

Bufo vulgaris. The substance is more toxic than bufagin. Solutions of 1:1,000,000 and higher concentrations produced in the frog's heart a primary acceleration soon followed by a decrease in rate and amplitude with the occurrence of ventricular extrasystoles, auriculo-ventricular block as shown by the 2:1 rhythm, arrhythmia, ventricular intermittence and systolic standstill, while the auricles continued their bradycardia until final arrest was brought about. Concentrations of 1:2,000,000 to 1:10,000,000 caused some depression of the contractions and the rate. The M. S. D. in frogs was determined to be 0.000005 gm. per gm. of body weight. In pithed cats of ordinary size, 0.5-1.0 mg. caused death. Smaller quantities also raised the blood pressure, but not so much as bufagin.

4. *Epinephrine*. M. P. 212° C. (uncorrected), gives the typical color reactions with ferric chloride. This is the first time that this principle also has been obtained in crystalline form from Ch'an Su. Its presence makes the traditional belief justifiable that Ch'an Su stops hemorrhages, and shrinks the nasal mucosa to drain the infected sinuses. Abel¹ discovered epinephrine in the secretions of *Bufo aqua* some 18 years ago. The epinephrine prepared from Ch'an Su reproduced all the known physiological responses in the animal body. When assayed biologically in pithed cats, it was proved to have exactly the same pressor activity as a commercial specimen.

Detailed accounts of this work will appear elsewhere.

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Influence of Cathode Rays on Leucocytes of Rabbits.

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It is well known that leucocytes are destroyed to a considerable extent if a large portion of an animal is exposed to about an erythema dose of roentgen rays which penetrate into the tissues under the skin. Bucky¹ has stated that very soft roentgen rays, "grenz rays," have a different effect on the leucocytes. According to him, a considerable portion of the leucocytes disappear from the circulating blood immediately after a small area of the skin has been exposed to

¹ Bucky, G., *Am. J. Roentg.*, 1927, xvii, 645.

these rays, which are all absorbed in the first millimeters of tissues, and reappear after a few hours. Cathode rays produced with less than 200 kilo volts are absorbed by the first millimeter of tissue. A very intense dose given to the skin will, therefore, not directly injure the underlying tissues. Such an intense dose can be given in a few seconds. Due to the rapid destruction of tissues a considerable amount of organic substances may be liberated. It is possible that they will be taken up partially by the skin capillaries and thus become mixed with the blood. What effect they may have on the system and on the blood itself is difficult to predict. It seemed likely that the effect should be similar to, though perhaps more intense than the effect of "grenz rays." We decided to study the effect on the leucocytes of rabbits and this is a preliminary report of the first results obtained.

We are obliged to Dr. W. Coolidge of the General Electric Company for supplying us with a tube of the construction which he has described in earlier papers,² and to the University of Minnesota for appropriating a special fund for needed equipment. The tube is connected to a system of vacuum pumps and has to be evacuated each time it is being used.

During the exposure of the first group of 3, we used 180 k.v., 0.5 m.a. and 1 cm. distance from the window of the cathode ray tube to the irradiated area which was on the inside of the right ear. The rabbit was placed behind a lead screen 1/16 in. thick. A square hole was cut in the lead and the ear was flattened out over this opening and fastened to the lead by strips of adhesive tape. Rabbit No. 1 had an area of 2x2 cm. exposed for 4 sec., rabbit No. 2 an area of 2x2 cm. exposed for 8 sec., and rabbit No. 3 an area of 3x3 cm. exposed for 8 sec.

For the second group of rabbits one (No. 3) was used for control. It was treated in exactly the same way as the other 2 rabbits with the exception that a piece of lead was placed in front of the hole in the lead screen during the "treatment". Instead of 180 k.v. we used 135 k.v. this time while the current was the same as before, 0.5 m.a. The distance from the window to the irradiated area was reduced to 1/2 cm. and the exposed area was kept at 3x3 cm. Rabbit No. 1 was irradiated for 10.9 sec. and rabbit No. 2 for 19 sec.

After normal counts were established for each rabbit, the total leucocyte count was taken and a differential count was made as follows: immediately before exposure to the cathode rays, 10 minutes after exposure and at hourly intervals during that day until the

² Coolidge, W. D., *J. Franklin Inst.*, 1926, 693.

leucocyte count became constant, and once daily thereafter until the leucocyte count returned to normal.

The effect of irradiation may be divided into 2 portions, the immediate reaction and the sustained reaction. In the first series the immediate reaction is characterized by a marked increase above normal, returning to normal in a few hours. The differential showed a rapid relative decrease and an absolute increase in the lymphocytes, while the neutrophiles showed both an absolute and relative increase. At the end of the immediate reaction the absolute and relative values of both the lymphocytes and the neutrophiles were practically normal. Three hours after irradiation the basophiles showed a slight relative and marked absolute increase, which at the end of the immediate reaction was still far above normal. The monocytes showed a relative and an absolute decrease throughout the immediate reaction.

The sustained reaction in the first series is characterized by a steady increase in the total number of leucocytes reaching a peak on the fifth day following irradiation, and gradually returned to normal about 10 days later. The lymphocytes and neutrophiles remained relatively normal throughout but showed an absolute increase which decreased in proportion to the decrease in the total count. The basophiles, however, showed both a relative and an absolute increase for a period of 8 days following irradiation and gradually decreased to normal. The monocytes showed both a relative and absolute decrease throughout the period of observation.

In the second series the immediate reaction also showed a marked increase above normal which returned to normal in about 5 hours. The lymphocytes showed at first a marked relative decrease and an absolute increase, but after the end of 5 hours there was a relative and absolute decrease throughout the rest of the immediate reaction. The neutrophiles on the other hand showed a marked relative and absolute increase during the entire immediate reaction. The basophiles also showed a marked relative and absolute increase, which returned practically to normal at the end of the immediate reaction. The monocytes showed a slight relative increase followed by a decrease, while the absolute value was increased during the first 5 hours and decreased during the remainder of the reaction.

In the sustained reaction 2 days after irradiation there was a slight secondary rise in the total leucocyte count with a slight relative decrease and absolute increase of the lymphocytes and a relative and absolute increase of the neutrophiles with a relative and absolute decrease of both basophiles and monocytes. From the third day after irradiation to the end of the period of observation the total

leucocyte and differential counts were normal with the exception of a slight relative and absolute decrease in the monocytes.

The rabbit which was used as a control showed the differential normal throughout the immediate reaction period. On the next day, however, the total leucocyte count was increased with an increase in neutrophils, but the characteristic basophilia did not occur. From this time the total leucocyte and differential counts were normal. This temporary rise in the leucocyte count was probably due to an infection, following thrombosis of the lateral vein of the left ear.

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Duration of Anticoagulant Action of Heparin in Vivo in Relation to Dosage.

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Reed¹ determined experimentally the "minimum dependable dose" of heparin as an anticoagulant. Takuji Shinoya,² upon injecting heparin intravenously into dogs, commented on the rapidity with which the coagulation time increased and then returned to normal. In the following experiments determinations were made of the rate of appearance and disappearance of the anticoagulant action of heparin *in vivo*.

Heparin was injected in varying amounts into the ear veins of rabbits, and the blood was collected from cut veins of the opposite ears. One method of determining clotting time which was used is as follows: Drops of blood were collected at intervals of 20 seconds or more upon glass slides cleaned with alcohol and ether. The time when each drop fell upon the slide was noted. Only blood which exuded and dropped readily was used. The blood was termed clotted when, upon being moved with a wire loop, clear or nearly clear serum was left behind. The slides were kept in a moist chamber at room temperature. A simpler method, used in the later series of experiments, is the capillary tube method. These 2 methods were

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¹ Reed, C. I., *Am. J. Physiol.*, 1925, lxxiv, 79.

² Shinoya, T., *J. Exp. Med.*, 1927, xlv, 21.