**Physiology**. — *"On Sensibilization to Radioactivity by the action of Hormones"*. By Prof. H. ZWAARDEMAKER.

(Communicated at the meeting of Sept. 25, 1920).

Sensibilization of organisms or organs to the energy of light has long since been a familiar process in physiology. It is especially H. VON TAPPEINER [1]) who has called attention to some fluorescent substances, which in the presence of oxygen largely increase the deleterious influence of light. This noxious influence resembles the influence of ultraviolet rays. Mr. and Mrs. HENRI [2]) have detected likewise an action of the colloidal selenium for the ultra-violet rays.

Long afterwards similar effects have been detected for the Röntgen-rays. This is instanced by the use of enzytol (10% solution of boric acid cholin) to increase the destruction of malignant tumors in Röntgenization [3])

In 1917 [4]) I have established sensibilization for Becquerel-rays. Here also there were fluorescent substances which brought it about, to wit fluorescein and eosin. The former had the stronger action for the $\alpha$-rays, the latter for the $\beta$-rays. Their action took place irrespective of the presence or the absence of light. In virtue of standard experiments with adsorbentia (e.g. talcum venetum) I correlated the sensibilization in these cases with a reinforcement of the adsorptions, which the radioactive ions undergo through the action of the sensibilizers. In these experiments we found a super-session of fluorescein adsorption by eosin and not the reverse, running parallel to a supersession of the sensibilization of fluorescein by eosin and not the reverse [5]). In general the adsorptions play a prominent part in the action of radio-active atoms of the circulating fluids, because the ions, moving freely in the fluid, exert an influence

[1]) H. VON TAPPEINER, die photodynamische Erscheinung (Sensibilisierung durch fluoreszierenden Stoffe). Ergebnisse der Physiol. Bd. 8. S. 698. 1909.

[2]) M. ET MME. VICTOR HENRI, Action photodynamique du sélénium colloidal, Soc. de Biologie. C. R. du 24 févr. 1912.

[3]) A full list of the literature on cholin action is to be found in DORN Strahlen-therapie Bd. 8. S. 499.

[4]) Kon. Akad. v. Wetenschappen, Amsterdam 27 Sept 1917.

[5]) See for the technique A. M. STREEF, Onderz. Physiol. Lab. Utrecht, 5e Reeks XVIII p. 59.



only when attached through adsorption to the surfaces of the cells, and not when they are located at various distances from the cells. An improved adsorption, by which a larger number of a certain group of ions attaches itself to the cells in a circulating fluid of a given composition, improves the result elicited by these ions.

There is a simple means to detect sensibilizers for radioactivity. One has only to start from radio-active antagonism [1]).

We, therefore, preferred to experiment on the heart of a cold-blooded animal, because the cells of this organ, the seat of automatic movement, are washed directly by the circulating fluid.

The heart of an eel or a frog beats only when, given the further necessary conditions, a radio-active component is present in the circulating fluid in the proper dosage. It does not matter whether the element under consideration is an $\alpha$-rayer or a $\beta$-rayer (our normal $\beta$-rayer is potassium). When applying the $\alpha$- and the $\beta$-rayer simultaneously, the quanta may be counterbalanced so as to inhibit each other's effect completely. At such a moment there is a standstill. A slight balance on the one side or the other will restore automaticity,

The dosage of $\alpha$- and $\beta$-rayers in the circulating fluid must be much smaller in summer than in winter. When taken alone, 5 mgr of potassium chloride or 0,1 mgr of uranylnitrate per litre circulating fluid is in summer sufficient to maintain the automaticity of sensitive hearts. In winter at least 20 mgr of potassiumchloride or 10 mgr of uranylnitrate per litre is needed. Accordingly the summer-, and the winter-equilibria differ very much. In summer a combination of 20 to 30 mgr of potassiumchloride and 0,1 mgr of uranylnitrate (per litre) may arrest the heart's action; in winter this result can be achieved only by 40 mgr of potassiumchloride and 10 mgr of uranyl-nitrate.

After having secured an equilibrium, no matter in what season, a number of substances will give a shifting, which again restores automaticity. Among the anorganic components it is especially the calcium-ion to which we must ascribe a great influence; among the organic substances I found a number of substances having in common the property of considerable surface-activity (as observed for the boundary layer air-water).

Shiftings may be observed on either side. When on the $\alpha$-side, so that a uranium-beat ensues, fresh potassium has to be added to obtain a standstill again. When the shiftings are on the $\beta$-side, uranium must be added to produce the same effect.

[1]) Kon. Akad. v. Wetensch. 27 April 1917.

The shifting does not at all prove that the substance, by which it is generated, is a sensibilizer; it only renders this probable. To ascertain this we have to find out the maximum-, and minimum-doses, between which the automaticity of the organ can be maintained; the potassium limits are the most important. In summer these extremes vary with the individuality of the animal, and range from 5 to 20 and from 10 to 300 mgr. of potassium chloride per Litre, a low threshold corresponding with a low upper-limit, etc.; in winter the extremes are more constant; 20—30 and 600—800 mgr. potassium chloride per litre. Similar observations were made for the other radio-active elements, but I pass them over in silence, since these elements do not occur in the animal organism. The same holds good for the majority of the sensibilizers found by us.

An exception is afforded by cholin and adrenalin, both hormones occurring in every organism. Their sensibilizing power for BECQUEREL rays is very strong, even when the dosis of cholin is one mgr. per litre of circulating fluid and of adrenalin 0,001 mgr. [1])

In the presence of one of these hormones the potassium-dosis that keeps up the heart's action, may be reduced to half the normal dosis, nay, to less even. In summer, therefore, these dosages are extremely small, even $^1/_2$ mgr. of KCl per litre. Then the greatest purity of chemicals is of the utmost importance.

However, there is a difference: Cholin shifts a potassium-uranium equilibrium towards the potassium-side, adrenalin towards the uranium-side. Whether this difference will also manifest itself in normal life is still an open question. For aught we know, there is nowhere in the organism an $\alpha$-rayer, unless it be the trace of rest-activity left behind by emanation, when it is inspired and expired in minimal quanta as an indifferent gas together with the atmospheric air.

Potassium, cholin, adrenalin are normal constituents of the organism. Accordingly, the study of their mutual relations is a true physiological study.

The bio-radio-activity of potassium has no temperature-coëfficient. Both the velocity of effect and the dosage remain the same with 4°, 10° or 20° [2]).

The small differences lie within the latitude of the experimental errors. In this respect physiological radio-activity is analogous to photo chemical actions, whose temperature-coefficient is likewise

[1]) W. LIEBRECHT used for the same purpose but in another connection 0,05 mgr. per litre. (Arch. int. de Physol. T. 15, p. 357).

[2]) Summer- and winterdosage do not differ on account of the difference of temperature. We mention the difference in hormones as a possible cause.



insignificant. Still, the two are not identical. On the contrary, physically corpuscular raying differs fundamentally from light-rays. Nor have we succeeded, in spite of strenuous efforts, not even by means of the most concentrated visible or ultraviolet light, in achieving a recovery of automaticity in an organ perfused with a potassium-free fluid. As regards the temperature-coefficient the analogy between radio-biological and photo-chemical action is still a matter of surprise, even though we are told by modern researchers that in many cases the action of light rests on the liberation of electrons.

These phenomena might be correlated by assuming that the charged particles which send the radio-active radiation with great velocity through the lipoid films on the surface of the cells, evoke inside the cells a catalytic effect, which we usually call a stimulus [1]).

[1]) On physiological radio-activity. Journal of Physiology. Vol. 53 p. 286.