

about 8.8 which lies within the range of alkalinity of the cervix during heat. Furthermore, 10 cc of cervical fluid with a pH of 8.3 requires 3 to 4 cc of N/10 HCl to bring it to pH 6.5. Thus the advocates of pH controlled vaginal douches for the control of sex must go beyond the cervix to make their procedure effective in the female bovine.

Summary. A study of the pH of the genital secretions of the cow has shown the vagina to be slightly acid in anestrus and slightly alkaline in estrus due to the distinctly alkaline character of the cervical discharge at that time. The fluids of the cervix during estrus average pH 8.3 with a range from pH 7.6-8.9. The fluids present in the uterus during estrus have an average pH of 6.8 which is a favorable one for sperm survival.

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Lessened Effectiveness of Bacteriostatic Agents vs. Tuberculous Infection in Rabbits with Impaired Functional Efficiency.

ARTHUR LOCKE, ROSE B. LOCKE AND HELEN SCHLESINGER.

From the Western Pennsylvania Hospital Institute of Pathology, Pittsburgh.

This is a report of a study of the effect of administered sulfanilamide (SA) and *p*-caproylaminobenzenesulfonhydroxamide (CH)* on the rate of increase in size of the local lesion produced by subcutaneous injection of a suspension of avian tubercle bacilli, in the rabbit, and on the bearing—on that effect—of the functional status of the rabbit as indicated by its reaction to chilling.^{1, 2}

Table I indicates the comparative intensity of the growth-restraining effect exerted by SA and CH in cultures of the avian tubercle bacillus in broth. The strain used was *M. avium* No. 30, from the Phipps Institute. It formed smooth, moist, cream-colored colonies on Lowenstein's medium. In broth, it grew in sedimenting, flocculent masses which formed an even suspension on agitation. The culture medium was glycerine veal heart infusion broth of pH 6.8, distributed in 25 cc amounts in 50 cc Erlenmeyer flasks. The

* Supplied by Dr. Maurice Moore, Sharp and Dohme, Philadelphia.

¹ Locke, A., *J. Infect. Dis.*, 1937, **60**, 106; *J. Immunol.*, 1939, **36**, 159; Locke, A., and Main, E. R., *Ibid.*, 173.

² Locke, A., Locke, R. B., Bragdon, R. J., and Mellon, R. R., *Science*, 1937, **86**, 228; Locke, A., Main, E. R., and Mellon, R. R., *J. Immunol.*, 1939, **36**, 183.

TABLE I.
Comparative Effects of Sulfanilamide (SA) and *p*-caproylamino benzenesulfonhydroxamide (CH) on the Growth of the Avian Tubercle Bacillus in Broth Culture.

Series	Total No. cultures in group	Drug added	Conc. millimolar	Avg vol of sediment from 10 cc of culture at 20 days, cc × 1000	Estimated avg % inhibition
2, 3, 5b (small inocula)	15	none		21	97
	5	CH	.26	<1	
	14	CH	.52	<1	93
	6	SA	.26	2	
	9	SA	.52	<1	
1, 4, 5a (heavier inocula)	18	none		24	60
	7	CH	.26	8	
	8	CH	.52	11	20
	7	SA	.26	20	
	11	SA	.52	19	

drugs were added in 0.1 and 0.2 cc volumes of 60% ethyl alcohol solution. Equivalent additions of 60% alcohol free of dissolved drug produced no recognized growth-checking effect. Ten cc aliquots of the cultures were centrifuged after incubation at 38°C for 20 days. The collected sediments were found to be pure.

The series in the lower group in Table I were inoculated from 3 to 5 times more heavily than those in the upper group. The average percent inhibition exerted by the CH in the upper group was 97; that exerted by the SA, 93. The equivalent averages for the group receiving the larger inocula were 60 and 20. The CH would appear to have been, in this *in vitro* comparison, more effective than the SA but less effective against a relatively large inoculum than against a small one. CH is, mole for mole, also more effective than SA in checking growth of the type I pneumococcus in broth culture but is less effective than SA in cultures containing blood.³ It has approximately the same effectiveness as SA in pneumococcus-infected mice.⁴

The usefulness of the reaction to chilling as an index of functional status, in the rabbit, was established in an investigation of factors determining non-specific capacity for resistance to pneumococcal invasion.¹ Rabbits with "warming times" of 30 to 33 were found to have a maximum non-specific capacity for surviving such

³ Main, E. R., Shinn, L. E., and Mellon, R. R., *PROC. SOC. EXP. BIOL. AND MED.*, 1940, **43**, 593.

⁴ Cooper, F. B., Gross, P., and Lewis, M., *PROC. SOC. EXP. BIOL. AND MED.*, 1940, **43**, 491.

TABLE II.
Comparative Size of the Local Lesion Developed Following Subcutaneous Injection of a Suspension of the Avian Tubercle Bacillus into Treated and Untreated Rabbits Making Optimal and Sub-optimal Reaction to Chilling.

Warming time ¹	Rabbit No.	Drug given	Per diem wt loss in g during treatment	Approx. area of lesion in cm ² on the indicated day of infection			
				9	20	40	60
Treatment begun immediately after infection.							
30-40	3	none		5	5	7	
	1	none		8G	8G	6GD	
	671	CH	5	1	1*	(9)	(6D)
	679	CH	0	1	2*	(6)	
	2	SA	23	4*	(13)	(13)	
	675	SA	63	4M			
>40	681	none		12	12	10D	
	677	none		9G	18G	20GD	
	667	CH	14	11*	(14)	(20GD)	
	664	SA	13	7*	(9)	(12)	
Treatment begun 20 to 40 days after infection.							
30-40	656	none			8	2D	3D
	639	CH	4		8†	10	
	649	CH	0		4†	4	0‡
	655	CH	0			6†	6D

*Day of discontinuance of treatment. The subsequent, bracketed values indicate extent of change in lesion size following cessation of treatment.

†Day treatment was begun.

‡Excision of the area revealed persisting tubercle bacilli. The notation M means dying. The terminal blood SA level, in this rabbit, 18 hr after the last preceding SA feeding, was 28 mg%. G denotes lymph-node invasion and D, drainage.

invasion and rabbits with warming times appreciably longer than 40, a minimum capacity for survival. Transition from a warming time of 40 or longer, to 33, could be induced through enforced rest, circulatory support and vitamin administration; and converse impairment from 33 to more than 40 through exhaustion, shock and starvation. The ability of SA to check pneumococcus invasion in rabbits with warming times less than 40 was observed to be more than double that observed in rabbits with warming times exceeding 40.²

The warming times of the upper group of rabbits in Table II lay between 30 and 40. Those of the lower group lay beyond 40. New Zealand White males were used, from 3 to 4 kg in weight. They were injected subcutaneously, within a shaved area over the abdomen, with 0.002 to 0.004 cc of sedimented, growing avian tubercle bacilli suspended in 0.5 to 0.75 cc of broth, one or more days after the last preceding estimation of warming time and from 0 to 2 hours before beginning drug feedings. The SA was given in capsule in a dosage of 0.3 g 8 x daily and the CH in a dosage

of 0.45 g 5 x daily or 0.23 g 8 x daily. Preliminary trial had indicated the ineffectiveness of smaller, less frequent dosage. The drugs could not be given, successfully, in admixture with food.

The infection was not rapidly fatal. The indicated death of rabbit 675 was due to sulfanilamide poisoning, not infection. The SA proved to be so toxic in effective dosage as to prohibit sustained use. Loss of appetite was induced, together with rapid decrease in weight. The comparative non-toxicity of the CH was the determining point in its choice for this study. CH produced no impairment in appetite, significant loss of weight or other directly recognizable injury during sustained, massive feedings over periods of 20 to 40 days. Adjuvant feedings were given, during protracted CH administration, of sodium bicarbonate, ascorbic acid and liver extract.

The lesions produced at site of injection in the control rabbits with warming times of 30 to 40 were, roughly, one half the size of those developed in the control rabbits with warming times longer than 40. A comparable relationship was apparent in the treated rabbits following cessation of treatment. During the period of treatment, the lesions in the 30-40 minute rabbits given CH from the outset of infection were approximately one-sixth the size of those observed in the controls but quickly grew out to normal size following discontinuance. The corresponding lesions in the 30-40 minute rabbits given SA were about two-thirds the size of those observed in the controls. No significant effect of CH or SA was indicated in the rabbits with warming times exceeding 40, either on a basis of lesion size at time of drug discontinuance or on a basis of extent of further development following withdrawal. CH administration begun 20-40 days after infection was without significant checking effect. The infection was in no case eradicated.

Summary. Sulfanilamide and *p*-caproylaminobenzenesulfonhydroxamide, producing 20 and 60% inhibition of growth, respectively, in broth cultures of the avian tubercle bacillus, exert a comparable degree of restriction on the rate of increase in size of the local lesion produced by subcutaneous injection of this organism, in rabbits with warming times less than 40, but not in rabbits with warming times appreciably longer than 40.