glomerulonephritis[4]—hyalinized glomeruli, and glomerular closure due to endothelial proliferation. These features were elucidated by staining with azo-carmine. In some cases not all the glomeruli were involved, whereas in others the process was general enough so that the term "diffuse glomerulonephritis" was applicable. Albuminuria was evidenced by casts in the tubules, but only a small degree of tubular degenerative change was present. Contracted kidneys have not been observed.

Preliminary chemical study has confirmed the morphologic diagnosis. Albuminuria, decreased total plasma proteins (5.0 g as compared with a normal for the mouse of 6.2-6.5 g %), and hyperlipemia have been demonstrated for one typical case.

[4] Bell, E. T., *Am. J. Path.*, 1938, **14**, 691.

The age of clinical appearance of the disease, when associated with edema, has ranged from 5 to 18 months; death ensued within 2 to 3 weeks in most cases after the development of massive edema. Glomerular pathology has been noted in animals which did not exhibit the nephrotic tendency. The incidence of the disease in untreated strain NH mice of the Minnesota stock has not been determined.† Further studies on the pathology of the disease in mice are being pursued; investigations on the genetic, chemical, bacteriologic, and nutritional aspects of the problem are being planned.

† The animals from which the Minnesota stock of the NH strain has been derived were obtained from Dr. L. C. Strong of the Yale University School of Medicine.

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Hormonal Influences on Chemically-Induced Tumors of the Reproductive System.

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In a recent study, Smith and associates[1] reported that a deficiency or excess of numerous hormones had, with few exceptions, little effect on the rate of development of chemically-induced tumors. In that study methylcholanthrene was introduced subcutaneously, in the present investigation the same carcinogen was placed directly into various organs of the reproductive system and attention centered upon gonadal and gonadotropic hormones as possible influencing agents.

Experimental. University of Denver strain white rats, whose spontaneous tumor incidence is practically zero, were employed. They were 3 months old at the time of carcinogen administration, those surviving were killed one year later. Small pellets of methylcholanthrene, in 20% suspension in paraffin, were introduced, under aseptic precautions, into the organ studied, the total dose per animal being 10 mg. All animals were examined carefully 3 times weekly, the date upon which a tumor of palpable size first was noted was recorded; if within a week it was apparent that the mass had increased in size (which was usually the case) the original date was accepted. If no growth ensued the site was directly inspected and a decision reached. Autopsy of the survivors at year's end revealed no tumors not previously diagnosed and the implanted carcinogen was found to have been retained in all animals which had not developed tumors.

Results. Tables I and II present the results obtained. The dosage of hormones shown is the amount given per injection. Injections were made 3 times weekly.*

[1] Smith, Donn L., Wells, J. A., and D'Amour, F. E., *Cancer Research*, 1942, **2**, 40.

* Our thanks are herewith expressed to the following companies for the generous amounts of hormone preparations supplied: G. W. Carnrick Co., Ciba Pharmaceutical Products, Inc., Parke, Davis and Co., The Schering Corporation, The Upjohn Co., and the Winthrop Chemical Co., Inc.

TABLE I.
Effect of Hormones upon Tumor Development.
Females.

Group	No. rats	Treatment	No. developing tumors	Avg time, days
A	10	Paraffin in Uterus	0	—
B	20	Methylcholanthrene in Uterus	2	180
C	10	Castrate; M.C. in Uterus	1	257
D	9	M.C. in Uterus, plus Stilb., 5 γ 3$\times$ weekly	6	179
E	10	M.C. in Uterus, plus Stilb., 15 γ 3$\times$ weekly	7	173
F	10	M.C. in Uterus, plus Progestin, 5 mg, 3$\times$ weekly	1	192
G	10	M.C. in Ut., plus Stilb. 5 γ and Progestin 5 mg, 3$\times$ weekly	1	226
H	10	M.C. in Uterus, plus P.U. gonadotropin, 1 I.U. 3$\times$ weekly	1	251
I	10	M.C. in Uterus, plus P.M.S. gonadotropin, 1 I.U. 3$\times$ weekly	3	140
J	10	M.C. in Ovaries	0	—
K	10	M.C. in Ovaries, plus P.M.S. gonadotropin, 1 I.U. 3$\times$ weekly	1	51

TABLE II.
Males.

Group	No. rats	Treatment	No. developing tumors	Avg time, days
L	10	Methylcholanthrene in Testes	0	—
M	10	M.C. in Testes, plus P.U. gonadotropin, 1 I.U. 3$\times$ weekly	0	—
N	10	M.C. in Testes, plus P.M.S. gonadotropin, 1 I.U. 3$\times$ weekly	0	—
O	10	M.C. in Testes, plus Testosterone, 20 γ 3$\times$ weekly	0	—
P	10	M.C. in Sem. Ves. and Prostate	3*	305
Q	10	Castrate; M.C. in Sem. Ves. and Prostate	10†	254
R	10	M.C. in Sem. Ves. and Prostate plus Testosterone, 20 γ 3$\times$ weekly	5‡	230

* Two tumors in prostate alone, 1 in seminal vesicle alone.
† Three tumors in prostate alone, 7 in both seminal vesicles and prostate.
‡ All 5 in prostate alone.

Discussion. Even under the stimulus of gonadotropic hormones, the gonads themselves appear to be highly resistant to the carcinogenic action of methylcholanthrene. Only one ovarian tumor developed in 20 females (groups J and K), and no testicular tumors in 40 males (groups L to O).

The stimulating action of estrogens upon some types of uterine tumors appears to be well established. Our results support this view as applying to tumors induced by methylcholanthrene, the incidence ranging from 10% in ovariectomized rats to 70% in the group receiving 45 γ of stilbestrol per week. It is interesting that progestin appears to inhibit this action, as is shown by comparing groups D and G.

In the paper previously mentioned, Smith reported a statistically significant hastening of the appearance of subcutaneous tumors under the influence of P.U. and P.M.S. gonadotropins, especially the latter. For P.M.S., this finding appears to be duplicated in the present study; the 4 tumors produced under its influence (groups I and K) having distinctly shorter incubation periods.

As regards the effect of testosterone on tumors of the male adnexæ, our results are contradictory. The animals having the lowest concentration, namely, the castrate group, had an incidence of 100% tumors, those receiving testosterone, 50%, and the normals, 30%. In view of the present trend toward castration in treating prostatic tumors in the human it would be interesting to see what effect castration would have if done after, rather than before, the development of the tumor. This point, as well as other inconsistencies in the male groups is now being investigated with larger numbers of animals.

Summary. An attempt was made to influence the development of methylcholanthrene-induced tumors of the reproductive system by means of gonadal and gonadotropic hormones. The results follow: 1. The gonads themselves were found to be highly resistant to

the carcinogenic action of methylcholanthrene. 2. Administration of stilbestrol increased the incidence of uterine tumors. 3. The effect of testosterone upon tumors of the male adnexæ was contradictory.

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An Ether-Extractable Substance from Blood Serum and Buffy Coat Which Contracts Smooth Muscle.

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The presence in blood serum and platelets of substances which contract smooth muscle has been recognized for the past seventy years. Although numerous investigators have prepared active extracts of serum and platelets by the use of alcohol and acetone, few have employed water-immiscible solvents. T. F. Zucker and Stewart[1] and Janeway *et al.*,[2] using strips of ox carotid artery as an indicator, reported that only a small fraction of the total activity of serum was extractable by ether. Recently, Wu, Fang, and Tsai[3] reported the separation of a fraction from dried rabbit serum by extraction with ether. This fraction was active on the rabbit intestine, but not on the vessels of the perfused rabbit ear, whereas rabbit serum was active on both of these indicators.* In the present paper, the properties of an ether extractable fraction which appears to be identical with that obtained by Wu *et al.*[3] will be described.

Methods. In the original method of Wu *et al.*,[3] the serum was dried on a steam-bath before extraction with ether. We were unable to obtain consistent results with this somewhat drastic method, but found that an ether extract made from serum dried at room temperature with Na_2SO_4 was uniformly active.

Rabbit serum was ground thoroughly with 5 times its weight of anhydrous Na_2SO_4. The powder was then extracted 4 times with dry ether and the ether was evaporated on a steam-bath from the combined extracts. Approximately 0.1 mg of residue was obtained from 1 cc of serum, of which about one-half was soluble in water. Extracts were prepared in a similar manner from cat and human serum. The portion of the residue soluble in Locke solution will be referred to as "extract of dry serum." Solutions were made up so that 1 cc of extract represented from 1 to 10 cc of the original serum. This made it possible to compare the relative activity of serum and extract because the activity of both could be made approximately equal. The dosage values given in Table I represent the volume, not of the extract, but of the serum from which it was obtained.

The activity of an extract of the buffy coat of human citrated blood was also studied. The buffy coat was mixed with an equal volume of acetone and filtered. The filtrate was freed of acetone by vacuum distillation. The resulting aqueous extract was dried by mixing

1 Zucker, T. F., and Stewart, G. N., *Zentralbl. f. Physiol.*, 1913, **27**, 85.

2 Janeway, T. C., Richardson, H. B., and Park, E. A., *Arch. Int. Med.*, 1918, **21**, 565.

3 Wu, C. H., Fang, H. S., and Tsai, C., *Proc. Chinese Physiol. Soc., Chengtu Branch*, 1942, **1**, 83.

* One of us (M.B.Z.), unaware of the work of Wu *et al.*,[3] had separated an active fraction from the buffy coat of human blood. The dry fraction was insoluble in ether. In doses of 0.5 to 2.0 mg it constricted the vessels of the perfused cat tail and stimulated the muscle of the rat and rabbit intestine. The recent visit of Dr. Tsai to this country presented an opportunity to compare the fractions studied in the Chinese and American laboratories. The present paper is a partial report of this joint study. Data on the fraction prepared by M.B.Z. and the comparison of the two fractions will be reported elsewhere.