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Concentration of Congo-Red in the Blood after Absorption from the Pneumonic Lung.

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The pulmonary circulation undergoes marked alterations in pneumonia, (1) to a condition of hyperemia and (2) to that of ischemia. Upon the state of efficiency of the circulation in the infected tissues must depend largely the rate of absorption of the toxic products of the infection, and upon the latter must depend the severity of the toxic symptoms. These experiments represent the initial phase in a study of the absorption rate as a basis for a better understanding of the symptomatology of pneumonia. Congo red was the substance injected into the lung for testing the absorption of soluble products, because it is identifiable and measurable in the blood, and, in the normal individual at least, is eliminated from the blood (by the liver) at a slow and uniform rate as compared with other non-toxic dyes. The only diseases known[1] to alter appreciably the rate of elimination of congo red are amaloidosis, which retards it, and nephrosis and cirrhosis, which sometimes accelerate it, but these are not found in dogs.

Pneumonia was produced in 24 dogs by the method of Terrell, Robertson and Coggeshall,[2] with the modifications that the pneumococci (type 1) were suspended in saline rather than in the more viscid medium, to allow them to reach the peripheral airways more easily, and that the inoculation was made bronchoscopically. Morphine, atropine and ether were given previously, and 3 cc. of a thin inoculum was injected into one bronchial branch of the right lower lobe. After an interval of 2, 4, 24, or 48 hours, the animals were anesthetized again, a sample of blood was obtained, congo red (1 cc. of 1.25% solution per kg. body weight) was injected very slowly into the same bronchus as was used for the inoculation, and samples of blood were collected at 10-minute intervals thereafter for nearly 2 hours. Each sample was drawn into isotonic solution of sodium oxalate (9 parts of blood to 1 part of solution), the mixture was fractionated by centrifuging, and the supernatant fluid was analyzed

[1] Bennhold, H., *Arch. klin. Med.*, 1923, **142**, 32; *Klin. Wchnschr.*, 1924, **38**, 1711.

[2] Terrell, E., and Robertson, O., PROC. SOC. EXP. BIOL. AND MED., 1930, **27**, 973. Terrell, E., Robertson, O., and Coggeshall, L., *J. Clin. Invest.*, 1931, **10**, 659.

colorimetrically. Immediately after the last sampling the animals were killed and autopsied, with special attention to the nature of the lesion and the distribution of the dye still remaining in the lungs. Six dogs were used as controls, treated in the same way except that the inoculation was omitted.

The control dogs began to show a trace of dye in the blood at 10 to 20 minutes after injection and a maximal concentration of dye of 6.25 to 11.25 parts per million at 40 to 60 minutes after injection. The dogs examined 2 hours after inoculation had an appearance-time of 10 to 30 minutes and a maximal concentration of 3.75 to 11.25 parts at 40 to 70 minutes. Those examined 4 hours after inoculation had an appearance-time of 10 to 40 minutes and a maximal concentration of 3.75 to 11.25 parts at 60 to 80 minutes. Those 24 hours after inoculation had an appearance-time of 20 to 50 minutes and a maximal concentration of 0 to 6.25 parts at 50 to 70 minutes. Three of this group presented no measurable amounts of dye at any time. Finally, the dogs examined 48 hours after inoculation had an appearance-time of 30 to 50 minutes and a maximal concentration of 0 to 6.25 parts at 60 minutes. Four of this group showed no measurable amounts of dye. Fig. 1, representing

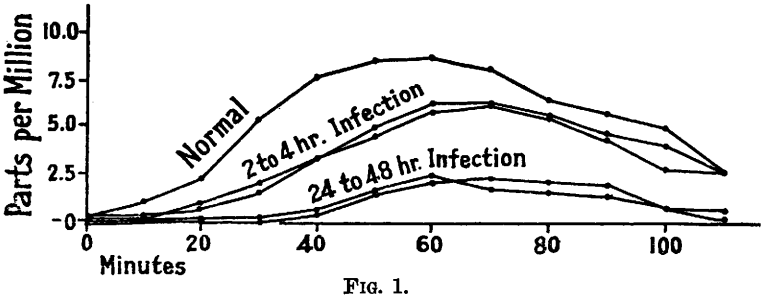

FIG. 1.

Curves representing the average behavior of the dye-concentration curves for each of the 5 series of dogs.

the simple averages for the 5 groups, demonstrates the outstanding characteristics, namely, the gradual rise and fall of the concentration of dye in the blood in all cases, and the tendency for a marked delay in the time of appearance and a great reduction in the maximal concentration in the cases with pneumonia, already distinctly in evidence 2 hours after inoculation. The lesions appeared at autopsy to be the same as those described by the authors of the method.[2] Those at 2 or 4 hours after inoculation were characterized by intense swelling, edema, congestion and hemorrhage, and those at 24 to 48 hours, by red-hepatization. There was considerable variation

in the extent and advancement of the lesions in the different individuals at each period after inoculation and, on the whole, this was proportional to the degree of the abnormalities in the dye-concentration curves. The dye was confined almost wholly to the right lower lobe. In the cases with pneumonia, the dye was in the tissues of the lesion, and also in the tissues immediately adjacent when the lesion did not occupy the entire lobe. That the dye penetrated well into the lesion was evidenced by its being visible plainly on both the pleural and cut surfaces of those tissues. The bronchi in the lesion large enough for gross examination were found to be patent but intensely stained.

The abnormalities of the concentration of dye in the blood of the dogs with pneumonia may have been due to one or both of 2 causes: (1) a delay in the onset, and a diminution in the rate, of absorption of the dye from the diseased lung, and (2) an increase in the promptness and rate of elimination of the dye from the blood. If the latter factor enters at all, it is probably of minor consequence, judging from what is known of the regularity of the process and elimination of congo red in disease in man; but to judge the rate of absorption from the lung with certainty, it will be necessary to determine whether or not the rate of elimination in dogs is affected by pneumonia after injection of the dye into the blood-stream. This is the next phase of the study.

The extremely early period of pneumonia at which marked abnormalities of dye absorption rate were seen is particularly noteworthy. Evidently the efficiency of the circulation in the infected tissues is greatly reduced at the stage of congestion in pneumonia, although not as greatly as at the stage of consolidation.