

advantage in the micro method lies in the possibility of greatly shortening the duration of the tests, thus making it possible to follow the time course of respiratory exchange over relatively short periods of time. Owing to the small volumes used, temperature adjustment is rapid.

With good manipulation the maximum error is less than 0.005 c.c. of O₂ gas. The method is being used in studies on oxygen consumption by small organisms such as protozoa, eggs and certain kinds of tissues.

35 (1782)

Does the introduction of an ethoxy group into aromatic compounds increase their bactericidal action upon the pneumococcus and the gonococcus?¹

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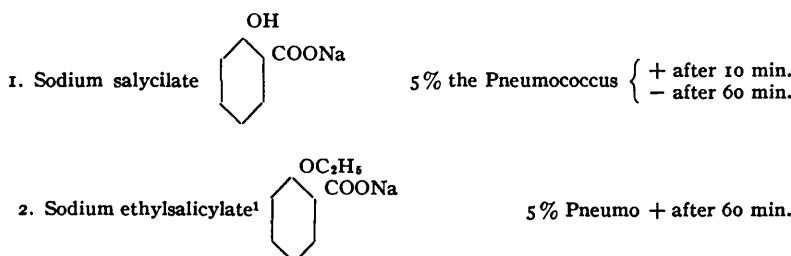
Morgenroth and his collaborators have shown that when an ethoxy group is substituted for the methoxy group in quinine derivatives and ethylhydrocuprein is produced, the substance takes on markedly increased pneumococcicidal action in vitro and in vivo. Solis Cohen, Kolmer and Heist found that ethylhydrocuprein hydrochloride was from eight to twenty times as strong an antiseptic for the pneumococcus as quinine hydrochloride. Morgenroth and Levy had shown that no such difference between quinine and ethyl hydrocuprein could be observed in the case of the streptococcus. We find that when cultures of gonococcus are exposed to starch bouillon containing quinine hydrochloride or ethylhydrocuprein in 1/10,000 dilution and then transferred to plates of rabbit's blood agar, growth occurs if the exposure to the drug has lasted only ten minutes but the bacteria are killed if the exposure has lasted thirty minutes. Ethylhydrocuprein has therefore no specific action against the gonococcus. However, as ethylhydrocuprein is too toxic for successful use in the chem-

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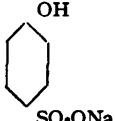
otherapy of lobar pneumonia, substances which are less toxic must be sought for.

The first question to be determined is whether pneumococcicidal properties are common to ethoxy compounds in general or whether this property is peculiar to ethylhydrocuprein and its closely related compounds. We have accordingly tested the bactericidal action of the ethyl ethers of various aromatic compounds, and compared them with the corresponding hydroxy compounds. In making the tests a suspension of pneumococcus type I. from the Rockefeller Institute was suspended for the desired interval in a broth solution of 0.9 per cent. NaCl containing the substance whose action was to be determined; and after the desired interval a loopful of this stroked across a rabbit's blood agar plate and incubated 24 hours. In the experiments with the gonococcus a strain was used which had been isolated from a case of typical anterior gonorrhoeal urethritis in the Outpatient Service of the Genito Urinary Division of the University of Minnesota, and which had been grown in Vedder's starch bouillon and on starch bouillon agar and rabbits' blood agar. Tests were made in the same way as for pneumococcus except that the drug was mixed with starch bouillon. The cultures were then transferred to rabbits' blood agar and incubated 24 hours.

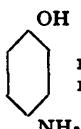
The following substances were tested, + indicating growth of the cocci after being exposed to the drug for the period indicated,—indicating that the cocci did not grow.

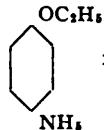


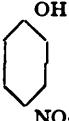
¹ Substances Nos. 2, 4, 10, 11, 12, 13 were prepared by Mr. Merrill C. Hart, chemical assistant in the department of pharmacology, University of Minnesota, and No. 9 was kindly furnished by Prof. Roger Adams, University of Illinois, to both of whom we extend our thanks.

3. Sodium phenolsulphonate  5% Pneumo + after 2 hours.
1% Gono + after 30 min.

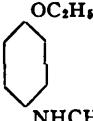
4. Potassium phenetolsulphonate  5% Pneumo + after 2 hours.
1% Gono + after 30 min.

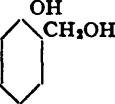
5. Para aminophenol  1% Pneumo + sometimes — sometimes after 30 min.
1: 1000 Gono — in 10 min.

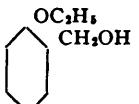
6. Para phenetidin  1% Pneumo + sometimes — sometimes after 30 min.
1% Gono — after 10 min.

7. Para nitrophenol  1% Pneumo + after 10 min. — after 30 min.
1: 500 Gono + after 10 min. — after 30 min.

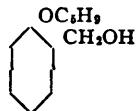
8. Para nitrophenetol  1: 1000 (sat. sol.) Pneumo + after 60 min.
1: 1000 Gono + after 60 min.

9. Phenetidinethylalcohol  Pneumo + after 30 min.
1: 250 Gono + after 30 min.

10. Saligenin  2% (in serum) Pneumo — after 60 min.
2% Gono + after 30 min.
— after 60 min.

11. Saligenin ethyl ether  Sat. sol. in 0.9% NaCl (about 1: 10,000).
Pneumo. Results vary.
8 repetitions — after 5 min.
16 repetitions + after 30 min.

12. Saligenin iso amylether



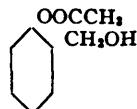
Sat. sol. less than 1: 10000.

Pneumo — after 5 min.

Gono — after 10 min.

Staphylococcus and *Bacillus coli*
both + after 30 min.

13. Acetyl saligenin



1: 200 Pneumo — after 5 min.

Gono — after 10 min.

From the above-recorded experiments it is evident that in the simpler aromatic substances, predominantly water-soluble like sodium phenolsulphonate and salicylate or predominantly lipoid-soluble like para amino phenol and para nitrophenol, whether nitrogen-free or containing nitrogen, the introduction of an ethyl group upon the ring does not confer pneumococcicidal or gonococcicidal powers. Whenever any difference is noted the hydroxy compound is a somewhat stronger antiseptic than the ethoxy. There is therefore no analogy in this regard between the simpler aromatic compounds and the quinine derivatives.