

Granular bodies were not seen in imprints, probably because of their fragility. The current custom is to depend on imprints or smears, which show elementary particles but not granular bodies. This may explain why the granular body has not been noted previously.

In a recent description of lesions caused by the Nigg strain,⁵ the presence of intracytoplasmic elementary particles is emphasized, this and other findings linking its agent to those of lymphogranuloma venereum and psittacosis.⁷ The intracytoplasmic collection of elementary particles in experimental lymphogranuloma venereum has been named by Miyagawa and associates⁶ "granulocorpuscle," and their work has been confirmed

⁵ Nigg, C., and Eaton, M. D., *J. Exp. Med.*, 1944, **79**, 477.

by Shaffer, Rake, and McKee.⁷ In the yolk sac infected with lymphogranuloma virus, Rake and Jones⁸ noted the formation of a "vesicle" containing minute spheroid particles, the whole being similar to the granular body noted by us in the lungs of mice.

Summary. A granular body composed of large numbers of minute spherical particles of uniform size is described in pneumonic consolidations. This lesion appears to be characteristic of certain transmissible non-bacterial pneumonias of mice.

⁶ Miyagawa, Y., Mitamura, T., Yaoi, H., Ishii, N., Nakajima, H., Okanishi, J., Watanabe, S., and Sato, K., *Jap. J. Exp. Med.*, 1935, **13**, 1.

⁷ Shaffer, M. F., Rake, G., and McKee, C. M., *Proc. Soc. Exp. Biol. and Med.*, 1940, **44**, 408.

⁸ Rake, G., and Jones, H. P., *J. Exp. Med.*, 1942, **75**, 323.

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Specificity of Cutaneous Allergy to Procaine in Man.

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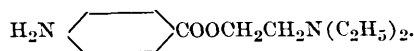
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This study was carried out on a 26-year-old dentist who was found to respond with itching, vivid erythema, edema, vesiculation, and oozing to contact with aqueous solutions of procaine hydrochloride. The threshold concentration at which this eczematous reaction was just visible, was found to be at 1:36,000 with aqueous solutions of procaine salts (hydrochloride, borate, butyrate), as well as with the base procaine dissolved in triethanolamine.

The cutaneous reactions to procaine and related compounds were tested by the simple drop method, which consisted of applying drops of equal size to the intact skin, and allowing them to remain there for exactly 5 minutes. The reactions were observed and noted 24 hours later. The standard test concentration of all solutions tested was 2½%,

i.e., 900 times the threshold concentration of procaine. Bases were dissolved in triethanolamine; salts in water.

Procaine has the structure of an ester:



The two compounds forming this ester, namely, the acid, *p*-aminobenzoic acid, and the alcohol, β -diethyl-amino-ethanol: $\text{HOCH}_2\text{CH}_2\text{N}(\text{C}_2\text{H}_5)_2$, when tested separately, yielded completely negative skin reactions in our subject. Similarly, seven alkyl esters of *p*-aminobenzoic acid up to C_5 , including the isopropyl and isobutyl esters, proved to be without any effect when dissolved in triethanolamine and tested in 2½% concentration. Several aliphatic compounds containing a tertiary amine-N, as does the side chain of procaine, such as triethylamine, $(\text{C}_2\text{H}_5)_3\text{N}$, and its hydrobromide, triethanolamine, $(\text{HOCH}_2\text{CH}_2)_3\text{N}$, and β -chloro-ethyl-diethyl-

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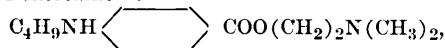
amine, $\text{ClCH}_2\text{CH}_2\text{N}(\text{C}_2\text{H}_5)_2$, were also ineffective.

The importance of the aromatic amino group for the reaction in question was demonstrated by testing 7 local anesthetics, apothesine, stovaine, alypin, metycaine, diothane, nupercaine, and intracaine, all having a tertiary amine in their side chains, but lacking the aromatic amino group on the benzene ring. None of these compounds caused a skin reaction in our subject.

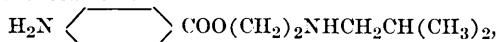
Further skin testing proved that the aromatic amino group has not only to be present on the ring but also must be present in the para-position. We synthesized the diethyl-amino-ethanol esters of ortho- and meta-aminobenzoic acids, compounds which were different from procaine only in the position of the aromatic amino group. The subject's skin did not respond to these compounds.

Positive reactions, to the same degree as elicited by procaine, were obtained with five compounds, all commercially available local anesthetics:

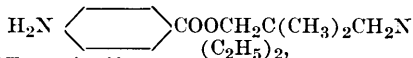
"Pontocaine":



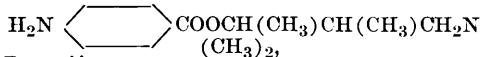
"Monocaine":



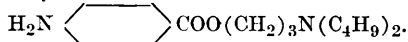
"Larocaine":



"Tutocaine":



"Butyn":



Pontocaine has a side chain similar to that of procaine inasmuch as there are 2 C atoms between the tertiary amine-N and the C atom of the carboxylic group. But it differs from procaine by having an H atom of the aromatic amino group substituted by a butyl radical, and having 2 methyl groups instead of 2 ethyl groups attached to the tertiary amine-N. In monocaine the position of the amine-N is similar to that in procaine and pontocaine but it is a secondary amine, and the attached alkyl chain is different. In the remaining 3 compounds the carboxylic group is separated from the tertiary amine-N by 3 instead of 2 C

atoms, and the length of the alkyl chain shows great variations.

Benzoic acid, anilin, *p*-aminophenol, *p*-phenylendiamine and *p*-amino-*m*-hydroxybenzoic-acid-methylester yielded negative results.

The passive transfer test of Prausnitz-Kuestner was negative, an indication that there were no antibodies circulating in the blood.

Discussion. Earlier attempts to establish the range of specificity in epidermal hypersensitiveness to procaine^{1,2,3,4} yielded incomplete or contradictory results. In the subject of the present study, the allergic response has required the presence of a *p*-aminobenzoic acid ester, in which the side chain contains a secondary or tertiary amine-nitrogen. The length of this chain may be different. Substitutions of H atoms by alkyl groups in the aromatic amino group or in the side chain have not altered the antigenic effect.

The paramount importance of the position of benzene ring substitutions for the specificity of serological reactions was demonstrated by Landsteiner.⁵ Pauling and co-workers⁶ showed that para-substituted compounds have greater antigenic effectiveness than compounds with meta- and ortho-substitutions. It seems that the pattern of group specificity in purely epidermal hypersensitiveness, without antibodies in the serum, follows a pattern similar to that of serological reactions.

Summary. In the subject studied eczematous contact type reactions were elicited with a group of *p*-aminobenzoic acid esters which contain a secondary or a tertiary amine in the side chain. The length of the side chain was irrelevant. Substitutions of H atoms by alkyl groups in the aromatic amino group or in the side chain did not alter the antigenic effectiveness. Benzoic acid esters

¹ Schwarzschild, L., *Arch. f. Dermat. und Syph.*, 1928, **156**, 432.

² James, B. M., *J. Am. Med. Assn.*, 1931, **97**, 440.

³ Waldron, G. W., *Proc. Staff Meet. Mayo Clinic*, 1934, **9**, 254.

⁴ Goodman, M. H., *J. Invest. Dermat.*, 1939, **2**, 53.

⁵ Landsteiner, K., *The Specificity of Serological Reactions*, C. C. Thomas, Springfield, Ill., 1936.

⁶ Pressman, D., Brown, D. H., and Pauling, L., *J. Am. Chem. Soc.*, 1942, **64**, 3015.

with a tertiary amine in the side chain but without an aromatic amino group, or with an amino group in meta- or ortho-position, were ineffective.

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Evidence that Testicular Androgen Stimulates the Inguinal Bursa of the Adult Rat.*

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In regard to factors which influence the descent of the testis, two recent and related suggestions have been made: (1) that androgen promotes descent by causing the inguinal bursa of Klaatsch¹ to become large enough to receive the testis and (2) that the gubernaculum acting as a mechanical factor assists androgen in expanding the bursa.^{2,3} These suggestions have grown out of certain observations upon man^{4,5} and rodents. In the ground squirrel, it was found that the gubernaculum is not requisite for the final stages of descent² and that injections of androgen increase the weight of the bursa.³ From earlier investigations it had become clear that in both ground squirrel⁶ and rat⁷ the weight of the bursa is influenced by 2 synergistic factors: (1) the hormonal action of testicular androgen and (2) the mechanical action of the contents of the bursa. The purpose of the present account is to report in greater detail

the earlier investigation in the rat which has been presented hitherto only in the form of an abstract.⁷ Recently, Almquist and Andrews have noted that injections of testosterone propionate increase the weight of the bursa and have given us permission to cite their forthcoming paper.⁸

Concerning materials and methods, 29 of 42 rats were castrated (Tables I and II). A median abdominal incision was made and castration was performed either bilaterally (25 cases) or unilaterally (4 cases). In all instances except 7, the gubernaculum and the mesentery, supporting epididymis and ductus deferens, were severed, then the spermatic vessels were ligated in the lumbar region, and the testis removed together with the epididymis, the greater part of the ductus deferens and most of the "lumbar fat body." In the 7 exceptional instances, no structure except the testis was removed from the left side of the animal; after the spermatic vessels had been ligated at a point near the mediastinum testis and then severed, the testis was removed by shelling it from the epididymis. Generally the orifice of the bursa was permitted to remain open. However, in each of 8 rats, a sterile pellet of paraffin was placed in the right bursa and the orifice was closed by sutures. At autopsy, the various bursæ were removed, weighed to the nearest tenth of a milligram and placed in Bouin's solution. Twenty-two of the bursæ were sectioned at 7 μ and the sections were stained with hematoxylin

* Aided by a grant from the medical research funds of the Graduate School of the University of Minnesota and a grant from the Research Council of the University of Missouri.

¹ Klaatsch, H., *Morph. Jahrb.*, 1890, **16**, 587.

² Wells, L. J., *Anat. Rec.*, 1944, **88**, 465 (Suppl. 4, April).

³ Wells, L. J., *Anat. Rec.*, 1944, **88**, 465 (Suppl. 4, April).

⁴ Wells, L. J., *Surgery*, 1943, **14**, 436.

⁵ Wells, L. J., *Bull. Minnesota Med. Found.*, 1944, **4**, 50.

⁶ Wells, L. J., *Proc. Soc. Exp. Biol. and Med.*, 1937, **36**, 625.

⁷ Wells, L. J., and Overholser, M. D., *Anat. Rec.*, 1937, **70**, 121 (Suppl. 1, December).

⁸ Almquist, J. O., and Andrews, F. N., *Anat. Rec.*, 1944, **80** (June, in press).