phrine given intravenously, the value for the blood pressure of each of the woodchucks was raised to about 200 mm. of mercury. There was considerable fluctuation below and above the control level but the blood pressure became stabilized within 4 minutes. At the completion of these observations, the animals were killed (Fig. 1).

8957 C

Carcinoma-Like Proliferations in Vagina, Cervix, and Uterus of Mouse Treated with Estrogenic Hormones.*

LEO LOEB, E. L. BURNS, V. SUNTZEFF AND M. MOSKOP.

From the Department of Pathology, Washington University School of Medicine, St. Louis, Mo.

We have referred[1] to the fact that in mice injected with preparations of estrogenic hormones over long periods of time abnormal proliferations of varying degrees of intensity may be induced not only in the mammary gland but also in certain parts of the vagina, cervix, and uterus. In a number of cases conditions were observed which in human beings would be considered precancerous lesions or as changes representing very early stages of cancer. In the monkey, Overholser and Allen[2] noted that in the cervix atypical epithelial proliferations were induced through administration of ovarian hormones. However, these investigators added traumatization of the tissue to the action of the hormones, while in our experiments the tissues were left intact. In two recent publications Lacassagne[3] described adenomatous proliferations of the uterine glands in the rabbit and in the mouse; in some cases the glands penetrated through the muscular layer. Quite recently we have autopsied a mouse in which proliferative changes had progressed further than in any of the others observed. This mouse, of the "Old Buffalo" strain in which spontaneous tumors are relatively rare, had been injected with estrogenic hormones for 24 months, 20 days, beginning at the age of 18 days. During the first 18

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1 Loeb, Leo, Burns, E. L., Suntzeff, V., and Moskop, M., *Canad. Med. Assn. J.*, 1936, **35**, 117.

2 Overholser, M. D., and Allen, E., PROC. SOC. EXP. BIOL. AND MED., 1933, **30**, 1322.

3 Lacassagne, A., *C. R. Soc. Biol.*, 1935, **120**, 685, 1156.

months this animal received 10 rat units of theelol in water daily; for the remaining 6 months, 20 days, daily injections of 30 rat units of theelin. At autopsy vagina, cervix, and uterus were very much enlarged. There were adhesions between the vagina and cervix and the surrounding pelvic tissues.

Microscopic examination showed very extensive proliferation in the upper part of the vagina near the cervix, in various parts of the cervix, and in the uterus. The proliferation in the upper part of the vagina consisted largely of squamous epithelium, forming many epithelial pearls containing hyaline material. However, there were also formed irregular ducts lined with columnar epithelium. In the cervix the proliferated tissue consisted largely of ducts lined with cylindrical or cuboidal epithelium, but there were also found some areas consisting of squamous epithelium. In some ducts both kinds of tissues were seen. Higher up in the beginning of the uterus the proliferating tissue consisted almost exclusively of strands or ducts of cuboidal epithelium, and squamous epithelium was rarely noted. These proliferated tissues penetrated deep into the wall of the vagina, cervix, and uterus, and often extended into the subperitoneal connective tissue, and where adhesions existed about the vagina and cervix some of these gland-like strands approached striated muscle tissue and at one point began to enter it. Furthermore some of these abnormally proliferating ducts had pushed their way into certain lymph vessels. Mitoses in this tissue, as a rule, were not numerous except in one area in cylindrical cell strands which took their origin in the uterine mucosa. Here mitoses were frequent and some of them seemed to be hyperchromatic. In various places we found considerable variations in the size of nuclei. In the mammary gland no definite tumor had been produced, but a considerable amount of a type of tissue, the development of which, as a rule, precedes tumor formation, was seen.

We do not believe it is possible at present to designate these abnormal proliferations of the vagina, cervix, and uterus as definitely cancerous, because we cannot be certain that the invasive growth would have continued indefinitely after cessation of injections of estrogenic hormones which served as stimuli in this case. But we may state that if such a condition had been observed in a human being it would have been called malignant.

Of special interest in these observations are the following facts: 1. Long continued application of estrogenic hormones not accompanied by traumatization of the cervix may produce very far going abnormal proliferations not only in the mammary gland, but also

in vagina, cervix, and uterus. 2. Estrogenic hormones may cause proliferations which are not limited to one organ, but affect vagina as well as cervix and uterus. 3. In the mouse observed by us the abnormally proliferating tissue formed under the influence of these hormones was specific in accordance with the actual and potential structures of the various tissues involved.

8958 P

Precipitin Reactions of Helminth Extracts.

LESLIE L. EISENBRANDT. (Introduced by T. C. Nelson.)
From the Zoological Laboratory, Rutgers University.

The serological technic of Boyden[1] offers a suitable means of investigating the preciptin reactions of some helminth extracts, and of studying the degree of relationship indicated by the tests. The limited research in this field has been done almost entirely with saline suspensions of powdered worms. The content of these suspensions was unknown, thus prohibiting the use of definite amounts of antigen which in turn prevented comparable interpretation of the results. Schwartz[2] and Hektoen[3] studied the precipitin reactions of a few dried helminths using the best methods available at the time.

In the present work fresh worms were extracted with sterile buffered saline, and the resulting extracts were passed through Seitz filters and bottled under sterile conditions. The antisera were produced in rabbits by injecting intravenously extracts having 0.00384 gm. total nitrogen per kilo body weight; they were divided into 4 doses of increasing amounts on alternate days. None of the rabbits were reinjected. The quantitative precipitin tests, constant in titer within ± one test tube as shown by repeated tests, permit accurate readings of an antiserum with its homologous antigen and with heterologous antigens.

The nitrogen content of the helminth extracts, as determined by the Kjeldahl method, is found to be much less than that of the mammalian blood sera studied by Boyden. He finds, also, that the non-protein nitrogen content of the mammalian sera is negligible,

[1] Boyden, Alan, *Am. Nat.*, 1934, **68**, 516.
[2] Schwartz, Benjamin, *J. Parasitol.*, 1921, **7**, 144.
[3] Hektoen, Ludvig, *J. Infect. Dis.*, 1926, **39**, 342.