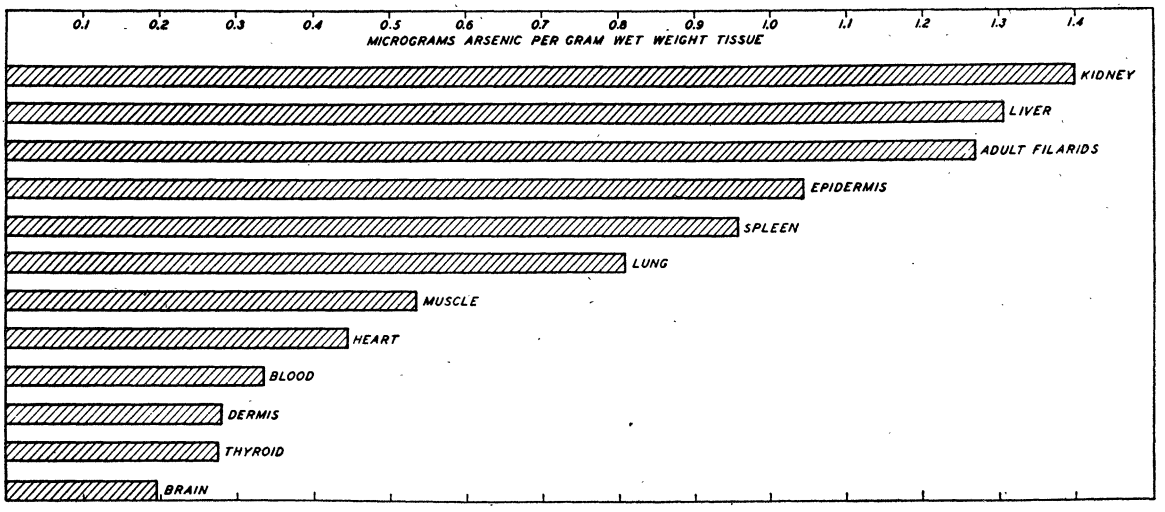

FIG. 1. Average arsenic concentrations of tissues of six cotton rats twenty-four hours after the intraperitoneal injection of 1.6 milligrams of arsenic per kilogram of body weight as sodium arsenite.

to take up sufficient quantities of the elements from the lymph to prove damaging to themselves. The fact that *Dirofilaria immitis* and *Litomosoides carinii* both showed specific affinity for arsenic makes such a hypothesis tenable.

In spite of the fact that *Litomosoides carinii* live in the pleural space, they showed a specific uptake of trivalent arsenic in five of the six cotton rats studied. Although the filarids in the sixth cotton rat appeared to be normal, they showed no specific uptake of the arsenic. In this rat, the only factor apparent to explain this difference was the presence of a chronic fibrous pleuritis. Such results suggest that treatment in human filarid infections might be more efficacious in early stages of the disease before the formation of extensive scar tissue.

CONCLUSIONS

Adult *Litomosoides carinii* of five of six infected cotton rats showed a specific affinity for arsenic after the injection of sodium arsenite. Lack of uptake in the sixth rat is attributed to the presence of a fibrous pleurisy. A specific localization of arsenic was shown in kidney cortex, liver, epidermis, spleen and lung of cotton rats.

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SYNERGISTIC ACTION BETWEEN SULPHONAMIDES AND CERTAIN DYES AGAINST GRAM-NEGATIVE BACTERIA

AS one of a number of possible explanations of the mode of action of substances that inhibit cell division of bacteria Henry[1] has suggested that the bacteriostatic agent may "poise" the oxidation-reduction potential in the immediate environment of the cell at a level which will preclude the normal functioning of one or more desmolytic enzyme systems.

Ingraham[2] has presented evidence in support of this hypothesis with respect to bacteriostatic dyes, a similar concept having been previously propounded by Dubos.[3] Henry[1] has indicated that inhibition of dehydrogenases by sulphonamides may, in part, be due to such a mechanism. More recently, Michaelis and Thatcher[4] have shown that the antibiotic substance, citrinin, depresses the action of certain desmolytic enzymes of susceptible species. These last workers also (unpublished) investigated the possibility of augmenting the "poising" effect of antibiotic substances by the addition of dyes of known E'o values. Various dyes brought about bacteriostasis, but a synergistic effect was not disclosed either between combinations of dyes or between dyes and citrinin.

The work of Soo-Hoo and Schnitzer,[5] however, confirms Ungar[6] in that a synergistic action does exist between penicillin and sulphonamides. Similar studies were therefore undertaken with sulphonamides and eH indicator dyes with respect to their activity against both *Staphylococcus aureus* and *Escherichia coli*.

It became immediately apparent that a pronounced synergistic effect was manifest, as is indicated by comparison of Tables 1 and 2. Moreover, the sulphonamides, which normally have little if any effect against

1 *Bact. Rev.*, 7(4): 175–262, 1943.
2 *Jour. Bact.*, 26: 573–598, 1933.
3 *Jour. Exp. Med.*, 49: 575–592, 1929.
4 *Can. Jour. Res.* (in press).
5 *Arch. Biochem.*, 5: 99–106, 1944.
6 *Nature*, 152: 245, 1943.

Gram-negative bacteria, would, in the presence of 1:28,000 methylene blue or brilliant cresyl blue, completely inactivate 10 million cells of a 24-hour culture of *E. coli* in 10 cc of nutrient broth buffered at pH 6.8 and containing a final concentration of 1:14,000 sulfapyridine, sulfathiazole or sodium sulfathiazole.

TABLE 1

THE CONCENTRATIONS OF INDIVIDUAL DYES AND SULFONAMIDES REQUIRED TO KILL 10^7 CELLS OF *E. coli* OR *Staph. aureus* IN 10 CC NUTRIENT BROTH BUFFERED AT PH 6.8, INCUBATED AT 37° C.

Reagent	Concentration *Staph. aureus*	Concentration *E. coli*
Methylene blue	1:100,000	1:13,000
Brilliant cresyl blue	1:130,000	1:20,000
Sulfathiazole	1:100	complete bacteriostasis not apparent at saturation levels
Sulfapyridine	1:100	
Sulfanilamide	1:100	
Sodium sulfathiazole	1:100	

TABLE 2

THE CONCENTRATION OF METHYLENE BLUE OR BRILLIANT CRESYL BLUE REQUIRED TO KILL 10^7 CELLS OF *E. coli* IN 10 CC NUTRIENT BROTH BUFFERED AT PH 6.8 IN THE PRESENCE OF SULFONAMIDES AT 1:14,000

Sulfonamide	Methylene blue	Brilliant cresyl blue
Sulfathiazole	1:28,000	1:32,000
Sulfapyridine	1:28,000	1:28,000
Sulfanilamide	1:18,000	1:18,000
Sodium sulfathiazole	1:28,000	1:32,000

Clinical studies undertaken in cooperation with Dr. J. T. MacLean at the Ste. Anne de Bellevue Military Hospital indicate a promising therapeutical value for the combination of sulfathiazole and methylene blue in the treatment of chronic genito-urinary infections by Gram-negative bacteria.

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ACID PHOSPHATASE IN GROWING AXONS AND DEGENERATED NERVE TISSUE

WOLF, Kabat and Newman[1] have reported the presence of acid phosphatase in the axis-cylinders of both the peripheral and central nervous system. The myelin sheaths appear to be devoid of the enzyme. Since phosphatase has been implicated in the metabolism of both phospholipids and sugars, it would appear that studies on this enzyme might give an indication of some of the metabolic processes going on within the nerve fiber and specifically in the axonal portion. This preliminary report deals with the results obtained from the study of (1) the growing nerve fibers of the cat from birth to neurologic maturity and (2) the behavior of the enzyme in the degenerating neuron.

It was found necessary to make considerable change in the existing technics for demonstration of acid phosphatase as applied to the tissue of the central nervous system. The method used, as well as a more complete description of our observations, will be published elsewhere.

Studies of the growing neuron have been made on cats of the following ages: 1, 2, 5, 10, 15, 20, 70 days and adult. The evidence from this series indicates that variations in the time of appearance of the enzyme in the axons are to be correlated with the phylogenetic background of the several nerve tracts as well as the ontogenetic age of the animal. Thus, at birth the ventral and dorsal roots, the sensory tracts within the cord, the medial longitudinal fasciculus and tecto-spinal tracts in the brain stem all give a marked positive reaction. At this age, the higher brain centers, as well as the great motor bundle, the pyramidal tract, show comparatively little or no phosphatase. Likewise, the tracts which react positively are known to be the first to become myelinated. In the later postnatal stages, a progressive increase in the reaction occurs in the higher brain centers. Comparatively, the pyramidal tract gives an incomplete reaction until some time after the 70th day. Thus, if the presence of acid phosphatase indicates a functional state in nerve conduction it would appear that the neuronal elements concerned with the cord and brain-stem reflexes are the first to show the presence of the enzyme.

Studies on the degenerating neuron have been made on the pyramidal tract in cats and monkeys following removal of the motor cortex. This bundle, in two monkeys with a post-operative survival time of four and five months, can be traced with ease from the cortex to the sacral cord segments. The entire degenerating field gives a marked acid phosphatase reaction. Since, in this breakdown, the affected axis-cylinders have disappeared the phosphatase must be associated with the glial tissue and possibly with chemical remnants of the myelin sheaths. One of the fundamental and unanswered questions in the field of neurology and neuropathology is why the medullated membrane should degenerate concurrently with the axis-cylinder when the cell body or nerve fiber is seriously damaged. There is the distinct possibility, on the basis of the present study, that the axon may liberate a substance (enzyme) which acts on the myelin sheath in a manner to cause its disintegration. Studies are in progress to determine the immediate or acute secondary and retrograde changes in phosphatase following injury to the neuron.

Two cats, similarly treated as the monkeys, but

[1] A. Wolf, E. A. Kabat and W. Newman, *Am. Jour. Path.*, 19: 423, 1943.