in different stages of intoxication. This procedure, we believe, should prove useful in many problems involving alcoholic intoxication.

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Hemorrhagic Necrotic Skin Lesions in Rabbit Produced by *Hemophilus influenzæ* and *Hemophilus pertussis.**

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When injected into the skin of rabbits, cultures of *H. influenzæ* can readily be distinguished from cultures of *H. pertussis.* While *H. influenzæ* causes slight inflammation, characterized by redness and swelling, *H. pertussis* produces bluish-violet discoloration in the involved part of the skin, frequently followed by necrosis.[1, 2] The observations to be reported are concerned with the influence of intravenous injection of *H. influenzæ* and *H. pertussis* on the skin lesions caused by the intradermal injection of the respective organisms.

For our experiments *H. influenzæ* is cultivated on Levinthal agar, *H. pertussis* on Bordet-Gengou medium, containing 25% rabbit blood. Twenty-four or 48-hour cultures of *H. influenzæ* and 48-hour cultures of *H. pertussis* are suspended in saline. The bacterial content of the suspension varies between 2 to 4 billion microbes per cc. Rabbits are injected intradermally with 0.25 cc. each of suspensions of *H. influenzæ* and *H. pertussis* and reinjected intravenously 24 hours later with 1 to 2 cc. of a suspension of *H. influenzæ.* Three to 6 hours later the areas prepared intradermally with *H. influenzæ* are transformed into a bluish-black lesion, and necrosis follows. The influence of the intravenous injection on areas inoculated with *H. pertussis* is only moderate, mostly none. The intravenous injection of *H. pertussis* produces the same results as the intravenous injection of *H. influenzæ.* It also may lead to hemorrhagic-necrotic lesions in the areas of the skin previously inoculated with *H. influenzæ,* while the areas inoculated with *H. pertussis* are usually not affected. We have the

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1 Takagi, Y., cited by Kasahara, M., *Klin. Wochenschr.*, 1933, 1609.

2 Gundel, M., and Schlueter, W., *Z. Blatt for Bact.*, Orig. 1933, **129**, 461.

impression, however, that the intravenous injection of *H. influenzæ* is more powerful than the injection of *H. pertussis*. It should be mentioned that in these experiments about one-third of the rabbits employed proved to be refractory.

TABLE I.

Influence of Intravenous Injection of *H. influenzæ* on Skin Areas 24 Hours Previously Injected with *H. pertussis* and *H. influenzæ*.

Aspect of Skin Areas	Rabbit skin inoculated with I. *H. pertussis*	II. *H. influenzæ*
A. Before intravenous injection	Bluish-violet lesion with indistinct outline	Redness, sometimes slight swelling with a tiny yellowish spot in the center
B. 5 hours after intravenous injection	No change	Dark bluish discoloration, distinct outline, beginning necrosis
C. 24 hours after intravenous injection	Appearance of small hemorrhagic - necrotic areas within or around the bluish-violet lesions	Hemorrhagic-necrotic lesions with distinct outline

According to Shwartzman, he and Frisch obtained an exotoxin from *H. influenzæ*, as did Gross, Mishulow, Mowry and Scott and later Koplik from *H. pertussis*.[3, 4, 5, 6, 7] We also succeeded in preparing effective agar-washing filtrates of *H. influenzæ* using the technique described by Shwartzman for the preparation of *B. typhosus* agar-washing filtrates. It seems however, unlikely that the skin lesions described in this paper can be attributed to exotoxins. Suspensions of *H. influenzæ* washed several times were equally able to produce the hemorrhagic-necrotic reactions while the corresponding wash waters and Berkefeld filtrates of the supernatant fluids were lacking in this ability. Heat-killed *H. influenzæ* were also able to induce hemorrhagic-necrotic skin lesions under the same experimental conditions as did living *H. influenzæ*. Thus the active principle must be connected with the bacteria themselves.

There exists, however, an interesting relationship between the agar-washing filtrates of *B. typhosus* and *meningococcus*,† on the one hand, and the effectiveness of *H. influenzæ* in the skin of the rabbit, on the other.

[3] Shwartzman, G., *Klin. Wochenschr.*, 1930, p. 1925.

[4] Shwartzman, G., *J. Exp. Med.*, 1930, **51**, 581.

[5] Mishulow, L., Mowry, I. W., and Scott, E. B., *J. Immunol.*, 1930, **19**, 227.

[6] Shwartzman, G., PROC. SOC. EXP. BIOL. AND MED., 1929, **26**, 843.

[7] Koplik, L. H., PROC. SOC. EXP. BIOL. AND MED., 1934, **32**, 309.

† We are grateful to Dr. Shwartzman for providing us with highly effective preparations of *B. typhosus* and *meningococcus* agar-washing filtrates.

B. typhosus agar-washing filtrates were injected intravenously into rabbits which 24 hours previously had received intradermal injections of *H. influenzæ* and *H. pertussis*. Three to 6 hours following the intravenous injection the areas of the skin treated with *H. influenzæ* became bluish-black, but there was no distinct change to be observed in the areas inoculated with *H. pertussis*. Conversely, living as well as dead *H. influenzæ* if injected intravenously also activate areas intradermally prepared with *B. typhosus* agar-washing filtrates.

The results of the above-mentioned experiments show that *H. influenzæ* may, under certain conditions, produce a hemorrhagic-necrotic lesion in the skin of rabbits. This ability is certainly not a specific characteristic of *H. influenzæ* alone. However, other organisms related to infections of the upper respiratory tract, such as pneumococci and streptococci, were not able to produce an identical effect under the same experimental condition as easily as did *H. influenzæ*.

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Subcutaneous Temperatures in Localized Infections.

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The mechanism of the increased production of heat at the site of a localized infection in the human body never has been definitely understood. The theory that the production of heat around an ordinary localized inflammation is due to the increased rate of flow of blood at the site has been upheld by the experimental studies of Marchand.[1] The belief that the local increase in temperature is due to heat-producing chemical processes active at the site of infection and that the hyperemia is really a compensatory phenomenon has been promoted by the work of Segale,[2] Schade,[3] Gessler[4] and others.

1 Krehl, Ludolf, and Marchand, F., *Handbuch d. allgem. Path.*, 1924, Vol. 4, Part I, S. Hirzel.

2 Segale, M., *J. Exp. Med.*, 1919, **29**, 235.

3 Schade, H., *Die Physik. Chemie in d. inneren Medizin*, 1923, 3rd edition, Steinkopff, Dresden and Leipzig.

4 Gessler, H., *Arch. f. exp. Path. u. Pharm.*, 1921, **91**, 366.