SUMMARY

The following pathological changes have been observed in rats given sulfaguanidine or sulfasuxidine in purified diets.

1. A granulocytopenia, leukopenia, hypocellularity of bone marrow and, occasionally, an anemia.

2. Hyalinization, necrosis and calcification of voluntary muscle.

3. Hyaline sclerosis and calcification of blood vessels.

4. A dermatitis which can be prevented or successfully treated with crystalline biotin.

We have also observed necrosis of heart muscle, hemorrhage into various organs and subcutaneous tissues, and liver damage.

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ATYPICAL RESPONSE OF THE RABBIT TO DESOXYCORTICOSTERONE ACETATE

WE have found[1,2] that administration of desoxycorticosterone acetate, progesterone, alpha-estradiol benzoate, testosterone proprionate and diethylstilbestrol to dogs results in a marked increase in the rate of entrance of Na and Cl into 5.5 per cent. dextrose solution introduced into the peritoneal cavity. No such effect was noted in rabbits following administration of desoxycorticosterone acetate, progesterone and diethylstilbestrol.[2] Certain additional findings are of interest in this connection.

Injection of 2.5 mg of DOCA daily for three days in two rabbits had no significant influence upon the urinary excretion of water or Cl during the experimental period. Two rabbits (2.0 and 1.8 kg) received 2.5 mg of DOCA daily for three months, the animals being weighed and the blood-pressure determined[3] bi-weekly. There was no significant change in weight for six weeks in one animal and eight weeks in the other, with a subsequent increase to a maximum of 47 and 40 per cent., respectively, over the pre-treatment levels at the end of the experimental period. There was no significant alteration in blood-pressure and no edema or other evidence of toxic effect of DOCA, as has been reported in the dog.[4] Two pregnant rabbits treated in the same manner showed no significant gain in weight, no edema and no increase in blood-pressure. Both aborted at about four weeks' gestation, one developed marked weakness of the hind limbs after five weeks of treatment and both died after six weeks. The weakness of the hind limbs may have been due to decrease in the serum K concentration; the serum Cl concentration was unaltered in the non-pregnant animals, but no chemical studies were performed in the pregnant rabbits. Dexter and Weiss[5] have reported a similar absence of effect of large doses of DOCA in pregnant and non-pregnant rabbits in experiments of shorter duration.

These observations suggest the existence of a marked species difference in the influence of DOCA and perhaps also progesterone, estradiol, testosterone and other steroid hormones upon water and electrolyte metabolism. This has an important bearing, perhaps, on the use of the rabbit in studies of the relation of these hormones to hypertensive "toxemia" of pregnancy.

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[1] A. Cantarow and A. E. Rakoff, *Endocrinology*, 27: 652, 1940.

[2] A. E. Rakoff and A. Cantarow, *Endocrinology*, 30: 816, 1942.

[3] R. I. Grant and P. Rothschild, *Jour. Physiol.*, 81: 265, 1934.

[4] D. Kuhlmann, C. Ragan, J. W. Ferrebee, D. W. Atchley and R. F. Loeb, SCIENCE, 90: 496, 1939.

UNIFORMITIES IN THE CONTENT OF B VITAMINS IN MALIGNANT NEOPLASMS

FOR two years[1] this laboratory has been interested in the possibility that cancer tissues might show peculiarities in vitamin distribution, characteristic of this type of growth. We have now completed an extensive series of determinations of eight B vitamins not only on various types of human, rat and mouse cancer material but also upon normal tissues from these same animals. This material is now in press.[2]

By analysis of the values obtained, highly interesting and important uniformities are observed which we wish to set forth briefly here. We shall use the term "vitamin uniformity" to designate the similarity of vitamin content in a group of tissues. For example, if in a number of samples of muscle tissue pantothenic acid had a mean level of 5 γ per gram with a standard deviation of 1, then $1/5 \times 100$, or 20, would equal the average deviation from the mean in per cent., or, to express the relationship in the opposite manner, there would be an average degree of uniformity in pantothenic acid content of 80 per cent. The average of the "vitamin uniformities" in a series of tissues calculated for the individual vitamins is designated the "Total B Vitamin Uniformity."

[5] L. Dexter and S. Weiss, "Preeclamptic and Eclamptic Toxemia of Pregnancy." Boston: Little, Brown and Company, 1941.

[1] R. J. Williams, SCIENCE, 92: 579, 1940.

[2] University of Texas Publication 4237, 1942.

It has been found (Table I) that normal tissues of the same type but taken from separate animals, such as myocardium from different hearts, have a relatively high "total B vitamin uniformity" (70 per cent. or more), while normal tissues which differ from each other in structure and function have a relatively low degree (less than 30 per cent.) of "total B vitamin uniformity" when compared with each other.

TABLE I

VITAMIN UNIFORMITY IN NORMAL AND CANCER TISSUES

Tissues	"Total B Vitamin Uniformity" in per cent.
Human Tissues	
8 diverse normal tissues	27
Myocardium from three separate hearts*	71
8 diverse cancer tissues	66
Normal mammary, ovarian and renal tissue	11
Mammary, ovarian and renal carcinoma	60
Rat Tissues	
8 diverse normal tissues	30
Myocardium from three separate hearts*	75
5 diverse cancer tissues	63
2 hepatomas	78
2 hepatomas with corresponding adjacent liver tissues	22
Mouse Tissues	
Myocardium from three separate hearts*	76
12 diverse cancer tissues	58
Human, Rat and Mouse Tissues	
Myocardium from three human, three rat and three mouse hearts	61.2
8 human, 5 rat and 9 mouse cancer tissues of diverse origins and sites	58.8

* Individual tissues other than the heart from different specimens (in human, rat and mouse) also show high "total B vitamin uniformity" but are not included in this table.

Examination of the tumor material in this manner disclosed that malignant tumors which differed from each other in tissue of origin, manner of induction and host species tended to have a relatively high "total B vitamin uniformity" when compared with each other.

Since in our observations on normal tissues a relatively high degree of "total B vitamin uniformity" has been found to be associated only with homogeneous and never with heterogeneous groups of tissues, it is concluded that malignant neoplasms of various types and from various animals tend to have similar cellular metabolism, forming in effect a common tissue type.

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SCIENTIFIC APPARATUS AND LABORATORY METHODS

THE DETERMINATION OF BLOOD VOLUME WITH RED BLOOD CELLS CONTAINING RADIOACTIVE PHOSPHORUS (P^{32})[1]

THE red cell, rather than the plasma component of the blood, has several advantages in determining blood volume. First of all, the fluid portion of the blood, because of its physiological connection with tissue, lymph and other fluid spaces, is not so anatomically delimited as that containing red cells. Secondly, changes in capillary permeability affect the plasma much more frequently and markedly than the red cells. Third, the dyes used to measure plasma volume, because of diffusion and adsorption, may themselves behave differently from the plasma they are supposed to measure.

Total red cell volume has been measured by the carbon monoxide method, which, however, has not achieved acceptance for a variety of reasons. More recently, blood volume methods have been described using red cells containing radioactive iron[2] and radioactive phosphorus.[3] Though radioactive iron has a long half-life and remains in the red cells for long periods it has a serious practical disadvantage of emitting such soft radiation that direct measure of the radioactivity of the blood is technically difficult and requires more or less complicated chemical manipulations. On the other hand, radioactive phosphorus, though its half-life is but 14 days, emits energetic beta particles which enables red cells containing it to be measured more easily. Nevertheless, in the phosphorus method described by Hahn and Hevesy[3] chemical extraction of the red cells was necessary; moreover, a large amount of blood (50 cc) was used for the extraction.

In the technic to be described herein, but two cc of blood were used and they were measured directly in the Geiger counter without any chemical manipulation whatever. A donor dog was prepared by the subcutaneous injection of sodium phosphate containing radioactive phosphorus. The dose was 0.4 millicuries (P^{32}) per day for 10 days. After several days the red cells became so intensely radioactive that the blood could be diluted 100 times and yet give a sufficiently high count for accurate measurement. Washing the cells in saline several times and suspending in saline for 24 hours resulted in very little loss of activity. For the determination of blood volume 10 cc or more of the donor dog's blood was heparinized, centrifuged and the plasma (which also contains radioactive phosphorus) removed. The cells were resuspended in

[1] Aided by a grant from the Commonwealth Fund.

[2] P. F. Hahn, J. F. Ross, W. F. Bale, W. M. Balfour and G. H. Whipple, *Jour. Exp. Med.*, 75: 221, 1942.

[3] L. Hahn and G. Hevesy, *Acta Physiol. Scand.*, 1: 3, 1940.