products formed bismuth complexes. Changes in chemical reaction might affect the results, but were not considered, the products being used as in therapeutics.

Conclusion. The amphoteric character of bismuth in 6 different products used in the treatment of syphilis, and variations in the behavior of the metal under different conditions, were demonstrated. These properties are believed to be of significance for the pharmacological and clinical actions of bismuth, such as absorption, toxicity, cerebral penetration, activity in cerebrospinal syphilis, etc. Correlation appears to exist between cerebral and spinal fluid penetration, and the electronegative (anionic) character of bismuth, which is consistent with the comparatively greater penetration of other anions than cations.

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Streptococcus Leucocidin and the Resistance of Clasmatocytes.

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Although long known (Ruediger[1]), the leucocyte destroying properties of virulent hemolytic streptococci have never been as fully investigated as they deserve. We agree with McLeod[2] that leucocidin formation is perhaps the most important factor in the virulence of this micro-organism. We have recently undertaken a more complete analysis of leucocidin which we believe is the first since that of Channon and McLeod.[3] The only other study that is at all complete is that of Nakayama.[4]

The presence of leucocidin in a broth culture of streptococcus is evidenced by the demonstrable disintegration of leucocytes that are exposed to it, or better, by interference with the oxygen absorption of these cells when living as contrasted by its absence when they are dead. This change is delicately measured by the methylene blue bioscopic test of Neisser and Wechsberg.

The precise mode of action of leucocidin under conditions of in-

[1] Ruediger, *J. Am. Med. Assn.*, 1905, **44**, 198.

[2] McLeod, *J. Path. and Bact.*, 1914, **19**, 393.

[3] Channon and McLeod, *J. Path. and Bact.*, 1929, **32**, 283.

[4] Nakayama, *J. Inf. Dis.*, 1920, **27**, 270.

fection has not been made clear. In our opinion it is operative primarily within the leucocytes that have already ingested streptococci and for this and other reasons is separable from the negatively chemotactic substances known as "virulins" and aggressins. Nakayama believed the leucocidin separate from the hemotoxin also liberally produced by the streptococcus but Channon and McLeod question this. In our experiments leucocidin seems clearly separable from hemotoxin. In the first place leucocidin is not present in many hemolytic or hemotoxin-forming streptococci. Leucocidin continues to increase in inoculated broth for at least 48 hours and remains there for several days, whereas hemotoxin is present in greatest potency in from 8 to 12 hours and may entirely disappear by the end of 24 hours. Leucocidin is much more thermostable than hemotoxin; it resists heating to 65° for an hour, whereas 56°C. for one-half hour destroys hemotoxin. Leucocidin may actually be concentrated by evaporation at a moderate temperature. Leucocidin may be filtered through porcelain candles, which procedure diminishes or eliminates hemotoxin. Nakayama found the two substances separable by specific absorption.

Our streptococcus studies extending over many years have continued to prove more and more conclusively that tissue macrophages are superior to the polymorphonuclear leucocytes in various conditions of resistance and immunity and particularly in streptococcus infections. Impressed with the direct relationship of streptococcus leucocidin to streptococcus virulence, it is now of great interest to us to find that macrophages are much more resistant to leucocidin than are polymorphonuclear cells. A 3-day pleural exudate of the rabbit, containing about 50% clasmatocytes, reduces methylene blue 2 to 4 times as well as a 24-hour exudate which is largely polymorphonuclear. A given number of clasmatocytes, moreover, resists destruction by leucocidin in a dosage that completely abolishes respiratory activity in an aliquot portion of polymorphonuclears. In other words, the relatively perfect resistance of macrophages against leucocidin would seem to account for their superiority in defending the rabbit against virulent streptococcus infection.