ployed by them in estimating polysaccharide produced.) These are also represented in Figure I; it is apparent that the major portion of polysaccharide in their experiment was found after completion of the logarithmic phase of growth. Of additional interest are the recent observations of Hoogerheide,[5] that the size of the capsule surrounding *Klebsiella pneumoniae (Bact. Friedlander)* begins to increase only after the completion of the logarithmic phase of growth, and the earlier observations of Cowan[6] that hemolysin appears in pneumococcal broth cultures only after completion of the logarithmic phase of growth.

Summary. The concentration of capsular polysaccharide appearing in blood-broth culture filtrates following the growth of a highly virulent, standardized strain of Pneumococcus III, was determined photronreflectometrically and correlated with the growth rate of the organism. An initial inoculum of 165 organisms per ml yielded a very small quantity of polysaccharide (0.5 mg %). An inoculum of 9,000 organisms per ml yielded 18 mg % of capsular polysaccharide in 48 hours. The greatest increases in concentration of polysaccharide occurred in two stages after the completion of the logarithmic phase of growth.

11264

Effect of Intravenous Injections of Yeast Extract on Spontaneous Breast Adenocarcinomas in Mice.

R. LEWISOHN, C. LEUCHTENBERGER, R. LEUCHTENBERGER AND D. LASZLO. (Introduced by Gregory Shwartzman.)

From the Laboratories of the Mount Sinai Hospital, New York City.

In this laboratory, studies on the action of different spleen extracts on transplanted and on spontaneous tumors have been carried out for several years. It was shown in previous publications[1, 2] that the complete retrogression of transplanted Sarcoma 180 could be accomplished in 60% of the treated animals following subcutaneous injections of biologically[2] or chemically concentrated spleen

[5] Hoogerheide, J. C., *J. Bact.*, 1939, **38**, 367.

[6] Cowan, S. T., *J. Path. and Bact.*, 1934, **38**, 61.

[1] Lewisohn, R., *Surg., Gyn. and Obst.*, 1938, **66**, 563.

[2] Lewisohn, R., Leuchtenberger, R., and Laszlo, D., Internat. Cancer Congress, Atlantic City, Sept., 1939.

extracts. Furthermore, we succeeded in producing total regressions in spontaneous breast carcinomas in 27 mice by intravenous injections of spleen extracts.

This report deals with the action of another extract on spontaneous malignant tumors in mice, namely a yeast extract.

Nevorojkin[3] injected concentrated suspensions of yeast into transplanted tumors and noticed retardation of growth and, in some cases, regressions.

Maisin, Pourbaix and Caeymaex[4] demonstrated that they could retard the growth of experimental cancer in rabbits by adding boiled yeast to the food of the animals.

The yeast extract which was used by us for intravenous or subcutaneous therapy of malignant tumors was prepared in the following manner: 2500 g of Brewer's yeast is washed several times with distilled water. The yeast is boiled for 7 minutes with 9000 cc distilled water to which 0.9 cc of glacial acetic acid has been added. The extract is filtered through paper-pulp and concentrated *in vacuo* at 70°C to 1500 cc. It is precipitated with 1500 cc of absolute alcohol. The filtrate is concentrated *in vacuo* at 70°C to 900 cc.

The yeast extract was used intravenously, sometimes in combination with subcutaneous injections. The average dose for intravenous treatment was 0.1 cm, whereas 0.5 cc was injected subcutaneously. The intravenous injections were given into the tail of the mouse. When used subcutaneously, the extract was injected as far away from the site of the tumor as possible in order to avoid the possibility of direct action of the extract on the tumor. Daily, or on alternate days, injections were given until the tumor disappeared or were discontinued when the tumor did not respond to treatment. Injections of yeast extract were continued after disappearance of the tumor in order to avoid a possible recurrence.

Thirty-three tumor-bearing mice were used for these experiments. Twenty-two came from the Jackson Memorial Laboratory, Strain A. Eleven were bought from the Rockland Farm. They did not belong to a pure inbred strain.

The average size of the tumor at the onset of the treatment can be recognized from the sketches of the regressed tumors in Table I.

In each instance the malignant character of the tumor was established by biopsy before treatment was started. The histologic criteria of malignancy were chiefly cytologic, such as many atypical mitoses

[3] Nevorojkin, J., *Vestnik. Roentgenol.*, 1935, **15**, 344.

[4] Maisin, J., Pourbaix, Y., and Caeymaex, P., *Comptes rendus Soc. biol.*, Paris, 1938, **127**, 1477.

Table I. Effect of yeast extract on spontaneous breast adenocarcinomas in mice. J.M.L.=Jackson Memorial Laboratory. R.F.=Rockland Farms.

No.	Source	Actual size of tumor	Treatment started	Healed	Injections	
					Intravenous	Subcutaneous
310	J.M.L		Nov. 9, 1939	Nov. 25, 1939	11	0
350	"		" 10, "	Dec. 20, "	13	11
352	"		" 10, "	Jan. 9, 1940	13	14
362	"		" 10, "	Dec. 16, 1939	11	8
402	"		Dec. 23, "	Jan. 13, 1940	11	10
		2 separate tumors 1 anterior 1 lateral			//// = Hemorrhagic.	
404	"		" 23, "	" 16, "	12	10
					3 cm.	
R 18	R.F.		Jan. 13, "	" 22, "	7	7
R 22	"		" 15, "	" 21, "	5	4

and striking cell irregularities, because actual invasion of the adjacent healthy tissue could hardly be established in a biopsy which had to be made as small as possible.

Controls were first deemed unnecessary since it has generally been assumed and has been confirmed by personal communication from Dr. Little that breast carcinoma of Strain A Jackson Memorial Laboratory, proven by biopsy, never disappears spontaneously. However, we believed it was necessary to establish whether biopsy alone might not influence the natural evolution of this tumor. In 60 mice, Strain A Jackson Memorial Laboratory, and in 5 Rockland Farm mice, in which only biopsy was performed, we have not observed so far disappearance of the tumor (Strain A Jackson Memorial Laboratory). However, temporary regressions in size were noted.

Of 33 animals treated with yeast extract, the tumors disappeared in 8 mice and have not recurred so far (see table). Naturally, the animals remain under further observation. In 10 animals the tumor was reduced in size. In 15 instances either no change in the size of the tumor was noted or they had even increased in size when treatment was discontinued or the animals died.

Details of the treatment and the source of the 8 mice in which the tumors regressed following treatment with yeast extract are presented in Table I.

It is impossible in this brief presentation to describe in detail the

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.

11265 P

Action of Sulfathiazole and Sulfamethylthiazole on *Staphylococcus aureus.*

GEOFFREY RAKE AND C. M. MCKEE.

From the Squibb Institute for Medical Research, New Brunswick, N. J.

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.