resistant to extraction by the fluorocarbon, as appears to be the case(3), then it is more likely to be a DNA than RNA virus, for there was no intact RNA in this particular preparation. Similarly, the fluorocarbon extract of the thymic tumor had no DNA, hence was more likely to be a RNA virus. The leukemic tissue had both RNA and DNA but by inference, only the RNA would be expected to contain a viral component.

Summary. RNA, DNA and protein are differentially removed by extraction of a tissue with fluorocarbon CCl_2F-$CClF_2$. These constituents occur in sedimentable (120,000 x g, 1 hour) and non-sedimentable forms. A unique component was observed in concentrated fluorocarbon extracts of 3 neoplastic tissues, which was absent from normal tissue. Its possible relation to viruses is discussed.

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Distribution Studies on Radioactive Hg^{203} Sodium Mercaptomerin in Animals. (25399)

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Many previous studies on mercurial diuretics have been performed on compounds administered clinically orally(1,2), or parenterally when combined with theophylline(3). This investigation was undertaken with Hg^{203} mercaptomerin sodium because, as employed clinically, it is not combined with any agent which might influence distribution or excretion. This study was done to determine general distribution, renal concentration, and rate of urinary excretion of this compound.

Materials and methods. Hg^{203} mercaptomerin sodium was synthesized in our laboratories,* and was identified by paper chromatography, quantitative determination of Hg and S, determination of temperature of decomposition, and determination of diuretic activity. The solutions were freshly prepared with pyrogen-free water and resterilized by filtering through type H. A. millipore filter. Specific activity of original material was 360 μc/mg mercury when assayed for gamma radiation. A standard dose of 1 mg Hg kg (equivalent to 3.5 mg kg mercaptomerin sodium) was used. Thirty-three albino rats (165-190 g), injected intraperitoneally, were divided into groups of 3 and placed in metal metabolism cages. Each group was deeply anesthetized with ether and sacrificed 15, 30, 60, 90, 120, 150, 180, 210, 240, 270, or 300 minutes after injection of the radioactive compound. Blood was obtained by cardiac puncture, using heparin as anticoagulant, and both kidneys were removed, decapsulated, weighed, and digested in concentrated nitric acid. Average radioactivity of renal tissue is expressed as μg of mercaptomerin sodium/g wet weight of tissue. Aliquots from pooled urines of 60, 120, 130, and 240 minute groups were collected and assayed for radioactivity. In addition, a series of kidney sections of the 1, 2, 3, and 4 hour groups was prepared for radioautographs. Sections 8 μ thick of kidney tissue were prepared by usual paraffin impregnation technic and mounted without removal of paraffin. The slides were covered with Kodak Panchromatic XX photographic film and firmly fastened with tape. Optimum exposure time was 14 days. In a second study, Hg^{203} mercaptomerin sodium was injected in-

* Method of synthesis supplied by Wyeth Inst. for Medical Research, Radnor, Pa.

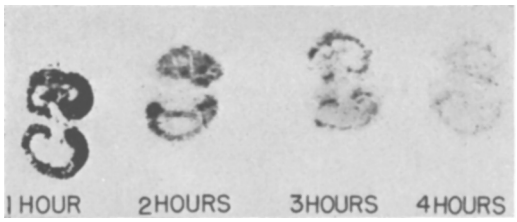

PLATE 1. Radioautographs of rat kidney following intraper. inj. of Hg^{203} mercaptomerin sodium (1 mg/Hg/kg).

tramuscularly into 28 albino rats (165-190 g) to study duration of radioactivity after a single injection. Fourteen groups of 2 animals each were kept in metabolism cages and a group sacrificed hourly for the first 3 hours, daily for the next 7 days, and finally weekly for the next 4 weeks. Twenty-four hour urines were collected for first 7 days. Plasma, renal tissue, and urine were assayed for radioactivity.

Results. Radioautographs (Plate 1) revealed that radioactivity was concentrated in renal cortical areas. Similar localization has been demonstrated after administration of radiomercuric chloride(4).

Intraperitoneally injected Hg^{203} mercaptomerin sodium (Fig. 1) produced a peak plasma concentration in 15-30 minutes and a peak renal accumulation in 30-60 minutes. On the other hand, when Hg^{203} mercaptomerin sodium was injected intramuscularly, peak plasma concentration occurred in 30 minutes and peak renal accumulation was 60 minutes (Fig. 2). Peak renal accumulation following intraperitoneal administration was approximately 25% of that produced by intramuscular injection. Wet weight of the rat kidney was 940 $\pm$ 26 (S.E.) mg.

We then calculated percentage of original material excreted in urine. The amount of mercaptomerin sodium recovered in urine during 4 hours following intraperitoneal injection was 301.1 μg or 42% of original dose. On the other hand, total amount recovered 24 hours following intramuscular injection was 41.2% of original dose. Only 78% of administered dose was recovered during first 72 hours and none was detected after 96 hours.

Additional studies were carried out on 2 apparently healthy male mongrel dogs, weighing 7.5 and 9.0 kg. These animals were anesthetized with pentobarbital sodium (30 mg/kg) and hydrated with normal saline by continuous intravenous drip at 0.1 ml/kg/min. throughout experiment. Renal venous samples were withdrawn through a polyethylene catheter introduced into left renal vein through an abdominal incision. Arterial blood samples were withdrawn through an indwelling needle in the carotid artery. Urine samples were collected with a urethral catheter introduced into the left side through the abdominal incision. Hg^{203} mercaptomerin sodium was injected into the femoral vein within 15 seconds. Blood samples were collected in syringes moistened with heparin. At 5, 10, 15, 30, 60, 90, and 120 minutes, samples were taken simultaneously from renal vein and carotid artery. Urine was collected at 10, 30, 60, 90, and 120 minutes. Arterial plasma concentration at the 5 minute period was only 5.8 μg/ml with an A-V difference of only 0.8 μg/ml (Fig. 4).

Discussion. Radioautographs indicate that mercury is most concentrated in the cortical areas with limited amounts in medulla of kidneys. This is in accord with the findings of Greif *et al.*(1) and de Metry and Aikawa(5). The radiopurity of Hg^{203} mercaptomerin sodium was ascertained by paper chromatography but no studies were performed to determine the chemical stability of this material in tissues. Although the locus of mercurial diuresis is presumably in the tubules, it has not been settled whether it is in the proximal or distal portion(6). However, all portions of the renal tubular structures are present in the region of highest radioactivity.

Radioactivity counts on whole kidney revealed that 91.7% of the injected radioactivity was present within one hour after intramuscular injection. This confirms the findings of Borghgraef *et al.*(2) and Weston *et al.* (7) who reported that mercury is rapidly taken up by the kidney. These data suggest that radioactive mercurial compounds are removed mainly by the renal cortex and are excreted into the urine. Delay in onset of excretion of mercury may be related to the time required to accumulate a critical concentra-

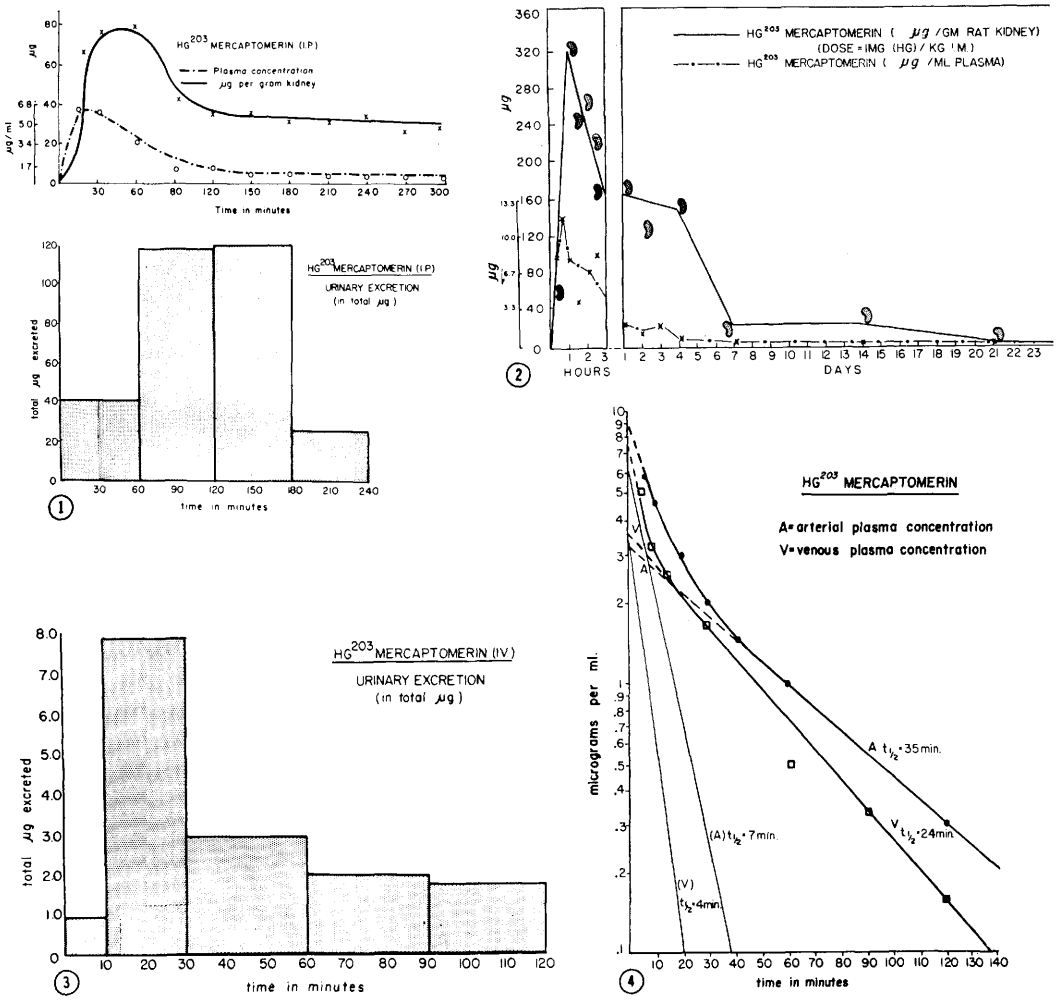

FIG. 1. Concentration of Hg^{203} mercaptomerin sodium in rats following intraper. inj. Urine values represent avg of 3 animals.

FIG. 2. Concentration of Hg^{203} mercaptomerin sodium in rats following intramusc. inj. Each "x" and each "kidney" represents avg of 2 observations.

FIG. 3. Urinary excretion pattern of intrav. Hg^{203} mercaptomerin sodium into dogs.

FIG. 4. Biological decay of plasma concentration following intrav. administration of Hg^{203} mercaptomerin sodium into dogs.

tion of this drug within the tubular cells. Following intravenous administration into dogs, renal excretion of Hg^{203} mercaptomerin sodium was most rapid during the first 30 minutes (Fig. 3) when the A-V difference was greatest (Fig. 4). Renal excretion decreased when the A-V difference diminished and approached a plateau between 90 and 120 minutes. The biological half-life, measured by rate of disappearance of radioactivity from plasma of arterial blood and venous renal blood, indicated at least 2 phases. Graphic resolution of the biological decay curves (Fig. 4) indicated the fast-moving component to have a half-life of 4 minutes for venous plasma and 7 minutes for arterial plasma. The slow-moving component has a half-life of 24 minutes for venous plasma and 35 minutes for arterial plasma. Similar regression curves were obtained by Borghgraef, Kessler, and Pitts(2) following intravenous administration of chlormerodrin.

Although peak plasma concentration and renal accumulation of Hg^{203} mercaptomerin

sodium, when administered intraperitoneally and intramuscularly, occurred at similar time intervals, intramuscular plasma concentration was approximately twice intraperitoneal concentration, and renal accumulation following intramuscular administration was 4 times that of the latter. This may indicate that renal tissue possesses a tremendous avidity or binding capacity for mercurial compounds.

Summary. 1. Using Hg^{203} labeled mercaptomerin sodium and studying radioautographs and renal distribution, 91.7% of an intramuscularly injected dose of 1 mg Hg/kg was found in the kidney within the first hour, and maximum concentration occurred in the cortical area. 2. Radioactivity was detected for 28 days in plasma and in renal tissue. 3. Intravenous administration of radioactive mercaptomerin sodium resulted in a rapid decline in plasma concentration during the first 5 minutes. Rate of urinary excretion appears to be a function of arterial plasma-renal vein plasma difference.

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In vitro Response of Mouse Testis to Human Chorionic Gonadotropin.* (25400)

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A number of investigators have cultured the mammalian testis successfully, either as entire organ or as fragments thereof(1-5). Irrespective of the medium employed or duration of culture, it was concluded that testicular explants had continued to develop in an essentially normal manner. These results are in contrast to those which I have obtained with ovarian explants from young post-natal mice in which an atrophy of the follicular and thecal cells occurs leading to a general loss of organization of the tissue; maintenance of ovarian structure *in vitro* was dependent upon incorporation of proper hormones into the basic medium(6). The following studies with isolated testis were therefore undertaken, using the same medium as that employed for the post-natal ovary, to determine response of the testis under these conditions. Human chorionic gonadotropin (HCG) and lactogenic hormone were the hormones selected for study.

Procedure. Testes from mice of the C57 Black strain, 3 days of age, were cultured on a medium made of 2 parts agar,‡ 1 part Tyrode's solution enriched with equal quantity of synthetic medium 199(7), and 1 part chick embryo extract. Details of the method have been discussed(8), and preparation of hormone-enriched medium has been described (6). Explants were cultured at 31 ± 1°C; every other day they were displaced to new sites on the media. In earlier experiments, the whole testis was cultivated 7 days on a medium enriched with lactogenic hormone or with HCG. In later experiments, each testis

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‡ Agar preparation containing 1 g agar (Difco)/100 cc Gey's solution.