Neurological correlations of ejaculation and testicular size in men with a complete spinal cord section

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SUMMARY This study was of 135 patients with a complete spinal cord section suffered from loss of ejaculation. The spinal cord injuries were classified following the upper and the lower limits of the lesion. The volume of the testes of the patients and of 13 normal control subjects were measured. Physostigmine allowed 75 patients to ejaculate and 15 of them procreated. The possibility of ejaculation after physostigmine mainly depended on the integrity of the T12-L2 metamers. The testicular volume was significantly smaller in patients with a lesion including the T12 metamer than in patients with a lesion sparing the T12 metamer. Six patients with a lesion including the T12 metamer had testicular atrophy. This suggests that T12 segment plays a role in testicular function in paraplegic patients.

The sexual potency of paraplegic patients has received much attention and many extensive surveys are available in the literature.¹⁻⁶ Although effective treatment of an ejaculation can now be offered to these patients,⁷⁻¹⁰ the number of those who have procreated remains low.¹¹⁻¹³ This survey of 135 patients with a clinically complete spinal cord section was performed in order to define the neurological basis for the prognosis regarding procreation. The capacity to ejaculate is an obvious prerequisite, but its relationship to the level of the cord lesion remains imprecise. In addition fertility obviously depends on testicular activity, which has been shown to be altered in patients with a spinal cord injury.¹⁴⁻¹⁸ The volume of the testicle was chosen as a measure of testicular exocrine capacity,^{19 20} since it can always be studied whether the patients are able to ejaculate or not.

Methods

Subjects

One hundred and thirty five paraplegic patients were all examined by the same physician (PAC) with regard to the

management of the sexual sequelae of their paraplegia. All wished very strongly to recover ejaculation, some of them were willing to procreate. The patients involved in this study suffered from a spinal cord section due to indirect trauma. The lesion was regarded as being complete on the basis of the clinical examination: below the level of the lesion sensory loss was complete and the patients were unable to perform the slightest voluntary movement. All were examined at least 6 months after the accident, by which time it was thought that no effects of spinal shock remained. The patients were aged 18 to 47 years and sustained spinal cord injury at an age ranging from 3 months to 41 years. The delay between the trauma and the first consultation ranged from 6 months to 33 years.

Neurological examination

The superior and inferior levels of the lesion were determined following a clinical neurological examination that has previously been described.^{21 22} Briefly, the upper limit of the lesion is the highest metamer displaying paralysis. The lower limit of the lesion was determined using both somatic and vegetative reflexes by successively testing spinal reflex activities from segment S5 to the higher levels. The lower limit of the lesion is the metamer just above the highest metamer which still displays automatic spinal activity (that is, corresponding either to the highest afferents that can induce a reflex and/or to the highest efferents driven by stimulation beneath the lesion). The somatic spinal reflexes used to determine the lower limit of the lesion are detailed in reference 22.

Spinal vegetative pilomotor and sudomotor reflexes may be obtained in response to a noxious and prolonged stimu-

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lation applied below the level of the spinal section, as by squeezing of the testicle.²¹ The extent of the pilomotor response can easily be determined by simply watching the surface of the skin. The extent of the sudomotor response was determined by gently slipping the back of a spoon on the skin and by feeling the brisk slowing down of its progression as the skin became damper. Simultaneously, the pupils were observed for mydriasis. As has been known since the observations of Thomas,²³ an upper extension of the sudomotor or pilomotor responses in the lower limbs, the upper limbs, the face together with mydriasis show that at least some of the related levels (respectively T10–L2, T4–T8, T4–T5, T2–C8) are below the level of the lesion.

Ejaculation

Patients with spinal cord section may ejaculate after pharmacological activation by physostigmine, as it has been described elsewhere.⁸ Routinely, three physostigmine tests were performed under medical control before self injections at home. Each test consisted of a subcutaneous injection of physostigmine 0.2 mg (in association with 40 mg N-buthylthioscine) followed by masturbation. Some patients included in this study before we used physostigmine received an intrathecal injection of neostigmine (0.3–0.5 mg) as previously described,¹² a method which was soon abandoned. Semen was systematically examined and the presence of spermatozoa verified. If the patient wished to procreate and if sexual intercourse proved to be ineffective, we taught the wife how to inseminate herself with fresh semen.

Testicle volume evaluation

The testicle volume was systematically measured at the first consultation. The testicle length (L) and thickness (diameter, D) were measured with a caliper. The testicle width was not taken into account since it was difficult to discriminate it from the epididymal enlargement. The testicular volume (V) was calculated assuming that it is ellipsoidal (formula suggested by Macomber and Sanders,²⁴):

$$V = \pi \times D^2 \times L \times 0.9/4$$

The volume was calculated for each testicle and the two measures added.

Thirteen normal subjects, examined by the same physician, were used as controls. These were young adult men, aged from 18 to 35 years old, who were admitted for a short period into hospital for acute benign orthopaedic problems. None of them had neurological lesions or medical illness.

Results

(1) Ejaculation and procreation

In 75 of 135 patients an ejaculation occurred after pharmacological activation, and spermatozoa were present in the ejaculate (EJ group). Among them, 15 were able to procreate: six by coitus and nine by auto-insemination. In other patients (60 out of 135), no ejaculation could be obtained (ANEJ group); most of them had at least three complete physostigmine tests but, in six, severe autonomic hyperreflexia during the first test prevented masturbation and contraindicated further tests. The occurrence of ejaculation did not

depend on age (respectively 22.5 ± 4.5 years old in the EJ group and 23.5 ± 5.6 years old in the ANEJ group) nor on the delay between the accident and the first test (respectively 7.4 ± 4.3 years and 8.2 ± 4.7 years).

(2) Level of the injured metamers

The extent of the spinal cord lesion is summarised on fig 1 for the patients who were able to ejaculate and for those who were not able to do so. In the upper part of fig 1, the spinal lesion of the 54 patients who could not ejaculate after three physostigmine tests is represented by a continuous line. As it can be seen, in all but three, the spinal lesion included L1 and in most of them (46 among 54) it extended at least from T12 to L2. In contrast (lower part of fig 1), only three out of 75 patients who could ejaculate had a T12–L2 metamer lesion (χ^2 test: $p < 0.001$). Within the EJ group of patients, the spinal lesions of the patients who procreated (dotted lines) did not differ from those of the other patients.

Fig 1 Extent of the spinal lesion. For each patient, the horizontal line represents the injured spinal metamers (indicated in abscissa) in which no reflex activity could be obtained. Upper part: patients who could not ejaculate. The stippled lines represent the patients who underwent AHR and did not sustain the three physostigmine tests. Lower part: patients who could ejaculate. The dotted lines represent the patients who procreated.

(3) Testicle volume and spinal lesion

Testicle volume estimates were available in 122 patients (67 in the EJ group and 55 in the ANEJ group). We excluded the patients who had urological or medical causes of testicular damage (orchiepididymis, destructive functional treatment of the lower urinary tract, cryptorchidism in one case, systemic lupus in one case). Fifteen patients from the EJ group and 12 patients from the ANEJ group had a testicular asymmetry of more than 15%. We considered that it probably indicated a previous orchiepididymis and we therefore excluded these patients even if they had no history of such a disorder. The patients who had an early prepubertal paraplegia (four from EJ group and two from ANEJ group) were also discarded. Hence the relation between the spinal cord injury and testicular volume was considered in only 86 patients (45 from the EJ group and 41 from the ANEJ group).

In all these patients, the mean testicle volume (28.55 ± 8.5 ml) did not significantly differ from that of the normal subjects (26.8 ± 5.3 ml). The testicle volume neither correlated with the age of the patients ($r = 0.12$), nor with their age at the onset of paraplegia ($r = 0.08$), nor with the delay between the accident and the date of examination ($r = 0.07$).

It appeared that the testicle volume was slightly lower in the ANEJ group of patients (26.8 ± 9.2 ml) than in the EJ group of patients (30.15 ± 7.7 ml), ($t = 1.8$, not significant). This is not directly linked to the possibility of ejaculation since the testicle were measured before any physostigmine test was performed in patients who previously could not ejaculate. The spinal lesion was obviously different in these two groups (see fig 1), not only in its level but also in its extent.

In order to evaluate a possible direct influence of the spinal lesion on the testicle, we considered each possible injured metamer. For each segmental level, the mean testicular volume of the patients who had a lesion including this metamer was compared with the mean testicular volume of the patients who had a lesion sparing this metamer (whether upper or lower). As is shown on fig 2, within the patients' group, the testicular volume was significantly smaller if the T12 segment was injured than if T12 was undamaged. This difference also appeared when the patients with a lesion including T12 were compared with the patients with T12 metamer placed below the lesion (table). The histograms of the testicular volume whether the patients had an injured T12 segment or not are shown in fig 3. It appears that the testicular volume is above normal range in 17 patients among 86 (19.8%); most of them (14) had an undamaged T12 segment. On the contrary, all the six patients who have a testicular volume below normal range have a spinal lesion

including T12 ($\chi^2 = \text{test: } p < 0.01$).

Discussion

Ejaculation

As has been reported, only a few paraplegic patients with a total spinal transection are able to ejaculate without any treatment (six among 108,² three among 49,³ 4% of 394,⁵ three among 100⁶) and in most of them the section was at low lumbar or sacral levels.²⁻⁵ In our study, as in the previous ones⁸⁻¹² pharmacological activation by the cholinesterase inhibitor physostigmine allows about half of the patients to ejaculate. The crucial importance of the T12-L1-L2 segments for ejaculation has been suspected since the pioneer work of Kuntz in animal²⁵ who concluded that ejaculation was mediated by a sympathetic reflex centre lying in the upper lumbar cord. Some patients with an upper limit at L2 or below can ejaculate without any treatment (even if reflex erection which depends on the integrity of the sacral segments is lost²⁻³⁻⁵ probably because the ejaculatory reflex centre is not separated from supraspinal control.³⁻⁷ The precise determination of the lower level in paraplegic patients indicates that ejaculation can be regularly obtained if the T12-L2 segments are not involved in the lesion, confirming with a greater number of patients the previous study.⁸ This suggests that the ejaculatory reflex centre lies in these segments and that it can be activated by physostigmine treatment as long as it is not destroyed but only isolated from supraspinal control.

In paraplegic patients, ejaculation may also be obtained after electrical rectal stimulation.⁷⁻¹⁰⁻¹¹⁻¹³⁻²³ Brindley⁷ provided evidence that electrical rectal stimulation acted by directly stimulating the preganglionic sympathetic fibres whose cell bodies are approximately at the T12 segment. The site for the efferent part of the ejaculatory reflex arc suggested by these data is consistent with our findings.

Hence, the prognosis for ejaculation mainly depends on the integrity of the low thoracic-high lumbar segments. In our practice, physostigmine treatment is routinely used at home and obtained a pregnancy in 15 patients' wives, after either sexual intercourse or auto-insemination of the fresh semen. The whole procedure is well accepted by the couples since it avoids excessive medical control of sexual life.

Testicular trophicity

Testicular volume is an important criterion of male reproductive function since seminiferous tubules and germinal elements account for more than 90% of the testicular mass.¹⁹⁻²⁰ The testicular volume may be evaluated with acceptable accuracy by the measure of its length and width, following the assumption that it

Fig 2 Testicular mean volume and spinal lesion. The testicular volume is expressed as a percentage of the patient mean. Each point represents the testicular volume of the patients who have a spinal lesion including the segment indicated in abscissa. The standard error to the mean (SEM) is indicated with a bar. The mean and SEM of the testicular volume in the whole population of paraplegic patients (P) and in normal subjects (N) are indicated on the left. The stars (**) indicate a significant difference ($p < 0.01$) between the testicular volume of the patients with a lesion including the related segment and the one of the patients with a lesion sparing this segment.

is ellipsoidal,^{24 26} (see critical review in ref 27). The authors usually emphasise the great variability of the results and the values obtained in normal subjects are consistent with the previously published values.²⁷

In our patients' group, the mean testicular volume did not differ from that of the normal subjects. However, within the patients' group, the testicular volume was smaller in patients with a lesion of the T12 metamer and six of these patients had true testicular atrophy. In contrast, some patients had a testicular volume above normal range. This does not seem to be due to the absence of ejaculation before the measure since it has been shown that vasectomy does not alter the testicular volume.²⁶ The mechanism of this

increased volume cannot be explained by our study, but it is unlikely to be due to a hypertrophy of the seminiferous tubules. However, it is possible that this volume increase may induce an underestimation of the number of patients with a testicular atrophy.

Testicular atrophy^{15 17} and anatomically evident testicular damage^{4 5 10 14 16 18} have repeatedly been reported in paraplegic patients. In these studies, testicular biopsy or necropsy material displayed selective alterations of germinal cells such as tubular atrophy or maturational arrest, without alterations of Leydig cells, in more than half of the paraplegic patients. The level of 17 ketosteroids in paraplegics was shown to be either elevated^{5 14} or decreased.¹⁵ Plasma FSH,

Table Testicular volume whether T12 is impaired or not

Patients	Mean	SD	Number
A: T12 injured	25.67	9.05	35
B: T12 metamer below the lesion	30.39	7.6	42 (A-B $t = 2.47$, $p < 0.02$)
C: T12 metamer above the lesion	31.22	8.4	9 (A-C $t = 1.65$, ns)

elevation of which may reflect a failure of tubular function,²⁸ was reported to be elevated in elderly paraplegics.²⁹ Nevertheless, more recent studies failed to observe any testicular atrophy³⁰ or persistent endocrinological changes: testosterone was shown to be decreased only at the acute stage of the tetraplegia³⁰ and was normal or slightly elevated in chronic paraplegia.^{17,30} Levels of FSH-LH in young paraplegics did not show any indication of a primary testicular failure.³¹

The mechanism of the testicular atrophy appears to be complicated. The cachexia due to severe medical complications of the paraplegia^{14,15,18} and urogenital infection¹⁸ are probably involved, but Stemmermann¹⁸ emphasised that the relation between cachexia and testicular atrophy was not strictly causal. Endocrine factors were also implied

via a possible adrenal cortical hyperfunction as a reaction to stress.^{5,14} It is probable that the low frequency of testicular damage observed in the more recent studies (since 1970), as in ours, is linked to the better clinical management of the paraplegic patients, since a chronic illness on its own may cause testicular atrophy.³²

In our study, the determination of the extent of the spinal lesion shows that the occurrence of testicular atrophy is linked to a lesion of the T12 segment. A neurological cause of testicular atrophy has previously been suspected and the possible role of the autonomic nervous system has been particularly discussed.^{14,18} But most of the previous studies, based on the upper limit of the lesion, failed to demonstrate a relation between the level of the spinal lesion and atrophy.^{4,14,18} However, our results are consistent with the findings of Tsuji⁵ who noted that patients who retained testicular sensitivity had testicular atrophy less frequently and at a lower degree since it is generally assumed that the testicular afferents reach the spinal cord at low thoracic-high lumbar level.³³ The testicle atrophy due to the T12 segment lesion could be related to the suppression of its sympathetic supply, as it has been described in the works of Kuntz in the dog.³⁴

In conclusion

The main clinical data that can influence the prognosis of procreation is the extent of the lesion, since we have shown that a lesion of the low thoracic-high lumbar segments impaired both the possibility of ejaculation after physostigmine and the testicular volume. This underlines the need to determine precisely the extent of the spinal lesion.

References

- 1 Bors E, Comarr AE. Neurological disturbances of sexual function with special reference to 529 patients with spinal cord injury. *Urol Surv* 1960;**10**:191-222.
- 2 Comarr AE. Sexual function among patients with spinal cord injury. *Urol Int* 1970;**25**:134-68.
- 3 Munro D, Horne HW, Paull DP. The effect of injury to the spinal cord and cauda equina on the sexual potency of men. *N Engl J Med* 1948;**239**:903-11.
- 4 Talbot HS. The sexual function in paraplegia. *J Urol* 1955;**73**:91-100.
- 5 Tsuji I, Nakajima F, Morimorito J, Nounaka Y. The sexual function in patients with spinal cord injury. *Urol Int* 1961;**12**:270-80.
- 6 Zeitlin AB, Cottrell TL, Lloyd FA. Sexology of the paraplegic male. *Fertil Steril* 1957;**8**:337-44.
- 7 Brindley GS. Electroejaculation: Its technique, neurological implications and uses. *J Neurol Neurosurg Psychiatry* 1981;**44**:4-18.
- 8 Chapelle PA, Blancart F, Puech AJ, Held JP. Treatment of an ejaculation in the total paraplegic by subcutaneous injection of physostigmine. *Paraplegia* 1983;**21**:30-6.
- 9 Guttman L, Walsh JJ. Prostigmine assessment test of fertility in spinal man. *Paraplegia* 1971;**1**:39-50.

Fig 3 Histograms of the testicular volume in patients with a spinal lesion sparing (upper part) or including (lower part) the T12 segment. The vertical continuous lines represent the mean testicular volume in normal subjects, the stippled lines the confidence limits (mean ± 1 and ± 2 SD).

- 10 Horne HW, Paull DP, Munro D. Fertility studies in the human male with traumatic injuries of the spinal cord and cauda equina. *N Engl J Med* 1948;**239**:959-61.
- 11 Brindley GS. The fertility in men with spinal injuries. *Paraplegia* 1984;**22**:337-48.
- 12 Chapelle PA, Jondet M, Durand J, Grossiord A. Pregnancy of the wife of a complete paraplegic by homologous insemination after an intrathecal injection of neostigmine. *Paraplegia* 1976;**14**:173-7.
- 13 François N, Maury M, Jouannet D, David G, Vacant J. Electro-ejaculation of a complete paraplegic followed by pregnancy. *Paraplegia* 1978;**16**:248-51.
- 14 Bors E, Engle ET, Rosenquist RC, Holliger VH. Fertility in paraplegic males. A preliminary report of endocrine studies. *J Clin Endocrinol* 1950;**10**:381-98.
- 15 Cooper IS, Rynearson EH, McCarty CS, Power MH. Metabolic consequences of spinal cord injury. *J Clin Endocrinol Metab* 1950;**10**:858-70.
- 16 Klein M, Fontaine R, Stoll G, Dany A, Frank P. Modifications histologiques des testicules chez les paraplégiques. *Rev Neurol (Paris)* 1952;**86**:501-3.
- 17 Mizutani S, Sonoda T, Matsumoto K, Iwasa K. Plasma testosterone concentration in paraplegic men. *J Clin Endocrinol* 1972;**54**:363-4.
- 18 Stemmermann GN, Weiss L, Auerbach O, Friedman M. A study of the germinal epithelium in male paraplegics. *Am J Clin Pathol* 1950;**20**:24-34.
- 19 Kothari LJ, Gupta AS. Effects of aging on the volume, structure and total Leydig cell content of the human testis. *Int J Fertil* 1974;**19**:140-6.
- 20 Sherins RJ, Howards SS. Male infertility. In: Harrison JH, Gittes RF, Perlmutter AD, Stamey TA, Walsh PC, eds. *Campbell's Urology, Vol 1*. Philadelphia: WB Saunders, 1978:640-97.
- 21 Chapelle PA, Leroy F, Roby A, Bussel B. Estimation topographique de la limite inférieure du syndrome lésionnel chez l'homme paraplégique complet. *Ann Réadapt Med Phys* 1984;**26**:369-77.
- 22 Grossiord A, Chapelle PA, Lacert P, Pannier S, Durand J. Le segment médullaire lésionnel chez le paraplégique. Applications à la fonction génito-sexuelle chez l'homme. *Rev Neurol (Paris)* 1978;**134**:729-40.
- 23 Thomas A. Les moyens d'exploration du système sympathique et leur valeur. *Rev Neurol (Paris)* 1926;**1**:767-928.
- 24 Macomber D, Sanders MB. The spermatozoa count. Its value in the diagnosis, prognosis and treatment of sterility. *N Engl J Med* 1929;**200**:981-4.
- 25 Kuntz A. *The Autonomic Nervous System*. Third edition. Philadelphia: Lea and Febiger, 1945.
- 26 Dias PLR. The effects of vasectomy on testicular volume. *Br J Urol* 1983;**55**:83-4.
- 27 Takihara H, Sakatoku J, Fujii M, Nasu T, Cosentino MJ, Cockett ATK. Significance of testicular size measurement in andrology. I. A new orchimeter and its clinical application. *Fertil Steril* 1983;**39**:836-40.
- 28 Nankin HR, Castaneda E, Troen P. Endocrine profiles in oligospermic men. In: Troen P, Nankin HR, eds. *The Testis in Normal and Infertile Men*. New York: Raven Press, 1977:529-37.
- 29 Hayes PJ, Krishnan KR, Diver MJ, Hipkin LJ, Davis JC. Testicular endocrine function in paraplegic men. *Clin Endocrinol* 1979;**11**:549-52.
- 30 Claus-Walker J, Scurry M, Carter M, Campos RJ. Steady-state hormonal secretion in traumatic quadriplegia. *J Clin Endocrinol Metab* 1977;**44**:530-5.
- 31 Young RJ, Strachan RK, Seth J, Nicol K, Frier BM, Corral RJM. Is testicular endocrine function abnormal in young men with spinal cord injuries? *Clin Endocrinol* 1982;**17**:303-6.
- 32 Handelsman D, Staraj S. Testicular size: the effects of aging, malnutrition and illness. *J Androl* 1985;**6**:144-51.
- 33 Dejerine J. *Sémiologie Des Affections du Système Nerveux*. Paris: Masson, 1926:952-3.
- 34 Kuntz A. Degenerative changes in the seminal epithelium of the mammalian testis. *Endocrinology* 1921;**5**:190-204.