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.

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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.

Following incubation, the tubes are transferred immediately to a mechanical blood-pipette shaking device and agitation is maintained until total white cell counts and films for differential counts can be obtained. It is necessary to have as many pipettes and counting chambers as there are tubes, to insure a minimal difference of time between the taking of the different counts. Tubes for counting are selected at random rather than in the order of dilution of the filtrate. Counts of control tubes are essential. After the differential counts have been completed, the total number of leukocytes of each type is calculated and the data plotted in order of dilution of the filtrate.

The action of typhoid leukocidin is manifested by a reduction in the number of leukocytes per cmm. of blood-toxin mixture as the concentration of the toxin is increased. When a potent filtrate is used the total count is reduced by about 50%, as compared with the number in the broth-control tube. Furthermore, the neutrophilic granulocyte is the only cell type which is reduced in numbers, and the surviving neutrophils show degenerative changes which are not apparent in the cells from the control tube. By the Neisser-Wechsberg method, leukocytic suspension is inactivated by a concentration of 0.001 cc. of the toxic filtrate. By our method a reduction in total cells and neutrophils is usually definite in 1:1000 dilution of the typhoid filtrate, and in certain experiments destructive activity has been shown by dilutions as great as 1:10,000.

Typhoid leukocidin may be removed from a filtrate by treatment with 3 volumes of 95% alcohol in the cold. The dried precipitate is stable for at least a year without loss in potency. Studies on the effect of heat upon the leukocidal activity of fresh filtrate indicate that potency is reduced 50% at 85°C. for one hour. Further inactivation necessitates holding the toxin at 100°C. for at least 2 hours.

Typhoid leukocidin (filtrate) is completely neutralized by an equal volume of specific concentrated immune globulin (Felix anti-typhoid serum). Increased toxicity for rabbit-neutrophils is apparent when the serum is diluted 1:20, but the neutralizing effect is not lost until the serum has been been diluted to about 1:50,000.

Our data indicate that human neutrophils are somewhat more susceptible to the action of typhoid leukocidin than are the leukocytes of the rabbit. We have found no difference between the leukocidal activity of the Rawlins strain of typhoid bacillus and a typical Vi strain. Filtrates of paratyphoid A and paratyphoid B bacilli also show leukocidal action but the potency is relatively slight.

It is conceivable that typhoid leukocidin may be responsible for the characteristic leukopenia of typhoid fever, the depletion of the myelopoetic elements of the bone marrow, and the absence of in-

flammatory cellular infiltration about foci of typhoid bacilli as seen in sections of tissue obtained postmortem. The postulation of a positive, selective leukocidal action of a soluble toxin *in vivo* is more compatible with the pathology of typhoid fever than is the accepted conception of a negative chemotactic or repellent influence of typhoid bacilli upon granulocytes.

9117

An Improved Optical System for Cathode-Ray Recording.

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Recent years have brought the cathode-ray tube into considerable prominence as an instrument for registering and recording electrophysiological phenomena. With the recent advances in high-mu amplifier tubes, the most infinitesimal biological currents come within the scope of cathode-ray study. This has created a need for a reliable and highly efficient optical system for recording on photographic paper. A number of expedients have already been suggested and used, among them those of Gasser and Erlanger,[1] Rijlant,[2] and McCulloch and Wendt.[3]

The methods fall into 2 main divisions: (1) still photography or contact prints of single waves or periodically recurrent phenomena, obtained by photographing a standing wave or the persistent after-image of a single excursion with a still camera, or by holding photosensitive paper in direct contact with the tube screen while the fluorescent dot executes a single excursion across the screen; and (2) photography on paper moving in one axis, of excursions of the dot in a perpendicular axis, this being the method of necessity in the study of continually changing wave forms.

For quite some time the fluorescent screens incorporated in cathode-ray tubes had such low actinic rating and such long persistence of the after-image, that registration was limited to the first type of recording, namely, still photography. However, with the improvement of highly actinic and extremely low persistence screens

1 Gasser, H. S., and Erlanger, J., *Am. J. Physiol.*, 1922, **62**, 496.

2 Rijlant, P., *Gaz. Med. France*, 1934, **4**.

3 McCulloch, W. S., and Wendt, G. R., *Science*, 1936, **83**, 354.