increasing body weight in the rats which could see in comparison with blind rats, may be related to the excretion of pituitary hormones. The findings[3] of smaller increase of lipoids and cholesterol and quicker increase of dry matter in the body of the rats which can see compared with blind rats, can be explained by the more intensive utilization of lipoids as energy donators for the synthesis of proteins stimulated by growth and other pituitary hormones, on the basis of elevated nucleic acids content. This greater increase of nucleic acids in rats beginning to see may be related to the completion of functional evolution of the eyes and to their action on the diencephalo-pituitary system. During postembryonal evolution, the influence of elevated secretion of pituitary hormones returned to normal limits and the procentual content of nucleic acids in the organism continued to decrease in agreement with the trend of ontogenetical evolution of the nucleic acids content in the rat body.

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Zusammenfassung

Bei Ratten wurde der Gehalt an Desoxyribonukleinsäure und Ribonukleinsäure von der Geburt bis zum 29. Lebenstag verfolgt. Mit Beginn des Sehens erhöht sich der gesamte Nukleinsäuregehalt des Organismus; vorübergehend zeigt sich auch ein prozentualer Anstieg. Diese Erhöhung des Nukleinsäuregehaltes wird als Folge der vermehrten Sekretion der durch den Lichtreiz stimulierten Hypophyse erklärt.

Influence of Oxidative Phosphorylation Inhibitors on the Histamine Release in the Anaphylactic Reaction *in vitro*

Several recent experiments have indicated that metabolic factors are closely involved in the mechanism of histamine liberation during the anaphylactic reaction. The importance of the metabolic factors could be demonstrated by employing specific enzymatic inhibitors[1], or studying the influence of metabolites consumed during the cellular work[2].

Using the latter method, it could be demonstrated that some metabolites, such as succinate, α-keto-glutarate, acetate[3], enhance the amount of histamine released from sensitized guinea-pig lung tissue by the anaphylactic reaction *in vitro*.

MONGAR and SCHILD[4], studying the effect of a series of enzymatic inhibitors, showed that histamine release can be inhibited by a large number of them, and that the substances which inhibited the release of histamine in anaphylaxis also inhibited oxygen consumption. MONGAR and SCHILD concluded that the anaphylactic reaction requires a functioning cell while admitting that the experiments provided little evidence on the precise nature of the reactions involved.

It seemed important to study the influence of some potent inhibitors of the oxidative phosphorylation on the anaphylactic reaction, since we showed that there is an increase in the oxygen uptake by the tissue[5] during the anaphylactic reaction, indicating an increase in the cellular work.

For the experiments, guinea-pigs were sensitized with horse sera previously treated by potassium alum, according to the Caulfield method. Sensitization of the animals was assayed by the Schultz-Dale reaction on a piece of the ileum. The lungs of sensitized animals were sliced by hand with a sharp razor and the slices transferred to the Ringer Barron medium of the main chamber of Warburg flasks. Sodium succinate, and the enzymatic inhibitor at the required concentration, were kept in the side-bulb of the flasks and tipped into the main chamber after thermal equilibration, or incubated together with the tissue. Antigen was added 30–150 min after incubation and left a further period of 30 min for the histamine liberation. Oxygen uptake was measured every 30 min, and calculated as mm^3/mg dry weight/h. Histamine was assayed in the supernatant fluid by the guinea-pig ileum method and calculated in μg of histamine dihydrochloride by g wet weight. As inhibitors of the oxidative phosphorylation, 2,4-dinitrophenol, pentachlorophenol, and sodium azide were investigated and the results are given in Table I.

All the three substances assayed caused an effective inhibition of the histamine release. 2,4-dinitrophenol at the concentration of 10^{-4} *M*, known as uncoupling phosphorylation from cellular oxidation[6], almost completely inhibited the liberation of histamine, leaving the oxygen uptake normal or even increased. Pentachlorophenol[7] and sodium azide[8] which are known to act like dinitrophenol, prevented significantly the histamine release by the antigen. Decrease in the Q_{O_2} observed in the experiments with the azide cannot explain the lowering in the histamine released. Using low tensions of oxygen (10% O^2 and 90 N^2), a decrease of the Q_{O_2} of around 50% can be obtained without decrease in the histamine released[9].

In another series of experiments, the influence of 2,4-dinitrophenol on the histamine released by the lungs was investigated in a medium containing succinate and α-ketoglutarate. The results of Table II show the strong inhibitory action of 2,4-dinitrophenol, both on the additional histamine released by the effect of substrates, and by the antigen alone.

These experiments give suggestive evidence that the histamine released during the anaphylactic reaction needs energy-rich phosphorylated compounds. The experiments with succinate and other metabolites of the Krebs cycle can be explained by supposing that the oxidation of these substrates led to an increase in available phosphorylated compounds[10].

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Table I

Action of some inhibitors of the oxidative phosphorylation on the oxygen uptake and histamine release by antigen from sensitized guinea-pig lung slices

Inhibitor			Histamine released (μg/g wet weight)		
Concentration	Incub. time* min	Q_{O_2}**	Without antigen (a)	With antigen (b)	(b–a)
0	90	5·84 ± 0·29 (4)	3·3 (1)	15·8 ± 1·4 (4) + +	12·5
2,4-dinitrophenol 10^{-4} *M*	90	5·89 ± 0·31 (4)	3·4 (1)	5·2 ± 0·35 (4) + +	1·8 + +
0	150	6·92 ± 0·20 (4)	2·5 (1)	9·4 ± 0·47 (4) + +	6·9
2,4-dinitrophenol 10^{-4} *M*	150	6·85 ± 0·34 (4)	3·1 (1)	5·1 ± 1·0 (4) + +	2·0 + +
0	30	7·62 ± 0·40 (2)	1·8 (1)	10·2 ± 1·4 (2)	8·4
2,4-dinitrophenol 10^{-4} *M*	30	9·00 ± 0·03 (2)	1·9 (1)	2·8 ± 0·5 (2) + +	0·9 + +
0	60	4·54 ± 0·15 (4)	2·5 (1)	3·9 ± 0·17 (4)	1·4
Pentachlorophenol 10^{-5} *M*	60	4·39 ± 0·19 (4)	2·4 (1)	3·4 ± 0·22 (4) +	1·0 +
0	60	6·95 ± 0·34 (4)	0·9 (1)	4·5 ± 0·13 (4)	3·6
Pentachlorophenol $2{\cdot}5 \times 10^{-5}$ *M*	60	6·40 ± 0·45 (4)	1·0 (1)	1·1 ± 0·13 (4) + +	0·1 + +
0	60	5·75 ± 0·31 (4)	2·2 (1)	17·0 ± 1·65 (4)	14·8
Pentachlorophenol 5×10^{-5} *M*	60	2·98 ± 0·20 (4)	3·0 (1)	3·4 ± 0·18 (4)	0·4 + +
0	120	4·18 ± 0·13 (4)	2·8 (1)	9·0 ± 0·67 (4)	6·2
Azide 1×10^{-3} *M*	120	3·25 ± 0·28 (4)	2·8 (1)	5·2 ± 0·26 (4) + +	2·4 + +
0	120	3·97 ± 0·16 (4)	2·0 (1)	16·9 ± 0·5 (4)	14·9
Azide $2{\cdot}5 \times 10^{-3}$ *M*	120	2·76 ± 0·04 (4)	2·4 (1)	4·1 ± 0·2 (4) + +	1·7 + +
0	120	5·42 ± 0·23 (4)	3·1 (1)	20·6 ± 1·1 (4)	17·5
Azide 5×10^{-3} *M*	120	1·96 ± 0·16 (4)	4·3 (1)	4·6 ± 0·2 (4) + +	0·3 + +

* Incubation time before antigen addition.
** Figures taken the 30 min following antigen addition (in parenthesis number of Warburg flasks used).
\+ '*t*' test between the means: $P < 0{\cdot}05$.
\+ + '*t*' test between the means: $P < 0{\cdot}01$.

Table II

Inhibition by 2,4-dinitrophenol of the effect of succinate and α-keto-glutarate on the histamine released during the anaphylactic reaction *in vitro*

2,4-dinitrophenol, succinate, and α-keto-glutarate			Histamine released (μg/g wet weight)		
Concentration	Incub. time* (min)	Q_{O_2}**	Without antigen (a)	With antigen (b)	(b–a)
0	120	5·31 ± 0·10 (3)	2·4 (1)	5·2 ± 0·17 (3)	2·8
Succinate 4×10^{-2} *M*	120	9·81 ± 0·27 (3)	2·8 (1)	7·2 ± 0·65 (3) + +	4·4 + +
Succinate 4×10^{-2} *M* + DNP 10^{-4} *M*	120	9·66 ± 0·79 (3)	3·8 (1)	3·6 ± 0·36 (3) + +	0·0 + +
0	120	4·10 ± 0·21 (3)	3·0 (1)	14·3 ± 0·95 (3)	11·3
Succinate 4×10^{-2} *M*	120	10·39 ± 0·83 (3)	3·0 (1)	21·9 ± 0·47 (3) + +	18·9 + +
Succinate 4×10^{-2} *M* + DNP 10^{-4} *M*	120	10·40 ± 0·13 (3)	3·1 (1)	3·5 ± 0·12 (3) + +	0·4 + +
α-keto-glutarate 10^{-2} *M*	30	7·69 ± 1·10 (2)	0·0 (1)	6·2 ± 0·7 (2)	6·2
α-keto-glutarate 10^{-2} *M* + DNP 10^{-4} *M*	30	9·95 ± 0·27 (3)	0·0 (1)	1·0 (3) + +	< 1·0 + +

* Incubation time before antigen addition.
** Figures taken the 30 min following antigen addition (in parenthesis number of Warburg flasks used).
\+ '*t*' test between the means: $P < 0{\cdot}05$.
\+ + '*t*' test between the means: $P < 0{\cdot}01$.

Résumé

Des expériences ont été faites pour étudier l'influence des inhibiteurs de la phosphorylation oxydative sur la libération d'histamine pendant la réaction anaphylactique.

Une inhibition de la libération d'histamine a été observée, suggérant que des composés phosphorylés riches en énergie sont liés au mécanisme de libération.

Sur les variations stressogènes quantitatives de la sérotonine dans le cerveau

L'étude du rôle de la sérotonine dans le syndrome d'adaptation présente un intérêt particulier. Au cours de nos recherches sur l'influence de la réserpine sur le système neuro-endocrine des lièvres soumis à l'émotion, nous avons constaté une réponse stressogène notable des cellules neuro-ganglionnaires de la région hypothalamique[1–3]. Ceci nous a suggéré l'idée d'une étude sur les variations quantitatives de la sérotonine au niveau du cerveau sous l'effet de la frayeur.

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