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Effect of Neoarsphenamin on the Number of Blood Platelets.

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The blood platelets show characteristic variations in number after the intravenous injection of certain toxic substances and during certain acute infectious diseases. At first, following the injection of the substance or during the febrile period of the disease the number of platelets is diminished. The period of thrombopenia is then usually followed by a rapid rise to the normal number (350,000 per cu. mm.) and often by a period of thrombocytosis, the number occasionally reaching 750,000 per cu. mm. or more.

It has been suggested that thrombosis may occur more readily as a result of the excessive number of platelets, although they are not the sole factor in the formation of thrombi.[1] Hartmann[2] has pointed out that the appearance of thrombosis which occurs during convalescence from typhoid fever coincides with the period of thrombocytosis. Recently a case in this hospital of cerebral thrombosis developing 5 days after the intravenous injection of 0.6 gm. of neoarsphenamin suggested the possibility of a similar relationship, although platelet counts were not made at the time.

Several investigators have observed the immediate diminution of the number of platelets following arsphenamin therapy and numer-

[1] Lee, R. I., Minot, G. R., and Vincent, B., *J. Am. Med. Assn.*, 1916, lxvii, 719.

[2] Hartmann, E., *Deutsch. Arch. Klin. Med.*, 1927, clviii, 1.

ous cases of purpura occurring after arsphenamin treatment are recorded. However, little or no attention has been given to the later period when thrombocytosis may occur. The following observations were made to determine whether or not thrombocytosis follows the period of thrombopenia subsequent to the intravenous injection of neoarsphenamin (novarsenobenzol "Billon").

The effect of the injection of the drug on the number of platelets of 14 patients was studied. The usual dosage given was 0.1 g. per kg. of body weight. The direct method of counting[3] was employed. Counts were made before the injection and then at intervals of from 10 minutes to 1 day after the injection for 5 days.

In 4 cases the number of platelets did not vary beyond the range of experimental error (±25,000). However, in agreement with other reports, there was a diminution in the number of platelets (170,000 to 300,000 per cu. mm.) from 10 to 30 minutes after injection in 10 cases. In 5 of these patients, flushing of the face, dizziness, nausea, chilliness and fever preceded the diminution in number. After a period of about 6 hours the number of platelets returned to normal and a period of slight overproduction followed which lasted from 1 to 3 days. The platelets during the period of thrombocytosis never exceeded 450,000 per cu. mm. in any case. A

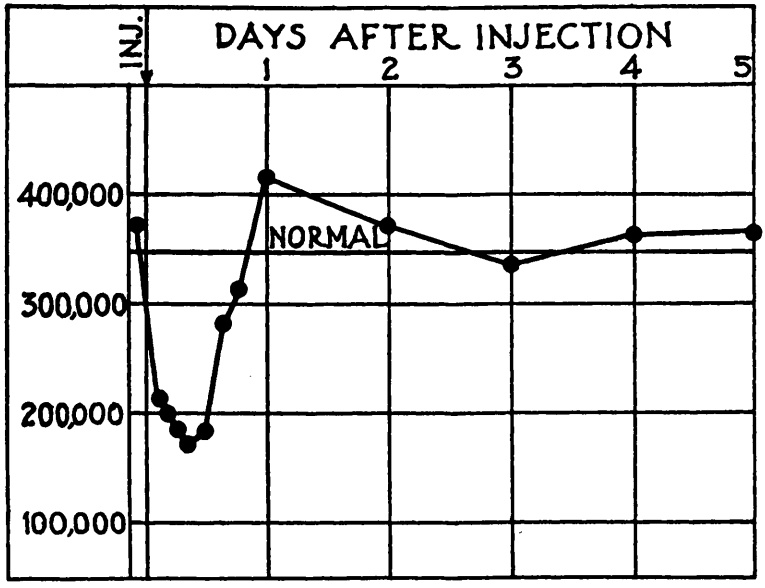

CHART 1.
Variations in the number of platelets following neoarsphenamin injection.

[3] Reimann, H. A., *J. Exp. Med.*, 1924, xl, 553.

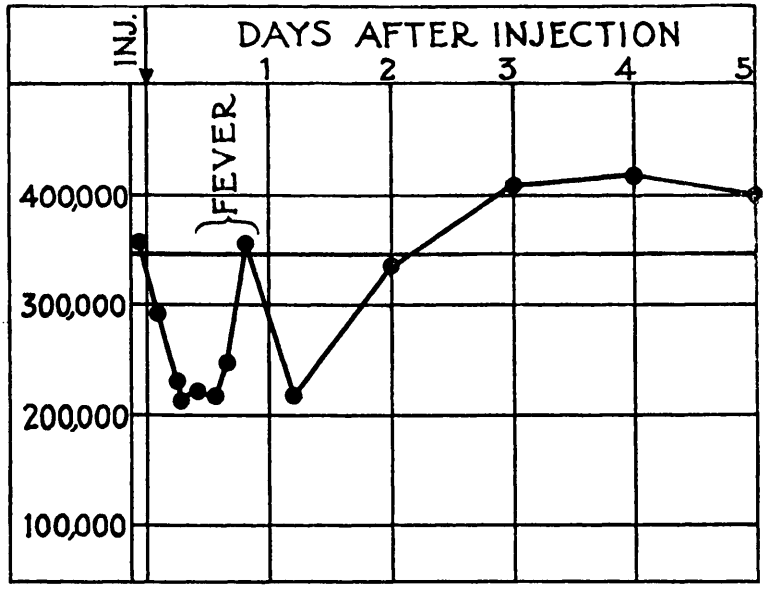

CHART 2.

The effect of a febrile reaction on the number of platelets following neoarsphenamin injection.

typical curve is illustrated in Chart 1. In 2 cases the diminution did not occur until 24 hours after injection. But in these 2 cases fever (38° to 38.5° C.) which appeared 12 hours after injection preceded the diminution. Chart 2 shows the effect of a febrile reaction occurring in another case 8 hours after the injection. The fever apparently caused a second diminution in the number of platelets which was followed in 2 days by thrombocytosis.

Summary: The number of blood platelets was diminished following the intravenous injection of neoarsphenamin in 10 out of 14 patients. The period of thrombopenia was followed by slight thrombocytosis. The number of platelets did not exceed 450,000 per cu. mm. in any of the cases observed. The variations in the number of platelets were usually greater in patients developing a febrile reaction after treatment. It would seem that only in the exceptional case does a reaction occur which is severe enough to provoke a marked thrombopenia and a subsequent marked thrombocytosis.