Respiratory Quotient, Heat Production and Blood Pyruvic Acid in Aneurin Deficient Rats after Glucose Administration

The determination of respiratory quotient (R.Q.) and metabolic rate is the most direct method of studying the oxidation processes and the glucide metabolism in aneurin deficient organisms. Nevertheless, the more or less severe starvation, which cannot be avoided in experimental avitaminosis, the difficulty of obtaining satisfactory measurements of heat production (H.P.) for the animals most frequently used in these experiments (rats, pigeons) and in estimating the degree of avitaminosis, and the frequent use of unsuitable diets deficient not only in aneurin but also in other B vitamins, are the most important disturbing factors which may explain the frequently contradictory results in this field. From the literature, we would refer especially to CHAHOVITCH[1], who noticed a decrease of the basal metabolic rate in avitaminosis B_1 (pigeon), and DRUMMOND and MARRIAN[2] according to whom the resting metabolism remains normal until the final phase, when marked malnutrition occurs. The R. Q. in avitaminosis B_1 has generally been found to be decreased[3]. MAGNE and SIMONNET[4] stated that the injection of glucose did not raise the R.Q. of the beri-beri pigeon, whereas MATTIL[5] found that the injection of cane sugar in vitamin B deficient rats immediately raised the R.Q. from 0·75 to 0·9 or more.

WHIPPLE, CHURCH and STEVENS[6] reported a decreased R.Q. in rats on aneurin-deficient diet; after subcutaneous injection of 1 g of glucose, the R.Q. were below the unity for deficient animals and above unity for controls.

More recently RING[7] confirmed the DRUMMOND and MARRIAN observations concerning the resting metabolism during avitaminosis; furthermore he found "no significant difference in the R.Q. of normally fed rats and those on thiamine deficient diets". In view of the discrepancy between the results reported in the literature, it seemed desirable to reinvestigate the problem under proper experimental conditions, determining the blood pyruvic acid as well as the R.Q. and the H.P.

In the present experiments we measured the H.P., the R.Q. and the blood pyruvate in normal and aneurin-deficient albino rats, taken from their cages in the morning without previous fast (not strictly basal conditions). The measurements were repeated after glucose administration *per os*. The heart rate, together with the body weight, has been used as a reliable index of the degree of avitaminosis.

The rats, with an initial weight of 55–70 g, were kept on a synthetic diet deficient in vitamin B_1 (wheat starch 65%, casein freed from fat and washed 18%, olive oil 10%, cod liver oil 2%, OSBORNE and MENDEL's saline mixture 5%), with appropriate quantities of other B vitamins (riboflavine, pyridoxine, niacine, pantothenic acid, biotin, inositol and choline). The control rats received, furthermore, 10 γ of aneurin hydrochloride each *pro die*.

All determinations have been carried out on animals fed in this way for 20–28 days. At the end of this time the rats were still in good physical condition, although avitaminosis was proved by the increased blood pyruvic acid, the decreased heart rate (about 23%) and the decreased body weight.

R.Q. and H.P. were determined on groups of 3 animals, kept for 10′ under a bell-shaped glass cover of known capacity. Air samples were analysed with the HALDANE-MARGARIA apparatus. The pyruvic acid was estimated by LU's method following FORNAROLI[1] on blood samples from rats kept in the dark for 30′–40′ before decapitation.

The glucose (1 g in 1 ml of water) was administered by means of sound. After administration the measurements were made between the 45th minute and the second hour for the R.Q. and H.P., and at the 45th minute for the pyruvic acid.

The results are reported in the Table

We note from the column *A* that the R.Q. and H.P. are significantly decreased during avitaminosis, whereas the blood pyruvic acid is considerably increased.

Glucose administration produces the following modifications:

(1) R. Q. is considerably increased. The difference between the values reached by the control rats and the avitaminotic rats is not statistically significant ($t = 0{\cdot}97$; $f.d. = 35$; $p = 0{\cdot}3$–$0{\cdot}4$). The increase due to the glucose administration was higher for the latter.

(2) H.P. is moderately but significantly increased both in control ($t = 2{\cdot}3$; $f.d. = 32$; $p = 0{\cdot}02$–$0{\cdot}05$) and in B_1 deficient rats.

(3) The blood pyruvic acid is also significantly increased both in the control rats ($t = 3{\cdot}2$; $f.d. = 25$; $p = 0{\cdot}001$–$0{\cdot}01$) and in the avitaminotic rats ($t = 3{\cdot}4$; $f.d. = 33$; $p = 0{\cdot}001$–$0{\cdot}01$). The difference between the two increases is not statistically significant.

The experiments reported in this paper show that the increase in R.Q. and H.P. after glucose administration in animals suffering from avitaminosis B_1, indicate an ability to use carbohydrate at a rate not lower than in controls.

The increase in the blood pyruvic acid after glucose administration in the avitaminotic animals is not significantly greater than in the controls. This result does not prove a diminished utilization of the glucides.

The lowered R.Q. and H.P. in aneurin-deficient rats can probably be explained only by a decreased food consumption. They are thus the manifestation of a partial fasting. Indeed it is known that anorexia is a precocious symptom of the avitaminosis B_1.

It is not easy to give a full explanation of our results at the present time in relation to present-day biochemical knowledge as to the point of attack of vitamin B_1 in the intermediate metabolism of carbohydrates.

Probably a great deal of importance must be given to the degree of avitaminosis, and therefore to the quantity of vitamin B_1 that still remains in the organism after treatment with a deficient diet.

Further researches are undoubtedly still necessary to clear up this point, and furthermore to demonstrate the

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	Rats	A Before administration			B After glucose administration		
		Number of determinations	Average	Standard deviation	Number of determinations	Average	Standard deviation
R.Q.	Controls	15	0·818 ± 0·010	± 0·042	19	0·936 ± 0·005	± 0·023
R.Q.	Avitaminosis	21	0·783 ± 0·007	± 0·0033	18	0·928 ± 0·006	± 0·026
Heat Produc. Cal/m²/hour	Controls	15	69·8 ± 1·90	± 7·4	19	75·1 ± 1·26	± 5·5
Heat Produc. Cal/m²/hour	Avitaminosis	20	58·1 ± 2·2	± 9·4	18	67·2 ± 1·97	± 9·4
Blood pyruvic acid mg/100 g	Controls	15	1·12 ± 0·075	± 0·291	12	1·55 ± 0·115	± 0·399
Blood pyruvic acid mg/100 g	Avitaminosis	25	2·38 ± 0·164	± 0·823	10	3·73 ± 0·471	± 1·493

degree of utilization of the carbohydrates in relation to the amount of aneurin in the tissues.

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Sommario

1° La produzione calorica e il quoziente respiratorio in ratti in avitaminosi B_1 diminuisce significativamente rispetto ai controlli.

2° La somministrazione di glucosio per sonda (1 g) provoca nei ratti in avitaminosi e nei controlli un notevole aumento del Q.R., accompagnato da un innalzamento della produzione calorica,

3° L'aumento di piruvato nel sangue conseguente alla somministrazione di glucosio è modesto e per gli animali in avitaminosi non è statisticamente significativo.

4° Questi risultati dimostrano che i ratti in avitaminosi conservano una non diminuita capacità di utilizzazione dei glucidi; resta da chiarire fino a che punto questo comportamento sia legato al permanere nell'organismo di piccole quantità di avitamina B_1.

Hemmung subkortikal ausgelöster Krampfpotentiale durch β-Hexachlorcyclohexan

Bei der Untersuchung der neurotropen Eigenschaften einiger Hexachlorcyclohexane (α-, β-, γ-Isomere) am Warmblüter (Ratten) wurden krampfhindernde Wirkungen nachgewiesen, deren Dauer nach einmaliger Applikation mehrere Tage betrug und von keinem bisher bekannten Pharmakon mit ähnlicher Wirkungsart erreicht wurde[1] Erhaltung der physiologischen Motilität, der normalen Temperaturregulation sowie unveränderte Funktion von Kreislauf und Atmung liessen darauf schliessen, dass die Nebenwirkungen bei den zur Erzielung der Krampfresistenz notwendigen Dosen des α- und β-Isomeren nur gering sein können[1]. Nur beim γ-Isomeren wurden vorübergehende initiale Krämpfe beobachtet, die für das Zustandekommen der antikonvulsiven Wirkung ohne Bedeutung sind. Die bisher gewonnenen Ergebnisse sprechen dafür, dass durch die Hexachlorcyclohexane im Stadium der Krampfresistenz eine eng umschriebene Funktionsänderung herbeigeführt wird, deren Existenz nur unter pathologischen Bedingungen durch das Ausbleiben experimenteller Krämpfe zu erkennen ist.

Durch einmalige Vorbehandlung der Versuchstiere mit den verschiedenen Isomeren liess sich eine Differenzierung der Wirkung von Krampfgiften erreichen, die mit den bisher üblichen Methoden nicht darzustellen war[2]. In Versuchen an dezerebrierten Ratten und bei Prüfung ihrer Rückenmarksreflexe konnte gezeigt werden, dass die Substrate für das Zustandekommen der krampfhindernden Wirkung im supratentorial gelegenen Vorderhirn lokalisiert sind. Es genügt schon die Abtragung einer Hemisphäre dieses Hirnanteiles, um den krampfhindernden Effekt zu beseitigen. Vorsichtige Durchschneidung der Kommissurenbahnen des Vorderhirns in der Mitte lässt dagegen die Behinderung der Krämpfe nach diesem Eingriff in vollem Umfange bestehen[2].

Zur weiteren Klärung des Angriffspunktes der Hexachlorcyclohexane haben wir elektro-enzephalographische Untersuchungen bei elektrisch und chemisch (Cardiazol) induzierten Reizzuständen des Gehirns durchgeführt. Bei diesen Untersuchungen interessierte uns hauptsächlich die β-Komponente, die generalisierte Krämpfe verschiedener Genese im Tierversuch beeinflusst[3].

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