interesting microscopic changes which occur in tumors during the treatment with yeast extract. Extensive cell necrosis presents a very striking picture which will be described in a subsequent publication.

Furthermore, we postpone for a later date reports on the treatment of malignant tumors with yeast in powder form or in pellets.

The factors responsible for this action of yeast extract are of course entirely unclear. Certainly, many different possibilities must be considered. For instance, it remains to be determined whether bacterial factors which may have been present in yeast extracts were operative in the effect described. Duran-Reynals[5] observed total regressions of some spontaneous mammary carcinomas of mice due to repeated injections of bacterial filtrates.

Summary. In 8 out of 33 treated mice complete regressions of spontaneous breast adenocarcinomas were effected with intravenous and subcutaneous injections of yeast extract.

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Action of Sulfathiazole and Sulfamethylthiazole on *Staphylococcus aureus.*

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Studies[1-4] on certain thiazole analogues of sulfapyridine[5, 6] have indicated that these drugs have a therapeutic activity equal to that of sulfapyridine when tested against pneumococci, streptococci, meningococci and the agent of lymphogranuloma venereum; and that the toxicity of sulfathiazole itself is usually less than that of sulfapyridine. More recently there have appeared several communications dealing with the activity of sulfathiazole and certain of its derivatives

5 Duran-Reynals, F., PROC. SOC. EXP. BIOL. AND MED., 1935, **32**, 1517.

1 van Dyke, H. B., Greep, R. O., Rake, Geoffrey, and McKee, C. M., PROC. SOC. EXP. BIOL. AND MED., 1939, **42**, 410.

2 McKee, C. M., Rake, Geoffrey, Greep, R. O., and van Dyke, H. B., PROC. SOC. EXP. BIOL. AND MED., 1939, **42**, 417.

3 Rake, Geoffrey, van Dyke, H. B., Corwin, W. C., McKee, C. M., and Greep, R. O., *J. Bact.*, 1940, **39**, 45.

4 Cooper, F. B., Gross, Paul, and Lewis, Marion, PROC. SOC. EXP. BIOL. AND MED., 1939, **42**, 421.

5 Fosbinder, R. J., and Walter, L. A., *J. Am. Chem. Soc.*, 1939, **61**, 2032.

6 Lott, W. A., and Bergeim, Frank H., *J. Am. Chem. Soc.*, 1939, **61**, 3593.

on staphylococci.[7-10] Herrell and Brown[7] found much greater *in vitro* bacteriostatic activity of sulfamethylthiazole than of sulfathiazole against *Staphylococcus aureus*. However, they give only one experiment and that in brief. They also state that "much more marked protection" was accorded mice infected with *Staphylococcus aureus* when these animals were treated with sulfamethylthiazole than when treated with sulfathiazole, but give no details. Lawrence[8] found that sulfamethylthiazole had a greater bacteriostatic activity than had sulfathiazole but his results would seem to be in part vitiated by the use of supersaturated solutions. Barlow and Homburger,[9] using small numbers of mice, give results which indicate little if any greater therapeutic activity of sulfamethylthiazole as compared with sulfathiazole. Finally, Helmholz[10] found that voided urine from patients treated with either of these two drugs was markedly bactericidal for *Staphylococcus aureus* even with drug concentrations as low as 16 mg %.

In carrying out *in vitro* studies with sulfathiazole, sulfamethylthiazole and sulfapyridine it has been found that minor variations in the technic used or in the broth menstruum have greatly influenced results. When, however, concentrations of drug of approximately 200 mg % are used, and supersaturated solutions are avoided, it has been found that the methyl derivative has greater bacteriostatic activity than sulfathiazole which, in turn, is more active than sulfapyridine. Table I shows such an experiment.

Poured plates inoculated with 0.1 ml of different dilutions of the

TABLE I.

Action of Sulfathiazole (ST), Sulfapyridine (SP), and Sulfamethylthiazole (SMT) on *Staphylococcus aureus in vitro*.

	ST	SP	SMT	Control
Immediate	40*	40	80	20
2 hr	80	50	140	230
4 "	170	1170	140	7100
6 "	1800	9200	1300	530,000
24 "	460 million	1260 million	7.4 million	1580 million

Drug concentrations in each case 198 mg% added to broth after autoclaving.
*Figures indicate number of colonies per ml.
Inoculum was 0.1 ml of 10^{-6} dilution of 18-hr culture of strain MK in 2 ml volume.

7 Herrell, W. E., and Brown, A. E., *Proc. Staff Meetings Mayo Clinic*, 1939, **14**, 753.

8 Lawrence, C. A., (a) *J. Bact.*, 1940, **39**, 46; (b) PROC. SOC. EXP. BIOL. AND MED., 1940, **43**, 92.

9 Barlow, O. W., and Homburger, E., PROC. SOC. EXP. BIOL. AND MED., 1939, **42**, 792.

10 Helmholz, H. F., *Proc. Staff Meetings Mayo Clinic*, 1940, **15**, 65.

cultures were made at the time intervals indicated. Counts were made and those recorded are from plates which gave the largest number of easily countable colonies.

Other experiments under similar conditions but with colony counts at different intervals of time confirm the relationship of activity, namely, sulfamethylthiazole > sulfathiazole > sulfapyridine. In certain cases, however, sulfapyridine and more particularly sulfamethylthiazole have not remained in solution during the test presumably because the starting solution was supersaturated. It would seem essential to avoid such precipitation of drug which may vitiate the results by decreasing the total amount of drug in solution. This condition of supersaturation seems to be rather a factor of the constitution of the broth than of the actual concentration of drug. Other factors, such as autoclaving the drug in the broth (with or without added glucose) or adding the drugs to the broth after the latter has been autoclaved (as in Table I), have also altered the results.

The agar cup plate method of testing *in vitro* activity[11] was also used.* When the drugs were mixed with 5% gum acacia, sulfathiazole was found to be the most active compound producing inhibition of growth in a dilution of 1:8000 as compared to 1:3000 for sulfamethylthiazole and 1:1000 for sulfapyridine. Differences in solubility and diffusibility probably account for these differences in activity.

In the *in vivo* experiments drugs were administered to mice in 1% of their normal dry diet.[2] Five different strains of *Staphylococcus aureus,* 3 hemolytic and 2 non-hemolytic, were used. The mice were inoculated intraperitoneally and received in each case approximately 500,000 organisms suspended in 1 ml of 5% mucin. Mice were kept on the drugs for 10 days and then observed for an additional 21 days after return to normal diet. At the end of the 31-day period survivors were autopsied and the persistence of infection noted by obtaining positive cultures from one or all of the following organs: spleen, liver and kidney. Deaths after 7 days were very unusual.

As seen in Table II, sulfapyridine had very little if any activity. Both sulfathiazole and sulfamethylthiazole protected mice and the former drug was slightly, but consistently better than the latter, as shown both by the number of surviving mice and by the percentage of residual infection in the organs as determined at autopsy. It may be noted that rough and other variants were found among the strains of

11 Ruehle, G. L. A., and Brewer, C. M., U. S. Dept. of Agriculture, 1931, circular No. 198.

* We wish to express our thanks to Dr. Brandt Rose of Philadelphia for suggesting the use of this test.

TABLE II.
Action of Sulfathiazole, Sulfapyridine and Sulfamethylthiazole *in vivo*.

Strain	No. of mice in each group	ST	SP	SMT	Control
MK NH	30	22*	3	22	0
Co. NH	40	17	4	14	3
469 H	30	15	2	9	2
687 H	30	21	3	15	1
631 H	20	20	6	18	2
Total	150	95	18	78	8
% of survivors whose organs gave positive cultures		14%	18%	25%	12.5%

H—Hemolytic strain. NH—Non-hemolytic strain.
* Figures indicate number of survivors over 31-day period.

Staphylococcus aureus recovered from the mice treated with each of the 3 drugs.

Summary. In *in vitro* experiments with *Staphylococcus aureus* sulfamethylthiazole has shown greater bacteriostatic activity than sulfathiazole; the activity of the latter was in turn greater than that of sulfapyridine. In *in vivo* experiments with the same organism sulfapyridine has had little, if any, activity. Both sulfathiazole and sulfamethylthiazole have protected mice and the former drug has been slightly but consistently more active than the latter.

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Mechanism of the Blood Pressure Response to Anoxia During Hypoglycemia.

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Gellhorn, Ingraham and Moldavsky[1] found that breathing a mixture of 6.2% oxygen in nitrogen caused a marked rise in blood pressure in dogs which had been made hypoglycemic by the injection of insulin. Intravenous injection of glucose made this blood pressure

[1] Gellhorn, E., Ingraham, R. C., and Moldavsky, L., *J. Neurophysiol.*, 1938, **1**, 301.