$$\alpha \frac{\partial f}{\partial x_1} + \beta \frac{\partial f}{\partial y_1} + \gamma \frac{\partial f}{\partial z_1} = 0,$$

and further according to the differential equation

$$(R-1)\, z_1\, \alpha\beta - R\, y_1\, \alpha\gamma + x_1\, \beta\gamma \text{ must be equal to } 0.$$

The two rays of the complex in the tangential plane have but to be made to coincide. The condition is:

$$-4\, R(R-1)\, z_1\, y_1\, f_2 f_3 = [-(R-1)\, z_1 f_3 + R\, y_1 f_2 + f_1 x_1]^2,$$

where f_1, f_2, f_3 represent the differential quotients of f according to x, y and z respectively, whilst analogous relations are easy to deduce.

From this ensues that the required curve is the intersection of

$$f(x, y, z) = 0$$

and

$$-4\, R(R-1)\, z\, y\, f_2 f_3 = [-(R-1)\, z f_3 + R\, y f_2 + f_1 x]^2.$$

Without entering into further details I only wish to observe that when $f(x, y, z) = 0$ represents a plane, the curve can be nothing but the conic of the complex. From the above mentioned equations we therefore find a parabola (the conic of the complex touches the tetrahedron plane at infinity) touching the three planes of coordinates of the rectangular system of axes.

Physiology. — "*On the excretion of creatinin in man*". By C. A. PEKELHARING. Report of a research made by C. J. C. VAN HOOGENHUYZE and H. VERPLOEGH.

As the muscle tissue in herbivora as well as in carnivora always contains a not unimportant amount of creatin, and creatinin is daily excreted with the urine it may be concluded, that creatin is formed as a product of metabolism in the muscles, and having entered the blood is at least for a part excreted by the kidneys in the form of the anhydride, creatinin.

But no agreement has been obtained about the question whether the forming of creatin is bound to the labour, the contracting of the muscles. To answer that question, researches have been made whether the amount of creatinin excreted by the kidneys augments after muscular labour. Different investigators have obtained different results. VAN HOOGENHUYZE and VERPLOEGH have resumed the research anew, using a new method to determinate the amount of creatinin in the urine, which was published some time ago by FOLIN [1]). The

[1]) Zeitschr. f. Physiol. Chemie, Bd. XLI, S. 223.

method of FOLIN is founded on the reaction of JAFFÉ, which consists in adding picric acid and an excess of caustic soda to a solution of creatinin, whereat the liquid takes a brown colour, which cannot be discerned from the colour of a solution of bichromate of potassium. This reaction is employed in the following way: 5 cc. of urine is mixed with 15 cc. picric acid 1,2 % and 5 cc. of caustic soda 10 %. After 5 minutes water is added to a volume of 250 cc. This solution is compared by FOLIN in the colorimeter of DUBOSCQ with a $^1/_2$ normal solution of bichromate of potassium of which a column 8 mm. high shows exactly the same intensity of colour as a column 8,1 mm. high of a solution of 10 mgr. creatinin with 15 cc. picric acid solution and 5 cc. caustic soda diluted to 500 cc. Instead of the colorimeter of DUBOSCQ, VAN HOOGENHUYZE and VERPLOEGH used a little instrument, constructed after their indication, which answered completely to their demands. Immediately after each determination each of them performed 5 readings of the height of the solution of creatinin at which its colour had just the same intensity as a column 8 mm. high of the solution of bichromate of potassium. The several readings of which the average was taken, never differed more than 0,2, only very seldom more than 0,1 mm.

It proved meanwhile that the temperature has influence on the reaction in that sense that the colour of the creatinin solution becomes deeper by increase of temperature. Therefore the water used for the diluting was always kept at a temperature scarcely differing from 15° C. The relation found by FOLIN was affirmed. A solution of 10 mgr. of pure creatinin in 500 c.c. treated in the indicated way produced as the average of 10 readings 8.14 m.m. (max: 8.2, min. 8.1) out of which a quantity of 9.951 instead of 10 mgr. would be deduced.

The results become less exact when the concentration of creatinin is much larger or smaller than 10 mgr. in 500 c.c. Therefore the determination was repeated when the readings became higher than 10.5 or lower than 5, with 10 c.c. urine, in the first case diluted to 250 in the second to 1000 c.c. The method of FOLIN had great advantages over the method of NEUBAUER used till now, in which the creatinin is precipitated out of an alcoholic extract of the urine by means of chloride of zinc and after that weighed. Not only that the method of FOLIN takes much smaller quantities of urine, so that it renders it easy to discern by the examination of different portions of urine the oscillations in the secretion in the course of the day, but it is also more reliable. With the method of NEUBAUER there is always some danger that under the influence of the alkaline reaction arising from the addi-

tion of milk of lime to separate the phosphates, a part of the creatinin is changed into creatin. This danger may be lessened but not wholly avoided by acidifying the filtrate before evaporation by means of hydrochloric acid, after which at the end the hydrochloric acid must be eliminated by addition of sodium acetate in order not to hinder the precipitation of creatinin zinc chloride. But there are other difficulties connected with the method of NEUBAUER which can never be totally removed. The urine is after the removal of the phosphates concentrated till it obtains the consistency of syrup and is than extracted with alcohol. In the mass of salts rendered hard by the contact with alcohol, a part of the creatinin may be retained undissolved. If in order to eliminate this difficulty the urine is not very much evaporated, there arises another source of error. The alcohol is diluted by the still resting water and the consequence is that now the creatinin-zincchloride crystallises only partially. For this compound is insoluble in absolute alcohol but not in alcohol containing water. A too small quantity of creatinin is therefore always found by the application of this method.

VAN HOOGENHUYZEN and VERPLOEGH have investigated the solubility of creatinin-zincchloride in alcohol by putting dried crystals, prepared from urine and purified as much as possible, in closed bottles under alcohol of different strength at the temperature of the room under repeated shaking and by determinating afterwards, by means of FOLIN's method, how much creatinin was dissolved in the alcohol. They found:

in 100 C.C. alcohol	99 %	trace	of	creatinin.
„ „ „ „	93 %	5.6 mgr.	„	
„ „ „ „	72 %	32.1	„	„
„ „ „ „	50 %	104.5	„	„

In connection with this they obtained out of urine more creatinin-zincchloride when the alcoholic extract before the addition of chlorid of zinc was again evaporated to almost dryness and then dissolved by strong alcohol, than with the usual method. They could still show creatinin in the liquid filtered off from the creatinin-zinc-chlorid as well by the reaction of WEYL as by that of JAFFÉ. So the method of NEUBAUER always gives a loss of which the amount cannot be estimated. One is therefore not entitled to attribute much value to the little oscillations in the output of creatinin found by applying this method.

By the method of FOLIN on the contrary such a source of uncertainty does not exist, when the time of the reaction — 5 minutes — is rightly observed, the liquid is brought to the exact volume with

water of the temperature of the room and when the determination is completed immediately afterwards.

VAN HOOGENHUYZE and VERPLOEGH have investigated by themselves whether increase of the secretion of creatinin in consequence of muscular labour could be observed. For that purpose in every series of experiments the urine was collected every day at appointed times namely in the morning, in the first series of experiments at 9, in the following at 8 o'clock, in the afternoon at 12 o'clock and at $4^1/_2$ o'clock, at night at $11^1/_2$ o'clock. Every portion was measured and divided into two equal halves. One of the halves was used for an estimation of creatinin, the other halves were mixed, after which the quantity of creatinin in the mixture was determined and moreover an estimation of nitrogen was performed after the method of KJELDAHL.

In this way the determination of creatinin was also controlled. In all the series of experiments the conformity of the figure of the total quantity of creatinin and the sum of the four portions was very gratifying. The quantity of urine of one day was that collected from 12 o'clock in the afternoon till the following morning 8 or 9 o'clock.

During each series of experiments a fixed amount of food was taken, every day the same. Only in the first series coffee and tea were still taken, in the later series only water.

I. From April the 8th—24th 1904, seventeen days at a stretch, food was taken which consisted of bread, butter, cheese, milk, oatmeal, sugar, meat, eggs, potatoes and rice, daily an equal portion of each.

The food contained:

for v. H. 118 gr. proteid 146 gr. fat, 326 gr. carbohydrat.; 40,8 Cal. p. Kg.
„ V. 115 „ „ 81 „ „ 327 „ „ 38.6 „ „ „

On working days moreover both consumed 50 gr. sugar.

The 11th, the 16th and the 21th of April bicycle excursions were undertaken at which they rode steadily on for $2^1/_2$ à 3 hours without resting. The other days were spent in the laboratory while the evenings were passed peacefully.

The excretion of creatinin underwent no perceptible change in consequence of the muscular labour. With both investigators it oscillated not unimportantly during the whole experiment. It amounted on an average to:

v. H.	14	days of rest	2.116 gr.	daily	(max.	2.401,	min.	1.821 gr.)
V.	„	„ „ „	1.998 „	„	(„	2.158 „		1.858 „)
v. H.	3	workingdays	2.147 „	„	(„	2.325 „		1.925 „)
V.	„	„	2.015 „	„	(„	2.058 „		1.949 „)

The difference is so small that no value must be attached to it. On the days which followed on the muscular exertion the figures of the creatinin remained within the usual daily oscillations.

The secretion of nitrogen was rather irregular with both during the whole experiment.

From June the 22nd till July the 2nd 1904 (eleven days) the experiment was repeated with less food which in particular was less rich in proteid. It contained:

for v. H. 71.5 gr. proteid, 125 gr. fat, 351 gr. carbohydr.; 33.7 Cal. p. Kg.
„ V. 80.5 „ „ 74.75 „ „ 358 „ „ 34.6 „ „ „

On July the 1st a bicycle excursion of three hours was undertaken (50 KM.).

The excretion of creatinin amounted on an average to:

	10 days of rest	Workingday
v. H.	1.983 (max. 2.042, min. 1.809 gr.)	1.997 gr.
V.	2.039 („ 2.174, „ 1.920 „)	2.049 „

On the days which followed the day of muscular labour the excretion of creatinin did not increase either.

III. Whereas till now meat was still taken, in the series of experiment II daily 50 gr., the experiment was now taken with food which contained no creatinin at all, moreover it was made poorer in proteid. The experiment lasted from July the 7th till the 29th 1904, 23 days at a stretch.

From July the 7th till 18th only bread, butter, cheese, rice and sugar were taken containing:

for v. H. 50 gr. proteid, 115 gr. fat, 344 gr. carbohydr.; 31.2 Cal. p. Kg.
„ V. 50 „ „ 74 „ „ 344 „ „ 33.8 „ „ „

From July the 18th rice was partly replaced by potatoes and the quantity of butter was decreased so that the ration became:

for v. H. 47 gr. proteid, 98 gr. fat, 337 gr. carbohydr.; 29,5 Cal. p. Kg.
„ V. 47 „ „ 64 „ „ 337 „ „ 30.1 „ „ „

On July the 28th and the 29th 5 eggs were daily added to this food.

On July the 15th, the 20th and the 23rd muscular labour was again performed while the other days were passed in the laboratory with occupations which exacted only little exertion of the muscles. On July the 15th a bicycle excursion was undertaken in which 54 K.M. were covered in three hours. On July the 20th and 23rd fatiguing indoors gymnastics were performed for $2^1/_2$ hours at a stretch with halters of 10 K.G. and with the chest-expander and

the combined developer of SANDOW; care was taken that all the muscles of the body and the extremities were used.

When the first three days of the scanty diet, July the 7th, 8th and 9th, in which the secretion of nitrogen fell with v. H. from 14,562 to 9,045 gr. and with V. from 13,721 to 10,234 gr. are not counted, as belonging to a transition-period, and neither the last two days, July the 28th and 29th at which about 30 gr. more proteids daily were taken, it appears that the excretion of creatinin has amounted in 15 days of rest on an average every day to:

v. H. 1.836 gr. (max. 1.935, min. 1.693 gr.)
V. 1.962 „ („ 2.079, „ 1.876 „)

while on the working days was found:

v. H. July the 15th 1.908, July the 20th 1.921 and July the 23th 1.974 gr. creatinin.
V. July the 15th 2.142, July the 20th 1.947, and July the 23rd 1.937 gr. creatinin.

Here then the figure with v. H. is always, with V. once above the average on the working day. Meanwhile the deviations do not surpass the oscillations, which are always found, also without important exertions of the muscles.

The figure found with V. on July the 15th does, it is true, surpass the maximum in the period of the days of rest, but the difference 0,063 gr. is so slight, that no value must be attached to that, in connection to the lower figures of the two other workingdays.

On the two last days of the series on which no muscular labour was performed, but on which more proteid was taken, the excretion of creatinin was:

v. H. July the 28th 1.955 gr., and July the 29th 1.959 gr.
V. „ „ „ 2.053 „ „ „ „ „ 1.984 „ .

while with both the secretion of nitrogen increased from about 8 gr. to 11 gr. daily.

IV. In September 1905 a new experiment was taken, to examine firstly whether preceding muscular exercise might perhaps bring some change in the result, secondly to investigate the influence of excessive labour and thirdly to see whether the excretion of creatinin would be increased with excessive labour and totally insufficient food.

After performing daily for three weeks at a stretch indoor gymnastics after the method of SANDOW, the experiment was begun September the 26th with food of the same composition as was used July the 18th till the 27th, hardly sufficient and poor in proteid. This food was

taken nine days at a stretch till Oct. the 4th. On September the 29th exercises were performed with SANDOW's implements for $2^1/_2$ hours with short intervals. On October the 2nd excessive labour was done, consisting of a walk of 21 KM. in the morning from 9 till 12 o'clock, a walk of 10 K.M. in two hours in the afternoon and working with halters for $^1/_2$ hour in the evening. On the six days of rest between September the 27th and Oct. the 4th (on the first day Sept. the 26th the urine was not examined) there was excreted on the average every day:

v. H. 1.859 (max. 1.977, min. 1.755) gr. creatinin
V. 1.925 („ 2.047, „ 1.860) „ „

while on Sept. the 29th there was found:

v. H. 2,001 V. 1.979, gr. creatinin
On October 2nd „ 1.859 „ 1,945, „ „

That not too much importance for the influence of muscular labour on the secretion of creatinin must be attached to the somewhat high figure of v. H. on September the 29th becomes clear when the separate portions of that day are considered. In the first portion of that day, that is in the urine excreted in the morning between 8 and 12 o'clock, so before muscular exertion was begun, 0,404 gr. creatinin was already found to 0,331 gr. and 0,345 gr. in the corresponding portions of the preceding and the following day.

After ordinary food had been taken for nine days, food was taken in absolutely insufficient quantity for five days at a stretch, consisting of bread, potatoes, butter and cheese. It contained:

for v. H. 36.6 gr. proteid 43 gr. fat 186 gr. carbohydrate; 15 Cal p. Kg.
„ V. 29.7 „ „ 34.7 „ „ 158 „ „ ; 15 „ „ „

On Oct. the 16th a bicycle ride of 42 K.M. in $2^1/_2$ hours was undertaken in the morning. In the first hour 20 K.M. were done but after that they could progress but slowly from hunger and fatigue.

In the afternoon a walk of 16 K.M. was taken from 2 till 5 o'clock and afterwards in the evening they worked with halters. The result was that both felt still very tired the next day.

The calculation of the average has no value in this short experiment. The course of the excretion of the creatinin was as followed:

		v. H.	V.	
Oct. the	14th	2.020	1.908	
„ „	15th	1.702	1.934	
„ „	16th	1.775	1.899	workingday
„ „	17th	1.831	1.938	
„ „	18th	1.861	1.868	

Here too where the food was not sufficient for the organism to defray the costs of the muscular labour, as appeared also from the increase of the nitrogen secretion on the workingday, one can certainly not speak of distinct influence of muscular labour on the excretion of creatinin.

It is however different when no food is taken at all for days.

VAN HOOGENHUYZE and VERPLOEGH had an opportunity to make observations about this too on the "Hungerkunstlerin" FLORA TOSCA a strong, young woman, who lent herself for the investigation during a starving period at the Hague, in a room which was opened to the public night and day. The urine was collected every day in three portions, in the morning from 10 o'clock till 4 o'clock in the afternoon, from 4 o'clock in the afternoon till 10 o'clock in the evening and from 10 o'clock in the evening till 10 o'clock the next morning; it was sent every day at a fixed time to the Physiological Laboratory in Utrecht and was there examined at once.

In the morning of June the 10th 1905 the last food was taken; after that nothing but mineral water (Drachenquelle) till June the 25th. Besides creatinin several other constituents of the urine were determinated daily; about this it will be sufficient to mention that from the course of the secretion of nitrogen, urea, uric acid and phosphoric acid it appeared sufficiently that no food was taken.

During the whole hunger-period of fourteen days complete bodily rest was observed as much as possible save on June the 17th when TOSCA during two hours with short rests, under direction of VERPLOEGH, was occupied with gymnastic exercises with halters of 1 KGr. 13 different movements were made, the first ten 20 times each, the last three 10 times each. The movements were so chosen that as many muscles as possible were set to work.

The examination of the urine showed now that in hungering the secretion of the creatinin as well as of the other products of metabolism steadily decreased. But the muscular labour suddenly produced an undeniable increase, not on the same day, but on the following. Still on the third day the influence was to be perceived, which however also was the case with connection to the total quantity of nitrogen. On the first day, when food was still taken, the quantity of creatinin amounted to 1,087 gr. Later on it decreased rapidly and rather regularly till on the 8th day. On June the 17th, the day of the muscular labour, it amounted only to 0,469 to rise the following day to 0,689. In the three days before the muscular labour 1,662 was secreted, in the three following days 2,006 gr. creatinin. After that the secretion decreased almost to 0,5 gr, daily, to remain rather constant then.

From the above mentioned it appears that even with perfectly regular food and with avoiding of all excessive muscular labour the daily secretion of creatinin, as was communicated already in 1869 by K. B. HOFMANN [1]), undergoes rather important oscillations. This is not sufficiently taken into consideration by those authors who as MOITESSIER [2]) and as GREGOR [3]) have deduced from their results with series of experiments of three, four or five days, where the creatinin was precipitated from the alcoholic extract of the urine as a compound of zincchloride, that the excretion of creatinin increased as a result of muscular labour. It seems therefore to me that more value may be attached to the conclusion, which v. HOOGENHUYZE and VERPLOEGH drew from their observations, that in man only then increase of excretion of creatinin is caused by muscular labour when the organism is forced, by abstaining from food, to live at its own costs

If the creatinin which is found in the urine of normal and normally fed men and animals is not to be considered, even were it for a small portion, as a product set free by the contraction of the muscle fibre, the question arises what signification must be given to this constituent of the urine.

Since MEISSNER's researches [4]) it is known that to make use of meat as a food must lead to the excretion of creatinin, as creatin and creatinin, brought into the blood either by resorption out of the intestinal canal or by injection under the skin completely or almost completely is excreted as creatinin by the kidneys.

The quantity of creatin in meat is rather important. It is usually mentioned as 0,2 à 0.3% of the fresh muscle substance [5]). With the aid of FOLIN's method v. H. and V. have determined the amount of creatin in muscle. 500 gr. meat freed as carefully as possible of fat and tendons and minced was mixed with chloroform water and was pressed out after standing for some hours at the temperature of the room. This was repeated twice. After that the pressed out meat was boiled for two hours with water and after cooling pressed out anew. The filtrates were mixed, boiled at weak acid reaction to remove proteids, after cooling filled up to 4000 c.c, and then filtered. 500 c.c. of the filtrate was concentrated to 100 c.c. and filtered anew, 80 c.c. of this filtrate was boiled with 50 c.c. *n*

1) Virchow's Archiv. Bd. XLVIII S. 358.

2) These Montpellier 1891.

3) Zeitschrift f. Physiol Chemie. Bd. XXXI S. 98.

4) Zeitschr. f. rat. Med. Bd. XXXI, 1868, S. 234.

5) VOIT. Zeitschr. f. Biol. Bd. IV, 1868. S. 77.

H_2SO_4 48 hours in the waterbath, to change all creatin into creatinin. After that the quantity of creatinin was determined colorimetrically. Every time a determination of the same kind of meat of different animals was made twice. So the following was found:

Beef	I	3.688	gr.	creatinin:	4.378	gr.	creatin	p.	Kg. meat
	II	3.898	„	„	4.522	„	„	„	„ „
Mutton	I	3.499	„	„	4.059	„	„	„	„ „
	II	3.608	„	„	4.185	„	„	„	„ „
Pork	I	3.718	„	„	4.313	„	„	„	„ „
	II	4.070	„	„	4.721	„	„	„	„ „
Horse	I	3.244	„	„	3.763	„	„	„	„ „
	II	3.395	„	„	3.948	„	„	„	„ „

Even with an abundant use of meat or beef-tea the creatinin excreted by the kidneys (1,5 à 2 gr. or still more in 24 hours) can but for a part be derived from the food. It is moreover well-known and by the above mentioned researches proved anew that the secretion of creatinin sinks not or scarcely under the norm, when the food does not at all contain creatin or creatinin. The organism itself forms creatin as a product of metabolism from the proteids. It would be possible that the nature of the proteid taken up as food was of signification for the forming of creatin. In that case it was possible that especially such proteids would produce creatin, out of which by hydrolysis much arginin, a more complicated derivative of guanidin could be obtained. According to the researches of KOSSEL and his disciples, from gelatin twice as much arginin can be obtained as from casein; out of gelatin 9.3 % [1]), out of casein 4.8 % [2]). VAN HOOGENHUYZE and VERPLOEGH have therefore examined by a new series of experiments whether the use of casein or gelatin increases the secretion of creatinin and if such is the case in what measure.

V. On April the 7th 1905 a beginning was made with the use of the same food as in series IV.

v. H. 47 gr. proteid, 98 gr. fat, 337 gr. carbohydr.; 29.5 Cal. p. Kg.
V. 47 „ „ 64 „ „ 337 „ „ 30 „ „ „

On April the 12th, 13th, 14th 50 gram casein was taken prepared after HAMMARSTEN from cow-milk, in the afternoon at 12 o'clock 25 gr. and in the evening at 6 o'clock once more 25 gr. To leave the total chemical energy of the food unchanged, so much fewer potatoes were taken on these days that the quantity of carbohydrates fell from 337 to 287. After that the food was taken as on April the

[1]) Zeitschrift f. Physiol. Chem. Bd. XXXI, S. 207.
[2]) Ibid. Bd. XXXIII, S. 356.

7th till April the 19th. April the 20th 21st and 22nd 50 gram commercial gelatin, well washed in water, was taken every time in two portions, each of 25 gr., just as the casein instead of 50 gr. carbohydrate. On April 23rd and 24th the first diet was again taken.

In 10 days in which the food daily taken contained 47 gr. proteid (the first two days April the 7th and the 8th, which were still under the influence of the food taken the preceding days, the urine was not examined) the secretion of creatinin amounted to:

v. H. on the average 1.813 gr. (max. 1.921 min. 1.706 gr.) daily
V. „ „ „ 1.850 „ („ 1.990 „ 1.723 „) „

On the days on which casein or gelatin was taken the secretion of nitrogen increased but the secretion of creatinin not or scarcely. It amounted on the three casein-days to:

v. H. on an average 1.913 gr. (max. 2.009, min. 1.836 gr.) daily
V. „ „ „ 1.897 „ („ 1.934, „ 1.834 „) „

and on the three gelatin-days:

v. H. on an average 1.800 gr. (max. 1.813, min. 1.783 gr.) daily
V. „ „ „ 1.872 „ („ 1.811, „ 1.868 „) „

Just as in the series of experiments III as was mentioned above, where, after the daily addition of 5 eggs to food which contained 47 gr. proteid, only a too insignificant increase of the secretion of creatinin was found to attach any value to it, it appeared now that the addition of casein and gelatin had no important influence whatever, although the added proteid was daily resorbed and desintegrated in the body, as the determination of nitrogen taught.

A short time ago FOLIN has communicated ample researches about the constituents of human urine and has come to conclusions [1]) with which the observations of VAN HOOGENHUYZE and VERPLOEGH are quite in accordance.

In 1868 MEISSNER has drawn the conclusion from his observations that the origin of creatinin in the organism of mammals must be quite different from that of the urea with which most of the nitrogen is excreted from the body [2]). FOLIN draws this conclusion anew and, in connection with his observations about the secretion of other nitrogen containing substances and sulphur-compounds, starts from this point in proposing a new theory about the desintegration of proteid in the animal body, which he puts in the place of the wellknown theories of VOIT and of PFLÜGER. In considering the desintegration of proteids in the body, there has been, argues FOLIN, generally laid

[1]) Amer. Journ. of Physiol. Vol. XIII, p 45. p. 66 p. 117.
[2]) l. c. S. 295.

stress almost only on the total quantity of nitrogen excreted, in relation to the quantity taken up in the food, and not enough attention has been paid to the quantities of each of the different nitrogenous products of metabolism which are excreted with the urine.

When the quantity of proteid in the food is enlarged or diminished then the secretion of nitrogen increases or decreases till after a short time a condition of equilibrium has been again obtained when intake and output of nitrogen are alike. The variability of the metabolism of proteids does not manifest itself in connection with all nitrogenous substances but for the greater part with connection to the urea. The secretion of creatinin on the contrary and also in a less degree that of uric acid is apparently independent of the richness of the food in proteid. We must distinguish a desintegration of proteid variable under the influence of the food, on which depends in the first place the forming of urea and which according to FOLIN's conception takes place for the greater part if not wholly in the digestive organs — in the cavity and in the mucosa of the intestine and in the liver — and beside a much less variable desintegration of proteid in the different organs which does not immediately depend on the food but on the function of the tissues. In the tissues there arise undoubtedly nitrogenous products of desintegrating of different composition. To them belongs as has been stated by NENCKI, SALASKIN and their collaborators ammonia, which is changed into the harmless urea by the liver. Moreover urea is formed in the organism in other places than the liver. This product of metabolism proceeds thus for a part, as FOLIN expresses it "endogenously" in consequence of the rather regular metabolism of proteid in the tissues and for another part "exogenously" in larger or smaller quantities, as more or less proteid is taken up in the digestive canal. It is however not possible to distinguish these two parts from each other in the urine.

But on the contrary the secretion of creatinin, on which the digestion of the food when it contains no creatin has no direct influence, gives an indication about the intensity of the desintegration of proteid in the tissues. In this respect the muscular tissue, must be thought of in the first place, but not exclusively, as creatin is formed undoubtedly in other tissues too.

It does not seem necessary to accept that all the creatin which is formed in the tissues is excreted as creatinin. The observations of MEISSNER give already rise to the supposition that creatin must be considered as an "intermediate" product of metabolism, as has been stated by BURIAN and SCHUR for the uric acid. MEISSNER at least could not quite retrace in the urine the creatinin brought into the

circulation. He did find, it is true, that after injection of creatin under the skin, not only the whole injected quantity was excreted again with the urine, but also 20 mgr. creatinin with it, but it remained uncertain how much of it proceeded from the metabolism of the animal itself.

To obtain an insight into this v. H. and V. have made anew an experiment in which the same food was taken, with 47 gr. proteid daily, as in the preceding experiment.

VI. The experiment lasted from Aug. the 17th till the 28th 1905. On the first day the urine was not examined. The oscillations in the secretion of creatinin were very insignificant. In five days from Aug. the 18th till the 22nd there was secreted:

v. H. average 2.023 gr. (max. 2.029, min. 2.017 gr.) daily
V. „ 2.028 „ („ 2.029, „ 1.930 „) „

On Aug. the 23rd each of them took in one portion 500 mgr. pure creatinin dissolved in water. On the same day there was excreted.

v. H. 2.420 gr. and V. 2.508 gr. The next day:
V. 2.030 „ „ „ 2.073 „ „ „

On Aug. the 26th each of them took again 500 mgr. creatinin but divided into 10 portions, 50 mgr. every hour. Now also the creatinin was found back the same day for the greater part in the urine. The excretion amounted to:

v. H. Aug. the 25th 1.998 Aug. the 26th **2.425** Aug. the 27th 1.940 Aug. the 28th 1.951 gr.
V. Aug. the 25th 2.045 Aug. the 26th **2.467** Aug. the 27th 2.035 Aug. the 28th 1.968 gr.

At least in three of the four determinations a part of the creatinin brought into the blood was not found back in the urine.

From this experiment, which has still to be completed with others, in which creatin will be taken instead of creatinin, it appears how distinctly every change of some importance in the excretion of creatinin can be shown with the aid of FOLIN's method. So it gives the more reason to trust the results of the above mentioned series of experiments, and the conclusion derived from them, that creatin is a product of metabolism which is not formed at the contraction of the muscle-fibre, but proceeds in muscles and other organs by the desintegration of proteid to which is bound the life of the cells, without regard to the developing of energy to which they are able in performing their peculiar functions. Only then when the organism is deprived of food and must therefore seek the power of performing

labour in itself, the material which the muscles want for contraction is taken from the proteids of the tissue, for this the tissues are forced to more vigorous life, of which an increased formation of creatin is the result.

Quite in accordance with the investigations and arguments of FOLIN, v. HOOGENHUYZE and VERPLOEGH also found that though the excretion of urea increases and decreases with the resorption of proteids, the excretion of creatinin is not directly dependent on it. There is dependence in so far that with total privation of food, the activity of the organs becomes as small as possible and that then with the intensity of the symptoms of life the secretion of creatinin becomes extraordinarily small. In connection with this a statement made on the last day of the hunger-period of TOSCA is worth mentioning. June the 25th she took milk and eggs in the evening after ten o'clock. The urine which was collected the following morning at 10 'clock contained 0.375 gr. creatinin, more than double the quantity which was excreted by her in the last days in that same period. This sudden increase can certainly not be put to the account of the food as such, as is shown by the very slight increase of the excretion of nitrogen in the same period, but must be attributed to the stimulation which the whole organism suffered by the putting into action of the digestive organs after such a long rest.

NOËL PATON investigated a short time ago with the aid of FOLIN'S method the excretion of creatinin of a dog which was fed with oatmeal and milk and moreover on one day with 5 eggs and which got no food at all on other days [1]). According to the author the results seem to indicate that in the dog there is a relationship between the production of creatinin and the intake of nitrogen.

The secretion of creatinin shows a somewhat too large irregularity in the communicated series to admit the making of conclusions. But if the impression of the author is right, there may be thought here also of a stimulating effect of the food on the whole organism.

Just as FOLIN, VAN HOOGENHUYZE and VERPLOEGH have observed not unimportant individual varieties in the excretion of creatinin with mixed food. Without doubt the quantity of meat which one is used to take, influences it. But with persons living pretty well under the same circumstances the difference seems to be less great when the weight of the body is considered. In 5 students a secretion of 26, 26.9, 27.4, 29,4 and 31,5 mgr. creatinin pro bodily weight of one Kgr. was found in 24 hours.

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[1]) Journal of Physiol. Vol. XXXIII, p. 1.

VAN HOOGENHUYZE and VERPLOEGH have also examined the urine of some sucklings. Always creatinin could be shown, more distinctly with the reaction of JAFFÉ than with that of WEYL. On account of the small concentration and the trifling quantities of urine which could be collected an accurate colorimetric determination was not possible. In four cases however a sufficient quantity of urine (15—60 cc.) was obtained, to admit at least of a somewhat reliable determination. In 10 cc. urine which was diluted to 50 cc. after having been mixed with picric acid and caustic soda, there was found:

I	child	8 days	old,	1.11	mgr. creatinine
II	„	32 „	„	0.91	„ „
III	„	2 months	„	0.41	„ „
IV	„	2 „	„	1.7	„ „

It is remarkable that in case III which concerned a weak child which was fed exclusively on cowmilk, the quantity of creatinin was so much smaller than in the three other children who were all strong and brought up by human-milk.

The above mentioned proves, as it appears to me, that the method of FOLIN is an acquisition of importance of which may be expected that it will aid in penetrating deeper than before into the knowledge of metabolism.

Physics. — "*On the theory of reflection of light by imperfectly transparent bodies.*" By Prof. R. SISSINGH. (Communicated by Prof. H. A. LORENTZ).

1. The laws of metallic reflection have been derived first by CAUCHY [1]), later by KETTELER [2]) and VOIGT [3]), while LORENTZ [4]) has developed them from the electromagnetic theory of light. By different

[1]) CAUCHY, Compt. Rend. **2**, 427, 1836; **8**, 553, 658, 1839; **9**, 726, 1839; **26**, 86, 1848; Journ. de Liouv, (1), **7**, 338, 1839. CAUCHY gives only general remarks on the way followed by him. Derivations of the results have been given, inter alia by BEER, Pogg. Ann. **92**, 402, 1854; ETTINGSHAUSEN, Sitzungs-Ber. Akad. Wien, **4**, 369, 1855; EISENLOHR, Pogg. Ann., **104**, 368, 1858: LUNDQUIST, Pogg. Ann., **152**, 398, 1874.

[2]) Pogg. Ann., **160**, 466, 1877; Wied. Ann., **1**, 225. 1877; **3**, 95, 1878; **22**, 204, 1884. KETTELER has, also in consequence of VOIGT's observations, modified his developments, and given a final form to them in the "Theoretische Optik", 1885.

[3]) Wied. Ann., **23**, 104, 554, 1884; **31**, 233, 1887; **43**, 410, 1891.

[4]) On the theory of reflection and refraction of light, 1875; SCHLÖMILCH's Zeitschr. f. Math. u. Physik, **23**, 196, 1878.