and riboflavine were fed. At this time symptoms of dermatitis began to appear. Factor 2 concentrates were added, and definite dermatitis appeared in a week. In 2 weeks, 16 of the rats developed severe dermatitis, 15 mild, and 12 rats showed no dermatitis. After 5 weeks of factor 2 feeding, only 4 rats remained without dermatitis. Three rats with slight dermatitis had cured spontaneously.

It thus appears, at least from these experiments, that dermatitis develops as a result of a factor 2 deficiency superimposed upon a pyridoxine deficiency. If rats are early exposed to such an extra deficiency, the effects, insofar as they affect dermatitis, seem to carry over after the addition of factor 2 concentrates, and the rats become deficient only in pyridoxine. The question may well be raised whether dermatitis or acrodynia is a reliable expression of uncomplicated pyridoxine deficiency.

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Experimental Necrotizing Arteritis. II. Mercuric Chloride as Effective as Uranium Nitrate in its Production.*

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In a recent publication[1] the senior author described well marked necrotizing arterial lesions affecting principally the large elastic arteries (aorta, sinuses of Valsalva, endocardium of the left auricle, coronary and pulmonary arteries) which appeared unexpectedly during the course of the experiments designed to determine whether heavy metal poisoning is influenced by altering the plasma protein level.

Normal adult dogs maintained on a standard low protein diet were made hyperproteinemic by repeated intravenous injections of plasma obtained from healthy donor dogs. Each dog then received a single subcutaneous injection of 5.0 mg of uranium nitrate per kilo. In 4 of the 5 dogs in which this procedure was carried out, acute necrotizing arterial lesions were found at necropsy 8-17 days after the injection of the heavy metal; and healed lesions were found when the 5th dog

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1 Holman, Russell L., *Am. J. Path.*, 1941, **17**, 359.

was sacrificed 11 months after the administration of uranium nitrate.

No definite conclusions were reached about the pathogenesis of the lesions but the suggestion was offered that the lesions "may be due to a hypersensitivity to some constituent of the blood of one or more of the donor dogs precipitated by uranium nitrate or made manifest in the disturbed metabolism consequent to the uranium nitrate injury."

In this paper are described the results of using mercuric chloride instead of uranium nitrate. Only 2 dogs have been tried but both yielded positive results showing that corrosive sublimate can be substituted for uranium nitrate in the production of these arterial lesions.

The methods were the same as those employed in the previous study, the only difference being that mercuric chloride (3.0 mg/kg *intravenously*) was used instead of uranyl nitrate (5.0 mg/kg *subcutaneously*). The standard basal diet consisted of: calves' liver (raw wet weight) 32 parts, cane sugar 25 parts, corn starch 25 parts, butter 12 parts, and cod liver oil 6 parts. Enough tomato juice was added to make a paste of which each gram contained 3 calories. One gram of McCollum-Simmonds salt mixture[2] and 5 g of kaolin were thoroughly mixed with each day's diet. The diet was fed in amounts to furnish 75 calories per kg per day.

The plasma injections used in making the dogs hyperproteinemic were carried out as follows: About 200 cc was bled from a healthy adult donor dog into a flask containing 2.5 cc of saturated solution of sodium citrate. The citrated blood was centrifugalized for 20-30 minutes at 3000 rpm in 100 cc centrifuge tubes. The plasma was then drawn off with suction, warmed to 40-45°C and injected into the jugular vein. Approximately 10 minutes was required for the plasma (usually 90-110 cc) to run into the vein. This procedure was repeated 6 times per week for 3-4 weeks before the heavy metal was injected.

The mercuric chloride was obtained from J. T. Baker Co. (lot 6939) and was injected to the jugular vein in 0.1% aqueous solution. Sufficient water was used to insure quantitative transfer.

Blood plasma protein and non-protein-nitrogen were determined by duplicate micro-Kjeldahl analyses. Trichloracetic acid (10%) was used to precipitate the protein for the determination of non-protein-nitrogen.

The dogs were necropsied promptly after death. Sections from all organs and from many of the tissues were stained routinely with

[2] McCollum, E. V., and Simmonds, N., *J. Biol. Chem.*, 1918, **33**, 55.

TABLE I.
Summary of Experimental Data.

Dog No.	No. of inj.	Total amt plasma inj. cc	Plasma protein concentration Before inj. g/100 cc	Plasma protein concentration After inj. g/100 cc	Body wt.* kg	Mercuric chloride inj. intrav. mg/kg	Height of non-protein nitrogen† mg/100 cc	Survival interval‡ days
40-63	24	2960	6.0	8.0	9.2	3.0	394	7
40-80	18	1840	6.7	9.4	5.8	3.0	466	6

*Body weight at end of period of plasma injections, *i.e.*, weight on date of mercuric chloride injection.

†In dog 40-63 the terminal blood sample was taken 2 hours before death; in dog 40-80, 3 hours before death.

‡Interval between injection and autopsy.

TABLE II.
Anatomical Distribution of Arterial Lesions.*

Dog No.	Ascending aorta	Sinuses of valsalva	Left auricle	Pulmonary artery	Arteries in lungs	Other arteries
40-63	+++	++	+++	+++	+†	
40-80	++†	++	+++	+++†	+	Innominate ++† (aneurysm)

*The lesions have been graded as follows: +++ = gross lesion over 1 cm in maximum diameter; ++ = gross lesion less than 1 cm in maximum diameter; + = lesion discovered in microscopic section.

†Thrombus associated with lesion.

——— Microscopic illustration.

hematoxylin and eosin. Special stains used in selected cases were: Verhoeff's for elastic tissue, Kossa's for calcium and VanGiesson's or Mallory's for the differentiation between muscle and connective tissue.

Table I summarizes the experimental data and Table II indicates the anatomical distribution of the arterial lesions. The cause of death in both dogs was presumably "uremia". The figures for the terminal non-protein-nitrogen and the extensive necrosis of the proximal convoluted tubules seen in histological sections of the kidneys substantiate this clinical impression.

The arterial lesions are similar in all respects to those previously reported with uranium nitrate.[1] Essentially the lesion is an acute necrotizing arteritis usually most marked in the intima but not infrequently involving all 3 coats. Polymorphonuclear neutrophils predominate in the cellular response. Hemorrhage and fibrin deposition are not infrequent. Sometimes thromboses occur. Typical lesions are illustrated in Fig. 1.

One lesion deserves special comment. A small saccular aneurysm about 8 mm in diameter and hemispheric in shape was found at the mouth of the innominate artery in dog 40-80. This aneurysmal bulge was partly filled with laminated thrombus and there was a slight

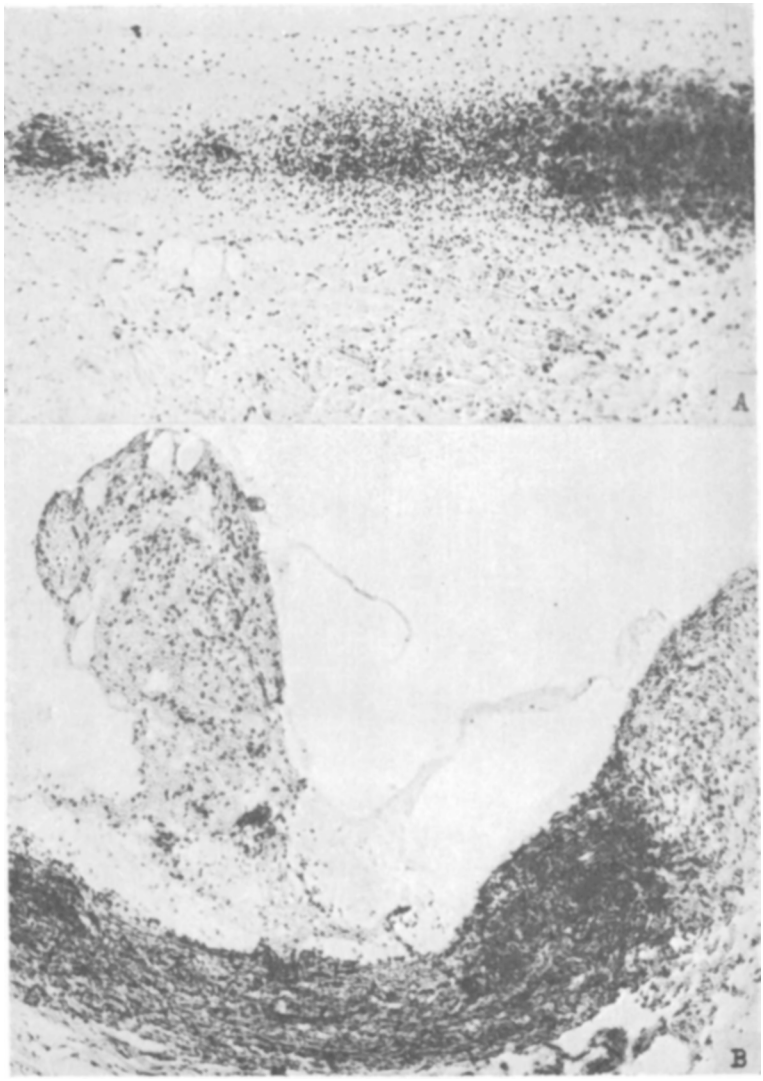

FIG. 1.

Dog 40-80. 6 days after mercuric chloride. × 110. Sections stained with hematoxylin and eosin.

A. Acute necrotizing auriculitis. Leukocytic infiltration and necrosis beneath intact endocardium.

B. Acute necrotizing arteritis of pulmonary aorta with thrombosis and aneurysmal outpouching.

amount of hemorrhage in the adventitia, but no definite rupture. Sections of the wall stained with Verhoeff's method show almost complete destruction of the elastic framework of the media. In

other respects this lesion resembles those previously described. This is the first aneurysm that has been observed in this series, but the possibility was suggested by the fragmentation and disintegration of elastic tissue seen in previous lesions.[1]

Thus the observations with uranium nitrate have been confirmed with mercuric chloride. Experiments are now in progress to determine whether the heavy metal as such or the renal insufficiency following the administration of the heavy metal is the essential factor in the production of these experimental arterial lesions. The other two factors apparently concerned in their production are diet and plasma alteration.

Summary. Mercuric chloride can be substituted for uranium nitrate in the production of necrotizing arterial lesions in dogs. An aneurysm developing on the basis of one of these lesions is described for the first time.

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Epithelial Hyperplasia of Hassall's Bodies of Thymus Gland Induced by Methylcholanthrene.

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The histogenesis and functions of the thymus gland are still imperfectly understood. Uncertainty exists concerning the essential nature of Hassall's bodies, the thymic reticulum, and the thymic lymphoid cells. The rôle of the thymus as a gland of internal secretion, and as a source of lymphocytes is also not clear.

During experiments designed to induce tumors in the thymus with a cancerogenic hydrocarbon observations were made which give support to the idea that Hassall's bodies are epithelial and not endothelial, and that some of the thymic reticulum may be epithelial in nature.

Procedure. Cylindrical pellets consisting of 10 mg of methylcholanthrene plus 10 mg of cholesterol and measuring approximately 1.75 mm in diameter and 8-10 mm in length were[1] implanted into the thymus gland of young guinea pigs of both sexes by open surgical operation.

Animals were sacrificed at 7, 14, 21, and 28 days and irregularly at

1 Shear, M. J., *Am. J. Cancer*, 1936, **26**, 322.