

INHIBITORY EFFECT OF THE RESTRICTION OF VITAMINS AND FOOD ON CARCINOGENESIS AND SURVIVAL OF GUINEA-PIGS WITH INDUCED TUMOURS

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Abstract — Tumours induced in guinea-pigs with injection of 3-methylcholanthrene developed after significantly longer latent periods and the survival with tumours was significantly longer in the experimental than in the control group of animals. The experimental animals were fed a low-vitamin diet which also was somewhat restricted in the amount of food in comparison with the diet of control animals. The control animals were fed an abundant diet which was rich in vitamins.

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Introduction — The aim of the experiment described here was to establish the effects of a diet low in vitamins on the genesis and growth of tumours in guinea-pigs, induced with injection of 3-methylcholanthrene.

Materials and methods — The experiment was performed in the following way: 40 guinea-pigs weighing 400—350 g were divided into a control and an experimental group. Twenty mg 3-methylcholanthrene dissolved in 1 ml olive oil was injected subcutaneously into the thigh of the right hind leg of each animal. The control group of animals was fed daily the following diet: 30 g guinea-pig chow with no vitamin added and 120 g grass in summer, and 30 g guinea-pig chow, 15 g unautoclaved hay and 135 g beet in winter. The experimental group was maintained on a diet of 30 g guinea-pig chow, 30 g grass and 15 g hay autoclaved for 1 hr at 121°C in summer, and 30 g guinea-pig chow, 15 g autoclaved hay and 45 g beet in winter. In the experimental group the quantity of foods containing vitamins was thus restricted to about a fourth of that given to control animals. This means that the daily intake of vitamins in the experimental animals was also a fourth of that in the control animals.

The first tumours, one in the control and one in the experimental group, were detected 144 days after injection of 3-methylcholanthrene. The animals were than inspected once weekly for the appearance and size of tumours. After the death of a tumour-bearing animal an autopsy was carried out and the tumour was histologically examined. The experiment was completed when the last tumour-bearing animal died.

Results — The results of the experiment are shown in table 1 and 2. Of the original 20 animals in each group one animal died before tumours began to develop. So 19 animals remained for analysis in each group.

Group	Latent periods of tumours in days
Control group (17 tumours/19 animals)	144, 151, 158, 165, 165, 172, 172, 193, 200, 200, 214, 214, 242, 242, 242, 256, 335
Experimental group (16 tumours/19 animals)	144, 151, 221, 229, 235, 249, 256, 286, 291, 376, 383, 392, 409, 409, 425, 431

Table 1 — Latent periods of tumours induced by methylcholanthrene in the control and experimental groups of guinea-pigs

Group	Survival with the tumour in days
Control group	42, 44, 57, 73, 76, 83, 83, 88, 91, 102, 103, 105, 111, 131, 135, 160, 179
Experimental group	67, 95, 96, 103, 105, 121, 122, 122, 127, 139, 145, 158, 165, 215, 265, 310

Table 2 — Survival of tumour-bearing animals in the control and experimental groups of guinea-pigs

Tumours developed in 17 animals in the control group and in only 16 animals in the experimental group. All the tumours were malignant, mostly fibrous histiocytomas and fibrosarcomas. A few were chondrosarcomas, liposarcomas and osteosarcomas.

The latent periods of the tumours in both groups of animals are presented in table 1. Statistical analysis with the Wilcoxon two-sample rank test showed that the latent periods in the experimental group were significantly longer than in the control group ($P < 0.01$). This result indicates that a diet low in vitamins has an inhibitory effect on carcinogenesis.

Table 2 shows the survival time of animals after the development of palpable tumours. Statistical analysis demonstrated that animals in the experimental group lived significantly longer after the development of tumours than the control group ($P < 0.02$). This suggests that a low-vitamin diet prolongs the survival with tumour.

Discussion — The results obtained are not surprising: they are in agreement with numerous published reports demonstrating the involvement of various vitamins in the genesis and growth of tumours. Many authors have shown that various vitamins, especially vitamin C and most vitamins of the B complex, promote the induction of tumours by carcinogens (1, 6, 8, 12, 14, 16, 17, 20) and enhance tumour growth when given in large doses (2, 4, 11), but act as tumour inhibitors when present in the diet in small amounts (3, 5, 7, 9, 10, 13, 15, 18, 19).

Like normal tissues, malignant tumours undoubtedly need vitamins for their growth. Being a rapidly proliferating tissue, they actually need much greater amounts of vitamins than normal tissues. Consequently, the restriction of vitamins in the diet to a level still sufficient for satisfactory function and growth of normal tissues, but no longer optimal for the growth of tumours, slows down tumour growth and significantly prolongs

the life of tumour-bearing individuals. Such a diet also inhibits carcinogenesis.

The average tumour size at the death was in our experiment in the control animals 6×5.3 cm and in the experimental animals 6×4.8 cm. Although no striking difference in size of tumours at the death was observed in both groups one may conclude with certainty that the low-vitamin diet significantly retarded the growth rate of tumours because the animals of the experimental group lived with tumours significantly longer than the control animals.

In the experimental group of animals, also the quantity of food was somewhat restricted, especially in winter. This in addition to the reduced vitamin content, may have contributed to the inhibitory effect of the diet on carcinogenesis and tumour growth. It should be stressed, however, that the animals of the experimental group were not underfed. The amount of vitamins in the diet, although restricted to a low level, and the quantity of food were still sufficient for a good growth of animals. The average weight gain in the first 16 weeks after the beginning of experiment was in experimental group 277 g and in the control group of animals 325 g. The difference was therefore not great.

In my opinion, the restriction of vitamins in the diet to about a third of the recommended daily allowance could be used in man both for partial protection against the development of malignant tumours in older people and as adjunctive therapy in tumour-bearing patients.

It must be stressed, however, that the term a »low level« is not identical with the term »deficiency«. Clearly, vitamin deficiency is not beneficial. Therefore, vitamins in cancer diet should never be restricted to a level inadequate for normal function and growth of normal tissues.

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Povzetek

ZAVIRALNI UČINEK RESTRIKCIJE VITAMINOV IN HRANE NA KARCINOGENEZO IN PREŽIVETJE BUDER Z INDUCIRANIMI TUMORJI

Tumorji, inducirani pri budrah z injekcijo 3-metilholantrena, so se razvili po signifikantno daljših latentnih dobah in preživetje s tumorji je bilo signifikantno daljše v eksperimentalni kakor v kontrolni skupini živali. Eksperimentalne živali so bile hranjene z dieto, ki je vsebovala le malo vitaminov in zmanjšano količino hrane v primerjavi z dieto kontrolnih živali. Kontrolne živali so bile hranjene z obilno dieto, ki je bila bogata z vitamini.

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