into normal male or female rats, simultaneously with oestradiol resulted in a partial suppression of the reaction of the anterior lobe to oestradiol, a result which has since been duplicated by injecting male hormone simultaneously with oestrone.[13]

Summary. 1. Skene's ducts in the female rat are usually rudimentary. Male hormone substance stimulates growth of these glands to a condition which resembles grossly and histologically the prostate of the male rat. 2. In the present series the incidence of these glands in 35 normal animals is 9.4%, in 13 oestrone-injected animals 0%, in 48 male hormone-injected animals 58.3%. 3. The state of Skene's ducts may be utilized as an indicator of the presence of male hormone. 4. In view of the growth response to male but not to female hormones, the occasional finding of Skene's ducts in an uninjected female rat suggests the presence of male hormone in the normal female. 5. The growth response of the female prostatic glands to the male hormone is further evidence of the masculinizing effect of male hormone substance of the female animal.

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The Localized Sanarelli-Shwartzman Phenomenon in the Rabbit Kidney.

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A new phenomenon of tissue reactivity to bacterial filtrates has recently been described. The filtrates of many bacteria, hitherto not considered to produce exotoxins, have been shown to exert a marked toxic effect when 2 injections into a rabbit, the second injection being intravenous, are separated by an interval of 24 hours. The generalized reaction resulting when the first, or "preparatory" injection is given intravenously was described by Sanarelli,[1] and studied in detail by Apitz,[2] Gratia and Linz,[3] and Gerber.[4] The localized reaction resulting when the preparatory injection is given

[13] Wolfe, J. M., and Hamilton, J. B., *Anat. Rec.*, 1937, **67**, 55.

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[1] Sanarelli, *Ann. de l'Inst. Pasteur*, 1924, **38**, 11.

[2] Apitz, K., *Virchow's Arch. f. path. Anat.*, 1934, **293**, 1.

[3] Gratia, A., and Linz, R., *Ann. de l'Inst. Past.*, 1932, **49**, 131.

[4] Gerber, I. E., *Arch. Path.*, 1936, **21**, 776.

intracutaneously was described by Shwartzman,[5] and subsequently by numerous other investigators. The present status of the phenomenon is summarized and discussed by Shwartzman, Klemperer, and Gerber.[6]

Localized reactions in numerous organs have been described when the preparatory injection was given into the parenchyma of the organ, or even when the organ was prepared by way of its local vascular supply (bibliography in ref. 6). Among the organs described as having been made the site of local reactions is the kidney. Shwartzman[7] clamped the left renal vein in rabbits, injected 0.5 cc. of *B. typhosus* filtrate into the left renal artery and released the vein 5 minutes later. The "provocative" intravenous injection was made 24 hours later, and after 48 hours the prepared kidney showed "severe hemorrhagic lesions in the cortex and medulla." No gross lesions were seen in the opposite kidney, and no microscopic sections were made of either kidney. Loi and Cardia[8] reported similar lesions when a preparatory injection of 0.3 cc. of *B. typhosus* filtrate was made directly into the parenchyma of a rabbit kidney which had been "denervated" by stripping surgically the renal capsule and vessels.

The present study was made for the purpose of investigating the possible use of the localized renal phenomenon in the production of experimental nephritis. Both parenchymal and local intravascular preparation of the kidney were attempted.

The bacterial filtrate used was prepared from *B. coli* communis by the method of Shwartzman.[9] For intravascular preparation, the following technique was used: Under paraldehyde anesthesia the left renal artery and vein were occluded by kinking each separately over the point of a probe, and an injection of 0.2 to 2.0 cc. of filtrate was made into the distal portion of the renal artery. Both vessels were held closed for 3 to 5 minutes. The artery was then released, the vein punctured, and the kidney "washed out" by the removal of 3 to 8 cc. of blood from the renal vein, which was then released. For preparation by direct parenchymal injection, the needle was inserted through the abdominal wall into the substance of the left kidney, and 0.2 to 0.5 cc. of filtrate injected without anesthesia. In

[5] Shwartzman, G., PROC. SOC. EXP. BIOL. AND MED., 1928, **26**, 207; *J. Exp. Med.*, 1928, **48**, 247.

[6] Shwartzman, G., Klemperer, P., and Gerber, I. E., *J. Am. Med. Assn.*, 1936, **107**, 1946.

[7] Shwartzman, G., *J. Exp. Med.*, 1930, **51**, 571.

[8] Loi and Cardia, *Boll. Soc. ital. di Biol. sper.*, 1934, **9**, 775.

[9] Shwartzman, G., PROC. SOC. EXP. BIOL. AND MED., 1929, **26**, 843.

all cases, a control injection of 0.2 cc. of filtrate was made in the abdominal skin at the time of the preparatory injection for the production of a localized Shwartzman phenomenon as a check on the susceptibility of the animal. Twenty-four hours later, 1 cc. of filtrate was given in the marginal ear vein.

Results. Intravascular preparation: Two control animals were given injections of 1 cc. of 0.4% phenol in normal saline into the left renal artery, and 2 more were given 1 cc. of *B. coli* filtrate in the same manner. No gross lesions were evident in any of these animals, and all the kidneys were normal histologically, when autopsy was performed 48 to 72 hours later. Five animals were then subjected to the intravascular preparation as outlined in the previous paragraph. Of these, one showed a negative control skin test, and at autopsy 12 days later all organs were grossly normal, and microscopic sections of liver, heart and both kidneys were normal.

The 4 animals showing positive skin tests were killed and autopsied 4 to 13 days after operation. The kidneys of all showed varying degrees of bilateral focal tubular necrosis in the convoluted tubules, less marked in the longer surviving animals, and 2 showed gross infarctions in the left kidney. There was a conspicuous absence of glomerular and other vascular lesions and of hemorrhage. The livers uniformly showed focal mid-zonal necrosis in various stages of fibrosis, and the myocardium in three showed fibrosing focal necrosis of muscle fibers. One animal developed a bloody diarrhea after 5 days, the intestine showing a severe non-specific inflammatory process microscopically.

Direct preparation of the renal parenchyma: Seven animals were used. In 2, the control skin tests were negative. Autopsies at 8 and 13 days respectively showed all organs grossly normal and both kidneys of each microscopically normal. In 5 animals, the control skin tests were positive. Autopsies from 6 to 13 days later showed in all the same bilateral focal necrosis of convoluted tubules in the kidneys, less marked in the longer surviving animals, that was seen in the animals prepared by way of the renal artery. No glomerular or vascular lesions were seen. In 3, the probable injection site in the left kidney was found, consisting of a sharply localized zone of bloodless glomeruli, dilated tubules and fibrosis extending from the capsule to fairly deeply in the cortex. Gross examination of the remaining viscera showed small focal necroses in the livers of 3, and in the heart of one, the latter proved microscopically.

The infarctions of the kidney with intravascular preparation and the sharply localized damage at the puncture site with direct paren-

chymal preparation may be fairly dismissed as the result of experimental trauma. In both series of experiments there remain the disappearing focal necroses of renal convoluted tubules, and the fibrosing focal necroses of liver and myocardium. These are undoubtedly later stages of the lesions described by Apitz and Gerber, and it would seem that because of the extreme vascularity of the kidney with anastomoses to surrounding vascular systems, sufficient bacterial filtrate escaped into the general circulation to prepare the entire animal for a generalized reaction in spite of the utmost care to restrict the reaction to the kidney. In the light of these results, it seems doubtful that the production of a localized Sanarelli-Shwartzman reaction in the kidney is possible.

The present author has observed small focal renal hemorrhages in the gross in animals dying a short time after the provocative injection, but these animals were discarded in favor of those surviving long enough to show late lesions at autopsy. The part played by the kidneys in a general reaction seems to have been a minor and transitory one, at least in animals that survived, compared to that played by the liver and myocardium, and in one case, the intestine.

Summary and Conclusions. 1. The production of a localized Sanarelli-Shwartzman phenomenon in the rabbit kidney was attempted, both by local vascular and direct parenchymal injection of *B. coli* filtrate. In neither instance was it possible to restrict the reaction to the kidney. 2. The results suggest that sufficient filtrate entered the systemic circulation from the preparatory injection to prepare the entire animal for a generalized reaction, and make it doubtful that the production of a localized renal phenomenon is possible. 3. The late lesions of the generalized phenomenon are described. These seem to indicate the relative insignificance of the renal lesions in surviving animals as compared to those of the liver and the myocardium.