

Group	Sack contents	Strike groups per fish per h	Touches per strike group	Duration (sec)
(i)	(ii)	(iii)	(iv)	(v)
A				
(20) Normal fish n = 10	worms	9.4 ^b	5.3 ^b	3.7 ^b
	stones	3.0	2.5	1.6
(10) Both olfactory tracts regenerated n = 20	worms	13.0 ^b	5.8	4.3
	stones	4.2	2.5	1.5
B				
(8) Normal fish n = 10	morpholine, 1·10 ⁻²	4.5 ^b	3.8 ^a	2.3 ^a
	stones	1.5	1.5	0.8
(4) Both olfactory tracts regenerated n = 6	morpholine, 1·10 ⁻²	11.8 ^a	4.6 ^b	2.8 ^a
	stones	3.6	2.1	1.2
(4) Both olfactory tracts regenerated n = 7	coumarin	5.4 ^a	2.2	1.5
	stones	0.6	1.8	1.2

^a $P < 0.05$. ^b $P < 0.01$.
In column (i) the number in parenthesis refers to the number of fish tested for each group; 'n' is the number of separate 1-h-long observations (on different days) from which were obtained the mean figures in columns (iii)–(v) for each group.

tracts learn and display clear positive responses to morpholine and to coumarin in an unambiguous test situation. Histological confirmation of tract regeneration and central reconnections was obtained. Further olfactory discrimination, histological and electrophysiological investigations are in progress.

der weitgehende Riechfähigkeit. Auch histologisch tritt Regeneration ein.

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Zusammenfassung. Wie mit einer neuentwickelten Methode gezeigt werden konnte, erlangen Karpfen 40 Tage nach Durchschneidung der Olfaktoriusbahnen wie-

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Alteration of Resistant *Staphylococcus aureus* Cultures by Contact with Yeast Products

From the residue of the brewing process we extracted two products: yeast protein, Malucidin, having antibiotic properties *in vivo* and purified yeast antibiotic having antibiotic properties *in vivo* and *in vitro*¹⁻⁹. Yeast antibiotic in 30 min contact with resistant and non-resistant staphylococcus killed about 95% of bacteria in doses of 0.75 mg and 0.035 mg/ml, respectively. Higher doses of yeast antibiotic, 1–1.5 mg/ml producing up to 98% mortality of resistant staphylococcus, have an alternative effect on this organism. Cultures grown from surviving cells were sensitive to penicillin and streptomycin and produced no coagulase or hemolysin. The effect of this treatment is highly increased sensitivity to standard antibiotics; original cultures of resistant staphylococcus which survived contact with 10 µg/ml of streptomycin after the treatment with yeast antibiotics were sterilized by 0.019 µg of streptomycin.

COHEN¹⁰ tested our cultures of resistant staphylococcus for penicillinase after we had treated them with the yeast antibiotic and found no detectable penicillinase activity.

A solution of Malucidin, in combination with soap and merthiolate, produced a similar alteration in resistant

staphylococci. They became sensitive to penicillin, streptomycin, tetracyclin and chloromycetin, produced no hemolysin or coagulase, and became non-typable for the phage pattern. Acquired new characteristics were inheritable and after eight transfers the new variant remained susceptible to standard antibiotics, and produced

Table I. Bactericidal effect of yeast antibiotic No. 260 on resistant and non-resistant staphylococci

Dose of yeast anti-biotic mg/ml	Resistant strain SA		Non-resistant strain C-1	
	No. of colonies	% mortality	No. of colonies	% mortality
2	0	100	0	100
1.5	1	99.9	0	100
1.2	3	99.6	0	100
1	3	99.6	0	100
0.75	2	97.6	0	100
0.6	77	91.2	0	100
0.4	750	84	0	100
0.35	750	84	12	99.6
0.035	1450	63.2	122	96

Table II. Characteristics of resistant staphylococcus before and after contact with Malucidin preparation

A. Resistance					
Preparation	Strain	Antibiotic concentration in $\mu\text{g/ml}$	Original resistance	Resistance after 1st contact	after 2nd contact
240A Dilution 1:1000 Mortality 97%	SA	Penicillin 10	+	-	-
		Streptomycin 10	+	-	-
		Tetracycline 5	+	-	-
		Chloromycetin 5	+	-	-
234 Dilution 1:2000 Mortality 94%	SA	Penicillin 10	+	-	-
		Streptomycin 10	+	-	-
		Tetracycline 5	+	-	-
		Chloromycetin 5	+	+	+
234 Dilution 1:1000 Mortality 98%	SG	Penicillin 10	+	-	-
		Streptomycin 10	+	-	-
		Tetracycline 5	-	-	-
		Chloromycetin 5	+	-	-
234 Dilution 1:2000 Mortality 96%	SG	Penicillin 10	+	+	-
		Streptomycin 10	+	+	-
		Tetracycline 5	-	-	-
		Chloromycetin 5	+	+	-
B. Other characteristics					
Preparation	Strain	Characteristic	Original	After 1st contact	
All	All	Coagulase	+	-	
		Hemolysis	+	-	

no hemolysin, coagulase or penicillinase. Treated with both yeast products staphylococci did not acquire resistance to these preparations.

Discussion. BLAIR¹¹ reported that by cross lysogenization of different strains of staphylococcus he was able in some cases to reverse resistance to penicillin. BARBER¹² has reported the spontaneous appearance of non-resistant colonies in her cultures of resistant staphylococci. In the cultures of resistant strains of staphylococci carried in our laboratories over a three-year period, we did not find the appearance of colonies susceptible to commonly used antibiotics. The discrepancy might be due to different methods of preservation of staphylococcus. In any event, if non-resistant mutants were present in the cultures of strain SA used in our experiments they would have been killed by treatment with Malucidin or yeast antibiotic since the lethal dose for the non-resistant organism is much smaller than that for the resistant one.

It is, therefore, not likely that the altered bacteria surviving treatment with yeast products represent spontaneous variants. The non-resistant form surviving treatment of resistant staphylococcus with toxic doses of yeast products appears, on the contrary, to represent a variant induced by the treatment.

The implication of our data might be the possibility of sensitization of resistant staphylococcus to commonly used antibiotics by pretreatment with a yeast product, as a new approach to chemotherapy. A similar phenomenon was observed in experiments with fungi¹³. Normal mice could not be infected with the strain of *Candida albicans* used in the experiment; however, pretreated with aureomycin or terramycin the animals succumbed very easily to inoculation with the same organism. The stimulation by aureomycin or terramycin of fungal infection in mice could be prevented by injection of Malucidin 24 h prior to the test.

Zusammenfassung. *Staphylococcus aureus*-Stämme wurden 3 Jahre lang in unseren Laboratorien gezüchtet. Hefeextrakt wirkte kurze Zeit auf sie ein, bevor sie wieder in den Nährboden geimpft wurden. Nach dieser Behandlung kam es zu einer Antibiotikaempfindlichkeit, und die Stämme bildeten weder Coagulase noch Hämolyisin. Die neu erworbenen Eigenschaften sind erblich und wurden durch mehrere Generationen beibehalten.

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