sections that the tubular ends were pushed into the space intervening between the glomerulus and Bowman's capsule. No tubular casts were observed. The glomeruli were in general hyperemic without showing the least trace of hemorrhage. A faint-staining amorphous substance, resembling albuminous exudate, often distended Bowman's capsule. No glomerular adhesions were seen and no cellular reaction of polymorphonuclear or round cell types was found in the interstitial substance, glomeruli or tubules.

Thymus: In several of the chinchilla rabbits the thymus showed similar histopathological changes, consisting in an intense vascular engorgement throughout the thymic substance.

Conclusions: A minimum and specific lethal dose of the concentrated scarlet fever toxic filtrate was not discernible in rabbits, although the chinchilla breed displayed a relatively greater susceptibility to the lethal toxic effects of scarlet fever toxin. The renal changes observed in the rabbit following intravenous injections of unconcentrated and concentrated scarlet fever toxic filtrates were not those of acute hemorrhagic glomerulo-nephritis but rather analogous to lesions observed in milder forms of tubular damage.

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Attempted Production of the Scarlatinal Syndrome with Whole and Filtered Scarlet Fever Faucial Exudate.

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The rôle of *Streptococcus hemolyticus* in scarlet fever is generally admitted to remain as unsettled as the question about the actual cause of this disease.[1] Both Ciuca[2] and Satake[3] failed consistently to produce experimental scarlet fever in a large series of Dick positive human volunteers by swabbing or injecting their tonsils with freshly isolated cultures of scarlet fever streptococci or scarlet fever blood. Specificity of the Dick toxin has not been granted by Bür-

[1] League of Nations. Health Committee, 1929, **3**, Nr. 7, 11; Freund, R., *Immunität, Allergie u. Infektionskr.*, 1929, **2**, 118.

[2] Ciuca, M., and Gheorghiu, I., *Compt. rend. Soc. da Biol.*, 1927, **97**, 1427.

[3] Satake, T., *Bull. de l'Office Internat. d'Hyg. Publ.*, 1927, **19**, 1627.

gers,[4] Cooke,[5] von Gröer and Redich,[6] Friedemann,[7] Meyer,[8] Molkte,[9] Parish and Okell,[10] Smith,[11] Wheeler,[12] Wadsworth,[13] Zlatogoroff and Derkatsch[14] and numerous other investigators. Serological specificity of *Streptococcus scarlatinae* has not been conceded by Bürgers and Wohlfeil,[15] Ciuca,[2] Friedemann,[7] Maclachlan and Mackie,[16] Smith,[11] Wadsworth,[13] Williams,[17] Zlatogoroff and Derkatsch[14] and many others. Failure of the scarlet fever antitoxin to abate septic complications is now generally admitted. This apparent lack of agreement with the group adhering to the streptococcic etiology of scarlet fever recently prompted Zlatogoroff[18] to review the filterable virus theory of the disease. In an extensive series of experiments on rabbits, monkeys and man he claims to have proven that during the incipient stages of scarlet fever a filterable virus is present in the faucial exudate which is capable of activating the otherwise ubiquitous and avirulent hemolytic streptococcus to assume toxigenic and pathogenic properties by which the clinical picture of scarlet fever is produced. When injected either intravenously or subcutaneously in rabbits, monkeys and man the filtered and sterile scarlatinal exudate almost constantly produces the scarlet fever syndrome, with subsequent typical histopathological lesions, as well as changes in the blood-picture, analogous to the epidemic form of the disease. The experimental disease bestows immunity for over 2½ years against reinfection. In rabbits and monkeys, however, the virus alone is capable of producing the disease in the absence of hemolytic streptococci, and yet, upon recovery the animals'

[4] Bürgers, *Klin. Wochenschr.*, 1928, **7**, 293.

[5] Cooke, J. V., *Am. J. Dis. Child.*, 1928, **35**, 762 and 781.

[6] von Gröer, F., and Redlich, F., *Monatschr. f. Kinderh.*, 1928, **37**, 558; *Z. f. exp. Med.*, 1928, **62**, 391, 414, and 444.

[7] Friedemann, U., *Klin. Wochenschr.*, 1928, **7**, 1474 and 2325; *Z. f. Hyg.*, 1928, **108**, 181 and 192.

[8] Meyer, S., *Ztschr. f. Kinderh.*, 1927, **43**, 258; *ibid.*, **45**, 105.

[9] Molkte, O., *Acta Path. et Microbiol. Scand.*, 1930, Suppl., **8**, 275.

[10] Parish, H. J., and Okell, C. C., *Lancet*, 1928, **1**, 746 and 748.

[11] Smith, J., *J. Path. and Bact.*, 1927, **30**, 651; *J. Hyg.*, 1927, **26**, 420 and 434.

[12] Wheeler, M. W., PROC. SOC. EXP. BIOL. AND MED., 1930, **27**, 570; *J. Prev. Med.*, 1930, **4**, 1.

[13] Wadsworth, A. B., *Am. J. Publ. Health*, 1929, **19**, 1287.

[14] Zlatogoroff, S. I., and Derkatsch, W. S., *Ztbl. f. Bakt. Ref.*, 1928, **90**, 399 and 507; *J. Inf. Dis.*, 1928, **42**, 56.

[15] Bürgers and Wohlfeil, T., *Klin. Wochnschr.*, 1928, **7**, 389.

[16] Maclachlan, D. G. S., and Mackie, T., *J. Hyg.*, 1928, **27**, 225.

[17] Williams, A. W., *J. Am. Med. Assn.*, 1929, **93**, 1544; *Am. J. Publ. Health*, 1929, **19**, 1303.

[18] Zlatogoroff, S. I., *Ztbl. f. Bakt. Orig.*, 1929, **113**, 97.

blood-serum contains agglutinins for hemolytic streptococci. When suspended in Ringer's or Locke's solutions Zlatogoroff's filterable virus resists dispersed sunlight for 33 days at room temperature and remains active for 35 days when left in the dark. In 0.5% phenol it remains viable for 15 days and heating for 1 hour at 60° C. completely destroys it. The burden of our communication is the results obtained in guinea pigs, rabbits and monkeys *(Macacus rhesus)* with material removed by Zlatogoroff's method from early and moderately severe cases of scarlet fever.

Scarlatinal Material: Exudations in the mouth, fauces and tonsillar crypts were removed on large sterile cotton swabs and immediately immersed in 50 cc. of saline solution contained in Ehrlenmeyer flasks with glass beads. This material was placed in the shaking machine for 2 hours. At that time half of the emulsion was passed through a Berkefeld V candle. Subsequent study revealed that the filtrate was sterile and that the whole faucial exudations contained about 90% of hemolytic streptococci, determined by the poured blood-agar method. Care was taken always to inject the material into the experimental animal within 2 days after removal from the patient. The pH of the filtrate was usually about 5.2-5.8, while the whole exudate varied between 4.8 and 5.2. When left in the refrigerator, the hemolytic streptococci in the whole faucial exudate remained viable about 6 days.

Animal Inoculations: Twelve guinea pigs, 16 rabbits and 30 monkeys were employed in this study. None of the animals reacted positively with 40 skin test doses of the Dick toxin. Previous to the inoculation with scarlatinal material the daily normal curves of temperature, number of leucocytes and differential blood cells were determined for one week in the guinea-pigs and rabbits employed. The absence of natural agglutinins for *Streptococcus scarlatinae* (Dochez N.Y. 5) was likewise determined in the guinea pigs and rabbits. The entire abdomen of all animals were carefully depilated without inflicting abrasions in the skin. Following the injection of the scarlatinal material, each animal was studied daily for changes in physical appearance, while the temperature, number of leucocytes and the differential blood picture were determined in the guinea pigs and rabbits. Except in the monkeys the Dick test was performed weekly with 1 to 40 skin test doses of toxin, while agglutination tests were made one month after inoculation, the antigens employed being *Streptococcus scarlatinae* (Dochez N. Y. 5) and the strain of hemolytic streptococcus isolated from the scarlatinal exudate injected. The following results were obtained: *Guinea pigs* (300-500

gm.): 6 normal guinea pigs injected subcutaneously with 2 cc. of the sterile filtrate of the scarlatinal faucial exudate showed nothing remarkable for one month following inoculation. Six other normal white guinea pigs were injected subcutaneously with a mixture of 0.5 cc. of whole scarlatinal faucial exudate, 0.5 cc. of a 24-hour broth culture of *Streptococcus scarlatinae* (Dochez N. Y. 5) and 1 cc. of melted guinea pig blood-agar reduced to about 50° C. These animals showed nothing unusual during the following month's observation except the occurrence of positive blood cultures of hemolytic streptococci in 3 animals on the fifth, seventh and eighth days respectively, and positive skin reactions (14 to 20 mm. diameters) with 40 skin test doses of the Dick toxin about the fourteenth day after inoculation with the scarlatinal material. Reinoculation of the whole group of animals took place one month after the first inoculation. Three cc. of the whole scarlatinal faucial exudate were injected subcutaneously. Within 24 hours a suspicious erythema appeared in 5 animals. All of these guinea pigs had previously been inoculated with the whole scarlatinal material and 3 had previously given positive skin reactions with 40 skin test doses of the Dick toxin. Definite flaky desquamation took place within a week in these animals. Neutralization of the skin reactions with scarlet fever antitoxin was not completely accomplished. Neither were any remarkable changes observed in the temperature, leucocytic count nor in the differential blood picture during the erythematous phase. Agglutination tests also remained inconclusive. The Dick tests became negative with 40 skin test doses of the toxin about 4 weeks after the second inoculation with the whole scarlatinal material. The erythematous reactions seemed definitely allergic in nature. *Rabbits* (1600-2200 gm.): 3 cc. of the sterile filtrate of the scarlatinal faucial exudate were injected intravenously in 3 white rabbits and subcutaneously in 3 others. Nothing remarkable was observed in these animals during the following 2 weeks. Six white rabbits were injected subcutaneously with 5 cc. of the whole scarlatinal faucial exudate. Within 24 hours 5 of these animals developed a generalized and suggestive scarlatinal rash which led to fine and flaky desquamation during the following week. These animals reacted positively with 40 skin test doses of the Dick toxin about the fifteenth day after inoculation and these reactions became negative 2 weeks later. One month after the appearance of the rash 3 rabbits presented agglutinin-titers of 1-80, 1-160 and 1-320 respectively with the strain of hemolytic streptococcus isolated from the exudate, while no agglutination occurred with the *Streptococcus scarlatinae*

(Dochez N. Y. 5). Reinoculation subcutaneously with 5 cc. of the unfiltered scarlatinal exudate one month after the first inoculation produced a diffuse and mild erythema in 2 rabbits previously injected with the unfiltered scarlatinal exudate. While the Dick test remained negative in all other rabbits these 2 rabbits reacted strongly with 40 skin test doses of the toxin. Neutralization of these reactions with scarlet fever antitoxin was inconclusive. The changes in temperature, number of leucocytes and differential blood picture during the erythematous phase were not remarkable from that observed in the non-reacting animals. The blood cultures remained consistently negative. *Monkeys:* Thirty monkeys *(Macacus rhesus)* were placed at our disposal by the kind permission of Dr. G. W. Corner. Each animal was injected subcutaneously with 4 cc. of the whole scarlatinal faucial exudate. Nothing remarkable was observed in any one animal during one month's observation except local swelling and slight redness at the site of inoculation, which cleared up rapidly without abscess formation.

Conclusions. Sterile filtrates of scarlatinal faucial exudations failed to produce the scarlatinal syndrome in guinea pigs and rabbits. Subcutaneous inoculation of the unfiltered scarlatinal faucial exudations into guinea pigs and rabbits produced irregularly an erythema suggestive of scarlet fever, without any remarkable changes in temperature, leucocytic cell count or differential blood picture. Development of marked skin sensitivity to the Dick toxin following the injection of scarlatinal exudations suggested an allergic basis for the suggestive scarlatinal rash which was followed by desquamation. Monkeys remained entirely refractory to the scarlatinal faucial exudations. A filterable virus in scarlatinal faucial exudations capable of producing the scarlatinal syndrome in guinea pigs and rabbits was not demonstrable.

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Effect of Epinephrine on the Oxygen Consumption of Frogs Before and After Hepatectomy.

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It has been shown that epinephrine injections in physiological doses liberate lactic acid in muscle. From the work of Meyerhof it is known that an increased formation of lactic acid in muscle is