observations, that any significant amount of additional free water in the livers of tumor-bearing rats is present in the sinusoids. This must be sought, rather, in the cells, the intercellular spaces, and the blood. In the adrenal cortex, the sinusoidal dilatation is relatively greater than in the liver though hardly enough to assume this as the only site of a greatly increased water content for this organ.

Summary. The increased water content of the livers and adrenal glands of tumor-bearing rats is not correlated with an increase in caliber of liver or adrenal cortex sinusoids.

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In vitro Antibacterial Activity of Dimethylaminoethyl Substituted Compounds. (18987)

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In the course of systematic investigations* of alkyl-substituted dimethylaminoethyl ethers and dimethylaminoethyl amines we have surveyed their antimicrobial activity *in vitro*. The results of preliminary screening tests are presented below.

Experimental. Tests were performed against *Staph. aureus* 209, *B. mycoides* ATCC 6462, *Klebsiella pneumoniae* Type A ATCC 6450, *E. coli* ATCC R 5190, *Vibrio metchnikovi* and *Sh. sonnei* ATCC grown in Difco nutrient broth, *Diplococcus pneumoniae* A 5 grown in blood broth, *Cl. welchii* ATCC 460 grown in thioglycollate broth, and *Mycobacterium tuberculosis* H 37 RV and B 1, both grown in Dubos' liquid medium. The inoculum of non-acid fast organisms was 0.1 ml of a 1-500 dilution of an 18-hour culture. The inoculum of tubercle bacilli was 0.1 ml of a 14-day culture in Dubos' medium which had been diluted to an optical density of 0.2 as measured in Lumetron colorimeter. Final readings were taken after 3 days incubation with non-acid fast bacteria, and after 2 weeks incubation with tubercle bacilli. In addition, some of the compounds were assayed against *Trichophyton mentogrophytes*† grown in 4% dextrose, 1% peptone broth. The inoculum was 0.1 ml of a suspension, containing 15,000-25,000 spores, prepared from a 10-day culture on Sabouraud's dextrose agar. Cultures were incubated at room temperature (20-22°C), and final readings were taken after 15 days incubation. The compounds were dissolved in the medium used for each organism at a starting concentration of 64 mg % (w/v). A 2-fold serial dilution method was used throughout. Controls were included in every series and each test was run in duplicate. Some of the more active compounds were tested against a wider spectrum of pathogenic fungi, including *Trichophyton rubrum* ATCC 671, *Sporotrichum schenckii* ATCC 10213, *Sporotrichum floccosum* ATCC 10227, *Microsporum canis* ATCC 10214, *Microsporum audouini*, and *Candida albicans* ATCC 2091, using the method outlined above.

Results. Using the compound R–O–CH_2–CH_2–N $(CH_3)_2$, and replacing R in the aliphatic series, no activity was found against any organism until R = heptyl (8 mg% against *M. tuberculosis* B 1). When R = octyl slight activity appeared (64 mg %) which gradually increased as R increased to dodecyl (0.5-4 mg %). In general *V. metchnikovi* was slightly more sensitive to these compounds than were the other organisms tested. Of the cyclic ethers tested, B-pyridyl, phenyl, cyclohexyl, and benzyl were inactive, thymyl and methyl were weakly active (64 mg %), while tetrahydro furfural was moderately active (4-8 mg %).

Using the compound R_1 R_2 N–CH_2–CH_2 N $(CH_3)_2$, and replacing R_1 and R_2 by ali-

* To be published from these laboratories.

† Obtained through the kindness of Dr. R. H. Benham, College of Physicians and Surgeons, New York City.

phatic or cyclic groups, marked activity was found against all the fungi under test when R_1 = dodecyl, R_2 = methyl, and when R_1 = naphthyl, R_2 = hexyl, heptyl, octyl, nonyl, and decyl (.25-8 mg %). Low or moderate activity was found when R_1 = naphthyl, R_2 = methyl, ethyl, and propyl (4-64 mg %).

No activity was observed among the lowest members of the series of aliphatic dimethylaminoethylamines. Using the compound $\begin{matrix}R_1\\R_2\end{matrix}> N\text{–}CH_2\text{–}CH_2\ N(CH_3)_2$, and replacing R_1 and R_2 in the aliphatic series, no activity appeared until $R_1 = R_2$ = butyl, when *M. tuberculosis* H37RV was inhibited by .5 mg %. The compounds $R_1 = R_2$ = methyl, $R_1 = R_2$ = ethyl, $R_1 = R_2$ = propyl, R_1 = allyl, R_2 = isopropenyl, R_1 = butyl, R_2 = ethyl, and R_1 = amyl, R_2 = methyl were all without effect on all organisms tested. When R_1 = amyl, R_2 = propyl, isopropenyl, or butyl, the compounds showed activity against *K. pneumoniae* and *Sh. sonnei* (.25 mg %) and weaker activity against gram positive organisms. When $R_1 = R_2$ = amyl antibacterial activity was low, as was the case when R_1 was hexyl, R_2 was methyl, ethyl, or propyl. In contrast R_1 hexyl, R_2 isopropyl inhibited *K. pneumoniae* and *Sh. sonnei* at .25 mg %. In ascending this series, when R_1 was amyl and R_2 was propyl, activity against gram negative organisms appeared. Bacteriostatic effects were maintained until R_1 was hexyl and R_2 was allyl. Activity then diminished, to reappear with a broader spectrum when R_1 was octyl and R_2 was hexyl. Maximal potency against both gram negative and gram positive organisms was obtained when R_1 was hendecyl or above. The most active members of this series of compounds were also effective against *Trichophyton mentagraphytes*. Optimal activity appears to be associated with a long chain hydrocarbon radical, but any such generalization would exclude the hexyl allyl derivative and would not account for the effectiveness of the lower members of the series against gram negative organisms.

Discussion. The more active members of the series of substituted dimethylaminoethylamines inhibited the growth of 4 g positive organisms, including aerobic and anaerobic spore formers, 4 g negative bacteria, and 2 varieties of tubercle bacilli. In addition, they were found to be active against a representative spectrum of pathogenic fungi. Although tests for bacteriostatic effects give no indication of germicidal activity, the above data indicate which of the compounds should be studied further. Work designed to evaluate the therapeutic potentialities of these compounds will be reported separately.

Conclusions. (1) No appreciable antimicrobial activity was found in an *in vitro* examination of a series of dimethylaminoethyl ethers. (2) Significant activity was observed in various long-chain di-aliphatic dimethylaminoethylamines. (3) When one of the aliphatic substituents was replaced by a naphthylene group marked antimicrobial activity was found.

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Thermolabile Antigens of *Shigella boydii* 2 Cultures with Special Reference to an Encapsulated Culture. (18988)

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The purpose of this paper is to report the natural occurrence of an encapsulated culture of *Shigella boydii* 2 (P288) and to describe the relationships of the thermolabile substance of the capsule to thermolabile somatic antigen in other *S. boydii* 2 strains and in *Klebsiella* and *Escherichia* cultures.

Fletcher(1) reported the occurrence of