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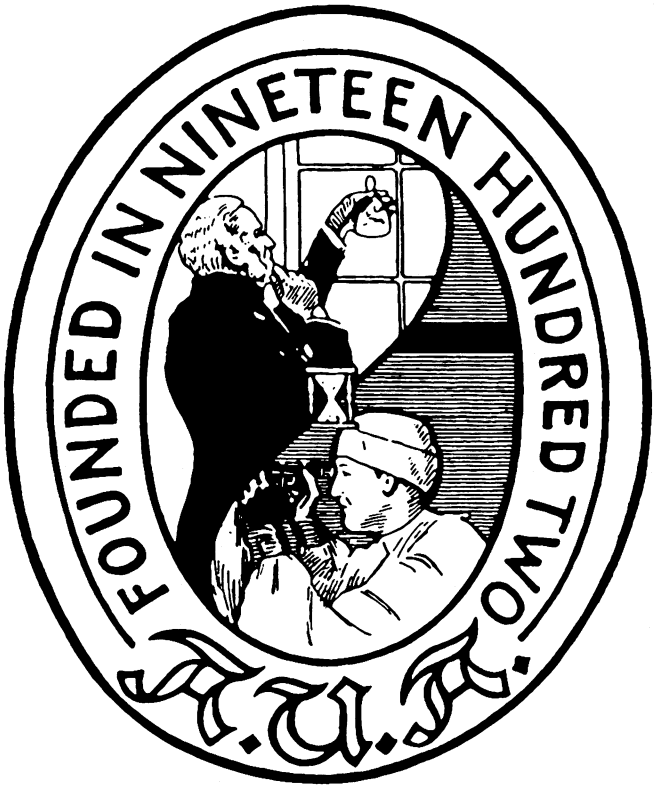

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Letters to the Editor

RE: SINGLE POTENTIAL ANALYSIS OF CAVERNOUS ELECTRICAL ACTIVITY IN SPINAL CORD INJURY PATIENTS

C. G. Stief, C. Hoppner, D. Sauerwein and U. Jonas

J. Urol., **151:** 367–372, 1994

To the Editor. While electrobiological phenomena are a common feature of many tissues, extracellular recordings of such events in complex tissues with multiple cell types must be interpreted with caution. This is particularly true of tissues that, although tonically contracted, still may experience dynamic local changes in smooth muscle tone. The recent article by Stief et al concerning corporeal electromyographic recordings clearly emphasizes this point. For the purposes of this discussion, we will refer to all of the recorded electrical activity as waveforms.

In this regard, what is fundamentally most disturbing about the article is that there are many possible interpretations of the recorded waveforms and the authors are ambiguous about this matter. For example, it is conceivable that the biphasic waveforms might represent "propagated action potentials." However, if the waveforms do represent regenerative electrical events then they should have the following characteristics: the waveforms should have a constant velocity and peak amplitude and, moreover, the area encompassed by the positive portion of a biphasic waveform must be equal to all area encompassed in the negative portion of the waveform.[1] There is no evidence that these conditions hold. The recorded monophasic waveforms might be considered to represent slow waves but this seems unlikely given the fact that slow waves have not been demonstrated in any other vascular smooth muscle.[2] Moreover, electrophysiological recordings on corporeal smooth muscle cells reveal no ionic basis for either slow waves or action potentials in this tissue.[3] Finally, the authors refer to triphasic waveforms, a phenomenon with well documented meaning and potential physiological significance[1] but they never even discuss this. In our opinion, the best possible interpretation of the data is that the recorded waveforms represent no more than an average evoked potential, which reflects the summed activity of groups of cells (neurons and smooth muscle?). However, it is important to note that the continual temporal phase shifting (that is the apparent unpredictability in the temporal sequence of the bilaterally recorded waveforms) in the recorded waveforms (between patients and within records from the same patient) implies that there may be a significant mechanical artifact in the recordings.

Although the authors believe that the results strongly support a major role of single potential analysis of cavernous electrical activity (SPACE) for the diagnosis of cavernous autonomic dysfunction, we disagree for all of the aforementioned reasons. Moreover, even if we assume that the waveforms reflect some physiologically relevant phenomenon, interpretation of the meaning of the observed alterations is greatly complicated by the fact that there is no accurate way to know the true extent of the putative autonomic lesions.

In short, the potential excitement concerning the use of SPACE in the diagnosis of erectile dysfunction should be greatly tempered. In the absence of any concrete information on the part of the authors concerning the suspected nature and/or origin of these waveforms, it is difficult to ascribe any particular interpretation or meaning to their existence. Thus, while we acknowledge the potential use of this technique and agree that the waveforms probably represent a bioelectrical phenomenon, it is clear that the authors have greatly overstated the current level of knowledge about the "electrical" events that occur in corporeal smooth muscle.

Respectfully,

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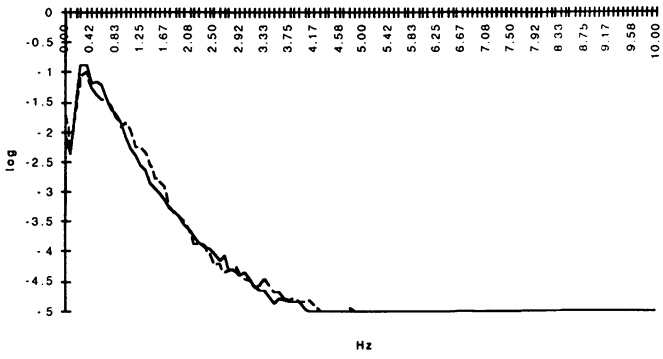
1. Plonsey, R. and Fleming, D. G.: Bioelectric Phenomena. New York: McGraw-Hill Book Co., 1969.
2. Hirst, G. D. S. and Edwards, F. R.: Sympathetic neuroeffector transmission in arteries and arterioles. Physiol. Rev., **69:** 546, 1989.
3. Christ, G. J., Spray, D. C. and Brink, D. C.: Characterization of K currents in cultured human corporeal smooth muscle cells. J. Androl., **14:** 319, 1993.

Reply by Authors. Clearly, extracellular recordings of electrical activity reflect events of mixed origin that are more or less dependent on electrical activity of the cells, intercellular connections and distribution of different cell types present. A situation similar to corpus cavernosum electromyography (the term SPACE was abandoned in 1993 at the First International Workshop on Corpus Cavernosum-Electromyography in preference for the more general term corpus cavernosum electromyography) is the recording of gastric smooth muscle activity during electrogastrography.[1] In the cavernous tissue, the majority of the electrically active cells are smooth muscle cells.

The myogenic activity can easily be examined in isolated tissue. In cavernous tissue, spontaneous rhythmical activity (frequency 10 to 20 per minute) of low amplitude was observed.[2] Additionally, sporadic larger contractions of lower frequency were noted. When compared to gastric electrical activity, cavernous electrical activity in vitro showed a lower amplitude, indicating a lower electrical coupling for coordinated activity in cavernous tissue in vitro. Therefore, in vivo recording (corpus cavernosum electromyography) with phases of electrical silence interrupted by typical fluctuations of the membrane potential (potentials in the article incorrectly termed) seems to reflect what really happens electrically. Of course, these registrations may be influenced by external factors, such as heart rate, breathing or electrogastrography. However, when corpus cavernosum electromyographic typical fluctuations of the membrane potential undergo fast Fourier transformation, it becomes obvious that they are of such a low frequency range (less than 2 Hz., see figure) that the aforementioned signals should be easily detected as of noncavernous origin. Furthermore, the signals are usually filtered out by band-pass filters. Nonetheless, mechanical artifacts, such as movements of the legs or strong coughing, are in a comparable frequency range and may jeopardize corpus cavernosum electromyography interpretation. Therefore, these influences must be excluded for proper interpretation.

It is true that slow waves (such as in electrogastrography or described by us) were not reported in vascular smooth muscle. However, events of low frequency (which means a slow wave) can easily be observed in many arteries and veins, such as the coronary artery or portal vein. The frequency of these coordinated contractions is in the range of 5 per minute.[3]

The term slow wave is properly used in gastric muscle and to our knowledge an ionic basis for this phenomenon is still missing. The investigation of Christ et al (reference 3 in Letter) was not specifically designed to uncover slow waves if present. However, in this and



Fast Fourier transformation of corpus cavernosum electromyography of normal subject shows frequency distribution of typical fluctuation of membrane potential to be in slow frequency range that is not compatible with cardiac or respiratory artifacts.

another recent study[4] it was shown that in cavernous tissue nearly the entire set of ionic channels, as described in other tissues, is present. It is obviously too early to attempt final conclusions about the origin, changes, shape and other aspects of corpus cavernosum electromyography. Based on this fact, we attempted to present a purely descriptive article of corpus cavernosum electromyography results obtained in spinal cord injury patients. For us it was important that the corpus cavernosum electromyograms obtained in spinal cord injury patients were different from those of normal subjects. Regarding the terms we used to describe our findings, these were also meant purely descriptively. We did not intend to use established terms in electrophysiology.

Similar data with significantly different corpus cavernosum electromyography recordings in patient groups with defined lesions compared to controls were presented by others during the second International Workshop on Corpus Cavernosum Electromyography held in February 1994. Thus, we believe that research on corpus cavernosum electromyography is promising and that knowledge will grow during the next years in that field, leading us to a better diagnosis of erectile dysfunction and, thus, providing better patient care. We believe that corpus cavernosum electromyography may evolve in a comparable manner as electrocardiography, which has had broad clinical acceptance and implications for years but required almost 5 decades for its fundamental bases (partially?) to be explained by physiologists.

Dr. Th. Noack, Department of Physiology, University of Marburg, Marburg, Germany, contributed to this Reply.

1. Stern, R. M. and Koch, K. L.: Electrogastrography. Methodology, Validation and Applications. New York: Praeger, 1985.
2. Mandrek, K. and Golenhofen, K.: The myogenic basics of smooth muscle motility in the corpus cavernosum penis. In: Cavernous Smooth Muscle Electromyography. Edited by K. Buchhauser. Gebel: Planegg/Germany, pp. 7–19, 1992.
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RE: VARICOCELE-RELATED INFERTILITY IS NOT ASSOCIATED WITH INCREASED SPERM-BOUND ANTIBODY

G. S. Oshinsky, M. V. Rodriguez and B. C. Mellinger

J. Urol., **150:** 871–873, 1993

To the Editor. We read this article with interest. We previously published work on this subject[1] and would like to point out some similarities rather than differences between these studies, raise questions regarding their methods and comment on their conclusions.

Both articles demonstrated an increase in sperm bound antibody in an infertile male population. Since the incidence of antisperm antibodies in an unselected male population is 7.8%,[2] the finding that 5 of 29 patients (17%) with a palpable varicocele and 9 of 82 (11%) without a palpable varicocele as described in this study is still a significant percentage, and suggests that in a subfertile male population there is an increased incidence of antisperm antibodies. The authors used duplex ultrasonography to confirm the physical examination. However, no details of how ultrasonography was performed or if it was performed on all of their patients were given. Did duplex ultrasonography detect varicoceles not palpable on physical examination (that is subclinical varicoceles)? In their article only clinically detected varicoceles were included in the varicocele group. Therefore, men with subclinical varicoceles (and possibly antibodies) might have been included in the nonvaricocele group. In addition, data were given on sperm density, volume and motility but no data were included on morphology, particularly tapered heads, which might have greatly supported their argument. The authors also discuss the possibility of infection confounding results from prior studies but did not give information regarding the urological history of the patients or quantification of leukocytes and/or bacteria found in the semen of these men, which might have confounded the data from the nonvaricocele group.

Therefore, we find their study to be inconclusive. Although much more work is needed to identify the physiological effect of varicoceles on fertility, all studies to date, including this study and a recent study using immunobeads by Knudson et al,[3] support the observation that men with varicoceles have a higher incidence of antisperm antibodies than the fertile male population, possibly the result of varicocele related damage to the seminiferous tubular epithelia. We have also found that serum antisperm antibodies are often elevated in men with varicoceles (unpublished data) and believe that positive serum antibodies might be a marker for varicocele.

Respectfully,
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1. Gilbert, B. R., Witkin, S. S. and Goldstein, M.: Correlation of sperm-bound immunoglobulins with impaired semen analysis in infertile men with varicoceles. Fertil. Steril., **52:** 469, 1989.
2. Clarke, G. N., Elliott, P. J. and Smaila, C.: Detection of sperm antibodies in semen using the immunobead test: a survey of 813 consecutive patients. Amer. J. Reprod. Immunol. Microbiol., **7:** 118, 1985.
3. Knudson, G., Ross, L., Stuhldreher, D., Houlihan, D., Bruns, E. and Prins, G.: Prevalence of sperm bound antibodies in infertile men with varicocele: the effect of varicocele ligation on antibody levels and semen response. J. Urol., **151:** 1260, 1994.

Reply by Authors. Our custom is not to perform duplex ultrasonography on every patient but only on those who have palpable findings. The accuracy of duplex ultrasonography in detecting subclinical varicocele has not been established. The entity of subclinical varicocele remains controversial. However, in our opinion these entities are most likely not clinically significant.

We did not include morphology data in our patients, since this parameter is highly subjective and varies from laboratory to laboratory, and the relationship between tapered sperm heads and antisperm antibodies remains unclear to us. The majority of our patients did not undergo routine quantification of seminal leukocytes or bacteriological studies, and there is no reason to suspect that these procedures would have altered the data from either group.

We agree that there appears to be a higher incidence of antisperm antibodies in an infertile male population compared to a normal fertile population. However, the aim of our study was to compare the incidence of antisperm antibodies in 2 groups of infertile patients (with and without a palpable varicocele). Our study clearly indicates that there is no statistically significant difference in the incidence of sperm-bound antibody in these 2 groups of infertile patients. This finding was also corroborated by Jarow and Sanzone, who also used an immunobead test.[1] The study by Gilbert et al (reference 1 in Letter) used an enzyme-linked immunosorbent assay for measurement of antisperm antibodies and because of the many problems associated with this assay, it has been abandoned by most laboratories measuring antisperm antibodies. In view of the problems associated with enzyme-linked immunosorbent assay for measurements of antisperm antibodies, we believe that the study by Gilbert et al is no longer valid or clinically relevant.

Therefore, we strongly disagree that our study was inconclusive and we stand by the data that men with varicocele do not have an increased incidence of antisperm antibodies compared with men without a palpable varicocele. Additionally, serum antibodies have never been shown to be reliably correlated with sperm-bound antibodies and we still believe that the best marker for a varicocele is a palpable dilated pampiniform plexus.

1. Jarow, J. P. and Sanzone, J. J.: Risk factors for male partner antisperm antibodies. J. Urol., **148:** 1805, 1992.