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Hereditary Influences on the Hematic Level of Adenosinetriphosphate

A Twin Study

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Adenosinetriphosphate (ATP) is a component of the adenylic system of great biological interest. The phosphoric bonds are fixed in it at a high energy level and are stable under ordinary conditions. The energy they release may be transformed into mechanical, electric or light energy, and may also be used for the synthesis of proteins, polysaccharides and lipids.

ATP is synthesized in the course of a number of different metabolic processes, such as anaerobic glycolysis and oxidative phosphorylation (OP). The energy output of this latter process is much higher than that obtained through fermentation.

In the course of OP, the energy of the substratum is gradually released during the transfer from hydrogen to oxygen, brought about by pyridinic coenzymes. This gradually released energy makes the synthesis of ATP possible. The integrity of the mitochondria is a basic condition for the orderly development of this process.

Thyroid hormones inhibit OP, thereby reducing the P/O quotient. Calcium has a similar effect, while manganese, magnesium and insulin act in the opposite way.

ATP is largely utilized. The free energy it contains may be transformed, as we have seen, into other forms of biological energy. And it may be used for the synthesis of various types of molecules, which occurs through absorption of energy.

The interaction between ATP and contractile proteins plays a central role in the process of muscular contraction. Myocardium being also involved, some Authors connect certain heart diseases with reduced myocardic concentrations of ATP.

The numerous biological syntheses which occur in the liver are conditioned by the presence of adequate levels of ATP in this organ. These levels might prove to be altered in a number of hepatic diseases. Satisfactory concentrations of ATP are also required by the brain and kidneys.

In the blood, ATP is present in the erythrocytes and thrombocytes. In the former, the energy it supplies allows the cell membrane to play its delicate role. It seems that the hemolysis taking place in the spherocytes may be related to the ratio (inverse with respect to normal cells) between organic and inorganic phosphates.

The hereditary, hemolytic, non-spherocytic anemias found in Caucasoid patients might be due to a deficit of ATP regeneration as a result of a shortage or absence of pyruvicokinase.

The importance of the metabolic role of ATP, with its impact on the pathology of pre-eminent organs, lead us to search into its possible relationship with the genotype.

A sample of 20, apparently healty twin pairs, only selected as to age (6 year-old twins being preferred), was drawn from the Mendel Institute's large twin file. Blood was drawn from both twins (fasting) of a pair on the same day.

The determination of ATP was carried out by means of an enzymatic method (based on the data by Bücher and Schuart), in which the quantity of ATP is proportional to the consumption of reduced diphosphopyridinenucleotide. The latter takes place in the course of the reduction of 1-3 diphosphoglycerate to glyceraldehyde-3-phosphate. 1-3 diphosphoglycerate is first obtained from 3-phosphoglycerate, the phosphorylation of which is made possible by ATP.

The determination was made by drawing 1 ml of peripheral blood from the radial vein, deproteinizing it with 1 ml of perchloric acid. The material for the determination was obtained from the supernatant resulting after 5 minutes washing and cen-

Tab. I. Material

Pair N.	Zygosity	Age (in years)	Δ (in %)	
6457	MZ	6	17	15
6855	MZ	5	15	12
6269	MZ	6	16	16
6368	MZ	6.7	14	14
6081	MZ	6.9	18	18
4546	MZ	4.10	13	13
6098	MZ	6.6	19	20
6291	DZ	5.10	11	9
6084	DZ	6.7	17	15
6378	DZ	5.5	18	17
6693	DZ	6.10	14	12
10169	DZ	6	14	16
6877	DZ	6.5	14	11
6317	DZ	7	13	16
6206	DZ	7	15	15
6402	DZ	5.6	17	13
6776	DZ	4.6	15	13
6715	DZ	5	12	15
6377	DZ	5.7	14	13
6370	DZ	7.9	13	14

trifugation (1300). Mixing 20 ml of this supernatant with 0.04 ml of DPNH and 2.40 ml of TRAPG solution, the original solution was obtained, from which the prime coefficient of spectrophotometric extinction (E_1) was determined. Five minutes after the addition of 0.4 ml of GAPDH/PGK, a new coefficient of extinction (E_2) was read, and the difference necessary for the calculation of the ATP content in the sample of blood observed) determined. Values were read at a wave lenght of 340. The results are shown in Tab. I.

The values of Δ express the difference of extinction (in %). Multiplied by two, they give the quantity of ATP in the blood (in ml%). Normal values ranging between 10 and 16 mg (according to Hotzland-Laudahn) and between 19 and 32 mg (according to Denemann), most of our results are to be considered as normal.

Our purpose being to evaluate the possible relationship between ATP blood level and heredity, twin zygosity had first of all to be determined. This was done through the polysymptomatic method, blood grouping, and interchangeability criteria. As

Tab. II. Analysis of correlation and hereditary quantum

	$\hat{r}$	Sr	$\hat{H}$	E_H
MZ	0.8205	0.1155	**67.09**	6.02
DZ	0.4545	0.2200		

a result, our sample was divided into 7 MZ and 13 DZ twin pairs. The intrapair correlation coefficient and the relative variations were then calculated in the two series.

The correlation coefficient is 0.8205 vs. 0.4545 and the variability 0.1155 vs. 0.2200, respectively in MZ and DZ twins, that is to say: MZ twins show a much higher correlation with respect to blood ATP values. By applying Holzinger's formula, the hereditary quantum was then estimated, together with its possible error:

$$\hat{H} = 67.09 \quad \text{and} \quad E_H = 6.02$$

It may be concluded that the hematic level of ATP is remarkably conditioned by heredity, namely for about two thirds.

Summary

Dosage of the hematic level of ATP has been afforded in 20 (7 MZ and 13 DZ) twin pairs aged 4-6 years. The intrapair correlation coefficient has been calculated and resulted to be significantly higher in MZ than DZ twin pairs. The hereditary " quantum " in the determination of the hematic level of ATP was also estimated and resulted to be of about two thirds.

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RIASSUNTO

È stato effettuato il dosaggio del livello ematico dell'ATP in 20 coppie (7 MZ e 13 DZ) di gemelli sani di 4-6 anni. Sui dati ottenuti è stato calcolato il coefficiente di correlazione intracoppia, che è risultato più alto nei gemelli MZ che nei DZ. È stato anche stimato il « quantum » ereditario nella produzione del livello ematico dell'ATP, che risulta dell'ordine di circa due terzi.

RÉSUMÉ

Le dosage du niveau hématique de l'ATP a été accompli chez 20 couples gémellaires (7 MZ et 13 DZ). Le coefficient de corrélation intra-couple résulte bien plus élevé chez les jumeaux MZ vis-à-vis des DZ. Le « quantum » héréditaire dans la production du niveau hématique de l'ATP est d'environ deux tiers.

ZUSAMMENFASSUNG

Bei 20 gesunden Zwillingspaaren (7 EZ und 13 ZZ) im Alter von 4-6 Jahren wurde der ATP-Spiegel im Blut gemessen. Aus den Ergebnissen wurde der Korrelationskoeffizient zwischen den einzelnen Paarlingen berechnet, der bei EZ höher als bei ZZ war. Es wurde auch das « Erb-Quantum » beim Zustandekommen des ATP-Spiegels im Blut bestimmt, das ungefähr zwei Drittel beträgt.

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