Table 3. Effect of *NN*′-Diphenyl-*p*-phenylenediamine in the Prevention of Carbon Tetrachloride Poisoning

No. of rats	Treatment with DPPD Time (hr. before carbon tetrachloride)	Dose (mgm.)	Carbon tetrachloride (ml./kgm.)	Deaths No.	Deaths Per cent
32	—	—	4·0	32	100
19	48, 24, 0	100	4·0	0	0
11	48	100	4·0	6	55
17	0	100	4·0	10	59
12	48, 24, 0	50	4·0	8	67
11	48, 24, 0	10	4·0	7	64

in 0·4 ml. arachis oil at 48, 24 and 0 hr. before giving 4 ml. carbon tetrachloride/kgm. protected all of 19 rats against death (Table 3). One dose of 100 mgm. DPPD either 48 hr. before or with carbon tetrachloride reduced the death-rate to 55 and 59 per cent respectively of 11 and 17 rats, as compared with 100 per cent of 32 rats given carbon tetrachloride only. Courses of 3 injections of 50 or 10 mgm. DPPD during the 48 hr. prior to administering carbon tetrachloride also reduced the death-rate.

The photomicrographs illustrate the protective effect of DPPD against histologically observable damage to the liver by carbon tetrachloride. Fig. 1 shows a section of the liver of a rat killed 24 hr. after having received 4 ml. carbon tetrachloride/kgm. The liver is typical for rats with severe acute carbon tetrachloride poisoning, showing centrilobular necrosis and fatty change. This contrasts with the virtually normal appearance of the liver section in Fig. 2, which is typical for rats killed 24 hr. after the same dose of carbon tetrachloride but which have been given 3 intraperitoneal injections of 100 mgm. DPPD during the 48 hr. before administration of carbon tetrachloride.

It seems likely that the antioxidants protect rats against the lethal effects of large doses of carbon tetrachloride by acting on a general permeability mechanism, and thus prevent the loss of mitochondrial and cellular pyridine nucleotides which would otherwise result from the physical damage to the cell produced by carbon tetrachloride.

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HÆMATOLOGY

Thromboplastic Activity of Red Cells

The problem concerning the relationship of the thromboplastic activity of red cells to that of platelets which Inglis and Halliday[1] have recently studied has, in part, been answered by the work of my associates and me.

It was repeatedly noted that in very mild hæmophilia the prothrombin consumption carried out by my original method was often normal when whole blood was clotted, but not when the platelet-rich plasma was clotted under otherwise identical conditions[2]. This observation led to an investigation of the clotting factor in red cells and its probable role in the generation of thromboplastin. It was found that the activity of hæmolysed erythrocytes (hæmolysate) is similar to that of platelets but quantitatively much greater[3,4]. It is significant that, when a concentrated extract of platelets is added to normal native platelet-poor plasma that has been in contact only with silicone-coated surfaces, the consumption of prothrombin is too small to be determined; whereas, when the plasma is first brought in contact with a glass surface or treated with a minute amount of thrombin, the addition of a platelet extract brings about good consumption of prothrombin[5]. In marked contrast, the addition of an extract of red cells results in a high consumption of prothrombin even when added to native plasma that has been exposed only to silicone-coated surfaces[6].

These findings suggest that platelets can enter the coagulation reaction only after a plasma factor has been activated. Because this activation can occur by exposure to glass, the agent has been designated 'contact factor'. It appears that a platelet constituent interacts with the activated contact factor and that the resultant product is either very similar to, or identical with, the clotting agent found in the red cell. The latter factor, which appears to be a phospholipid[7], does not require contact factor to enter into the clotting reaction. From recent work it appears that some of the clotting agent formed from the platelets during clotting is removed by the red cells[8].

Whether the clotting activity of the intact red cell, which is feeble, has physiological significance remains unanswered. The alternative view that the red cell may be constantly removing this potent agent, which perhaps is being produced continuously, also deserves recognition and consideration.

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We freely acknowledge the priority of Prof. Quick in discovering and reporting the platelet-like thromboplastic activity of red-cell hæmolysate. No reference was made to his work, as it was our opinion that it would be well known to all workers in this field.

The activity reported by us is, however, manifested by non-hæmolysed cells. According to previous reports, non-hæmolysed red cells are capable of exerting only feeble platelet-like activity. Prof. Quick concurs with this. Our work, however, has shown that this is true only in regard to the initial stages of coagulation, but that after the formation of fibrin becomes evident red cells which are still intact develop much greater activity. We have not, as yet, investigated whether this is due to the envelope of the red cell being attacked by thrombin. The activity may be due to the same element in the red cell as is responsible for the platelet-like activity of red cell hæmolysate; but if so, this element can act while still attached