Lewin[6] showed that (1) acrolein is lethal to mammals only in large amounts (0.25 gm. per kilo), (2) acrolein-vapor appears in the breath shortly after subcutaneous injection, (3) the symptoms of acrolein-poisoning in man are dizziness, nausea, and diarrhea. These symptoms have been observed in our laboratory in subjects who have eaten several ounces of garlic. The fact that detectable amounts of acrolein appear in the breath after injection of acrolein suggest its possible value as a disinfectant of the respiratory tract. Since it is lethal only in large amounts and bactericidal in small amounts, we propose to investigate its therapeutic possibilities further.

Summary. The well known sulfides responsible for the peculiar odor of garlic are not responsible for its bactericidal activity. Acrolein was found to be a highly active bactericide. Its properties are such that it gives promise of being a respiratory disinfectant. Its general properties suggest that it or related compounds may be the bactericide of garlic.†

The writers are grateful to Dr. Henry Borsook for his encouraging advice.

9115 P

Acidosis Associated with the Administration of Para-amino-benzene-sulfonamide (Prontylin).

HAMILTON SOUTHWORTH. (Introduced by P. H. Long.) (With the technical assistance of Florence White.)

From the Johns Hopkins Hospital, Baltimore, Md.

In the last 3 months at Johns Hopkins Hospital about 50 cases have been treated with para-amino-benzene-sulfonamide (Prontylin) in doses of 0.04 to 0.12 gm. per kilo per day. Two of these cases have shown clinical acidosis.

Case A. G. J., 29 yrs., colored female, was admitted for an acute beta hemolytic streptococcal tonsillitis. Prontylin was started by mouth and her temperature fell to normal in 36 hours. After 48 hours, however, she began definitely overbreathing and the CO_2 combining power of her plasma was 36.2 vol. %. At this point

[6] Lewin, L., *Arch. Exp. Path. Pharm.*, 1900, **43**, 1351.

† Our recent results show that acrolein is much more poisonous than Lewin found. Proof that acrolein, croton aldehyde, or a similar substance is present in garlic has been obtained by a color reaction.

TABLE I.

Case	Name	Age	Sex	Wt. kg.	CO_2 value before	CO_2 value after	Mean drop	Relation of test to dosage	Aver. dose in gm.	Aver. dose gm./kg.	Aver. dose Days	Aver. dose previous 24 hr.	Total dose gm./kg.	Diagnosis	Organism
1	M.A.	58	F	51	54.1	52.2	1.9	2 days later	3.7	.08	2½	—	.19	Acute tonsillitis, diabetes	Beta strep.
2	A.A.	14	M	49	63.3	44.7	18.6	2 " "	3.1	.07	3	—	.19	" " peritons. abscess	" "
3	W.M.	21	M	73	58.9	54.1	4.8	1 " "	3.1	.04	4	—	.18	" "	" "
4	M.B.	13	F	34	56.0	49.4	6.6	1 " "	2.7	.06	5	—	.32	Erysipelas	—
5	C.A.	30	F	64	59.8	40.9	18.9	1 " "	4.1	.06	4	—	.25	Acute rheumatic fever, mitral lesion	No beta strep.
6	L.T.	22	F	75	54.1	48.5	5.6	1 " "	4.9	.07	2	—	.13	" tonsillitis and laryngitis	Beta strep.
7	W.P.	27	M	69	59.8	52.2	7.6	During dosage	3.7	.05	12	.05	.65	Cellulitis and osteomyelitis of hand	" "
8	R.B.	19	F	45	59.8	40.9	18.9	" "	3.6	.08	4	.08	.32	Strep. pneumonia and otitis media	" "
9	C.K.	17	M	68	59.8	40.9	18.9	" "	4.3	.06	3	.06	.17	Acute otitis, mastoiditis, sinusitis	" "
10	H.F.	28	M	54	57.9	52.2	5.7	" "	3.5	.06	2½	.07	.14	Scarlet fever	" "
11	M.D.	20	F	44	63.5	45.7	17.8	" "	5.4	.12	3½	.12	.43	Subac. bact. endocarditis	Alpha strep.
12	A.G.	31	F	34	63.6	40.9	22.7	" "	5.4	.16	4	.16	.56	" " "	" "
13	E.H.	17	F	46	65.5	39.0	26.5	" "	6.0	.12	13+	.12	3.1	" " "	" "
14	M.S.	23	F	50	64.5	37.2	27.3	" "	5.4	.11	33	.11	3.5	" " "	" "
15	C.S.	30	M	60	54.1	40.0	14.1	" "	5.3	.08	8	.12	.68	" " "	" "

Prontylin was stopped (a total of 6.0 gm. or 0.12 gm./kg. had been given) and 8 days later the CO_2 combining power of the plasma had risen to 54.1 vol. %. Two months later, when afebrile and suffering from no apparent streptococcal infection, the patient was readmitted and voluntarily took 6.9 gm. of Prontylin in 60 hours. Again her CO_2 combining power fell, this time from 59.8 to 37.2 vol. %, though there was no definite clinical evidence of acidosis.

Case B. R. E., 45 yrs., white male, had a craniotomy performed with the removal of a dural tumor and 6 days later beta hemolytic streptococci were obtained from the wound. Prontylin was started by mouth and 0.8% solution of para-amino-benzene-sulfonamide was given both subcutaneously and intrathecally, the total dose averaging about 4 gm. or .06-.07 gm./kg. per day. After 6 days he showed marked Kussmaul breathing with a CO_2 combining power of 31.5 vol. %. Later the CO_2 fell to 27.7 vol. %. At a secondary operation the lateral ventricle was entered and the patient died a week later.

Because of these cases a series of 15 consecutive Prontylin-treated patients have been studied for changes in the CO_2 combining power of their blood plasma. In each instance a determination was made prior to the giving of the drug and at least one subsequent one, during or shortly after its administration. The results are given in Table I. Every single case showed some fall in this value. This varied from 1.9 to 27.3 vol. %, and the average decrease for all cases was 14.1 vol. %. In spite of this there was no clinical evidence of acidosis in any case.

It is generally conceded that the CO_2 combining power may be slightly lowered as long as the temperature is elevated, but no specific studies of streptococcal infections are recorded. The effect of fever can be excluded in the first 10 cases, because the preliminary determinations, made during the acute fever, were all normal, and the low values were recorded only in the secondary determinations, all of which were made during convalescence when the temperature was lower, if not normal. It seems unlikely also that the fall was due to any peculiarity inherent in streptococcal infections, because the patients were admitted at all stages of their disease and yet all the preliminary determinations were above 50 vol. %. Moreover, in the second test on Case A, reported above, when she was afebrile and suffering from no streptococcal infection, the CO_2 combining power fell from 59.8 to 37.2 vol. % after the ingestion of 6.9 gm. of Prontylin.

The degree of fall has been found to show a moderate correlation with the dose of Prontylin, in grams per kilogram, given in the

previous 24 hours. Less correlation was found when it was charted against either the average dose or the total dose. However, the fact that in cases 1 and 2 a decrease still persisted when no Prontylin had been given for 2 days shows that the amount given 48 hours previously may still produce an effect.

The mechanism of the acidosis is as yet unknown. Studies to determine its nature are now in progress.

Summary. Two cases of clinical acidosis due to the administration of Prontylin (Para-amino-benzene-sulfonamide) in large doses are reported. Fifteen consecutive cases treated with this drug showed a consistent though variable drop in the CO_2 combining power of their blood plasma.

9116 P

Typhoid Leukocidin.

E. W. DENNIS AND HARATUNE SENEKJIAN.

From the Department of Bacteriology and Parasitology, School of Medicine, American University of Beirut, Beirut, Lebanon.

Typhoid leukocidin may readily be demonstrated in the filtrate of a 24-hour culture of *Eberthella typhosa* grown in plain sodium chloride veal infusion broth, pH 7.4-7.6, without addition of peptone. Typhoid leukocidin passes readily through Berkefeld N, Chamberland L3, and Seitz EK filters. The leukocidin may be adsorbed by the filter unless suitable precaution is taken.

The demonstration of leukocidal activity may be accomplished by the Neisser-Wechsberg[1] method as used by Gay and Oram,[2] but we have used a method of direct determination which is simple in principle and has yielded more satisfactory quantitative and qualitative data than the older method. For this purpose we have utilized normal rabbit's blood and non-immune human blood. The blood is collected directly into heparin, mixed, and distributed to tubes before there has been any opportunity for the leukocytes to settle out. Equal volumes of varying dilutions of the toxic filtrate are quickly added to the tubes of blood; appropriate control tubes of blood plus plain broth are always included. The tubes are sealed with paraffined corks and incubated at 37°C. in a rotating box for one hour.

[1] Neisser and Wechsberg, *Z. f. Hyg. u. Infektionskr.*, 1901, **36**, 299.

[2] Gay, F. P., and Oram, F., *J. Immunol.*, 1933, **25**, 501.