duced a 19.5-fold decrease in the binding of SN-12868 by the ribonucleate anion. This suggests that the interactions of cationic acridines and quinolines with polyvalent nucleate anions involve, at least in part, the phenomenon treated theoretically by Danielli (*3*). However, the

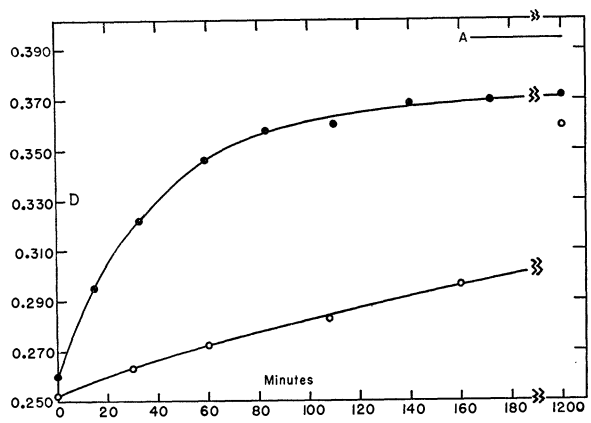

FIG. 3. Change in binding of SN-12868 by ribonucleate during incubation of the latter in 0.5 N NaOH at 24° C (●), and in 0.05 N NaOH at 37° C (○).

difference in binding of SN-12868 and SN-7618 suggests that forces such as hydrogen bonding and van der Waals' forces, are involved in addition to coulombic forces. The interactions reported here should be compared with those between nucleic acids and streptomycin which have been described by Cohen (*2*), and von Euler and Heller (*4*).

That the interaction of these antimalarials with nucleic acids is dependent upon the molecular size of the nucleic acids is suggested by experiments summarized in Fig. 3. Ribonucleic acid was incubated in aqueous solutions of sodium hydroxide. At intervals, aliquots of the solution were transferred to phosphate buffer, HCl equivalent to the alkali in the aliquot was added, SN-12868 was introduced, and the mixed solution was diluted with phosphate buffer in such manner that in every case the solution was 4×10^{-5} M with respect to SN-12868 and contained the equivalent of 0.046 g of ribonucleic acid per 100 ml. Final pH was 5.9 in each case. Optical densities were determined at wavelength 425 mμ. The progressive increase in optical density (Fig. 3) corresponds to progressively diminished binding of SN-12868. The rate of change in 0.5 N NaOH at 24° C was much greater than the rate in 0.05 N NaOH at 37° C, but after 20 hr the optical densities of these two solutions appeared to be approaching an equivalent limiting value, which was less than the optical density (0.394) that would have been observed in the complete absence of binding of SN-12868. The bridging phosphate ester linkages of nucleic acids undergo hydrolytic cleavage in alkaline solution, and these experiments suggest that the binding of acridine derivatives can be used as an indirect measure of such cleavage. Application of these observations in the study of the action of various nucleases is suggested.

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A Rationale for Plasma Therapy in Poliomyelitis

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During the 1948 epidemic of poliomyelitis in Los Angeles, a research program was suggested by one of us (R.M.E.), and initiated by both, in which it was observed that the serum albumin level was frequently lower than normal, and that there seemed to be a correlation between the degree of reduction and the severity of the disease. Because of the importance of serum albumin in maintaining the normal osmotic pressure of blood and of the osmotic pressure in regulating the equilibrium of tissue fluids, and because of the possibility that edema of the cord may contribute to the pathogenesis of the paralysis in poliomyelitis, the suggestion was made that a detailed study be conducted to determine: 1) the alterations in serum proteins which occur during the course of the disease, and 2) the effect on both the serum proteins and the neurologic residual of paralysis as a result of intensive administration of plasma. The results obtained were highly suggestive of a beneficial effect of plasma and will be reported in the near future, with the Los Angeles County Hospital group. It was thought desirable to describe briefly the theory that prompted the suggestion, in the hope that other workers will be stimulated to explore these therapeutic possibilities.

Because the spinal cord is encased in a bony framework, it is particularly susceptible to injury from the edema which consistently accompanies the virus-induced nerve cell damage. Any decrease in serum albumin caused either by accelerated protein catabolism or disturbed protein synthesis and occurring as one of the systemic manifestations of the disease would lower the plasma osmotic pressure and accentuate the spinal cord edema. Conversely, if the serum albumin (and osmotic pressure) were raised by the administration of plasma, the process might be reversed.

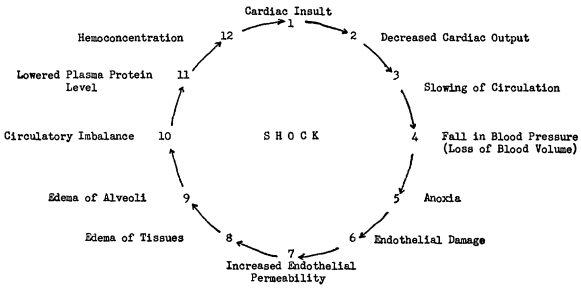

FIG. 1. It is probable that the shock state may be produced by a type of chain reaction initiated at any one of the above 12 points. Hemorrhagic shock emanates from point 4 as an actual loss of blood volume. Infectious shock would start at point 6 with endothelial damage.

In uncomplicated hypoproteinemia, the osmotic pressure of plasma proteins must be reduced to approximately 20 mm of mercury or below before edema is clinically evident. However, when factors tending to precipitate shock are operative, much more moderate decreases in plasma protein may become important in the pathogenesis of generalized or local edema. For instance, it has been shown by Eaton (*2*) that after an acute hemorrhage is induced in dogs, a degree of pulmonary edema rapidly develops which seems to be the result of a shock syndrome, in which there is a decrease in cardiac output, slowing of the circulation, drop in blood pressure, anoxia, endothelial damage, increased permeability of endothelium, transudation of fluid through the impaired endothelial structure, lowering of serum protein levels, and subsequent pulmonary edema (Fig. 1). In these experiments only a slight lowering of the already depressed serum albumin level existent in the shock state was necessary in one group of hemorrhaged dogs to accelerate significantly the accumulation of free fluid in the pulmonary tissue as compared with a control group of hemorrhaged dogs in which no added alteration of serum albumin was made. In poliomyelitis, on the other hand, it is postulated that the virus-induced infection itself may initiate a similar, although at first local, shock syndrome (infectious shock) at point 6 in the diagram, and cause damage to capillary endothelium, vascular congestion, and anoxia, and consequently lead to the transudation of fluid across the impaired endothelium and into the cord. Here again, slight lowering of the plasma osmotic pressure, caused by increased protein catabolism and disturbed protein synthesis as a systemic manifestation of the disease, could lead to a prompt increase in both the degree and the rate at which the local edema of the cord develops.

According to reports in the literature, plasma in moderate amounts has been given in the past to patients with poliomyelitis, with the idea of introducing the immune bodies of the globulin fraction. In one brief study reported by Barnum and Bower in 1944 (*1*), large amounts of plasma were intravenously administered with apparently good results, but again with the apparent intent to administer γ-globulin. The present paper suggests that the therapeutic value of plasma in poliomyelitis may more correctly be attributed to the albumin fraction and to its effect in reducing cord edema. Our preliminary results with a group of 76 Los Angeles patients, soon to be reported, are in accord with this hypothesis and indicate that generous amounts (600 to 900 ml daily) are required.

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A Photoelectric Microdensitometer

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The photoelectric microdensitometer was designed for the semiquantitative determination of colorimetric histo- and cytochemical tests. Visual judgment of color intensity is not sufficiently reliable to permit comparison of the degree of color in experimental and control preparations. This instrument completely eliminates the subjective element of judging color intensities. It is possible to duplicate the values of different sets of tests (e.g. the Feulgen reaction) on comparable material within ±2%.

The microddensitometer is based on ideas from a number of sources, particularly Dempsey *et al.* (*2*), and Stowell (*3*). Although this densitometer assembly is not new in principle, its adaptability and reliability make it a valuable laboratory aid.

As shown in Fig. 1, the assembly consists of a monocular microscope, a Leitz Makam with a ground glass back, and a model 512 Photovolt Electronic Photometer with a Type C search unit. The phototube search unit is mounted in a traversing mechanism which can be used to move the search unit over the ground glass screen. This assembly in turn is mounted on an arm that can be moved up and down a vertical post. The arm is counterbalanced by a spring-activated steel tape fixed to the top of the vertical post and is provided with a collar which will lock the assembly at any height by a simple set screw. Details of the arm and traversing mechanism are shown in Fig. 2.

Illumination of the Kohler type, as described by Copeland (*1*), is provided by any good microscope lamp and

[1] U. S. Public Health Service, National Cancer Institute Research Fellow.