Résumé

L'auteur a obtenu dans le lapin un sérum antimitochondre du foie de rat. Le sérum antimitochondre a une faible action inhibante sur la succinoxydase des mitochondres du foie du rat, tandis qu'il accélère l'activité des mitochondres du rein. Les sérums normaux de cobayes, de lapins, de rats, de souris, de chiens et d'hommes ont une action accélérante qui est supprimée après incubation à 37,5°C pour 30 minutes.

L'auteur démontre, par les inhibiteurs de la lipase du sérum, que l'action des sérums normaux doit être rapportée à cet enzyme.

Enzymatic Activity and Protein Amounts in the Liver

VIRTANEN and coll.[1] relate interesting observations on the behaviour of certain enzymatic activities of *Escherichia Coli, Torulopsis utilis, Pseudomonas fluorescens*, when the protein amount of the cell of the microorganisms is reduced by the development of such microorganisms on satisfactory culture media.

When their nitrogen content diminishes, the activity of certain enzymes [enzymatic systems of respiration (*Escherichia coli, Torulopsis utilis*), catalase (*E. coli, Torulopsis utilis, Pseudomonas fluorescens*), proteolytic enzymes (*E. coli, Torulopsis utilis, Pseudomonas fluorescens*), saccharase (*Torulopsis utilis*)], remains almost the same as in that of the normal cell; other enzymes, on the contrary [saccharase (*E. coli*), lactase (*E. coli*), formic dehydrogenase (*E. coli*), enzymatic system of the anaerobe glycolysis (*E. coli*)], show a remarkable decrease in their activity. Therefore in the cells of microorganisms and perhaps of animal organisms, certain enzymes must be present (VIRTANEN and WINKLER[2]) which are indispensable for life and which maintain their activity even when the nitrogen content is reduced, and other enzymes, not indispensable for life, which lose most or all their activity when the nitrogen content of the cell is reduced. Yet, MILLER[3] observed in the liver of fasting rats after 7 days a decrease in the activity of some enzymes (catalase, alkaline phosphatase, xanthine dehydrogenase, cathepsin) of the same degree or higher than the protein loss of the tissue. HARKNESS, SEIFTER, NOVIC, and MUNTWYLER[4] also in the liver of rats receiving a protein-deficient diet, found a decrease in the concentration of A co-enzyme, which is essential for the sulfamide acetylation, proportional to the reduction of the protein concentration in the liver. Therefore the behaviour of the enzymes in the tissues of animals deficient in nitrogen analogous to that observed in micro-organisms is not yet ascertained.

To examine the question, I compared the activity of some enzymes (esterase, phosphomonoesterase, pyrophosphatase, adenosintriphosphatase, dipeptidase, arginase, catalase, succinic dehydrogenase, choline dehydrogenase) of the liver of rats receiving a qualitatively and quantitatively suitable diet, with that of rats receiving a protein deficient diet, followed by a remarkable decrease of the nitrogen content of the tissue.

Therefore 10–12 weeks old rats (♂) were fed during 25 days on a diet composed of saccharose (87%), olive oil (8%), a salt mixture (4%), dry yeast (1%), with the addition of a suitable amount of thiamine, riboflavin, niacin, pantothenic acid, pyridoxine, inositol, choline, axerophthol, calciferol, tocoferol, 2-methyl-1,4-naphtoquinone. Ten rats fed with the same diet, but with casein substituted for part of the saccharose (24%), were used as animals of control. After 25 days, the rats were killed by decapitation, after fasting 18 hours. Immediately their liver was removed and used to test the enzymatic activity as a homogenate, prepared in Potter and Elvehjem's apparatus.

The esterase was determined according to LENTI[1]. Phosphomonoesterase and adenosintriphosphatase were measured in accordance with methods suggested by CAFIERO[2]. The determination of dipeptidase was obtained by measuring the carboxyl groups liberated in the glycil-glycine hydrolysis after formaldehyde blocking of the aminic groups. The arginase was determined according to LENTI[3]. For the catalase we used the method suggested by VON EULER and JOSEPHSON[4] Succinic dehydrogenase and choline dehydrogenase were tested, measuring the O_2 loss in Warburg's apparatus.

The quantity of water, lipids and nitrogen was ascertained in parts of the liver. Water was calculated from the difference of weight after drying to 103°, lipids after ether extraction of the dry material. Nitrogen was determined on dried and lipide-free material using Kjeldahl micromethod.

Under the above mentioned conditions, the liver of the rats receiving a protein-deficient diet shows, as has been long known, a decrease of nitrogen content and an increase of lipide content in relation to the liver of animals receiving a quantitatively and qualitatively normal diet, while the water content is not appreciably modified (Table I).

Table I

Water, lipid and nitrogen content of the liver of rats receiving a normal and a protein-deficient diet

Diet	Water g/kg	Lipide g/kg	Nitrogen g/kg
Of control	677 (643–699)	54 (31–79)	30 (20–35)
Protein-deficient . . .	685 (639–717)	96 (62–130)	19 (13–23)
Difference in %	−1·2	+77·8	−36·7

The behaviour of the examined enzymatic activities differs highly. Phosphomonoesterase shows a very remarkable increase. Esterase, catalase, choline dehydrogenase show a remarkable decrease, a less remarkable decrease is to be observed for pyrophosphatase, adenosintriphosphatase, arginase, and succinic dehydrogenase. Dipeptidase remains unchanged (Table II).

From such various changes of the activity of the examined enzymes it is impossible to assume, at least under the adopted experimental conditions, a definite relation between the concentration of the above-mentioned enzymes and the protein concentration of the liver. Even a division of the liver enzymes into indispensable and

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[2] M. CAFIERO, Boll. Soc. Ital. Biol. Sper. *24*, 1322 (1948); *26*, 159 (1950).
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Table II

Enzymatic activities of the liver of rats receiving a normal and a protein-wanting diet enzymes

Diet	Esterase ml. 0·01 *n* NaOH	Phosphomonoesterase inorganic P split off γ	Pyrophosphatase inorganic P split off γ
Of control . . .	3·19 (2·30–3·96)	13·7 (9·5–20·9)	54·6 (45·6–74·1)
Protein-deficient	0·76 (0·33–1·12)	49·8 (28·5–64·7)	39·8 (31·3–49·4)
Difference in % .	– 76·2	+ 263·5	– 27·1
	Adenosintriphosphatase inorganic P split off (γ)	Dipeptidase % of hydrolised glycil-gycline	Arginase % of arginine split off
Of control . . .	109·1 (93·1–125·4)	88·3 (79·6–97·3)	93·3 (80·1–99·0)
Protein-deficient	84·4 (76·0–93·0)	81·3 (69·9–90·0)	70·7 (52·5–85·0)
Difference in % .	– 22·6	– 7·9	– 24·2
	Catalase $K_{10^{-2}}$	Succinic-dehydrogenase QO_2	Choline-dehydrogenase QO_2
Of control . . .	2·2 (1·5–3·4)	70·9 (52·6–88·9)	69·6 (55·0–85·4)
Protein-deficient	0·70 (0.43–0·93)	55·9 (42·1–76·6)	14·1 (2·3–26·3)
Difference in % .	– 68·2	– 21·1	– 79·7

not indispensable according to VIRTANEN and WINKLER[1] for the microorganisms does not seem to be feasible at present.

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Zusammenfassung

Die Verfasserin hat die Wirkung einer eiweißarmen, im übrigen aber quantitativ und qualitativ ausreichenden Diät auf den Gehalt verschiedener Enzyme der Rattenleber untersucht. Geprüft wurden Esterase, Phosphomonoesterase, Adenosintriphosphatase, Pyrophosphatase, Dipeptidase, Arginase, Katalase, Succinodehydrogenase und Cholindehydrogenase. Unter den erwähnten Versuchsbedingungen wurde folgendes gefunden: Vermehrte Aktivität der Phosphomonoesterase; verringerte Aktivität der Esterase, Katalase, Cholindehydrogenase, Pyrophosphatase, Adenosintriphosphatase, Arginase, Succinodehydrogenase und eine unveränderte Aktivität der Dipeptidase. Diese Effekte sind mit einer Stickstoffabnahme und einer Zunahme in der Lipoide der Leber verbunden, während der Wassergehalt ungefähr der gleiche bleibt.

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Cloroamine e anergia mesenchimale

La reazione delle cellule del sistema istiocitario del polmone, come noi l'abbiamo osservata a seguito della iniezione intraparenchimale di una piccola dose di istamina, in vari animali da esperimento, presenta, come caratteristica essenziale, la iperplasia intensa di tutti gli elementi istiocitari locali[1]. Il polmone si presta bene per lo studio di questa reazione perchè è un organo prevalentemente vascolo-connettivale. Per i suoi attributi anatomici (formazione di barriere cellulari) e funzionali (formazione di globuline anticorpo, di principi protettivi-opsonine, proteasi, alessina, ecc.)[2] questa reazione mesenchimale iperplastica ha significato altamente difensivo.

Si deve ritenere che la moltiplicazione delle cellule mesenchimali sia regolata, come avviene per le cellule di altri tessuti, dalle modificazioni del rapporto glicolisi-respirazione[3] nel senso che ogni influenza che può dare la spinta alla moltiplicazione cellulare mette in funzione sempre lo stesso meccanismo di emergenza, la glicolisi, quello stesso che ha luogo ogni qualvolta non vi sia O_2 sufficiente per adeguare le esigenze della respirazione alla richiesta energetica di un tessuto[4]: in funzione della nota regola di Pasteur, un parziale deficit di O_2 deve agire come stimolo della moltiplicazione delle cellule. In questo senso l'istamina, riducendo gli scambi respiratori delle cellule[5], ne attiverebbe i processi glicolitici e quindi la capacità moltiplicativa.

Poichè questa reazione connettivale iperplastica risulterebbe così in funzione di un elevato rapporto glicosio glicolizzato: glicosio ossidato, apparirà interessante che a noi sia riuscito di dimostrare, in conigli gravemente diabetizzati con allossana, la quasi completa anergia del connettivo polmonare, dopo stimolo istaminico, pneumotoracico e papainico[6]. In base a questi risultati possiamo ritenere probabile che anche altre condizioni sperimentali che compromettano il metabolismo glicidico, siano in grado di inibire la reazione connettivale iperplastica: modernamente infatti si accetta come dimostrato[7], che molte sostanze che impediscono la moltiplicazione cellulare hanno in comune la capacità di ledere i meccanismi enzimatici del metabolismo carboidrato.

Così come in animali gravemente diabetizzati con allossana[6], anche con dosi tossiche di azoipriti abbiamo potuto dimostrare la inibizione della reazione istiocitaria iperplastica da istamina, nel polmone.

Sono evidenti i punti di contatto fra le due condizioni, diabetica e tossica da cloroamine: l'ostacolo frapposto dalle azoipriti (corpi tioloprivi[8]) ad una rapida utilizzazione glicidica sarebbe da riferire in particolare, all'inibizione di una serie di enzimi —SH, vettori di fosfati,

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