2.6 ± 1.3 ml/sec) and calf pump function has been sustained.

The authors of the letter note the absence of crural vein reflux. This was discussed in detail during presentation of the data to the American Venous Forum. Although these patients were not selected because of this characteristic, the data support the current importance assigned to the popliteal and crural valve segments. As noted in our discussion, and referenced in their letter,[5] it is likely that popliteal or crural reflux will confer a worse prognosis.

They suggest that "insignificant femoral vein reflux that did not contribute to the overall calf pump dysfunction" may have accounted for some of our findings. On the basis of our data, we question the significance of isolated proximal vein reflux. Six of 11 limbs reported had popliteal valvular reflux. Thus we concur that if these results remain unchanged, one of the conclusions from our data may be that proximal reflux alone may be effectively treated with primary superficial venous ablation alone.

Currently, we disagree with their assertion that superficial and perforator ablation confers no hemodynamic benefit in patients with "deep reflux across the knee" as defined by grade 3 to 4 descending venography. To date, these patients have demonstrated sustained improvement in both hemodynamic and clinical reassessments. Although the magnitude of initial reduction in VFI did not achieve statistical significance, the most recent mean VFI in the grade 3 to 4 group is now 2.3 ± 1.2 ml/sec, which is significantly different ($p < 0.05$) when compared with the preoperative VFI. However, we remain cautious in this recommendation on the basis of the small sample size and duration of follow-up. The alleged "deterioration" in two limbs (page 712) is merely a duplex finding of an additional valve segment with incompetence that was identified during the first postoperative reassessment. The role of deep vein valvular reconstruction is an issue beyond the scope of these letters.

Correction of the superficial venous component in limbs with primary, combined deep and superficial venous insufficiency with ulceration has produced excellent results to date. Outcome in patients who have crural and popliteal valvular incompetence ultimately may prove to be less satisfactory, but our current data do not corroborate this conclusion at this time. As a group, these patients remain as satisfied as any group I have been privileged to manage and will continue to be observed closely.

*Frank T. Padberg, MD*
Department of Surgery
Veterans Administration Medical Center
East Orange, N.J.

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### Branham's sign is an exaggerated Bezold-Jarisch reflex of arteriovenous fistula

*To the Editors:*

Nicoladoni-Branham (Branham's) sign, a decrease in pulse and increase in blood pressure that immediately follows the sudden occlusion of an arteriovenous (A-V) fistula, is familiar to all vascular surgeons. Since its description in 1890, it has been considered the standard test of the hemodynamic significance of an A-V fistula.[1] Although the validity of Branham's sign is generally accepted, there have been recent reports of patients who did not exhibit Branham's sign but had seemingly significant A-V fistulae for unclear reasons.

We propose that Branham's sign is an exaggerated Bezold-Jarisch (B-J) reflex. Described in 1867, the B-J reflex causes bradycardia by stimulation of baroreceptors residing in the left ventricle. Certain receptors respond primarily to chemical stimuli (i.e., acetylcholine,[2] 5-hydroxytryptamine[3]), whereas others respond primarily to mechanical effects (volume loading, balloon distension[2]) and some to both. One study showed that the inhibition of nitric oxide (NO) synthesis led to enhancement of the bradycardic reflex.[3] Both Branham's sign and the B-J reflex are abolished by atropine administration,[1,2] and are diminished by the standing position.[2,4]

When a hemodynamically significant A-V fistula is placed in the circulation, cardiac output will rise in an attempt to return systemic blood flow to the baseline level present before the creation of the fistula.[1] Occlusion of the fistula, therefore, momentarily increases systemic blood pressure, reflecting the adjustment period during which the excess cardiac output is forced to pass throughout the higher-resistance peripheral vascular beds rather than the low-resistance fistula. The bradycardic response that follows the occlusion of the fistula occurs within one or two heart beats. This immediate effect has been attributed to be the effect of blood pH on the action of choline esterase.[4] Furthermore, there is now additional evidence that it is initiated by the baroreceptors and is also mediated through

the vagus nerve.[1] We propose that the occlusion of the A-V fistula leads to stimulation of left ventricular chemoreceptors and mechanoreceptors, initiating a bradycardic response.

In addition, in patients who have a hemodynamically significant fistula, NO production is increased, possibly as a result of increasing shear stress in both veins and arteries.[5] Sudden closure of the fistula immediately coincides with decreases in NO production and cardiac output. An abrupt reduction in cardiac output causes a vigorous contraction in an almost empty ventricular chamber, triggering a paradoxical increase in firing of inhibitory left ventricular receptors.[2] These mechanism suggest that the transient bradycardia and hypertension of Branham's sign is a result of the physiologic responses described as the B-J reflex. In some cases of high-output cardiac failure, Branham's sign may be negative in spite of a significant A-V fistula as a result of an impaired B-J reflex from loss of sensitivity of chronically overloaded cardiac sensory receptors.[2]

In conclusion, it appears that inhibitory reflexes that originate in the heart explain the typical physiologic responses of significant A-V fistulae. Failure of a patient to exhibit Branham's sign is suggestive of impairment of cardiac baroreflex control. In such patients, closure of the fistula may not reverse high-output failure.

*Somkiat Wattanasirichaigoon, MD, MS*
*Frank B. Pomposelli, Jr., MD*
Division of Vascular Surgery
Beth Israel Deaconess Medical Center
West Campus, Harvard Medical School
110 Francis St., Suite 5B
Boston, MA 02215

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