Determinations of the calcium and phosphorus of these samples were made in duplicate.[6, 7]

The percentage of calcium and the percentage of phosphorus were essentially the same in all specimens. The ratio of the phosphorus and calcium was even more constant. Any variation shown in these ratios is entirely within the range of analytical error (Table I).

These results indicate that the phosphate-calcium ratio in the bones is not changed by the ingestion of phosphorus.

Conclusions. 1. The bone in the phosphorus bands produced in the metaphyses of growing long bones by the ingestion of phosphorus is of normal chemical composition. 2. The increased density represents deposition of radio-opaque salts in greater amount per unit of tissue calcified, since calcification and ossification have continued unchecked while the cartilaginous growth was inhibited. 3. This observation constitutes additional evidence that the zones of increased density in metaphyses of growing bones, produced by ingested phosphorus, are in fact "growth arrest lines."

10202

Heptaldehyde as a Tumor Inhibitor.*

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In connection with studies on tumor-inhibition by oil of wintergreen, Strong identified heptaldehyde in the active fraction of the oil.[1, 2, 3] He then fed a diet containing commercial heptaldehyde to mice with spontaneous tumors, and observed liquefaction in most of the tumors followed in many cases by regression. More recently, Strong and Whitney reported a similar response in dogs with spon-

6 Fiske, C. H., and Logan, M. A., *J. Biol. Chem.*, 1931, **93**, 211.

7 Fiske, C. H., and Subbarow, Y., *J. Biol. Chem.*, 1925, **46**, 285.

* Supported by the Jonathan Bowman Cancer Fund and the Wisconsin Alumni Research Foundation.

1 Strong, L. C., *Am. J. Ca.*, 1936, **28**, 550.

2 Strong, L. C., *Am. J. Ca.*, 1938, **32**, 227.

3 Strong, L. C., *Science*, 1938, **87**, 144.

taneous mammary tumors when heptaldehyde was injected subcutaneously.[4]

The question arose whether heptaldehyde would inhibit all tumors or whether its action was restricted to certain tumor types. We have, therefore, studied the effect of heptaldehyde on 5 kinds of mouse tumors: (1) spontaneous mammary adenocarcinoma in strain A mice, (2) primary ear tumor induced by ultraviolet light, (3) primary epithelial tumor induced by painting benzpyrene, (4) primary sarcoma induced by the subcutaneous injection of benzpyrene, (5) transplantable spindle-cell sarcoma originally induced by benzpyrene.

The heptaldehyde (Eastman technical) was fed mixed in various amounts with Steenbock stock ration† (Table I). In general the mice were placed on the diets when the tumors were approximately one centimeter in diameter, although some of the spontaneous tumors were larger. The mice with transplantable tumors were given the various diets from the day of inoculation. In each series the animals were divided such that the tumors in the various groups were of comparable sizes. The tumors were measured at weekly intervals and all mice were carefully autopsied.

When 2% heptaldehyde was fed to mice bearing U.V. tumors, the tumors grew more slowly than in animals on the stock diet. However, these mice ate so little that the limiting factor in the

TABLE I.
Effect of Heptaldehyde on Survival of Tumor Mice.

Type of Tumor	Amt. of Heptaldehyde %	No. of Mice	Survival Avg No. days
Ultraviolet irradiation	0.	30	39.7
" "	0.4	10	18.8
" "	0.8	20	31.5
" "	2.0	10	19.4
Benzpyrene injected	0.	3	33.0
" "	0.8	4	27.0
Benzpyrene painted	0.	12	16.6*
" "	0.8	13	43.8
Benzpyrene transplant	0.	36	24.3
" "	0.8	6	12.0
" "	2.0	23	25.0
Spontaneous mammary	0.8	11	17.7

*The cause of early death of the controls in this group is unknown. In a repetition of this experiment, the survival of mice on both diets was the same.

[4] Strong, L. C., and Whitney, L. F., *Science*, 1938, **88**, 112.

† In one series the heptaldehyde was also injected subcutaneously, but the resulting ulceration and the high mortality of the injected animals rendered the results meaningless.

growth of the tumors appeared to be the reduced caloric intake rather than the heptaldehyde. This was demonstrated by feeding stock ration to tumor-bearing mice in the small amounts consumed by the animals receiving 2% heptaldehyde. Under these conditions the growth rate of the tumors was also markedly restricted.

When 0.8% heptaldehyde was fed, food consumption was more nearly normal. This level approximates the amount fed by Strong. However, in our experimental animals the tumors grew at the same rate as those in the controls. The feeding of heptaldehyde failed to prolong the life of the tumor-bearing animals; in fact in several groups it appeared to hasten death (Table I). Nor did it alter the character of the tumors. Of 97 tumor-bearing mice treated, only one small spontaneous tumor regressed and the animal in question died shortly thereafter. Heptaldehyde also failed to inhibit the growth of the Flexner-Jobling rat carcinoma. The discrepancy between our results and those of Strong demonstrate that heptaldehyde is not a universal tumor inhibitor.

10203 P

Production of Cirrhosis in Fatty Livers with Alcohol.*

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It was previously shown that depancreatized dogs develop cirrhosis of the liver when maintained with insulin and a diet containing meat, sucrose, bone ash and vitamins. The cirrhosis was observed as early as 2.6 years after pancreatectomy and was preceded by the infiltration of massive amounts of fat, the latter appearing as a rule within 20 weeks after excision of the gland. It was concluded that the scar tissue developed in response to the presence of the large amounts of fat in the liver. In the present study cirrhosis in normal dogs is shown to occur when the feeding of large amounts of alcohol is superimposed upon a previously established fatty liver.

For 30-35 days each dog received daily 10 g lard and 7 g lean meat per kilo. Vitamin sources and Cowgill's salt mixture were fed throughout the experiment. At the end of this period, the adminis-

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