line only when sufficient emanation was present, f.i. 1/100 microcuries p. Litre.

The zone between these two curves is the zone of regularly pulsating hearts. Such an automatism can be maintained for any length of time if only care is taken to fix up a new Mariotte bottle when the old one has been emptied.

It is of course possible to discover the horizontal centres of these two lines. These points answer to the following.

Emanation in curies	Calcium in gramme molecules	Em. × Ca.
0.5×10^{-7}	5×10^{-3}	2.5×10^{-10}
0.8×10^{-7}	3.6×10^{-3}	2.9×10^{-10}
1×10^{-7}	2×10^{-3}	2.0×10^{-10}
1.5×10^{-7}	1.5×10^{-3}	2.25×10^{-10}
2×10^{-7}	1.3×10^{-3}	2.6×10^{-10}
3×10^{-7}	0.82×10^{-3}	2.46×10^{-10}
4×10^{-7}	0.75×10^{-3}	3.0×10^{-10}

As may readily be seen a line drawn through the above-mentioned points, (see dotted line), satisfies the equation:

$$\text{Em} \times \text{Ca} = \pm \text{ constant.}$$

We have not dared to presume upon the biological significance of this relationship. One of us (F) formerly found: $\frac{K}{Ca} = \pm 2$ (K and Ca in gram molecules) using the same object to experiment upon; we now found: $Em \times Ca = 2.5 \times 10^{-10}$ (averaged), Em in curies, Ca in gram molecules.

Both formules point to a relationship between the radioactive element and calcium. A closer examination of the first relationship has proved that it is an exceptional case of a general balance of ions, which always finds expression in a quotient. Such a quotient is supposed by some authors to mean an antagonism; SPIRO[1]) has, however shown that one should speak of pseudo-antagonism, as the quotient only expresses that numerator and denominator weaken, but by no means neutralize one another.

In the case before us we are dealing with neither antagonism nor pseudo-antagonism, for in the product $Em \times Ca$ both factors support one another. A closer examination shows that both factors have a limit, which lies at approximately $^1/_{100}$ microcuries per Litre for emanation, and at a few milligram per L. for Ca, and in the latter case the electrocardiogram remains visible if only sufficient microcuries are present. Calcium can, therefore be dispensed with, not emanation. In other words, calcium is not an emanation substitute, but an emanation-intensifier.

We have not yet been able to discover a physical cause for the intensifying influence of Ca on emanation for the automatisms we examined. Emanation is a pure alpha radiator and a heart pulsating on emanation entirely possesses the character of an organ in alpha automatism, with respect to paradoxes and radiophysiological equilibria. The intensifying influence which Ca exerts must, therefore, be an influence on the alpha radiators, unless one may accept that the presence of Ca aids the adsorption of emanation. For emanation is highly absorbed not only by charcoal[2]) but also by animal tissues. As soon as occasion offers we will try to discover whether Ca exercises any influence on this adsorption. If this were the case it would offer an explanation, for it is not the emanation atoms in the centre of the perfusing fluid which are of biological significance. It is the atoms adsorbed by the cells which revive the automatism which was forfeited by removing the radioactive element. In order

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[1]) K. SPIRO, Baseler Antrittsvorl. 1921, and Schweiz. med. Wochenschr. 1921, N°. 20.

[2]) Mixtures are of great importance. Cocoa-nut absorbs best, compare ST. MEYER v. SCHWEIDLER, Radioaktivität 1916, p. 329.

to obtain a similar result by radiation from without the bombardment of alphaparticles must of necessity be a million times stronger.

Some time ago one of us (Z) examined this, together with GRIJNS [1]), in experiments in which a pulsating heart was brought to a standstill by removing the potassium after which the regular pulsations were revived by radiation with polonium, applied externally.

The experiments took place in completely quiet surroundings (camera silenta of the laboratory) so that no jerks or shocks could reach the heart. Nevertheless the hearts revived spontaneously, while the perfusion with potassium-free Ringer continued. This research was repeated a short time ago by VOORSTAD [2]) on a more systematic and extensive scale, with the same results. The number of particles emitted in these experiments is almost infinitely large, as appears from the strong scintillating effect which polonium produces; only a few of these, however, penetrate to the depths as their penetrating power is fairly limited. As far as we could discover the Ca present in the fluid had neither a stimulating nor an inhibitory influence. In the case we speak of in this communication we substituted the microradioactivity of a perfusing fluid for the macroradioactivity of the external radiation.

We are of opinion that the fact that the lost automatism can, all the same, be revived with the same certainty, must be ascribed: 1° to the large area of the walls of the lacunes in the muscles, 2° to the greatly increased concentration, which it attained by the adsorption on the limiting membrane between cells and perfusing fluid, 3° the almost entire lack of distance between the source of radiation and the seat of automatism.

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[1]) ZWAARDEMAKER en GRYNS, Arch. néerl. t. 2, p. 500, 1918. Comp. also Verslag Kon. Akad. v. Wetensch. Amsterdam Dl. XXVIII (1919), p. 370; these Proc. Vol. XXII, p. 383.

[2]) J. N. VOORSTAD. Diss. Utrecht 1923.