Physiology. — "*On the Transitory Arrest of the Heart's Action*". By Prof. H. ZWAARDEMAKER and W. WITANOWSKI. (Communicated by Prof. H. ZWAARDEMAKER).

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When the conditions under which the heart functionates are of a sudden considerably altered, it often happens that the organ ceases to beat for some time and resumes its pulsations a few moments later. One receives an impression that the heart wants to accommodate itself before getting used to the new condition.

These transitory conditions have often been studied before, also with the isolated heart. NOYONS and LIBBRECHT [1]) were confronted with them during sudden changes of temperature; during a sudden change of pressure every researcher must have observed them; during a sudden change of osmotic pressure and of concentration of hydrogen-ions ODINOT [2]) noted them; during sudden changes of potassium-concentration in the circulating fluid they are quite common. (NOYONS, LIBBRECHT, BUSQUET) [3]).

Lately we could establish them also with abrupt changes in the concentration of Na and Ca, and also in artificial systems with a change in the concentration of NH_4, Rb, Cs, UO_2, Th., so that it is safe to say that nearly all sudden changes are attended with transitory standstills.

Together with the visible movements the action-currents of the heart disappear in all these cases [4]).

Besides transitory standstills other transition phenomena can appear with abrupt quantitative transitions. (T, p, π, P_H, Conc, Na, Conc. K, Conc. Ca, Conc. Rb, Conc. Cs, Conc. NH_4. Conc. U. Conc. Th.). Among these we reckon, e. g., also the group-formation appearing for some time in the pulsation instead of a transitory arrest. Sudden changes of force or relaxation have also been observed.

We purpose to discuss very briefly the significance of these transition-phenomena.

All of them have one characteristic in common: they are generated by an abrupt quantitative modification in a certain condition and they all have the peculiarity that they appear and disappear critically with extreme rapidity, with a latent period of half a min. We suspect, therefore, that we have to do here with a surface phenomenon, and we

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1) NOYONS and LIBBRECHT, Arch. internat. de Physiol. T. 16, p. 451.

2) Unpublished investigation in the Physiol. Lab. of Utrecht.

3) Only calcium forms an exception. See Mines, Arbeiter, etc.

4) An investigation by STEYNS has lately cleared up the Ca-controversy.

naturally feel inclined to correlate this with the so-called antagonisms, resp. pseudo-antagonisms of the ions. The ions of which this antagonism, resp. pseudo-antagonism has been established are Na, K, Ca. The numerical relations are represented schematically:

A. In the case of single antagonism by the fraction $\frac{Na + K}{Ca} =$ = constant.

B. In the case of threefold antagonism or pseudo-antagonism by the triangle

$$\begin{array}{ccc} Na & - & K \\ & \diagdown\;\diagup & \\ & Ca & \end{array}$$

Geometrically the triangle is the base of a pyramid, whose apex is located in the origin of coordinates of a three-dimensional system of coordinates Na. K, Ca. The base of the pyramid may be displaced in a direction parallel to itself, but a displacement in another direction is not consistent with normal functions.

It should not been imagined, however, that the relations in question $\frac{Na}{Ca}$ = constant, $\frac{K}{Ca}$ = constant, $\frac{Na}{K}$ = constant, must be kept invariable. On the contrary, in practice ample variation is admissible as well in J. LOEB's classical researches as in the most recent ones.

The antagonisms are most often correlated with softening or hardening of the surface layer (H. MEYER, SPIRO, HÖBER), and the pseudo-antagonisms are ascribed to the necessity of maintaining a proper permeability (J. LOEB, H. J. HAMBURGER).

We shall not enter into a discussion of these explanations as we prefer to say something about the phenomena as real facts, premising that we deal only with transition-phenomena that arise with abrupt transitions between the several conditions, in which the antagonism as well as the pseudo-antagonism of the ions, of themselves, are fairly well maintained, so that after some time, say for the space of 60 minutes, regular cardiac action is guaranteed.

A. Inotropies and tonotropies as transition-phenomena conforming to the fractional scheme.

For instance sudden changes of lifting-power are met with both in a positive and in a negative sense. They generally reveal themselves with a staircase. The latent period is short, yet in the cold-blooded heart it is mostly not shorter than some seconds.

A very frequent transition-phenomenon is a sudden tonotropy, sometimes in a positive, sometimes in a negative sense. This may be a staircase or a steep reaction. The latent period is longer, it may last several minutes.

From the occurrence of a staircase and from the rather long latent period we infer that the surface layer in which this occurs should not be looked for too close to the surface of the cell. Considering that in fraction $\frac{Na + K}{Ca}$ increase of the numerator brings on rapid relaxation, and increase of the denominator induces strengthening of the muscle, we localize this transition-phenomenon in the surface-layer of the fibrils, which is probably also the location of the elastic tonus (LANGELAAN, FEENSTRA).

A long series of other ions may also be included in the numerator of our fraction. In the series Li : Na : NH_4 : K we know the quantitative relation 1 : 3 : 12 : 120 (v. d. BOVENKAMP). Afterwards the series could still be prolonged via Rb to Cs. (SMITS). In the denominator Sr and Ba find a place beside Ca, but Be and Mg appeared to be inactive. Quite foreign ions, viz. U and Th can exert, together with calcium, an influence analogous to that of calcium, not, however, when the calcium is absent.

In the glucose heart of NOYONS [1]) the denominator prevails over the numerator as far as tonus is concerned; as regards force the denominator is inferior to the numerator.

B. Chronotropies as transition-phenomenon conforming to the triangle-scheme:

As already stated, the phenomena themselves admit of a division into three groups:

1^0. transitory standstills;

2^0. group-formations;

3^0. transient increase of the frequency.

The latent period of these phenomena is very short, sometimes even no longer than a few seconds, in a coldblooded heart equal to the periodical time of one pulsation.

The duration is very variable, sometimes the standstill lasts only a few seconds, then again a few minutes up to 20. The group-formation manifests itself after 10 minutes or less, and perhaps persists for half an hour. The increase of the frequency has again a short latent period (1 min.) and continues only for 1, 2 to 5 minutes (J. B. ZWAARDEMAKER).[1])

The phenomena are closely allied, for not only can we let them come and go by the same contrivances, but they can also link up to each other, those with a short latent period, of course, coming first and later on those with a longer period.

Their character is exclusively chronotropic. For instance, instead of Na half the substance can be replaced by Li. The vertex of the triangle is then Li + Na. Partially K can be replaced by NH_4, also by Rb. The vertex is then NH_4 + K + Rb. In place of Ca Cs can be used. Entirely new triangles may also appear when we introduce the radio-

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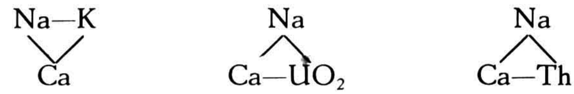
[1]) J. B. ZWAARDEMAKER, Arch. néerl. de physiol. T. 8 p. 414, 1923.

active ions U or Th. Then the following schemata are obtained that are analogous inter se.

I II III



Meanwhile this time the transitions are no longer purely quantitative, as the radio-active elements K and U, when acting separately (or all but separately) are, indeed, interchangeable, but when acting simultaneously (which they do of necessity in such transitions), the radio-physiological antagonism asserts itself. The transitions I ⇄ II, resp. I ⇄ III will, therefore, acquire a quantitative and a qualitative character. The transitions I ⇄ III on the other hand are of a qualitative nature.

From what has been set forth here it appears, then, that the following phenomena reveal themselves:

1^0. transition-phenomena of a quantitative origin conforming to the fraction scheme;

2^0. transition-phenomena of a quantitative origin conforming to the triangle-scheme;

3^0. transition-phenomena of a qualitative origin.

I must not omit to call attention to the following remarkable peculiarity:

Wheras the transition-phenomena sub 1 and 2 still show some difference in their mode of appearing (gradual development, resp. recession sub 1 sudden coming and going sub 2), not any outward difference is noticeable in the transition-phenomena sub 2 and 3. We there observe the same suddenness in appearing and disappearing, equal latent period (on an average 30 sec.) equal duration (on an average 1 or 2 minutes), mostly complete relaxation of the muscle during the standstill. Yet they originate in a different way. In the one case the standstill is brought about by the sudden modification in the quantity of a condition, in the other by a sudden modification in the nature of a condition (alpha-radiation, i.e. emission of positively charged, very large ions over against beta-radiation, i.e. negatively charged, very small particles). True, there is no denying the fact that between alpha-, and beta-radiation there is besides a qualitative also a quantitative difference (e.g. in the amount of kinetic energy), but it would not do to attach value to this quantitative difference alone, for in doing so the difference in positive and negative charge would be eliminated, and the biological contrast between the two radiations (radio-physiological antagonism) would not be taken into account. The connection will be readily understood, however, when we examine the frequency of the occurrence of the standstills, i.e. when we compare e.g. a frequency with purely quantitative difference with the frequency of the standstills in case of a complex of quantitative difference and qualitative difference. The frequency of the standstills amounted, for purely quantitative difference, to 33 % of the expressly examined cases (VAN DISHOECK), over against 50 % when qualitative and quantitative differences were combined. Occasionally the two transitions will appear the one after the other. The artificial Na Ca UO_2-system, and the equally artificial Na Ca Th-system have not yet been dealt with systematically. Provisionally we are impressed with the idea that in the main (not entirely) [1]) they are analogously related to the natural Na K Ca-system.

[1]) Not entirely, as there is no abrupt increase of frequency in Petromyzon on a sudden removal of the UO_2, resp. Th. from the circulating fluid. In fact also the abrupt transition-standstills and transition-groupings are less frequent in the artificial systems. Meantime there remains a possibility that owing to the slow diffusion of the UO_2- and Th-ions the transitions are not comparable.