

INCONSTANCY AND VARIABILITY OF THE VASCULAR FRAGILITY TEST EVEN IN PURPURIC CONDITIONS

By J. ROSKAM, M.D., CH. RENARD, M.D., AND L. SWALÛE, M.D.

THE PATHOGENESIS of purpura is mysterious and complex. This is true for the origin of uncontrollable hemorrhages in Werlhof's disease and similar conditions. Clinical and experimental observations have indeed proved that the very long bleeding times occurring in hemogenic and hemophilo-hemogenic syndromes are due to the association of a hemic and a vascular factor (Roskam, ¹¹⁻¹³). Although the existence of the latter factor is established beyond doubt, its nature is not yet completely elucidated.

The breaking out of intradermal purpura seems also to result frequently from multiple factors (Grenet⁴; Bedson¹), seldom analyzed as yet.

Several authors have, however, emphasized the importance in the production of petechiae of the fragility of vessels of purpuric patients, as namely evidenced by the ease with which venous stasis produced a petechial eruption in these patients.

This induced purpura was described in 1911 by Frugoni and Guigni,² later by Weill (of Lyon) and Chalié¹⁶ in certain hemorrhagic conditions. The same year, Leede⁵ erroneously considered it as pathognomonic of scarlet fever. Later this phenomenon was systematically studied and was found by many authors in various conditions: intoxications, avitaminoses, diseases of the endocrine organs, of the spleen, the reticulo-endothelial system, of the sympathetic nervous system (Stephan¹⁵), in hypertension, solitary or combined with arteriosclerosis, in nephritis, in endocarditis lenta (Weissman¹⁷), in diabetes, in rheumatic patients given large amounts of sodium salicylate, in patients with gastro-duodenal ulcers treated with a milk diet and alkaline powders, in patients with chronic glaucoma (Roskam⁹), in erythremia, icterus, certain forms of tuberculosis (Schour¹⁴), etc.

The intensity of the purpura induced by venous stasis, "signe du lacet," capillary fragility test, capillary resistance test, or tourniquet test, etc., is approximated by the number of petechiae which appear during the test.

One of us has, however, repeatedly pointed out the "qualitative" and not "quantitative" aspect of the eruption; i.e., the importance of the size of the different purpuric elements. Petechiae with a diameter above one millimeter possess a significance similar to that of increased bleeding time (Roskam¹⁰).

These proportionally large petechiae are observed in subjects with a hemorrhagic condition. The more severe the condition, the larger is generally the diameter not of all petechiae, but of a certain number of them.

After this brief review, we will take the opportunity of describing two recent clinical observations to underline the diverse results in different circumstances of the "vascular" fragility test, as we prefer to call the "capillary" fragility test, for no one has proved that only capillaries are involved in that test.

From the Institute of Medical Clinic and Pathology, University of Liege, Belgium.

CASE HISTORIES

Case 1: V. Michel, male, 16, high school student.

Family history: irrelevant.

Personal history: measles, scarlet fever, diphtheria, appendectomy in childhood.

Present disease: At the beginning of December 1946, appearance of an eruption not disappearing by "vitropression," made up of small elements grouped in clusters on the antero-medial aspect of the forearms and thighs. Later extension of this eruption mainly to the shoulders, to the anterior side of the legs, and to the ankles. Purple at their appearance, the small eruptive elements turn later brown-pink and yellow before disappearing. Several eruptive waves follow, always occurring in the skin areas involved in the first attack.

Physical examination: On Jan. 10, 1947, nothing unusual, except for pigmented sequelae of previous eruptions and for a few small submaxillary and axillary nodes.



FIG. 1

Sedimentation rate: 3 mm. in the first hour (Westergren).

Hemoglobin: 55 per cent.

R.B.C.: 4,200,000. *Morphology:* normal.

W.B.C.: 7,200.

Differential: Neutrophilic polymorphonuclears, 48 per cent; eosinophilic polymorphonuclears, 3 per cent; lymphocytes, 43.5 per cent; monocytes, 5.5 per cent.

Platelets: 220,000. *Morphology:* normal.

Bleeding time: Right ear, 1'30"; 1', 1', 3'30", 2'. Left ear, 1'30", 1', 1'30", 2'30", 1'30".

Clotting time: 22', 22', 22', 22' (normal: 16' to 24').

Prothrombin time (Quick): 100 per cent.

Bordet-Wasserman, Meinicke, Paul and Bunnel reactions: negative.

*Vascular fragility test**: quantitative, ++++: qualitative, +++; only in the cutaneous areas corresponding to previous eruptions, as the petechiae induced by venous stasis are grouped in clusters and form eruptive blotches separated by areas of normal or almost normal skin (figs. 1, 2, and 3).

One week later, despite the daily intake of 40 mg. of citrin, similar vascular fragility test: quantitative, ++++: qualitative, +++ in the cutaneous areas with sequelae of previous eruptions, almost negative between these areas.

Case 2: Jacques, male, 17, high school student.

Family history: irrelevant.

Personal history: measles, chicken pox, mumps, whooping cough in childhood; appendectomy in 1942; frequent bronchitis; gastro-intestinal upset with fever in October 1946.



FIG. 2

Present disease: On Saturday, January 25, 1947, the patient ate lobster with cocktail sauce, duck, and *pâte de foie gras*. Normal activity from January 26 to 28, but exposure to very cold weather during these three days. On Tuesday 28, purpuric stripes (length: $1\frac{1}{2}$ -7 cm; width: $\frac{1}{2}$ -2 $\frac{1}{2}$ cm) suddenly appeared on the face and neck. On the 29th, fever (about 38 C) which lasted for two days, headache and nausea, whereas the eruption faded out progressively and disappeared on Feb. 10.

On Feb. 2, at 8 P.M., intake of two boiled eggs and again exposure to severe cold. At 9 P.M., as his

* The vascular fragility test which we used is the test described by one of us in 1929 under the name of "signe due brassard": application above the elbow of the cuff (brassard) of Boullitte's oscillometer inflated half-way between the maximal and minimal arterial pressure of the patient. The pressure is held for 15 minutes. After decompression, there is examination of the induced purpura on the whole surface of the forearm and hand, and not, as later proposed by Wright and Lilienfeld,¹⁸ in a small area of the supero-medial aspect of the forearm.



FIG. 3



FIG. 4

father was weighing and measuring the patient, he saw the appearance of a new eruption which reached its maximum in a quarter of an hour. More numerous, the purpuric spots were localized on the face, neck, upper part of the chest, forearms, and wrists. Soon afterwards, fever (38.2 C), headache and nausea.

Physical examination: On Feb. 3, 1947, in addition to the cutaneous eruption (figs. 4 and 5), there were slight fever (37.5-38.5 C) which disappeared progressively in ten days, a few petechiae on the soft palate, a few small nodes in the neck, groins and axillae, and a palpable spleen reaching the costal margin on percussion.

Sedimentation rate: 4 mm. in the first hour. (Westergren)

Hemoglobin: 100 per cent.

R.B.C.: 4,750,000. *Morphology:* normal.

W.B.C.: 6,000.



FIG. 5

Differential: Neutrophilic polymorphonuclear, 60; eosinophilic polymorphonuclear, 2; lymphocytes, 31; monocytes, 7.

Platelets: 225,100. *Morphology:* normal.

Bleeding time: Right ear: 1', 1', 1'30", 2', 3'. Left ear: 3', 2', 1', 1', 2'.

Clotting time: 21', 23', 21', 23'. (normal: 16' to 24').

Prothrombin time (Quick): 100 per cent.

Bordet-Wasserman, Meinicke, Widal, Wright's reactions: negative.

Paul and Bunnell's test: + at 1/8.

Hemoculture: negative.

Takata-Dohmoto's flocculation figure: 59 (low, but still normal.)

Weltman's coagulation band: 0.4 (normal).

Vascular fragility test: quantitative and qualitative practically negative on this day, as well as later, when the eruption was fading or had disappeared.

As the history and tests suggested an anaphylactic purpura, preparations of egg white, mayonnaise, foie gras, and lobster were scratched into the skin: no reaction. Similarly, intradermal reactions with milk, tuberculin, Dmelcos, antistaphylococcic vaccine remained negative, as well as attempts to find a possible focal infection. The intake of foie gras on Feb. 20 did not bring any of the reactions characteristic of Widal's digestive hemoclasia, nor any rash.

However the patient—who had been kept at normal temperature—ate on Feb. 6, at noon, lobster cocktail sauce and, in the evening, some foie gras. On the next morning, the purpuric stripes appeared at the base of the neck and on the anterior aspect of the forearms; the latter spots were surrounded by an area of congestion without pruritus. The eruption induced on February 6 and 7 was much milder than the previous ones. This was the last of the purpura of this patient.

On Feb. 14, Paul and Bunnel's reaction: 1/16 ++++, 1/32 ++, 1/64 +.

COMMENTS

Both cases reported had a purpuric eruption.

In the first one, the eruption was symmetrical and made up of innumerable petechiae grouped in cluster, in maplike areas 0.5 to 2 cm. in diameter, separated by areas of almost normal skin. This relapsing purpura simplex had a protracted course or at least a subacute one. The etiology remained mysterious, as well as the cause of the different attacks. However, outside any purpuric attack, the vascular fragility test was twice strongly positive, quantitatively and qualitatively, but only in those cutaneous areas where the previous eruptions had spontaneously occurred.

In the second patient, the eruption, also symmetrical, was formed by rather homogenous hemorrhagic streaks not resulting from the coalescence of smaller petechial elements. The only real petechiae were observed on the soft palate. The etiology of the syndrome probably was alimentary. However, it is noteworthy that the cuti-reactions with the suspicious foods remained negative, as well as Widal's tests of digestive hemoclasia, and that the purpura simplex of this patient occurred at the same time as an attack of infectious mononucleosis. The vascular fragility test was completely negative at the place of the purpuric spots and outside them.

Thus, in one of the two reported cases of purpura simplex, a strongly positive quantitative and qualitative vascular fragility test was present.

In the other, the vascular fragility test was completely negative.

In order to explain the different behavior of the vessels of the two patients during venous stasis, one might consider the different nature of the two cases of purpura, as also evidenced by differences in the clinical course and in the purpuric eruption.

This simple interpretation is probably accurate.

Nevertheless a case of constitutional athrombopenic hemorrhagic purpura published by one of us in 1929 (Roskam⁸) might be taken as an argument against it.

For this patient we noted on April 5, 1927, at the time of his admission to the hospital:

"Tourniquet test after 15 minutes of compression at 70 mms. of mercury with the blood pressure machine: there appeared below the right elbow several large petechiae measuring 1-3 mms. About 50 were seen on the anterior aspect, 40 on the posterior aspect of the forearm. Under the same conditions, the test being repeated twice, no purpuric elements were seen over the left forearm. On April 29 we noted:

"Tourniquet test: after 15 minutes of compression of the arm at 80 mms. of mercury, identical numbers of petechiae appeared over the right forearm as had been noted on April 5. The left forearm at this time showed a very marked purpuric eruption with enumerable punctate petechiae. 195 petechiae were present on the anterior aspect of the left forearm together with 6 ecchymoses of about 5 mms. in diameter. Posteriorly 175 petechiae of about 1 mm. in diameter were seen. Tourniquet test after 15 minutes of compression at a pressure of 100 cu. mms. of mercury; an intense purpuric eruption about the same both in the right and left arms occurred. Numerous petechiae were seen. These extended over the dorsum of the hands and over the fingers."

We have thus observed a case of constitutional athrombopenic hemorrhagic purpura with, during an acute period, a vascular fragility test quantitative +, qualitative ++ on the right side, completely negative on the left side; a few days later, quantitative +, qualitative ++ on the right side, quantitative and qualitative ++++ on the left. Two years later, without hemorrhagic episode, the vascular fragility test was strongly and equally positive on both sides.

This observation indicates the great variability of the vascular fragility test at different times, and also at different sites, in symmetrical areas of the skin in a case of chronic hemorrhagic purpura.

Together with the two new cases reported in this paper, it shows the complexity of the factors producing the purpuric eruption. The appearance of cutaneous hemorrhages is in no way a simple phenomenon and its mechanism is still unknown. The observations of Bedson has shown that the experimental induction of petechiae and hemorrhages sometimes requires the cooperation of a hemic and a vascular factor. Reilly, Rivallier, Compagnon, Laplane, and Du Buit,⁶ later confirmed by Frumusan,³ have demonstrated the role of the autonomous nervous system in animals in the production of some hemorrhagic lesions of the gastrointestinal tract. These very interesting experiments do not, however, afford a satisfactory explanation of the clinical observations concerning the apparition of purpura.

We hope that this paper will draw attention to this important problem, and that it will make experimenters and clinicians conscious of the inconstancy and variability of the vascular fragility test.

SUMMARY

Two unusual cases of purpura simplex raise the problem, as yet unsolved, of the pathogenesis of the purpuric eruption. Together with a previous observation of hemorrhagic purpura made by Roskam, they show the inconstancy and variability of the vascular fragility test.

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