

The resemblance of certain chemical properties of indium to those of bismuth suggested its trial as antisyphilitic agent. The citrated solution of the chloride, an oily suspension of the hydroxide, and an aqueous suspension of the metal are being tested in this respect by Dr. E. E. Ecker. Although these studies are not yet completed, they appear to indicate that indium in these forms has no curative effect on luetic lesions in rabbits.

6280

Biological Characteristics of Ovary-Stimulating Extracts Made from Blood of Pregnant Women*.

C. F. FLUHMAN

From the Department of Obstetrics and Gynecology, Stanford University School of Medicine

The demonstration that ovary-stimulating extracts prepared from human placenta (Collip *et al.*¹), or from urine of pregnant women (Evans, Meyer, and Simpson²) differ from anterior pituitary gland implants in their influence on the weights of immature rat ovaries, is of considerable biological interest. It seemed of importance, therefore, to determine if extracts made from the blood of pregnant women were similar in this characteristic.

A crude estrin-free extract was prepared from blood by a method developed with the assistance of Dr. M. L. Tainter of the Department of Pharmacology, based on that of Wallen-Lawrence and Van Dyke³ for the extraction of "hebin" from anterior pituitary glands. Forty to 50 cc., obtained by venapuncture, from each patient was placed in a receptacle containing a few crystals of sodium citrate, centrifuged, the red blood cells discarded, and the resultant clear blood plasma shaken up 5 times with ether. Ten volumes of 95% alcohol were then added to the blood plasma, the solution centrifuged, and the resultant precipitate washed twice with ether, dried, powdered, and extracted over night with 20 to 30 cc. of an isotonic sodium acetate-acetic acid buffer solution having a

*Supported by a grant from the Rockefeller Fluid Research Fund of Stanford University School of Medicine.

¹ Collip, J. B., Thomson, D. L., McPhail, M. K., and Williamson, J. E., *Can. M. A. J.*, 1931, **24**, 201.

² Evans, H. M., Meyer, K., and Simpson, M. E., *Am. J. Physiol.*, 1932, **100**, 141.

³ Wallen-Lawrence, Z., and Van Dyke, H. B., *J. Pharm. and Exp. Therap.*, 1931, **43**, 93.

pH of about 4.4. The next morning it was centrifuged and to the clear supernatant solution was added 6 volumes of 95% alcohol. A white precipitate resulted which was recovered by centrifugalization, again washed with ether, dried and powdered. This powder contained the active element and was fairly readily dissolved in small amounts of the buffer solution for injection. It was generally so made up that 1 cc. of the extract was equivalent to 2.3 cc. of blood plasma and various dilutions were prepared from this stock solution.

Collip and his co-workers state that the injection of large doses of A.P.L. placental extract could not stimulate the ovaries of immature rats to develop to a size beyond that reached in adult life, while Evans, Meyer, and Simpson found that with prolan a curve in which ovarian weight is plotted against dose level quickly reaches a plateau and that a further 5-fold or even 10-fold increase in dose did not cause a further increase in ovarian weights. On the basis of the present preliminary work involving the use of over 80 immature rats it may be stated that the same characteristic can be ascribed to pregnancy blood extracts which readily induce the development of graafian follicles and lutein bodies. As shown in Table I, it has been impossible to produce any great increase in ovarian weight over a period of 5 days even by increasing the dose 50 times. This is in startling contrast to the tremendous increase in ovarian weights produced by anterior pituitary implants, as originally reported by Aschheim and Zondek and Smith and Engle.⁴

TABLE I

At end experiment Age days	Body wt.	Duration experiment days	Amount injected	No. of injections	Wt. ovaries	Wt. uterus + tubes
27	36.0013	.054
27	40.0	5	0.024	6	.009	.089
27	40.0	5	0.024	6	.011	.110
26	35.0015	.032
26	35.0	5	0.05	5	.024	.114
26	34.0	5	0.05	5	.018	.118
26	31.0008	.026
26	29.0	5	1.25	5	.012	.202
26	29.0	5	1.25	5	.014	.188
50	70.0016	.054
50	62.0	20	0.33	33	.020	.253
50	55.0	20	0.33	33	.023	.293
54	79.0014	.049
54	68.0	24	0.41	41	.049	.360
54	50.0	24	0.41	41	.033	.344
26	48.0	5	3 rabbit	pituitary implants	.104	.139
26	47.0	5	“	“	.069	.128
26	49.0	5	“	“	.077	.094

⁴ Smith, P. E., and Engle, E. T., *Am. J. Anat.*, 1927, 40, 159.

Of considerable interest, however, is the pronounced increase in weight shown by the uterus under the influence of this extract. These weights are out of all proportion to the ovarian response and show a progressive increase according to the amount of extract administered. This is also marked even with small doses when the preparation is given over a prolonged length of time. In the appended table are a few examples illustrating the effects obtained with one of the extracts, and for comparison are listed the findings in 3 immature rats each of which received one rabbit anterior pituitary gland implant daily for 3 days. However, as pointed out by Smith and Engle,⁴ the uterine weights do not represent the absolute tissue gain as they were almost all done at a stage of uterine engorgement when the vaginal smear showed cornified or nucleated epithelial cells. The factors concerned in this phenomenon are not clear, but it is believed that the uterine growth is not due to ovarian hormones present in the extracts since these were ineffective in immature spayed rats.

6281

Observations on Mørch's Method for Standardization of Thyroid Gland Preparations.

W. W. PALMER AND J. P. LELAND.

From the Department of Medicine, College of Physicians and Surgeons, Columbia University, and the Presbyterian Hospital, New York City.

Mørch¹ devised a method for the standardization of thyroid preparations based on the percentage increase of the carbon dioxide output of white mice after administration of thyroid preparations. Gaddum and Hetherington² compared the physiological activity of thyroid preparations with the thyroxine content as determined by Harington and Randall.³ It seemed desirable to investigate the question whether the thyroid glands of patients with exophthalmic goiter contained some substance other than thyroxine itself which might cause an increase in the basal metabolic rate. An answer seemed possible by feeding animals equi-thyroxine doses of dif-

¹ Mørch, J. R., *J. Physiol.*, 1929, **67**, 221.

² Gaddum, J. H., and Hetherington, M., *Quart. J. Pharm. and Pharmacol.*, 1931, **4**, 183.

³ Harington, C. R., and Randall, S. S., *Quart. J. Pharm. and Pharmacol.*, 1929, **2**, 501.