minor modifications. The prothrombin time was determined six times for each chick at the intervals indicated in the table, counted from the intravenous injection of aqueous colloidal, or crystalloid respectively solutions of the substances. The amounts used were stoichiometrically equivalent to 100 times the limit dose of menadione (0·03 micrograms per gram of body weight) which results in normal prothrombin time after 22 h when given orally in oil solution.

Prothrombin times in seconds at various intervals after the intravenous injection of vitamin K_1, Menadione and Synkavit. Normal value = 25 s.

	0 h	0·5 h	1 h	1·5 h	2 h	22 h
Vitamin K_1 . .	223	44	30	27	28	22
Vitamin K_1 . .	153	39	32	31	30	24
Menadione . .	165	155	59	40	30	22
Menadione . .	251	206	79	43	33	25
Synkavit. . .	154	120	41	31	27	23
Synkavit. . .	170	151	59	39	34	25

A similar difference between vitamin K_1 and the other substances is observed when the comparison is carried out at much lower or higher levels.

Further details of this study will be published elsewhere.

H. Dam and Ebbe Søndergaard

Department of Biochemistry and Nutrition, Polytechnic Institute, Copenhagen, November 1st, 1952.

Zusammenfassung

Die Wirkungsgeschwindigkeiten von intravenös injiziertem Vitamin K_1, Methylnaphthochinon und Synkavit in Vitamin-K-frei ernährten Küken wurden verglichen. Es zeigte sich, dass in den ersten Stunden nach der Injektion Vitamin K_1 die Prothrombinzeit viel schneller zum Absinken brachte als die beiden anderen Verbindungen.

Nucleic Acids and Proteins in the Liver of Guinea Pigs dying from Experimental Ascorbic Acid Deficiency

At present it is generally accepted[1] that total pentosenucleic acid (P.N.A.) of the liver and of many other tissues is readily diminished by protein-deficient diet or starvation, whereas total desoxypentosenucleic acid (D.N.A.) remains unaffected, and that the loss of P.N.A. is paralleled by that of proteins as well as phospholipids. Studying the relation between the P.N.A. content and the basophilic pattern of mammalian livers, we had an occasion of examining scorbutic guinea pig livers which showed a marked diminution of total protein content without any sign of concomitant loss of P.N.A.

Guinea pigs weighing about 300 g were fed on ascorbic acid-deficient diet by removing green grass and vegetables from stock diet. In some four weeks the animals became typically scorbutic and began to die. During this period they did not grow but lost body weight gradually, while control animals on normal diet gained much body weight. After the appearance of scorbutic symptoms animals ate little, and their body weight decreased rapidly. It might seem as if the animals died from starvation during the last few days; but this can not have been the case, as shown below. Livers of three dying animals, two of which (II and III in the Table) showed a typical picture of premortal enlargement of mitochondria[1], were subjected to determination of nucleic acids and proteins by Schneider procedure[2]. As many guinea pigs on normal diet weighing about 300 g (equal to the initial body weight of experimental animals) served as the control. Livers of individual animals were perfused with ice-cold saline and analyzed separately. Orcinol and diphenylamine tests and digestion with $H_2SO_4 - H_2O_2$ followed by hypobromite-iodometry were employed for the determination of P.N.A.-P, D.N.A.-P., and protein-N, respectively[3]. The D.N.A. content of the average liver nuclei was also determined as reported elsewhere[4], and the total number of liver nuclei was calculated from D.N.A. contents of the nuclei and the whole tissue.

The results are summarized in accompanying Table. For comparison, our own data on rats dying from prolonged starvation[5] are also listed. Total D.N.A. and D.N.A per nucleus of the liver, and hence the number of liver nuclei showed no change from the normal values in both the scorbutic guinea pigs and the fasted rats, suggesting that no necrotic degeneration of liver cells had occurred before the final death. This adds a new example to the concept of the stability of D.N.A. in the liver of adult animals[6]. Now, total P.N.A. of the scorbutic guinea pigs remained constant, whereas that in the fasted rats decreased down to about one third of the control, although the loss of the body weight was nearly comparable in both cases. The striking stability of P.N.A. in the scorbutic liver might be partially reflected by less pronounced decrease of liver weight in these animals than in fasted rats, but this may rather be due to other constituents such as glycogen and lipids. Protein-N of scorbutic animals, however, does show a loss comparable in order with the body weight, but to a lesser extent than in fasted animals. As the number of nuclei in the scorbutic liver is the same as that of the control, the above findings concerning P.N.A. and proteins hold in cell unit also.

The link between the protein and P.N.A. contents of the liver tissue is noted by several workers[7]. As shown in the table, in prolonged starvation the decrease of P.N.A. was, indeed, even more extensive than that of proteins. Therefore, it is rather surprising that the ascorbic acid deficiency resulting in a marked loss of liver protein does not affect the liver P.N.A. at all. Here it should be remembered that the metabolism of our scorbutic animals had been damaged so severely that they were almost dying at the time of analysis.

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Nucleic acids, proteins, and cell number of normal and scorbutic guinea pig livers at the same growth stage

	Animal	Body weight initial g	Body weight at death g	Liver weight g	Total D.N.A.-P. mg	D.N.A. per nucleus μμg	Cell number ×10⁶	Total P.N.A.-P. mg	Total protein-N mg	P.N.A.-P protein-N
Normal	I	285	285	10·0	2·59	9·03	2890	6·32	247	0·026
	II	300	300	11·0	2·78	9·06	3100	6·63	253	0·026
	III	290	290	9·0	2·61	9·04	2920	5·89	202	0·029
	Mean	292	292	10·0	2·66	9·04	2970	6·28	234	0·027
Scorbutic	I	290	220	9·5	2·64	9·13	2920	6·52	212	0·031
	II	290	220	8·6	2·83	9·06	3150	6·08	158	0·039
	III	290	200	7·6	2·54	9·14	2810	6·14	161	0·038
	Mean	290	213	8·6	2·67	9·11	2960	6·24	177	0·036
	Per cent of normal	99	73	86	100	101	100	99	76	133
	Rats in starvation: per cent of normal	100	66	47	99	98	101	35	44	76

There is a report of Russian workers[1] suggesting that nuclei of scorbutic guinea pig livers contain less D.N.A. and more P.N.A. than nuclei from normal animals. They have speculated that ascorbic acid may be involved in the mechanism of D.N.A. biosynthesis. Nothing in our data seems to support such an idea, although these were obtained with whole liver tissues. The reason of the stability of P.N.A. in the ascorbic acid-deficient liver is not clear. Nor can the quetion be answered at present of whether this represents a blocking of both the breakdown and the biosynthesis of P.N.A. or the maintenance of balanced turnover activity during the whole period of ascorbic acid deficiency. The role of ascorbic acid in the metabolism of P.N.A. may be disclosed by enzymatic studies and isotopic experiments with scorbutic livers. It may then contribute something to the formulation of the underlying mechanism of the possible link between turnover or biosynthesis of P.N.A. and that of proteins[2], a question being at present subject to much discussion[3].

MICHIO FUKUDA and ATUHIRO SIBATANI

Microbial Diseases Research Institute, University of Osaka, Doozima-Nisimati 7, Kitaku, Osaka, Japan, September 9, 1952.

Zusammenfassung

Ein Experiment mit an Skorbut sterbenden Meerschweinchen. Der Proteinverlust der Leber bei diesen Tieren wird nicht von einer gleichzeitigen Verminderung der Pentosenukleinsäure begleitet; letztere bleibt vielmehr bis zum Tod normal.

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Cortison und die Leukozytenphagozytose

Wiederholt berichteten wir, dass infolge Reizung des N. splanchnicus in der Nebenniere ein Prinzip frei wird, welches die phagozytosefördernde Fähigkeit des Blutserums steigert. Nach unseren Untersuchungen hatten weder Adrenalin noch wässerige Rindenextrakte, noch das «DOCA» *in vitro* eine unmittelbare Wirkung auf die Phagozytose[1]. Es schien uns daher geboten, auch die Wirkung des Cortisons zu untersuchen.

Die Versuche wurden an Kaninchen bzw. an Ratten durchgeführt. Die Cortisonwirkung wurde zunächst an überlebenden Reizleukozyten geprüft, die wir aus der Bauchhöhle der Ratten nahmen. Mit der Methode nach WRIGHT wurde der Grad der Phagozytose bestimmt. Unsere Systeme enthielten 0,5 cm³ Leukozytensuspension (1 mm³: 10000 Zellen), 0,1 mm³ Rattenserum, 0,1 cm³ Bakteriensuspension (1 mm³: 10 Millionen Keime) und Cortisonlösung (Cortisone Acetat «MERCK») bzw. physiologische Kochsalzlösung. Nach einer einstündigen Inkubation im Thermostat wurde in gefärbten Ausstrichpräparaten die Zahl der von 400 Leukozyten aufgenommenen Bakterien (Staphylococus pyogenes aureus bzw. Typhusbazillen) bestimmt. Die Resultate sind durch statistische Berechnungen belegt. Fehlergrenze der Berechnung (Streuung): $\sigma = \pm 9{,}57\,\%$.

Auf Grund der Untersuchungen lässt sich einheitlich feststellen, dass die Bakterienphagozytose der Leukozyten durch Cortison in einer Endkonzentration von 1 mg% nicht verändert wird[2], woraus folgt, dass das auf Wirkung der Splanchnikusreizung in der Nebenniere frei werdende phagozytosefördernde Prinzip nicht mit dem Cortison identisch sein kann.

In einer weiteren Versuchsreihe wurden 10 Kaninchen für die Dauer von 1–3 Tagen i.m. mit Cortison behandelt. Die phagozytosefördernde Fähigkeit wurde nach 24 h mit Rattenleukozyten wie oben bestimmt. Über mehrere Tage hinweg wurde auch die Phagozytosetätigkeit der zirkulierenden Leukozyten des Tieres mit dem von uns modifizierten Verfahren von PLATONOV bestimmt.

Die Veränderungen der Mittelwerte unserer Versuche sind in beiden Abbildungen zu sehen.

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