

# The Journal of UROLOGY®

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## CLINICAL UROLOGY

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# FUNCTIONAL EVALUATION OF PENILE HEMODYNAMICS

CHRISTIAN G. STIEF,\* WOLFGANG BÄHREN, HELMUT GALL AND WOLFGANG SCHERB

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## ABSTRACT

A multidisciplinary study was performed on 200 consecutive patients with erectile dysfunction more than 1 year in duration, which included a standardized intracavernous injection of a vasoactive substance mixture (15 mg. per ml. papaverine plus 0.5 mg. per ml. phentolamine). The multidisciplinary findings correlated well with the intracavernous dose needed for full erection. The group without pathological hemodynamic findings (36 patients) needed an average of 0.67 ml. and the group with pathological inflow (107) needed an average of 1.07 ml. In the venous insufficiency group (57 patients) only 18 achieved full erections with an average of 2.1 ml. (39 achieved tumescence only to 3 ml.). The results show that standardized intracavernous injection of a vasoactive substance mixture is a useful method to evaluate penile hemodynamics. This pharmacological test appears to be effective in the differential diagnosis of nonvascular and vascular erectile dysfunction. (*J. Urol.*, 139: 734-737, 1988)

Owing to the complex nature of erection and the often multifactorial genesis of erectile dysfunction, the diagnosis of erectile disturbances requires a comprehensive testing program.<sup>1-5</sup> Only by multidisciplinary collaboration can the specialization and expertise of the individual physician be achieved, which are needed to perform extensive examinations. Most of the current therapeutic possibilities of organic erectile dysfunction aim at influencing penile hemodynamics.<sup>6-8</sup> Therefore, the differentiation among arterial, venous and nonvascular causes has a decisive role with respect to therapy. Lue and associates demonstrated that the hemodynamic changes induced by intracavernous injection of vasoactive drugs are identical to those observed after direct neurogenic stimulation: for example papaverine leads to an increase in arterial inflow, a relaxation of the cavernous sinus and venous constriction or compression.<sup>9</sup>

We examine a possible correlation between the multidisciplinary findings in our patients with erectile dysfunction and the response to standardized intracavernous pharmacological testing.

## PATIENTS AND METHOD

We evaluated 200 consecutive patients between 19 and 65 years old (mean age 45.6 years) who had suffered from erectile dysfunction for at least 1 year with respect to the disturbance via a multidisciplinary approach. In anamnesis 28 patients had a primary (congenital) erectile dysfunction and 19 had had insulin-dependent diabetes for more than 5 years, while 15 suffered erectile dysfunction after pelvic trauma, 6 after radical prostatectomy, 4 after surgery on the large abdominal and pelvic vessels, 2 after abdominoperineal proctectomy and 2 after radiotherapy of the pelvis. Three patients had multiple sclerosis and 6 had undergone a revascularization procedure without permanent success (see table).

The detailed history of the patients was taken via questionnaire. Apart from inquiries about the social environment as well as the sex life and behavior of the patient and his female partner, great importance was attributed to risk factors, the situation-related erection process and libido.<sup>10,11</sup> Moreover, the patients underwent physical examination, laboratory tests (including testosterone and prolactin), nocturnal penile tumes-

cence measurements by means of a Snap-Gauge† (showing adequate correlation with the sleep laboratory for screening purposes),<sup>12</sup> bulbocavernosus reflex latency and, if necessary, somatosensory evoked potentials, upper abdominal and pelvic sonography, Doppler ultrasonography of the 4 penile arteries (proximal and distal),<sup>2</sup> sexual history and psychometry (Minnesota Multiphasic Personality Inventory and Freiburger Personality Inventory). Selective pharmaco-angiography of the pelvis and penis was performed in 59 patients<sup>4</sup> and dynamic cavernosography<sup>13,14</sup> was done in 69. The correlation between the result of Doppler ultrasonography and angiography was 94.5 per cent.<sup>15</sup> Dynamic cavernosography as an invasive diagnostic method requires strict indications, such as insufficient rigidity to maximum dosage of intracavernous drugs or only full rigidity to high doses together with intact penile arterialization.<sup>16,17</sup>

After the patient was appropriately informed, the first 55 patients received a 1 ml. intracavernous injection. The following patients received 0.5 ml. to reduce the high rate of prolonged erections (8 of 55 patients: 4 with a neurogenic, 1 a psychogenic and 3 an arterial etiology) with 1 ml. of a standardized vasoactive substance mixture (15 mg./ml. papaverine hydrochloride plus 0.5 mg./ml. phentolamine methane sulfonate). The injection was performed via a 26 gauge half-inch needle into the dorsum of the extended penis at about 1 cm. from the abdominal wall and 2 to 3 mm. laterally from the midline. In a control group of 10 men with normal potency 0.5 ml. induced a complete erection at least 30 minutes in duration. Under dose variation an erection duration of 30 to 90 minutes was to be achieved in

† Dacomed, Minneapolis, Minnesota.

## Underlying diseases in 200 consecutive patients with erectile dysfunction

	No.
Primary erectile dysfunction	28
Insulin-dependent diabetes	19
Post-traumatic	15
Radical prostatectomy	6
Cystoprostatectomy	1
Large abdominal and pelvic vessel surgery	4
Abdominoperineal proctectomy	2
Radiotherapy of the pelvis	2
Multiple sclerosis	3
Failed penile revascularization	6
No underlying disease	114

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the patients and the maximum dose was set at 3 ml. At least 3 injections (1 injection per day) per patient were performed at the hospital without psychogenic or reflexogenic stimulation. The interval until maximum onset of action as well as quality and duration of maximum response were recorded by the urologist. The penile reaction was divided into 6 degrees according to the palpatory findings: 0—no reaction, 1—slight tumescence, 2—medium tumescence, 3—complete tumescence with no rigidity, 4—complete tumescence with medium rigidity and 5—complete rigidity.

Severe hypoplasia or aplasia of both penile arteries on angiography and/or Doppler ultrasound was considered an arterial etiology. A bulbocavernosus reflex latency exceeding 42 msec. was regarded as a neurogenic etiology. On dynamic cavernosography, a maintenance flow greater than 80 ml. per minute was considered a venous etiology.

### RESULTS

During the diagnostic use of vasoactive substances in the 200 patients studied 19 experienced 21 prolonged erections (duration of more than 6 hours). The first 4 erections were treated successfully by aspiration of blood from both corpora cavernosa, while the remainder were treated by intracavernous injection of 2 mg. of the  $\alpha$ -adrenergic stimulator metaraminol.

According to the results of the multidisciplinary evaluation, the etiology was purely arterial in 58 patients, arterio-neurogenic in 42, arteriovenous plus neurogenic in 11, arteriovenous in 19, arterio-psychogenic in 7, neurogenic in 27, venous in 24, psychogenic in 9 and neurogenic-venous in 3. The doses required by the individual patients to achieve a complete erection at least 30 minutes in duration are shown in figure 1.

If one arranges these groups under hemodynamic aspects, basically different reactions to the intracavernous injection can be classified as 1—no effect on hemodynamics, 36 patients (fig. 1, *f* and *h*), 2—disturbance of arterial inflow with venous competence, 107 patients (fig. 1, *a*, *b* and *e*) and 3—excessive outflow, 57 patients (fig. 1, *c*, *d*, *g* and *i*). Mean patient age in these 3 groups was 44.7, 46.9 and 45.3 years, respectively. The age distribution curves showed no significant differences. In contrast to the normal subjects, 20 of 36 patients without pathological hemodynamic findings achieved a complete erection

after administration of 0.5 ml. or less within 5 to 8 minutes. In this group a mean dose of 0.67 ml. was needed to achieve a complete erection (fig. 2, *a*). All patients with arterial insufficiency achieved a complete erection by means of vasoactive substances. The response time was markedly prolonged (up to 40 minutes) and the mean dose was 1.07 ml. (fig. 2, *b*). Only in 18 of 57 patients with venous insufficiency (maintenance flow more than 100 ml. per minute) could a complete erection be achieved by intracavernous injection of vasoactive substances and the mean dose was 2.1 ml. in these patients (fig. 2, *c*).

### DISCUSSION

Intracavernous injection of a papaverine-phenolamine mixture induces an erection with complete rigidity provided the penile hemodynamics are intact and the dosage is adequate.<sup>9</sup> This effect is achieved mainly by relaxation of the smooth muscles of the cavernous sinus. Juenemann and associates demonstrated the importance of a decrease in penile outflow to achieve complete rigidity as a result of this cavernous relaxation.<sup>18</sup> Patients in whom the erectile dysfunction is not of arterial or venous etiology have a complete erection in response to a standardized intracavernous injection of vasoactive substances. Arterial insufficiency produces prolongation in the response time from a normal of 5 to 8 minutes up to 40 minutes and, depending upon the extent of the inflow disturbance, an increase in dosage is required to achieve complete rigidity. A mild inflow disturbance cannot be differentiated from an intact penile blood supply by means of this test. If complete rigidity cannot be achieved even by maximum doses (45 mg. papaverine and 1.5 mg. phenolamine) marked insufficiency of the smooth cavernous muscles or abnormal venous channels must be assumed based on the results of animal experiments.<sup>16</sup> The insufficient reduction in venous outflow prevents the intracavernous pressures that are necessary to achieve complete rigidity and it can be demonstrated as venous leakage by means of dynamic cavernosography. This cavernous reaction to intracavernous injection of vasoactive substances can be modulated by external and psychological factors, respectively, in terms of an increase adrenergic tone but it can be inhibited completely only in rare cases. This penile response to certain intracavernous doses of vasoactive substances is well reproducible in the same

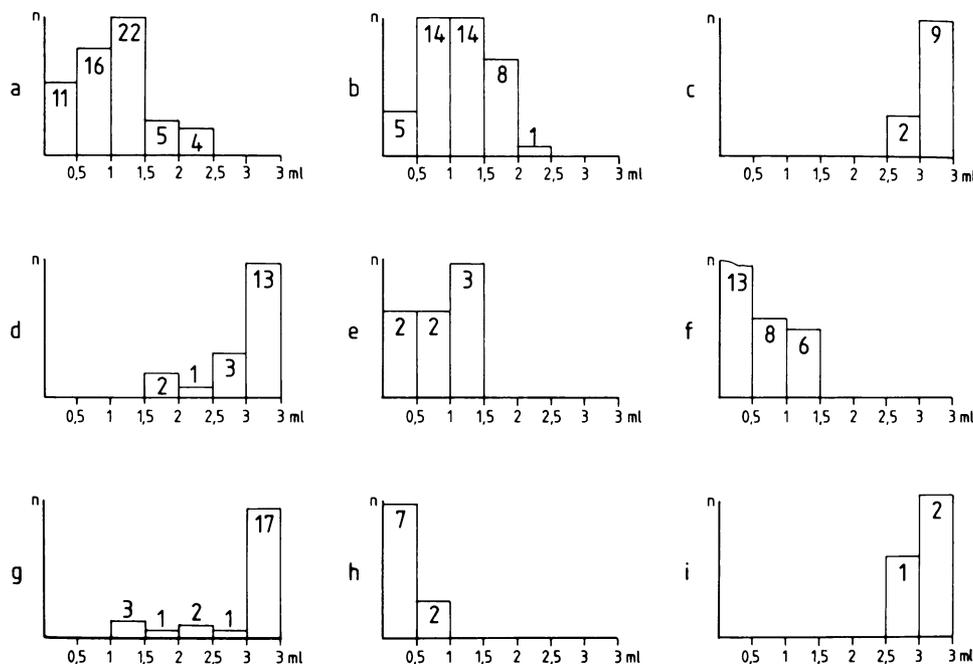


FIG. 1. Etiology of erectile dysfunction according to results of multidisciplinary approach (200 patients) in correlation to dosage required for full erection. *a*, arterial etiology, 58 patients. *b*, arterio-neurogenic etiology, 42 patients. *c*, arteriovenous plus neurogenic etiology, 11 patients. *d*, arteriovenous etiology, 19 patients. *e*, arterio-psychogenic etiology, 7 patients. *f*, neurogenic etiology, 27 patients. *g*, venous etiology, 24 patients. *h*, psychogenic etiology, 9 patients. *i*, neurogenic-venous etiology, 3 patients.

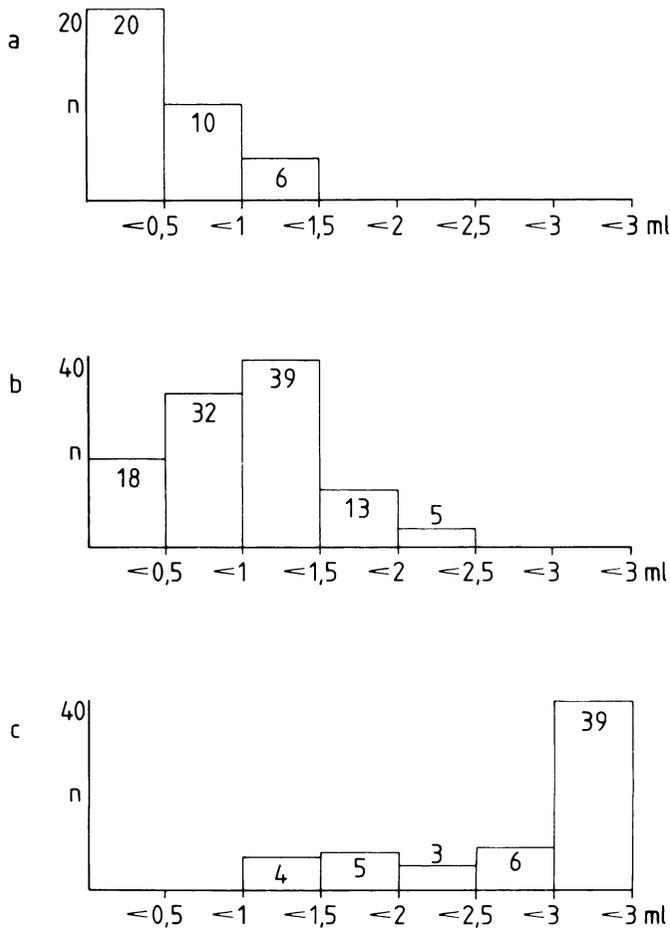


FIG. 2. Distribution of erectile dysfunction in patients according to penile hemodynamic status and dosages required for full erection. *a*, intact penile hemodynamics. *b*, pathological inflow, venous competence. *c*, venous leakage.

individual and some patients reported that in certain stress situations "it didn't function as well as usual". Therefore, the dose testing to achieve a 30-minute erection was repeated at least twice.

Virag and associates studied the diagnostic possibilities of intracavernous papaverine injection.<sup>19</sup> They divided their 45 patients examined by a multidisciplinary approach into a control group, as well as nonorganic and organic erectile dysfunction groups. They observed identical reactions in the control and the nonorganic (psychogenic) groups. The organic group achieved no complete rigidity after an identical papaverine injection following a prolonged response time. These results as well as those by Nadig,<sup>20</sup> and Jünemann<sup>21</sup> and Sidi<sup>22</sup> and their associates are compatible with our results. Buvat and associates<sup>23</sup> performed the papaverine test (80 mg.) recommended by Virag and associates<sup>19</sup> following dynamic cavernosography. No significant difference could be found between patients with marked pathological arterialization and psychological origin without organic causes. These results, which contradict the findings of the other investigators, could possibly be attributed to the increased adrenergic tone following the invasive dynamic cavernosography and the 2 needles still present in the penis. This assumption is supported by our experience. In the course of dynamic cavernosography vasoactive substances were injected intracavernously in more than 40 patients at a dose that was 4 times as high as that normally required for complete erection and it induced a complete erection in 7 patients only under these circumstances.

## CONCLUSION

Intracavernous injection of vasoactive substances in a standardized form represents a simple and reliable method to evaluate penile hemodynamics. To avoid serious side effects such injection should be performed only by physicians experienced with this technique. By means of this pharmacological test a rationalized 3-step program was developed to answer therapy relevant questions: 1) baseline examination included history, physical examination and laboratory testing, 2) specific non-invasive examinations included pharmacological testing, Doppler sonography and sexual history plus psychometry, and abdominal and pelvic sonography, and 3) specific invasive examinations (only in certain indications) included dynamic cavernosography, angiography, bulbocavernosus reflex latency testing and evaluation of the somatosensory evoked potential.

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## EDITORIAL COMMENTS

The authors support serial intracavernous injections of vasoactive agents in the differential diagnosis of impotence and evaluation of penile hemodynamics. The diagnosis of impotence is based on the quality of the response, time required to achieve the response and dose required to induce a full erection. Men with intact penile vasculature responded to vasoactive agents with full, rigid erections. Men with vasculogenic impotence (that is venous, arterial or mixed), if they respond at all, usually require higher doses of medication to induce this response, the onset of which may be delayed.

Several factors should be considered when vasoactive agents are used intracavernously in the differential diagnosis of and screening for impotence. The same dose administered to the same patient at different times may induce a different response. The response may differ if the patient is in the supine, standing or sitting position during injection, if he is anxious or if there is sexual stimulation. Patients with penile arterial insufficiency may have a normal response. An attenuated response may occur in up to 44 per cent of the patients with normal vasculature despite repeated injection.<sup>1</sup>

Vasoactive agents injected intravenously have great potential for the differential diagnosis of impotence. However, this potential is not yet realized. More test standardization is required so that specificity, sensitivity and accuracy can be defined. Factors that should be standardized include the vasoactive agent used, dose, whether single or multiple injections are given, test conditions, use of visual sexual stimulation, position during injection and methods to assess the response.

Currently, it appears that a diagnosis of severe venous incompetence or severe arterial insufficiency can be excluded with certainty if a full erection is achieved after carefully performed intracavernous injection. The significance of a partial response or no response still is uncertain.

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1. Buvat, J., Lemaire, A., Marcolin, G., Dehaene, J. L. and Buvat-Herbaut, M.: Intracavernous injection of papaverine (ICIP). Assessment of its diagnostic and therapeutic value in 100 impotent patients. *World J. Urol.*, **5**: 150, 1987.

I agree with the authors that intracavernous injection of pharmacological agents is useful in the evaluation of penile hemodynamics.

However, owing to the imprecise nature of most of our current diagnostic tests to differentiate various types of impotence, the etiological classification in this article is oversimplified. A prolonged bulbocavernosus reflex only implies that the patient may have some neurological deficit and not necessarily neurogenic impotence. During evaluation of the cavernous artery, penile arteriography and Doppler analysis currently are imprecise and there will be large numbers of false negative or positive results in the diagnosis of arteriogenic impotence.

It must be emphasized that the dosage mentioned by the authors is for diagnostic purposes (without sexual stimulation). If the patient is to perform self-injection before sexual intercourse the dosage required would be much lower. We prefer to start with 0.1 ml. (3 mg.) papaverine alone in patients with neurogenic impotence and 0.5 ml. (15 mg.) in those with other types, and then we increase the dosage gradually until a desirable result is obtained. Use of 2 to 4 mg. metaraminol to treat priapism is dangerous. Two deaths have been reported in France owing to complications from acute severe hypertension. We prefer a small dose of epinephrine (10  $\mu$ g./1 ml. normal saline) repeated every 5 minutes after aspiration of 15 to 20 ml. blood. Others prefer irrigation with phenylephrine solution.

Standardization of a dynamic test for erectile dysfunction is a difficult task owing to the psychological inhibition that invariably occurs in such an artificial environment. I congratulate the authors on this endeavor and I stress that when results are equivocal the test should be repeated 2 or 3 times to rule out psychological overshadowing of organic disease.

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## REPLY BY AUTHORS

We appreciate the editorial comments and are in complete agreement that, although techniques may be standardized, patients will never be. In particular, psychogenic influences may alter the individual response to standardized intracavernous pharmacological testing. Accordingly, to avoid an attenuated response in an anxious or nervous patient, we recommend that pharmacological testing not be performed as the first diagnostic procedure for erectile dysfunction. Rather, it should be introduced after the urologist has gained the confidence of the patient. It should be performed in a secure, quiet environment and it should be repeated to prove reproducibility. The complexity of the erectile phenomenon and the current gaps in our knowledge of it currently make a precise diagnostic method unavailable. However, we believe that standardized intracavernous pharmacological testing, besides minimizing the use of invasive techniques, provides a useful evaluation of penile hemodynamics as an aid to choosing the appropriate therapeutic option.