

eosinophilic, and young and mature neutrophilic elements. These changes are accompanied by a significant diminution in the percentages of nucleated erythroid elements, with a consequent decrease in the values of the erythroid-myeloid cell ratios, as compared with the untreated and sham-operated controls.

Administration of whole adrenal cortical extract³ (1–2 ml daily) to adrenalectomized rats, beginning with the first day of operation, although effective in preventing the development of the peripheral anemia and increased red cell resistance, is without significant influence upon the marrow components, except for a concomitant decrease in the percentages of blast cells. Table 1, however, indicates that Compound E (17-hydroxy-11-dehydrocorticosterone acetate⁴), in dosages of 0.5–1.0 mg daily, is partly effective in restoring the bone marrow myelograms to normal values. This substance significantly reduces the degree of myeloid immaturity, and the most significant decreases occur in the eosinophilic and young neutrophilic cell groups, with accompanying increases in the percentages of mature neutrophilic forms. Erythroid-myeloid cell ratios are increased, but completely normal values are not obtained with these dosages of hormone. Significant decreases in the eosinophilic levels of the peripheral blood are also observed when this hormone is given to the adrenalectomized animal.

It is thus apparent that the marrow of the adrenalectomized rat is characterized by increased percentages of myeloid elements, associated with elevated levels of eosinophilic and young neutrophilic forms, tending toward a leukemoid state. The decreased nucleated erythroid cell percentages could account for the peripheral anemia that develops in the salt-maintained adrenalectomized animal. Despite the changes that occur in the granulocytic percentages in the marrow, however, no consistent trends were observed in the peripheral white cell picture with chronic adrenal insufficiency. It should be borne in mind that peripheral blood cell values may be influenced by a variety of processes, of which type and rate of cell production are only two. A complete elucidation of the question as to how the adrenal cortex influences the numbers of circulating blood cells can be achieved only after the effects of adrenal insufficiency and replacement therapy are studied in connection with such additional factors as total functional marrow mass, rate of release of cells from the marrow, longevity of the cells in the circulation, and possible redistribution of the cells to other organs.

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³ We are indebted to D. A. McGinty, Parke, Davis & Co. for generous supplies of the cortical extract Eschatin (Compound E content, 164 µg/ml).

⁴ Compound E acetate (cortisone acetate) was supplied through the kindness of Harry J. Robinson and Augustus Gibson, Merck & Co., Inc.

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Modified Laboratory Lyophil Apparatus

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A modification of the lyophil apparatus of Holzman (2) has been in use in this laboratory for several months and has been free from one objectionable feature of the original design. The ring seal at the top of Holzman's apparatus is a point of weakness, since any movement of the center tube will cause breakage, even though this tube is supported on glass pins.

Our apparatus replaces the sealed-in center tube with a female standard taper joint, so that the body of the apparatus consists of six 34/45 female joints arranged symmetrically and at right angles to each other (Fig. 1).

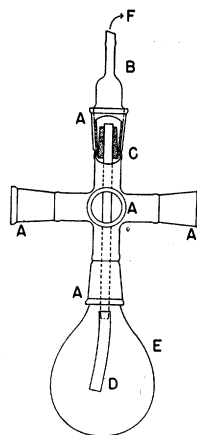


FIG. 1. Lyophil apparatus, side view: A, ports, ST 34/45 female, for flasks; B, exhaust tube, ST 34/45 male; C, cork insert in exhaust tube; D, removable glass center tube with flexible end (Tygon) extending into receiver flask; E, receiver constructed from 800-ml Kjeldahl flask; and F, connection to vacuum.

A male joint is drawn and sealed to 10-mm glass tubing, and the center tube of the same diameter is inserted through a cork in the lower end of this joint. It is not necessary to achieve a completely gas-tight seal by insertion of the cork, as there is no restriction on gas flow through the center tube, the purpose of the latter being

to direct the atmosphere through the trap flask during the early stages of evacuation. This assembly is inserted through the top female joint of the body.

The operation and efficiency of this modification are as described by Holzman. The advantages are a more rugged structure and a simpler construction.

As pointed out by Campbell and Pressman (1), it is convenient to stopper unused ports of the apparatus with sealed-off standard tapers, which may also be used for drying small samples of material.

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Sulfapyrazine Precipitated in Cancer Tissue upon Repeated Glucose Injections¹

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Cancer tissue, unlike most normal tissues, produces large quantities of lactic acid aerobically. The acid production can be increased by intraperitoneal injection of glucose to the point that the pH of the extracellular fluid often drops below 6.4, as measured by glass electrode (1). This fact has enabled us to produce high local concentration in cancer tissue of a compound administered at a site distant from the tumor. The compound used, sulfapyrazine, was precipitated in the tumor presumably because it is less soluble at acid pH than at pH 7.4. Rats with Walker tumor 256 were used.³

As an example we give the concentrations of sulfapyrazine found in 2 implants of tumor 256 and in other tissues taken from a 400-g rat injected 3 days earlier with sulfapyrazine. The tumors were subcutaneous in the interscapular region. When they were 16 days old, the rat was given a single subcutaneous injection in the hind leg of 55% aqueous sodium sulfapyrazine containing 0.5 g of sulfapyrazine. During the 3-day period 14 g of glucose were given intraperitoneally in 50% solution. The rat was then killed by bleeding under ether anesthesia. The tumors were flecked with white precipitate and were necrotic throughout. Tissues were weighed, digested in alkali, aliquots were precipitated with *p*-toluenesulfonic

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³ Tumor supplied through the courtesy of John B. Storer, Department of Pathology, University of Chicago.

acid, and the sulfapyrazine was determined colorimetrically by the Bratton and Marshall technique (2).

Serum taken from the heart at sacrifice contained 87 mg of sulfapyrazine/100 ml, the blood 93% as much, the small tumor (4.5 g) 330%, the large tumor (6.6 g) 280%, kidneys 100%, stomach (without forestomach) 95%, hide 94%, small intestine (upper 8 cm) 83%, heart 73%, lungs 72%, liver 69%, spleen 61%, leg muscle 55%, and testes 54%.

TABLE 1

DATA ON 250 RATS WITH WALKER TUMOR 256 KILLED AFTER SUBCUTANEOUS INJECTION OF SULFAPYRAZINE

| Mg of sulfa injected/ 100 g body weight | Hours be- tween sulfa in- jection and killing | Sulfa/g of tumor divided by sulfa/ml of serum | | Sulfa/g of kidney divided by sulfa/ml of serum | | | |
|--|--|--|-----|---|----------|----|----------------|
| | | > 1 | < 1 | > 1 | < 1 | | |
| | | | | | | | |
| | | No. rats | | Chi square* | No. rats | | Chi square* |
| <i>Repeated injections of glucose</i> | | | | | | | |
| 100-200 | 20-97 | 31 | 14 | 6.4 | 9 | 36 | 14 |
| <i>Single injection of glucose</i> | | | | | | | |
| 200-1,000 | 3-20 | 26 | 79 | 27 | 31 | 74 | 18 |
| <i>No glucose injected</i> | | | | | | | |
| 200-1,000 | 3-20 | 29 | 71 | 18 | 75 | 25 | 25 |

* All probabilities are less than 0.01 except for the smallest chi square, of which the probability is between 0.01 and 0.02.

Table 1 illustrates conditions in which similar concentration of sulfapyrazine in tumors did and did not occur. Highest concentrations were found in necrotic tissue. The quantities injected are generally lethal. The tumors had a median weight of 1.28% of the body weight, none more than 13%.

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Measurement of the Extract of Cornstalks

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By extract is meant the water-soluble content in terms of the Brix sugar scale (3). In its measurement the assumption is made that the water, as well as the soluble solids, is uniformly distributed throughout the sample. It is necessary to know the total moisture content, and the Brix reading of the juice at or near 20° C. If sufficient juice cannot be obtained, a known amount of water is mixed with the sample, the diluted juice is expressed, and its Brix reading measured. The method is rapid, does not require expensive equipment, and is far more easily operated than any of the other sugar estimation methods. Clark (1) has found that approximately two-