pertension by 3 weeks after operation.

Systolic blood pressures having been followed by repeated indirect measurements for 60 days, these conclusions as to the severity of the hypertension were verified by direct determinations using the Hamilton manometer. Three rats of each group were lightly anesthetized by injecting intraperitoneally 3 mg sodium pentobarbital per 100 g body weight. Their pressures were measured (a) plethysmographically and (b) immediately afterward directly from the femoral artery. Table II summarizes this comparison and, within the usual respiratory variations of blood pressure when a tracheal cannula is not used, shows the quantitative accuracy of conclusions drawn from previous indirect measurements.

Comment. The pathogenesis of hypertension in these animals appears to be similar to that produced by other chronically irritative materials such as silk or cellophane. Within a few days after the application of the rubber capsule the superficial tissues of the renal cortex reacted by forming first a fibrinous, then a definitely fibrous, envelope. The latter can become very thick and tough as shown in Fig. 1F. In this specimen the latex capsule has been applied to the kidney 57 days before. The microscopic changes were also similar to those produced by other types of irritative capsule. Similar results have also been observed in a few rabbits.

Summary. Enclosing both kidneys in molded latex rubber capsules to produce perinephritis can be recommended for its simplicity and effectiveness, particularly when large numbers of hypertensive rats are required.

15812

On Use of Urea- and Phenol-Treated Skin Test Antigens for Diagnosis of *Lymphogranuloma venereum.*

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It has been shown in an earlier report from this laboratory[1] that urea in concentrations of 1 to 2% inactivated the virus of *Lymphogranuloma venereum* in 10% yolk sac suspensions prepared from infected chick embryos. Suspensions so inactivated with urea were satisfactory both as complement-fixing and skin test antigens. Urea-inactivated skin test antigens (containing 0.25% phenol and 1-20,000 merthiolate as preservatives) have been prepared in these laboratories for clinical testing for over 4 years.[2-5]

When later studies[6,7] revealed that the addition of phenol to yolk sac suspensions enhanced their complement-fixing activity from a titer of approximately 1-200 to 1-3200, and in some instances to 1-6400, the question of the possible enhancement with phenol of the skin test activity naturally presented itself.

Methods. To investigate the effect of phenol on the reactivity of skin test antigens, saline suspensions were prepared as previously described[7] from yolk sac membranes heavi-

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TABLE I.
Comparison of Urea- and Phenol-treated Skin Test Antigens.

Susp. 96 10% saline Susp.-YS membranes fractions:	Description			Complement fixation titer with standard positive serum pool	Skin reactions with antigens diluted: 1-500*		1-2000*		1-8000*	
	Inactivation 3 wks with:	Preservative added to diluted antigens Phenol	Merthiolate		Pt. weak reactors†	7 days	Pt. moderate reactors†	7 days	Pt. strong reactors†	7 days
A	Urea 2% 2-4°C	0.25%	1-20,000	1-200	Hun	30‡	Dea	30	DeL	49
					Bla	36	Jen	42	Ben	49
					Wil	4	DeV	36	Tho	48
B	Urea 2% 2-4°C	—	,,	1-200	Hun	24	Dea	30	DeL	25
					Bla	25	Jen	49	Ben	36
					Wil	9	DeV	30	Tho	48
C	Phenol 0.5% 37°C	0.25%	,,	1-3200	Hun	36	Dea	16	DeL	49
					Bla	49	Jen	104	Ben	64
					Wil	9	DeV	56	Tho	48

* Dilutions are expressed in terms of original yolk sac weight.
‡ Score equals product of the axes of the erythematous papule in mm.
† Patients used in testing the three dilutions were selected on the basis of previous tests.

ly infected with the virus of *Lymphogranuloma venereum* and fractions thereof were treated as shown in Table I. Fraction A was prepared by the method in use in these laboratories for the routine production of *Lymphogranuloma venereum* skin testing antigens. Fraction B was prepared in identical manner. Fraction C was treated at 37°C for 3 weeks with phenol in a final concentration of 0.5%. This procedure effected enhancement of complement-fixing activity.[7] The final dilutions of Fractions A and C contained 0.5% phenol and 1-20,000 merthiolate as preservatives, while Fraction B contained only merthiolate. Control material for each fraction was prepared in identical manner from normal yolk sac membranes (in approximately the same stage of development) for simultaneous testing.

When all preparations had passed the necessary tests for sterility and inactivation of virus, they were tested on clinically and serologically positive cases of *Lymphogranuloma venereum,* using the 1-500 dilutions of each preparation on each of several patients, the 1-2000 dilutions on each of another group of patients and the 1-8000 dilutions on each of a third group. Such a procedure was followed to rule out differences in individual response to the same test material. The test dose of each preparation was 0.1 ml injected intracutaneously on the flexor surface of the forearm. The reactions were recorded at 2- and 7-day intervals following injection.

Results. Some patients show, during the first 2 or 3 days following the test injection, a more or less extensive edematous, erythematous area with or without induration. The erythema may recede fairly rapidly, leaving a characteristic erythematous papule which regresses slowly with or without central necrosis, requiring several weeks for its complete disappearance. This more persistent reaction, as seen one week after injection, was thought to present a more reliable criterion for the comparative evaluation of the various preparations. Table I, therefore, shows only the 7-day readings. The product of the axes of the erythematous papule in mm was used as a basis for scoring

the reactions. In no case did the control Fractions A, B and C, give a positive reaction with 1-500 dilution. The results present at the most only slight and probably insignificant differences in reactivity between the 3 preparations, whether phenol was used in the preparations (Fractions A and C) or was completely absent (Fraction B).

The skin test results are in contrast to the comparative complement-fixing activities of Fractions A and B with a titer of only 1-200, and Fraction C, with a titer of 1-3200, constituting a 16-fold enhancement.

Summary. 1. Saline suspensions prepared from yolk sacs heavily infected with the virus of *Lymphogranuloma venereum* and inactivated with 2% urea or 0.5% phenol constituted satisfactory diagnostic skin test antigens in high dilutions.

2. Yolk sac suspensions treated with phenol so as to enhance their complement-fixing activity 16-fold were not appreciably more active as skin test antigens than urea-treated suspensions.

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Trypanocidal and Spirochetocidal Compounds Derived from BAL and Organic Arsenicals.

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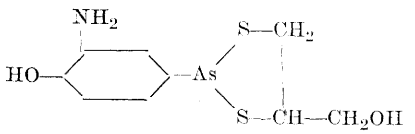
This study is part of an investigation of the chemotherapeutic activity of organometallic compounds as affected by chemical combination with dithiols.

War research has brought out the fact that BAL (British Anti Lewisite, 2,3-dimercaptopropanol) protects man and experimental animals against the toxic effect of organic arsenicals, including 4-arsenoso-2-aminophenol (I), *i.e.*, oxophenarsine U.S.P., and counteracts *in vitro* the trypanocidal effect of this drug.[1-3]

The limited information published to date (February 18, 1947) suggests that the compound resulting from the condensation of I with BAL, *i.e.*, 2-amino-4-[methylol-(ethylenedimercaptoarsino)]-phenol (II)



(II)

would be significantly less toxic than its parent substance (I), but devoid of chemotherapeutic activity.

With a view to evaluating this proposition, we have synthesized (II) and tested *in vivo* its trypanocidal and spirochetocidal activity.

(II) crystallizes from methanol as white needles, soluble in propylene glycol and dilute hydrochloric acid, insoluble in water and anhydrous acetone. It gives a negative nitroprusside reaction at pH 8, positive at 10.

Analysis:

Calcd. for $C_9H_{12}O_2NS_2As$:	N 4.59,	As 24.6
Found:	N 4.52,	As 24.0
	4.49	24.8

(II) forms a crystalline hydrochloride (III), soluble in water, ethanol and propylene glycol, insoluble in anhydrous acetone.

Analysis:

Calcd. for $C_9H_{13}O_2NClS_2As$:	N 4.11;	As 22.0
Found:	N 4.10;	As 21.2

The free base (II), and more so its hydrochloride (III), are quite stable. Propylene glycol solutions of the hydrochloride may be sterilized by heating for one hour at 100°.

(III) cures the experimental *T. equiperdum*

[1] Peters, R. A., *Nature*, November 24, 1945.

[2] Waters, L. A., and Stock, C., *Science*, 1945, **102**, 601.

[3] Sulzberger, M. B., and Baer, R. L., *J. Am. Med. Assn.*, 1947, **133**, 293.