Then we have:

$$\omega_1 = \omega_2 + 2n\pi \ (n \geqq 0)$$
$$\omega_2 = 2\pi$$

Hence $\omega_1 = 2n\pi \ (n \geq 1)$, so that inside $\mathfrak{P}'$ there would have to lie an invariant point.

With this we have completely proved the following

THEOREM. *For a continuous one-one transformation with invariant indicatrix of a two-sided surface in itself a circular continuum with two separated invariant complete circumference segments contains at least two invariant points.*

ERRATA.

In the 3rd communication on this subject, these Proceedings Vol. XIII

p. 767, l. 6 from top	for: indicated. but	read: indicated but
l. 20 from top	for: *paraboli*	read: *parabolic*

Physiology. — C. A. PEKELHARING reads a paper on: "*The excretion of creatinin in man under the influence of muscular tonus*", after experiments by Mr. J. HARKINK.

(Communicated in the meeting of September 30, 1911).

Some time ago I reported here on an investigation by Mr. VAN HOOGENHUYZE and myself, proving that in vertebrates the content of creatin in the voluntary muscles increases during the tonus, but not during simple contractions of the muscles. We may therefore expect that by increase of the muscular tonus more creatin passes into the blood than in other circumstances. Moreover a later investigation showed us that creatin, when gradually introduced into the circulating blood, is partly excreted by the kidneys as creatinin [1]). So we may conclude that an increased tonus will lead to a larger excretion of creatinin.

A series of estimations by VAN HOOGENHUYZE and VERPLOEGH showed indeed that less creatinin is excreted per hour during the night when the muscles as a rule are relaxed in sleep, than in the daytime, when the muscles are now in a tighter, now in a less intense tonus. Besides they stated that a smaller amount of creatinin

[1]) Onderzoekingen Physiol. Laborat. Utrecht, 5de R. XI. p. 236.

was excreted by old people and by those suffering from considerable muscle-paralysis, than by normal, healthy persons [1]).

However all this is no inquestionable proof that these fluctuations in the excretion of creatinin are necessarily caused by changes in the muscular tonus. For it may safely be granted that, although the muscles contribute mostly to the formation of it, yet creatin is formed in several other organs. People that are asleep, as well as persons weakened by old age or other causes, show a greatly reduced metabolism, not only in the muscles but also in other organs. Under these circumstances we might be inclined to attribute the diminished excretion of creatinin not entirely, nay perhaps not even in the first place to the muscles, but to the weakened function of other organs. Therefore I thought it desirable to examine whether a larger output of creatinin can be stated by purposely intensifying the muscular forms, while all other causes of changes in metabolism are excluded as much as possible.

It stands to reason that in this case vertebrates have to be experimented upon, no creatin being found in invertebrates. However it seems impossible in animals simultaneously to cause a protracted tonus of a number of muscles without producing at the same time other, unreliable changes in metabolism. On man, however, the experiment may be satisfactorily performed. Therefore I invited Mr. HARKINK, who had shown genuine interest in the problem, and who had distinguished himself by accurate and careful work in the laboratory, to subject himself to a number of experiments, proposal with which he fell in most graciously.

Our plan of research was a very simple one. Leading a scrupulously regular life and passing the greater part of the day in the laboratory, engaged on work that required little muscular exertion, Mr. HARKINK took every day the same amount of food, which contained neither creatin nor creatinin. On some days, however, the muscles of the trunk and the limbs were maintained in tension as much as possible by assuming the so-called "stramme Haltung" every time during four hours. Then we had to ascertain whether this intensified muscular tonus led to a larger output of creatinin.

The experiment began on June 20 and ended on July 20. Every day his food consisted of:

8.30 a. m. 200 gr. wheaten bread, 20 gr. butter, 50 gr. cheese, 400 cc. milk.

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[1]) Ned. Tijdschr. v. Geneesk., 1908, III, p. 1689.

12.30 p. m. 350 gr. potatoes, 50 gr. rice, 20 gr. butter, 100 gr. sugar, 300 cc. milk, 300 cc. water.

7. p. m. 150 gr. wheaten bread, 50 gr. cheese, 20 gr. butter, 300 cc. milk.

During the rest of the day he took neither food nor drink.

From June 20 to July 5 the urine was collected in 3 portions, from 8 to 3, from 3 to 10 and from 10 to 8. From July 6 till July 19 the morning-portion was divided into one of 8 to 12 and one of 12 to 3. In each portion the content of creatinin was stated after the method of FOLIN by means of the colorimeter of VAN HOOGENHUYZE and VERPLOEGH, first in the unchanged urine and next after the urine + 2 Vol. n. HCl had been heated at 115° C. for half an hour in order to ascertain whether any creatin could be found. The total output of nitrogen was stated after the method of KJELDAHL.

SIX times, viz. on June 30, on July 3, on July 9, on July 15 and on July 18, each time from 8 to 12 a. m. the muscles were kept in tonus as much as possible. In order to compare this to the influence of muscular labour Mr. HARKINK took a walk of 20 K.M. from 8 to 12 a. m. on July 12. On June 20 he weighed 72.5 K.G., on June 29 73, on July 10 71,7 and on July 20 72 KG.

The examination of the urine proved that on the days of the tonus more creatinin was excreted than on other days. On the other hand the performance of mechanical work — a four hours' walk over against a four hours' tonus, which was kept up as much as possible, yet not continually — had no perceptible influence on the amount of creatinin excreted on that day, in accordance with the statement of VAN HOOGENHUYZE and VERPLOEGH. Also on the day after the tonus the creatinin-figure was every time comparatively high and no wonder. For creatin introduced into the circulating blood is not immediately nor entirely removed in the shape of creatinin, as far as it is not decomposed, as experiments on animals have shown.

The average excretion per day was:

normally (18 days)	1.493 (max.	1.527,	min.	1.361)	mgr.
tonus (6 days)	1.614 („	1.640	„	1.573)	„
next day (6 days)	1.525 („	1.545	„	1.454)	„
walk (1 day)	1.534 mgr.				

The minimum of the normal days regards the first day of the whole series of experiments. For the rest it never fell below 1.444 mgr. Creatin was not once found in the urine.

On the tonus-days there soon was an increase of the excretion. This was especially evident, when from July 6 onward, the urine

was daily examined from 8 to 12 and from 12 to 3 separately. On those days (8—12) remarkably little creatinin was excreted during the tonus, while the quantity in the period of 12—3 increased considerably. On those days the average amount per hour was:

July 6, 8—12 (during the tonus) 51.7, from 12—3, 82 mgr.
„ 9, „ „ „ „ 48 „ „ 85 „
„ 15, „ „ „ „ 52.5 „ „ 95.5 „
„ 18, „ „ „ „ 55 „ „ 78 „

on the other days the average excretion was: July 6—19, from 8—12 60.6, from 12—3 75.6 mgr.

More than the ordinary amount of urine (235 cc.) and at the same time more creatinin (74.3 mgr. per hour) was excreted in the first period of July 12, after a walk from 8—12, but during the rest of that day the creatinin did not exceed its usual limits, as the above figure of the total excretion shows.

Corresponding to the series of experiments by VAN HOOGENHUYZE and VERPLOEGH the average excretion of creatinin per hour was found to be less during the night than in the day time. And as a rule the figure of excretion was still low in the first period of the day from 8—12. For the whole series, from June 20 to July 20, excluding the tonus-days, it amounted to:

from 8— 3 on an average 65.6 mgr. per hour
„ 3—10 „ „ 67.6 „ „ „
„ 10— 8 „ „ 57.7 „ „ „

Undoubtedly a considerable part of the creatin, formed during the muscular tonus and passed into the circulation, was not changed into creatinin and excreted as such, but was further decomposed. However this is not evident from the total amount of excreted nitrogen which is subject to fluctuations, dependent on numerous unaccountable circumstances, notwithstanding the uniform nourishment and the regular way of living.

If we compare the products of decomposition of creatin to the nitrogenous matter of the urine being of an other origin, they occupy but a secondary place. In this series of experiments about 1.5 gr. creatinin was excreted per day, equivalent to about 0.5 gr. nitrogen, i.e. a small part of the total amount, about 13 gr., which was per day found in the urine. Over against the nitrogen produced by the protein, that is digested in the alimentary canal and afterwards is desamided, the increased production of creatin in the tonus cannot possibly be of much influence, even though we must take it for

granted that the creatinin excreted by the kidneys, represents only a part of this creatin. Yet, stating the average excretion of nitrogen and creatinin per hour, the fact is remarkable that on the tonus-days the proportion of the amount of nitrogen to that of the creatinin is largest in the afternoon in the period of 3—10, after the creatinin has reached its maximum in the preceding period.

So the above experiments confirm the conclusion, drawn from the content of creatin in the muscles of vertebrates, that chemism in the muscular tonus is totally different from that in the contraction of the muscles. In the first case a nitrogenous metabolite, creatin, is formed, in the second non-nitrogenous products are consumed.

In performing mechanical labour the influence of the tonus is greater proportionally to a more or less careful control of the movements. Consequently we might admit the supposition that intense muscular labour will produce an increase of the excretion of nitrogen, if not only powerful contractions are called forth, but the movements are regulated with great care by tonic contraction of the antagonists, as is often the case with athletic performances.

Physiology. — "*The effect of substances which dissolve in fat on the mobility of Phagocytes and other cells.*" By Prof. H. J. HAMBURGER and J. DE HAAN.

The investigations which will be described in the following treatise, are a continuation of those published in the Proceedings of March 25th 1911 [1]).

It will be remembered that their starting-point was formed by an investigation relating to the favourable effect of Iodoform on the treatment of wounds, and that we arrived at the result that even a slight quantity of this substance (a dilution of 1 to 5000000) has the faculty of accelerating the amoeboid motion of the white blood-corpuscles and of promoting at the same time their phagocytarian capacity. In order to explain this property of Iodoform we assumed that the outer layer of the phagocytes consists of a fatty (lipoid) substance. Now, when Iodoform is dissolved in it, this fatty substance is softened and the amoeboid motion is facilitated. If this view was the correct one, then other substances, soluble in fat, such as Choroform, Chloral, Benzene, Camphor, Turpentine must likewise increase

[1]) HAMBURGER, DE HAAN and BUBANOVIC: On the influence of Jodoform, Chloroform and other substances dissoluble in fats on Phagocytosis.