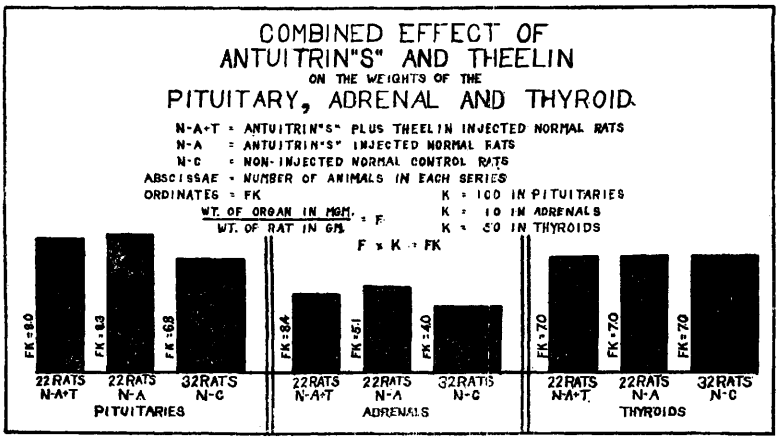

Resulting from the injections of 2 rat units of Antuitrin "S", the pituitaries were increased in weight 22% and the adrenals 27.5%, as compared with the normal control animals. Whereas, the injections of 2 rat units of Antuitrin plus 20 rat units of Theelin only caused an increase of 17.7% for the pituitaries and 20% for the adrenals as compared with the normal control rats. No significant changes in the weights of the thyroids were found.

Conclusion. 1. A combination of Antuitrin "S" and Theelin increases the weight of the pituitary and adrenal in the normal rat. 2. Antuitrin "S" alone causes a slightly greater increase than Antuitrin "S" plus Theelin.

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Lipolytic Activity of Rat Lepromata During Treatment with Various Antileprotics.*

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We previously discussed the distribution of lipase in tissues of normal and experimentally infected leprous rats,[1] as observed by us preliminary to a study of changes in lipolytic activity during

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treatment of infected animals. Our subsequent observations demonstrating that there is no significant change in lipolytic activity of tissues of leprous animals during treatment are reported elsewhere.[2] This present report is concerned with changes in the lipase content of the leproma during intensive "plancha" treatment[3] with various antileprotic drugs.

The lipolytic activity of 60 untreated lepromata and 36 treated lepromata was estimated by Loevenhart's method[4] as used by us previously, and was found to be $0.16\pm0.03\%$ and $0.15\pm0.04\%$ respectively. Approximately half the material in both cases was obtained by biopsy and the other half from animals dying or sacrificed. It is apparent from these determinations that there is no tendency during treatment for the lipolytic activity of lepromatous subcutaneous tissue to approach the value of $0.83\pm0.07\%$ found by us for normal subcutaneous tissue of rats with "early stage" leprosy.

No correlation was found between apparent lipase content of lepromata and type of antileprotic drug used. The average lipolytic activity of lepromata of rats treated over 6 months with maximum tolerated doses of the more important drugs considered was: ethyl chaulmoograte, $0.15\pm0.03\%$; "Alepol," $0.15\pm0.05\%$; ethyl di-n-heptyl acetate,† $0.11\pm0.04\%$; sodium dihydrochaulmoogryl p-phenetidine sulfonate, $0.12\pm0.05\%$; sodium chaulmoogryl p-phenetidine sulfonate, $0.13\pm0.02\%$.

Two possible explanations of the cause of the low lipolytic activity of leprous tissues were examined experimentally. First, the absence of any lipase-inhibitory substance in lepromata was shown by the addition of leproma brie to other tissue extracts which results in a summation of lipolytic activity, even if both are incubated together for a short time. Secondly, mechanical dilution of tissue by the leprosy bacillus, which has a low lipase content, was considered.

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[2] Anderson, H. H., Emerson, G., and Leake, C. D., *Am. J. Trop. Med.*, 1933, in press.

[3] Lara, C. B., and Nicolas, C., *J. Philip. Is. Med. Assn.*, 1929, **9**, 321; Velasco, F. I., Alonso, J. M., Limkako, G., and Fernandez, G., *Ibid.*, 1929, **9**, 327; Lara, C. B., *Ibid.*, 1929, **9**, 336.

[4] Kastle, J. H., and Loevenhart, A. S., *Am. Chem. J.*, 1900, **24**, 491; Loevenhart, A. S., *Am. J. Physiol.*, 1902, **6**, 331.

† We are indebted to Dr. Roger Adams, Department of Chemistry, University of Illinois, for kindly furnishing us with a quantity of di-n-heptyl acetic acid, and to Dr. Richard Wrenshall, Department of Chemistry, University of Hawaii, for generously supplying us with various new chaulmoogryl derivatives as well as with ethyl chaulmoograte.

Determination of the ethyl butyrate esterase content of *Mycobacterium leprae hominis* (Mary Puhulahula strain, isolated in pure culture by Dr. E. L. Walker) gave values of 0.27 to 0.28% for a 10% suspension on duplicate analyses. Kendall, Walker and Day[5] have also reported extremely low values for the human leprosy bacillus. Since this organism is not the pathogen of rat leprosy, these results have no exact relation to the values found for lepromata, which are themselves nearly pure cultures of *M. leprae muris*. They give a strong indication of the lack of lipase in the rat leprosy bacillus, however. It is unfortunate that *M. leprae muris* cannot be cultivated *in vitro* sufficiently well to make possible a similar study with it (Koch[6]).

It is concluded, therefore, that the apparent low lipase content of lepromata is real, and that this condition is probably brought about by the dilution of normal tissue by tremendous numbers of *M. leprae*.‡ This holds for other tissues of infected rats as well, since massive invasion of most internal organs may occur (Schlossberger and Koch[7]). The explanation of the wide variation of lipolytic activity previously found is obvious. Also, none of the drugs studied produces lipase activation *in vivo*,§ confirming the work of Neill and Dewar[8] with ethyl chaulmoograte in human lepers. In view of the failure of leprosy therapy with a specific lipase activator ("javanin," Eubanas[9]) and the reputed clinical efficacy of chaulmoogra derivatives, it is doubtful that the latter act therapeutically through an indirect stimulation of the lipolytic activity of the tissues, as suggested by Shaw-Mackenzie and Rogers.[10]

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[6] Koch, F., *Z. f. Haut- u. Geschlechtskrankh.*, (orig.), 1932, **40**, 433.

‡ A somewhat similar explanation of the cause of the apparent low lipolytic activity of tubercular guinea pig tissues has been proposed. Happold, F. C., and Taylor, A., *Brit. J. Exp. Path.*, 1927, **8**, 101; Susman, W., and Happold, F. C., *Ibid.*, 1927, **8**, 106; Happold, F. C., and Taylor, A., *Ibid.*, 1931, **12**, 272.

[7] Schlossberger, H., and Koch, F., *Z. f. Bakt., Parasitenkunde u. Infektionskrankh (Sitzber.)*, 1932, **106**, 382; Schlossberger, H., and Koch, F., *Gedenkschrift f. Joannovic*, Belgrad, 1932.

§ We have been unable to confirm Shaw-Mackenzie's report of *in vitro* activation, also. Further work on this is in progress.

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[10] Shaw-Mackenzie, J. A., *J. Trop. Med. Hyg.*, 1921, **24**, 161; Rogers, L., *Brit. Med. J.*, 1923, **2**, 11; *Lancet*, June 28, 1924, 1297.