plastic goiter seems to differ from the reported spontaneous goiter, in that it does not alter the natural resistance of the rat to thyreotropic stimulation.

9499

The Purpuric Reaction Produced in Animals by Derivatives of the Pneumococcus.

KENNETH GOODNER AND FRANK L. HORSFALL, JR.
From the Hospital of the Rockefeller Institute for Medical Research, New York.

Julianelle and Reimann[1] have described the purpura that develops in white mice following the intraäbdominal injection of pneumococcal autolysates. This reaction is most evident in those portions of the skin on which hair is either scanty or absent. They concluded that some autolytic derivative of the bacterial cells damaged the endothelium of the capillaries in these areas.

The experiments of Julianelle and Reimann have been largely repeated and extended. One of the most striking features of the reaction is that the purpura produced is seldom evenly distributed over the ears, feet, tail, snout, and genitalia. Even on the ears the distribution may be splotchy while along the tail the reaction is always most irregular, certain points showing a very intense reaction while others may be completely negative. These irregularities as well as the anatomical distribution of purpura suggested that some factor such as a mild trauma might be involved in the localization of the reaction. As a test of this hypothesis several experiments have been carried out of which 2 typical examples may be cited.

Experiment 1. An area of one sq. cm. of the abdominal skin of a mouse was carefully shaved. Immediately thereafter 0.5 cc. of an autolysate of rough pneumococci prepared by the method of Julianelle and Reimann was injected intraäbdominally at a point removed from the shaved area. At 24 hours the shaved lesion was markedly purpuric but the removal of hair from neighboring areas showed these to be free of purpura. A second injection of the autolysate was then given. Twenty-four hours thereafter the freshly shaven areas were purpuric but further removal of hair showed that the adjacent skin was completely clear. It seems reasonable to

1 Julianelle, L. A., and Reimann, H. A., *J. Exp. Med.*, 1926, **43**, 87, 97; 1927, **45**, 609.

conclude that the irritation associated with the shaving determined the localization of the purpura.

Experiment 2. Mice were placed in individual jars lined with cotton. After a preliminary period of 24 hours during which the animals were not handled, each mouse received an intraäbdominal injection of 0.5 cc. of an autolysate of rough pneumococci. In the course of these injections great care was taken to avoid handling the ears except as noted in Table I. From these results it will be noted that, in general, the purpuric reaction occurred in those areas previously subjected to mild irritation.

TABLE I.

Mouse	Handling	Results at 12 hours; presence of purpura	
		Left ear	Right ear
1	Ears avoided	+	—
2	" "	—	—
3	" "	—	—
4	Left ear handled, right avoided	++	—
5	Right ear handled, left avoided	—	++
6	Both ears handled	++	++
7	" " "	++	++
8	" " "	++	++

A somewhat similar predilection for cutaneous areas subjected to mild irritation is manifested by the eruptions of certain exanthemata and some forms of clinical purpura. In these instances the local pressure of clothing or of applied adhesive tape will frequently determine the sites of the initial cutaneous lesions.

Previous reports[2] have described the purpura observed in the dermal pneumococcal infection of the rabbit. This reaction not infrequently develops in the course of the infectious process and is almost invariably associated with the development of bacteriemia. The extent and intensity are sometimes increased after the intravenous administration of certain substances as, for example, a bacterial extract containing a specific enzyme.[3] This purpuric reaction in the rabbit is always confined to the locally infected area and has not been observed on other parts of the body-surface. It has now been found that if one injects pneumococcal autolysate intravenously in a dermally infected rabbit the entire dermal lesion becomes purpuric within a very short time, but that purpura occurs only in this area.

In summary, the autolysis of pneumococci under certain condi-

[2] Goodner, K., *J. Exp. Med.*, 1928, **48**, 1; Goodner, K., and Rhoads, C. P., *J. Exp. Med.*, 1931, **54**, 41.

[3] Goodner, K., Dubos, R., and Avery, O. T., *J. Exp. Med.*, 1932, **55**, 393.

tions gives rise to a substance capable of producing purpuric reactions in mice and in rabbits but the presence and location of these reactions is dependent upon the condition of the capillaries in the various cutaneous areas.

9500 P

Differentiation of Glomerular and Tubular Function in Glomerular Nephritis.

WILLIAM GOLDRING AND HOMER W. SMITH.

From the Departments of Medicine and Physiology, New York University College of Medicine, and the Third (New York University) Medical Division of Bellevue Hospital, New York City.

It was recently shown that at low plasma levels about 94% of the phenol red clearance in the normal human kidney is accomplished by tubular activity.[1] In view of this fact this clearance is a sensitive index of tubular excretion, and when observed simultaneously with the inulin clearance, affords evidence of the respective functional activities of the tubules and of the glomeruli. The present investigation concerns the study of these clearances together with the urea clearance in 21 subjects with glomerular nephritis either during a first attack, during an exacerbation, or in the chronic stage.

We have endeavored to maintain the urine flow above the augmentation limit wherever possible so that the urea clearances would be physiologically comparable. The urea clearance has ranged from 64.6 to 5.4, the inulin clearance from 131 to 6.2 cc. per minute; the urea/inulin clearance ratio has ranged from its normal value of 0.55 to a value of 0.88. In no case has the urea/inulin clearance ratio been observed to fall significantly below the normal value in any stage of the disease. In general it tends to rise, so that in advanced chronic glomerular nephritis it has a value of 0.85 or higher. Our observations do not bear out the belief that in renal disease there is increased back-diffusion of urea, or that the elevation of the blood urea is due to such back-diffusion.

A full discussion of the behavior of the phenol red clearance and its relation to the inulin clearance in various stages of disease must be deferred to a later time, but a few interesting features may be noted here. In general, in those individuals in whom renal impair-

[1] Goldring, W., Clarke, R. W., and Smith, H. W., *J. Clin. Invest.*, 1936, **15**, 221.