132. *Vitamins and Tumor Growth.*

I. The Deficient Vitamin B Content of Chicken Sarcoma Tissue.

By Waro NAKAHARA and Eiichi SOMEKAWA.

Institute of Physical and Chemical Research, Tokyo.

(Rec. June 30, 1928. Comm. by U. SUZUKI, M.I.A., July 12, 1928.)

In an investigation of the relations of vitamins in the growth physiology of tumor cells, the determination of the vitamin contents of tumor tissues should be of importance. Vitamin A is said to be absent in tumor tissue (Burrows and Jorstad,¹⁾ but previous workers are at variance as to the vitamin B content, since Drummond²⁾ states that this vitamin is negative in tumor tissue, while Burrows and Jorstad¹⁾ report that it is especially abundant, both based on growth experiments using rats. Partly in view of these conflicting reports, but more especially because of recent evidence pointing to the composite nature of vitamin B, we considered it worth while to reinvestigate this subject. The present paper is a brief account of our experiments in which we attempted to determine the vitamin B content of the Rous chicken sarcoma, using both pigeon and rat tests.

Pigeon Tests. In preliminary experiments, attempts were made to cure pigeons of polished rice polyneuritis by feeding 3 to 4 grams of dried tumor tissue, but these were uniformly unsuccessful. On the other hand, 2 to 3 grams of similarly dried chicken liver were found to bring about an undoubted cure. Not content with these results, we have carried out the following experiments with the hope of obtaining more conclusive evidence.

Young pigeons weighing around 250 to 300 grams were kept on an exclusive polished rice diet and water (free feeding) so as to induce polyneuritis. In addition, McCollum's salt mixture was forcibly fed at the rate of 0.5 gr. per pigeon per day. Tumor tissue was removed from freshly killed chicken, avoiding as much as practicable the admixture of blood, surrounding normal tissues and necrotic material. It was then chopped up and rapidly dried in an open glass dish over water bath at 70–80°C. The dried tumor tissue was forcibly fed to a part of the pigeons, and the development of polyneuritis in these pigeons was compared with that in control pigeons on the polished rice diet, not fed with tumor tissue.

1) Burrow, M.T., and Jorstad, L.H. Amer. Jour. Physiol., vol. **77**, 24, 1926.

2) Drummond, J.C. Biochem. Jour., vol. **12**, 25, 1918.

Both tumor fed and control pigeons developed and died of polyneuritis at about the same rate as shown below :

Table I. Experiments 1 and 2.

	Pigeon no.		Initial weight gr.	Final weight gr.	Death from polyneuritis in
Exp. 1.	1	0.4 gr. tumor per pigeon per day throughout experiments.	312	217	32 days
	2		284	205	37 „ (average
	3		232	202	41 „ (36 2/3 days.)
	4	Control	298	218	20 days
	5		274	225	42 „ (average
	6		252	205	47 „ (36 1/3 days.)
Exp. 2.	7	1 gr. tumor per pigeon per day from 10th day of experiments.	250	156	24 „
	8		250	173	23 „ (average
	9	Control	262	172	25 „
	10		287	162	23 „ (average
					24 days.)

In both experiments, polyneuritis manifested by the pigeons was of a spastic form sometimes showing a tendency toward atrophic type. These symptoms were invariably associated with the gradual decrease of the body weight and progressive paralysis, especially of legs, and were accompanied by a marked fall in body temperature.

Rat Tests. Two series of experiments were carried out using the growth of the rat as the method of assay. Young rats were fed on a vitamin B deficient diet consisting of meat protein 15 per cent, starch 65 per cent, butter 15 per cent, and McCollum's salt mixture 5 per cent. About at the time when the growth came to a standstill or began to decline, some of the rats were given a weighed amount of dried sarcoma tissue, and their subsequent growth compared with that of control rats. Also, for the sake of comparison, dried chicken liver which is rich in vitamin B was fed to some of the rats. Tissues were dried over hot water bath as before.

Table II. Experiments 3 and 4.

	Rat No.	Initial body wt. gr.	Body wt. 17th day, gr.		31st day body wt. gr.	Average effect of test feeding
Exp. 3	1	63	92	Tumor feeding started 24th day : 0.1 gram per rat per day	75	Loss 17 gr.
	2	68	86		68	
	3	68	75		55	
	4	61	71	Liver feeding started 24th day : 0.1 gram per rat per day	75	Gain 2.5 gr.
	5	59	78		79	
	6	59	73	Control	57	Loss 11.5 gr.
	7	63	85		78	
Exp. 4			Body wt. 20th day, gr.		28th day body wt.	
	8	50	66	Tumor feeding started 21st day : 1 gram per rat per day	60	Loss 1.7 gr.
	9	50	78		77	
	10	51	64		66	
	11	50	68	Liver feeding started 21st day : 0.5 gram per rat per day	84	Gain 17.3 gr.
	12	53	71		100	
	13	7	81		88	
	14	50	78	Control	80	Gain 1 gr.
	15	46	60		55	
	16	48	78		84	

It is evident from the result of Experiment 3 that the daily intake of only 0.1 gram of dried liver is sufficient for the maintenance of body weight in vitamin B deficient rats, while Experiment 4 shows that ten times that amount (1 gram) of similarly dried sarcoma tissue fails to produce any recognizable effect. In both experiments, the growth of tumor fed rats was not materially different from that of controls, while the liver fed rats invariably showed distinctly more favorable growth than either tumor fed or control rats.

Comments. Our results support Drummond and show that vitamin B is present in tumor tissue only in a small amount or may even be absent. It is difficult to arrive at a more definite conclusion as it is practically impossible to obtain tumor tissue entirely free from other tissue elements. We fail to explain the opposite result reported by Burrows and Jorstad, especially since these authors make no mention of controls.

The marked deficiency of vitamin B in tumor tissue might signify that this vitamin is unnecessary for the growth of malignant cells. It might be true, on the other hand, that the growing tumor tissue so thoroughly consumes this vitamin that it is itself free from it, though this idea does not seem reasonable in view of the growth behavior of tumor bearing animals on vitamin B deficient diet (Drummond,¹⁾) We shall consider this question more adequately in a further investigation.

Summary. Pigeons fed on polished rice and dried chicken sarcoma manifest symptoms and die of polyneuritis at about the same rate as control pigeons fed on polished rice alone. Also, while the daily intake of only 0.1 gram of dried chicken liver protects rats from the reduction of body weight on vitamin B deficient diet, ten times that amount of similiary dried sarcoma tissue fails to give similar protection. From these facts, it may be concluded that vitamin B content of the tumor tissue may be very small, if not practically nil.

1) Drummond, J.C. Biochem. Jour., vol. **11**, 325, 1917.