

TABLE I.

| Guinea pigs Weight-groups gm. | No. animals used | Dose per kilo mg. | Average lethal dose mg. |
|-------------------------------------|------------------|----------------------|----------------------------|
| 200-299 | 178 | 47.5-67.5 | 57.5-60 |
| 300-399 | 158 | 45 -65 | 57.5-60 |
| 400-599 | 130 | 42.5-60 | 52.5-55 |
| 600-799 | 44 | 45 -60 | 45 -47.5 |

those that died, less of the drug per kilo body weight being required for both of these effects with the heavier animals than with the smaller pigs.

8438 C

Nutritional Value for Planarian Worms of Vitamin Depleted
Mammalian Tissues.*

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The planarian worm has proved itself a useful instrument for demonstrating changes in the composition of mammalian tissues resulting from changing conditions in the animal as a whole. (Bahrs.¹) This research was undertaken to ascertain what the planarian worm could reveal as to modification of the nutritional value of tissues derived from animals fed diets with and without the recognized vitamins.

Guinea pigs and white rats were used to furnish the tissues. The animals received standard basal diets for a month or more. (For diets used, see Table I.) When definite signs of vitamin A deficiency and polyneuritis were apparent in the respective groups of rats, the planarian worm experiments were started. Guinea pigs showed definite signs of scurvy before their tissues were used in the planarian worm experiments. The guinea pigs maintained upon the vitamin D-free diet, of course, appeared entirely normal when their tissues served for the planarian worm diets.

Each group of planarian worms (probably *Planaria agilis*) consisted of 30 newly regenerated worms, all of the same length. Experimental groups were kept in finger bowls of heat-sterilized river

* Aided by a grant from the General Research Council of the Oregon State System of Higher Education.

¹ Bahrs, Alice M., *Physiol. Zool.*, 1931, 4, 189.

water, and maintained at a constant temperature, 23°C.-24°C. The worms were fed twice per week on thoroughly mashed tissues of freshly killed guinea pigs or rats, taken from groups fed the specified vitamin diets. They always ate the tissues well. Spleen, lung, liver, heart and in one case kidney cortex were the tissues used.

Two types of observations were made upon the worms receiving these various tissues: Weekly individual length measurements, and regular inspection for abnormalities in shape, indicating the presence of dietary disease. It was found that the worms did not remain in a healthy condition on all of the tissue diets, but developed a well-marked symptom complex. When gliding freely, planaria have a very smooth outline, and the first sign of disease was a roughening of this smooth border. This was followed by a deepening in color of the whole worm, and as the disease advanced, the surface of the worm shrivelled and became almost black. Irregular lumps developed which in the worst cases became so large as to bend the worms into abnormal shapes and render movement impossible. Although worms developing this pathological condition continued to eat, the result of disease was shown very early by a decrease in growth. (Table I.) This syndrome is essentially different from the one observed by us in connection with the administration to planaria of liver and egg white in graded amounts. (Wulzen and Bahrs.²)

Reference to Table I shows that lack of any vitamin from the diet of rats and guinea pigs lowered the growth-promoting power, for planarian worms, of all the tissues investigated. What change has occurred in the tissues to make this true is of course unknown. It might be that the weakened condition of animals deprived of vitamins gave rise to metabolic changes which affected the tissues so as to reduce their growth-promoting power. However, the lowered growth-promoting power of tissues from animals on the various vitamin-free diets was not uniform, and also the vitamin D-free guinea pigs were certainly not in a weakened condition, as far as could be observed. Nevertheless, their tissues showed lower growth-promoting power than those of the controls.

The development of disease due to dietary deficiency among the experimental groups of planarian worms was a striking feature of these experiments. Lung and spleen never gave rise to disease, no matter what vitamin was absent from the diets of the animals furnishing the tissues. If guinea pigs had been on the deficient diets for longer periods of time, we have experimental evidence

² Wulzen, Rosalind, and Bahrs, Alice M., *Physiol. Zool.*, 1931, 4, 204.

TABLE I.
Growth-promoting and disease-producing power, for planarian worms, of tissues from rats and guinea pigs fed standard basal diets with or without vitamins A, B, C, and D. All worms in each experimental group (30 worms) were of the same original length, and the experiments were of 4 weeks' duration.

| Series | Tissue and Diet | Animal | Orig. Length mm. | Terminal Length mm. | Gain mm. | Gain % | Stand. Dev. | P.E. | Dietary disease in |
|--------|-----------------|------------|------------------|---------------------|----------|--------|-------------|------|--------------------|
| A. | (A+) spleen† | rat | 252 | 555 | 303 | 120 | 18.538±.132 | | none |
| | (A-) "† | " | 252 | 465 | 213 | 84 | 15.500±.163 | | " |
| | (A+) lung | " | 252 | 486 | 234 | 92 | 16.214±.163 | | " |
| | (A-) " | " | 252 | 447 | 195 | 77 | 15.414±.171 | | " |
| | (A+) liver | " | 252 | — | — | — | — | | all |
| | (A-) " | " | 252 | — | — | — | — | | " |
| | (A+) heart | " | 252 | 357 | 105 | 41 | 10.800±.146 | | 19 |
| | (A-) " | " | 252 | 324 | 72 | 28 | — | | all |
| B. | (B+) spleen | rat | 217 | 387 | 170 | 78 | 12.928±.146 | | none |
| | (B-) " | " | 212 | 323 | 111 | 52 | 10.793±.164 | | " |
| | (B+) lung | " | 217 | 406 | 189 | 87 | 13.814±.160 | | " |
| | (B-) " | " | 212 | 343 | 131 | 61 | 11.464±.188 | | " |
| | (B+) liver | " | 217 | 260 | 43 | 19 | 8.678±.105 | | 20 |
| | (B-) " | " | 217 | 230 | 16 | 7 | 7.730±.106 | | all |
| | (B+) heart | " | 215 | 268 | 53 | 24 | 8.933±.139 | | 17 |
| | (B-) " | " | 212 | 278 | 66 | 31 | 9.392±.122 | | 18 |
| C. | (C+) spleen | guinea pig | 240 | 455 | 215 | 89 | 15.178±.172 | | none |
| | (C-) " | " | 240 | 429 | 189 | 78 | 14.310±.134 | | " |
| | (C+) lung | " | 240 | 401 | 161 | 67 | 13.366±.119 | | " |
| | (C-) " | " | 240 | 374 | 134 | 55 | 12.482±.133 | | " |
| | (C+) liver | " | 210 | 457 | 247 | 117 | 15.233±.170 | | " |
| | (C-) " | " | 210 | 306 | 96 | 45 | 10.400±.164 | | all |
| | (C+) heart | " | 210 | 347 | 137 | 65 | 11.586±.105 | | none |
| | (C-) " | " | 210 | 332 | 122 | 58 | 11.066±.091 | | 12 |
| | (C+) kidney | " | 210 | 354 | 144 | 68 | 11.800±.101 | | none |
| | (C-) " | " | 210 | 253 | 43 | 20 | 8.461±.172 | | all |

| D. | (D+) spleen | guinea pig | 240 | 513 | 273 | 113 | 17,115 ± .164 | none |
|----|-------------|------------|-----|-----|-----|-----|---------------|------|
| | (D-) | " | 240 | 487 | 247 | 102 | 16,241 ± .095 | " |
| | (D+) lung | " | 210 | 396 | 186 | 88 | 14,071 ± .117 | " |
| | (D-) | " | 210 | 388 | 128 | 60 | 12,179 ± .148 | " |
| | (D+) liver | " | 240 | 460 | 220 | 91 | 15,370 ± .164 | 23 |
| | (D-) | " | 240 | 414 | 174 | 72 | 13,793 ± .215 | 26 |
| | (D+) heart | " | 210 | 325 | 115 | 54 | 10,827 ± .087 | none |
| | (D-) | " | 210 | 317 | 107 | 50 | 10,571 ± .108 | " † |

- A. Vitamin A supplied as 5% cod liver oil.* Basal diet: purified casein, 18%; salt mixture No. 185, 4%; yeast, 8%; dextrin, 69%; NaCl, 1%.
- B. Vitamin B supplied as 15% of dried yeast.* Basal diet: casein, 18%; salt mixture No. 185, 4%; dextrin, 72%; cod liver oil, 5%; NaCl, 1%.
- C. Vitamin C supplied in form of 10 gm. fresh kale per animal daily. Basal diet: ground barley, 40%; bran, 20%; baked milk powder, 26%; CaCO₃, 3%; NaCl, 1%; clarified butter, 10%.
- D. Vitamin D supplied in form of 2 drops Viosterol* per animal every other day. Basal diet: yellow corn meal, 76%; wheat gluten, 20%; CaCO₃, 3%; NaCl, 1%. Vitamin C supplied in form of canned tomato juice.
- *Yeast, cod liver oil and Viosterol very kindly supplied by Mead Johnson and Company.
- †(A+) liver, spleen, etc. = tissue from animal supplied vitamin A.
- ‡(A-) liver, spleen, etc. = tissue from animal devoid of vitamin A.
- ‡‡Two worms definitely affected after 6 weeks' feeding.

which leads us to believe that these tissues would also have become disease-producing. Liver, kidney cortex and heart (for one exception, see (D+) heart, Table I) constitute another group, all the tissues of which gave rise to dietary disease in planarian worms, regardless of what vitamin was present or absent, or what type of basal diet was consumed by the animals furnishing the tissues. This last statement requires an important modification. We found that when fresh, green kale served as the source of vitamin C, liver, kidney cortex and heart of the animals so fed were never disease-producing for planarian worms. The nature of this effect of green plant tissue upon the tissues of guinea pigs is under investigation at the present time. In this investigation we are demonstrating, from the condition of the guinea pigs themselves, that the use of vitamin A from certain other sources beside butter does not affect the outcome; neither have other sources of vitamin C beside kale, such as tomato juice, orange juice and ascorbic acid, a protective effect.

The results presented in this paper correlate with those detailed in a recent publication by the authors. (Wulzen and Bahrs.³)

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Relative Actions of Di-hydro-morphinone Hydrochloride and Morphine Sulphate on the Excised Ureter and Bell's Muscle.*

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It has been shown that morphine sulphate, when added to the bath in which an excised pig's ureter is contracting, increases the general tonus and increases the rate and force of the rhythmical contractions of the tissue.¹ These findings have been supported by those of Ockerblad, Carlson and Simon² on the intact human ureter. Recently Krueger and Howes,³ Gruber and Brundage,⁴ and Mitchell

³ Wulzen, Rosalind, and Bahrs, Alice M., *Physiol. Zool.*, 1935, **8**, 457.

* This research was made possible through a grant from the Therapeutic Research Committee of the Council on Pharmacy and Chemistry of the American Medical Association.

¹ Gruber, *J. Pharm. and Exp. Therap.*, 1928, **33**, 191.

² Ockerblad, Carlson and Simon, *J. Urol.*, 1935, **33**, 356.

³ Krueger and Howes, *J. Pharm. and Exp. Therap.*, 1934, **51**, 139.

⁴ Gruber and Brundage, *J. Pharm. and Exp. Therap.*, 1935, **53**, 120